Published in final edited form as:
Expert Rev Cardiovasc Ther. 2010 July ; 8(7): 917–932. doi:10.1586/erc.10.56.

Smoking and stroke: the more you smoke the more you stroke

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Abstract

Cigarette smoking is a well-established risk factor for all forms of stroke. While both the general public and the global healthcare system are aware of the vascular risks associated with smoking, the prevalence of tobacco use has remained largely unchanged over the last quarter of a century. Approximately one in five US adults are classified as regular smokers, with the initiation of smoking typically occurring during the teenage years. Although the increased risk of stroke associated with smoking is generally acknowledged, it is less well recognized that considerable scientific evidence implicates a strong dose–response relationship between smoking and stroke risk. In this article, we summarize the literature regarding smoking-related stroke risk, the dose–response relationship, and the costs of this detrimental habit to both the individual and society as a whole.

Keywords

cigarettes; dose; risk; smoking; stroke; tobacco

"Cigarette smoking is clearly identified as the chief preventable cause of death in our society and the most important public health issue of our time". This statement was first articulated in 1982 by the then US Surgeon General C Everett Koop, and unfortunately it remains accurate today, over 25 years later. Hence, over the last quarter of a century, one can argue that efforts regarding smoking prevention and cessation, and public awareness campaigns describing the associated health risks regarding smoking, have had only limited success. The aim of this article is to reinforce the awareness of healthcare providers, healthcare organizations and the population at large to the perils of cigarette smoking. Summary information focusing on US smoking statistics, worldwide vascular outcomes data and dose–response findings are presented. It is our hope that this article will instill a sense of

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Financial & competing interests disclosure

John W Cole was supported in part by the Department of Veterans Affairs, Baltimore, Office of Research and Development, Medical Research Service; the Department of Veterans Affairs Stroke Research Enhancement Award Program; the University of Maryland General Clinical Research Center (grant no. M01 RR 165001); the General Clinical Research Centers Program; the National Center for Research Resources, the NIH (grant no. R01 NS045012-05) and an American Heart Association Beginning Grant-in-Aid (grant no. 0665352U). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.
No writing assistance was utilized in the production of this manuscript.

purpose and motivation in the reader to decrease this well-established and highly detrimental health risk factor.

Smoking prevalence

Despite growing knowledge about the adverse health and economic consequences of smoking, the prevalence of smoking in the USA remains alarmingly high. According to the CDC, their most recent data indicates that 20.8% of the US adult population smokes. This represents only a 3% decline in smoking prevalence over the last 10 years [101]. Due to the current rates of population growth, even with a small percentage decline of tobacco consumption over the years, absolute consumption continues to grow and will continue to do so unless more aggressive measures are taken to promote smoking cessation [102]. In short, over 1 billion more cigarettes were consumed worldwide in 2000 compared with 1980.

Who smokes?

An impetus to begin smoking is clearly present during the teenage years. While only 6% of middle-school students were smokers in 2006, data collected 1 year later showed a prevalence of 20% among high-school students [103]. This 20% prevalence among high-school students is consistent with the overall US adult smoking prevalence. Hence, these statistics clearly argue for the need for more aggressive smoking prevention programs in our schools, notably in the middle-school years (grades 6–9) or earlier. In general, the prevalence of smoking peaks between the ages of 18 and 44 years and decreases dramatically after the age of 65 years; this is directly related to smoking-related illnesses [101].

Currently, the prevalence of smoking among US male adults is still greater than that of females – 23 versus 19%, respectively [101]. Among women of reproductive age, those aged 18–24 years were most likely to have attempted to quit (68.4%) but least likely to have quit smoking (26.3%), bringing to light another important target population [104]. The prevalence among African–Americans and Caucasians is similar at approximately 21%. Hispanic individuals and Asians are about half as likely to smoke [101].

Socioeconomic status is also an influencing factor. Adults with a bachelor’s degree or greater are less likely to be current smokers and more likely to have never smoked compared with less educated individuals. Adults in families that are poor, or near poor, are more likely to be current smokers than adults in families who are not poor. Finally, a fact that is bound to pique the interest of health economists and raise concern over the public health burden of cigarette smoking – individuals who are uninsured or have Medicaid are more likely to smoke (33–37%) than those with private health insurance coverage (18%) [101]. In summary, the less educated, uninsured poor are more likely to smoke. Over time, these individuals will eventually succumb to smoking-related diseases, be unable to pay for their healthcare and in doing so further stress our already tenuous healthcare system.

The association between smoking & stroke

The evidence linking smoking to stroke is extremely convincing. Table 1 summarizes the results of numerous globally based studies evaluating the association between stroke and cigarette smoking. In short, these studies performed across various ethnicities and populations demonstrate a strong association between smoking and stroke risk, with current smokers having at least a two- to fourfold increased risk of stroke compared with lifelong nonsmokers or individuals who had quit smoking more than 10 years prior. In one study, the risk increased to sixfold when this population was compared with nonsmokers who had never been exposed to environmental tobacco smoke (i.e., second-hand smoke) [1]. In a

separate study, this sixfold increase in risk persisted when cigarette-smoking women with smoking spouses were compared with smoking women with nonsmoking spouses, further demonstrating the effect of second-hand smoke on stroke risk [2].

More recently, the deleterious consequences of second-hand smoke have been at the forefront of public health organizations and the subject of numerous government reports [3–5]. These studies have convincingly shown that environmental (second-hand) smoke increases the risk of stroke even in nonsmokers. Bonita *et al.* found that the odds of a first stroke, fatal or nonfatal, were increased among nonsmokers and long-term ex-smokers exposed to second-hand smoke at home or at work compared with those not exposed (odds ratio [OR]: 1.82; 95% CI: 1.34–2.49) [1]. In an Australian study investigating the effect of spousal smoking, the risk of stroke was twice as high in individuals with spouses who smoked compared with sex-matched neighborhood controls [6]. In New Zealand, second-hand smoke exposure at work was estimated to cause around 100 avoidable deaths per year from lung cancer, coronary heart disease and stroke collectively [7]. Finally, in the USA, a cohort study of over 27,000 individuals has shown a 1.50-fold (95% CI: 1.07–2.09) increased risk of first ischemic stroke in women exposed to 20 h or more per week of environmental tobacco smoke at home compared with those exposed to less than 1 h per week [8].

Plausible mechanisms by which primary and environmental tobacco smoke exposure can increase the risk of stroke and heart disease are numerous and include carboxyhemoglobinemia, increased platelet aggregability, increased fibrinogen levels, reduced HDL-cholesterol, and direct toxic effects of compounds such as 1,3-butadiene, a vapor phase constituent of environmental tobacco smoke that has been shown to accelerate atherosclerosis in animal models [9]. Environmental tobacco smoke exposure has also been linked to the progression of atherosclerosis as measured by B-mode ultrasound of the carotid wall [10–12], as well as to early arterial damage as assessed by endothelium-dependent brachial artery dilatation [13]. Last, the pathogenesis of increased stroke risk in populations exposed to cigarette smoke has been suggested to be that of advanced atherogenesis, potentially in relation to chronic infection [10,14].

Atherosclerosis and arterial damage thus explain how smoking predisposes individuals to large- and small-vessel lacunar stroke. Impaired endogenous fibrinolysis and reduced blood flow in the brain secondary to smoking-induced vasoconstriction may also contribute to lacunar stroke. While atrial fibrillation and hypertension may outweigh the risk of smoking for cardioembolic stroke, an association is believed to exist for this stroke subtype as well. The Atherosclerosis Risk in Communities (ARIC) study demonstrated a relative risk (RR) of 2.30, 1.61 and 1.94 for lacunar, nonlacunar and cardioembolic strokes in current smokers, respectively [15].

Ischemic stroke is not the only form of stroke associated with smoking; both intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) risks are also elevated. In 2003, Kurth *et al.* published two articles outlining the risk of hemorrhagic stroke in male and female smokers [16,17]. These studies showed an increased risk of total hemorrhagic stroke, ICH and SAH in females smoking 15 or more cigarettes per day (RR: 3.29 [95% CI: 1.72–6.29], 2.67 [95% CI: 1.04–6.90] and 4.02 [95% CI: 1.63–9.89], respectively) and males smoking 20 or more cigarettes per day (RR: 2.36 [95% CI: 1.38–4.02], 2.06 [95% CI: 1.08–3.96] and 3.22 [95% CI: 1.26–8.18], respectively). Results of the Multiple Risk Factor Intervention Trial showed a strong relationship between smoking and SAH, ICH and nonhemorrhagic stroke [18].

The increased risk of SAH appears to be related to the increased incidence of aneurysms seen in smokers. Heavy smoking (>20 cigarettes/day) men and currently smoking women have been found to have adjusted RRs of aneurysmal hemorrhage of 7.3 (95% CI: 3.8–14.3) and 2.1 (95% CI: 1.2–3.6), respectively, as compared with men who had never smoked and with women who were not current smokers [19]. Smoking may cause ICH by damaging the walls of small intraparenchymal arteries, leading to their rupture [16,17]. The Hemorrhagic Study Project found cigarette smoking to be an independent risk factor of primary hemorrhage [20]. A more recent study of 39,484 patients by Andersen *et al.* demonstrated that high alcohol intake and smoking favor hemorrhagic stroke over ischemic stroke [21]. A dose–response relationship has also been shown in a case–control study by Fogelholm *et al.*; the OR was 3.33 (95% CI: 1.05–10.6) for those smoking 1–20 cigarettes per day and was 9.78 (95% CI: 2.25–42.5) for those smoking more than 21 cigarettes per day [22].

It has been suggested by some that the relationship between smoking and ICH is weak and inconsistent. For example, a recent pooled cohort of the ARIC study and Cardiovascular Health Study (CHS) by Sturgeon *et al.* did not find any consistent or independent relationship between smoking and ICH [23]. As this was a pooled analysis, this study had limited power with confounding and study interactions potentially altering the results in unpredictable ways [23]. However, this and other such studies raise the possibility that the association between smoking and ICH may be somewhat less straightforward. For example, one study showed that current smoking increases the risk of ischemic stroke only, while former smokers have a 50–60% increase in the RR of both ischemic and hemorrhagic stroke [24]. Another study has shown that smoking may be unrelated to nonlobar primary ICH, but doubles the risk for lobar primary ICH [25]. A study on a select group of Korean men with low cholesterol found no overall association of smoking with ICH, but an increased risk in those with a BMI less than 25 kg/m^2 (p-value for interaction = 0.003), and a pooled Japanese analysis found a significantly increased risk of ICH in female current and ever-smokers, but not in men [26,27]. Finally, the Melbourne Risk Factor Study Group showed no increase in risk of ICH with smoking, but *post hoc* analysis suggested a significant interaction between smoking and hypertension on the risk of ICH (OR: 8.13; 95% CI: 2.04–32.42) [28].

Smoking discontinuance results in a considerable reduction in stroke risk across gender, race and age. This fact has been demonstrated in numerous studies both in the USA and worldwide. In a Nurse's Health Study manuscript by Kawachi *et al.*, the RR of total stroke among US nurses who smoked compared with never-smokers was 2.58 (95% CI: 2.08–3.19). The RR among former smokers was 1.34 (95% CI: 1.04–1.73). For total and ischemic stroke, the excess risks among former smokers dissipated 2–4 years after cessation. This pattern of decline was observed regardless of quantity smoked, age at initiation of smoking or other stroke risk factors [29]. Likewise, in a cohort of Asian men, heavy smokers (>20 cigarettes/day) who quit smoking showed significantly lower risks of ischemic stroke and SAH compared with heavy smokers who continued to smoke (HR: 0.66 [95% CI: 0.55–0.79] and 0.58 [95% CI: 0.38–0.90], respectively) [30]. An Australian study investigating the effect of smoking cessation among Asians and Australasians found that current smokers had a HR of 1.38 (95% CI: 1.24–1.54) compared with nonsmokers, whereas ex-smokers had a HR of 0.84 (95% CI: 0.76–0.92) compared with current smokers [31]. Mechanistically, the return to baseline or near-baseline stroke risk is thought to be related to normalization of the procoagulant state seen in smokers. However, not all studies demonstrate a full return to nonsmoker risk status, which may in part be related to several factors including the duration of smoking, concomitant risk factors and the quantity of atherosclerotic disease developed while smoking. Per Shinton's well-cited meta-analysis reviewing the relationship between cigarette smoking and stroke, ex-smokers under the age of 75 years retained an appreciable

increased risk of stroke with a RR of 1.5 [32]. Nevertheless, smoking cessation produces a major reduction in stroke risk across all race, gender and age groups.

Stroke-related morbidity stems from the fact that tobacco smoke contains over 4000 different chemicals including heavy metals and other toxins that promote the development of free radicals, inducing vascular endothelial dysfunction and inflammation, ultimately leading to the development and acceleration of the atherosclerotic process. Smoking also causes the development of a global circulatory procoagulant state thought to be induced by altered hemostatic and inflammatory marker concentrations. As previously mentioned, among its other detrimental effects smoking causes an increase in fibrinogen concentration, a decrease in fibrinolytic activity, an increase in platelet aggregability, and polycythemia [33]. Last, smoking also decreases cerebral blood flow, which may further increase the risk of clot formation and subsequent stroke risk through a slowed flow or stasis phenomenon [34].

The dose–response relationship: the more you smoke, the more you stroke

For as long as 20 years, the dose–response relationship between tobacco consumption and stroke risk has been well established. Unfortunately, this relationship is little publicized. Notably, this relationship provides smokers with an opportunity to garner definitive measurable health benefits if they can reduce their daily number of cigarettes smoked. Table 2 demonstrates the key studies performed worldwide implicating the dose–response relationship across the age spectrum.

In a 1989 32-study meta-analysis investigating the dose–response relationship between smoking and stroke, individuals who consumed a low amount of tobacco (<10 cigarettes/day) were found to have a RR of stroke of 1.37 compared with smokers consuming high amounts (≥20 cigarettes/day) who had a RR of 1.82 [32]. Likewise, in a more recent study evaluating young females, the risk of stroke as associated with smoking demonstrated a strong dose–response relationship. Using never-smokers as the reference group, multivariate-adjusted analysis demonstrated an increasing OR with an increasing number of cigarettes smoked per day: 2.2 for 1–10 cigarettes/day; 2.5 for 11–20 cigarettes/day; 4.3 for 21–39 cigarettes/day; and 9.1 for 40 or more cigarettes/day. The dose–response relationship between smoking amount and stroke risk was not modified by any of the covariates, including race. In a multivariate logistic model, smoking amount remained highly significant ($p = 0.002$) but smoking duration was not statistically significant ($p = 0.6$). Former smokers did not have an increased risk of stroke [33].

Similarly, nonsmokers exposed to spousal second-hand smoke have a higher prevalence of stroke that increases relative to the intensity and duration of their spouse's smoking. In a study by Zhang *et al.*, the adjusted ORs of stroke in Chinese female non-smokers was 1.28 (95% CI: 0.92–1.77), 1.32 (95% CI: 1.01–1.72) and 1.62 (95% CI: 1.28–2.05), dependent on the number of cigarettes smoked by their husbands; 1–9, 10–19, and 20 or more cigarettes per day, respectively (p-value for trend = 0.0002) [35].

The mechanisms through which the dose of smoking affects stroke risk has been a topic of interest over the last several years. Certainly one could argue that the numerous smoking-associated risk mechanisms as mentioned previously could manifest in a dose–response type fashion, with greater exposure increasing risk. Similarly, it also plausible that the number of other coexisting vascular risk factors such as hypertension, diabetes and hyper-lipidemia, among others, also influence stroke risk in synergy with the daily quantity of cigarettes smoked. Last, the duration of smoking in years coupled with the daily quantity consumed probably also plays a key role in stroke risk; particularly in risk as associated with the development of atherosclerosis. A recent cross-sectional observational investigation carried

out in a cohort of patients attending a lipid clinic showed that carotid intima-media thickness was highest in current smokers, lower in former smokers and lowest in never-smokers ($p < 0.0001$). Carotid intima-media thickness was positively related to the number of pack-years smoked in both former and current smokers ($r = 0.34$ and 0.37, respectively; both $p < 0.0001$). There were no differences between smokers of cigarettes with high or low nicotine, tar or carbon monoxide content ($p > 0.05$) [36].

The cost of smoking to current smokers

Up to one-quarter of all strokes are directly attributable to cigarette smoking. This percentage can rise up to 50% for young adults admitted for a cryptogenic ischemic stroke [37].

If one assumes an attributable risk of stroke as associated with smoking of 20%, taken in conjunction with the 700,000 strokes that occur in the USA annually, then, if all Americans stopped smoking, there would be 140,000 fewer strokes. The cost benefits alone would be enormous, potentially saving one-fifth of the US$43 billion per year spent on stroke care in the USA.

In addition to the risk of stroke, data from the National Health Interview Survey and death certificate data from the National Center for Health Statistics suggest that smoking causes 30% of all cancer deaths and 80% of all chronic obstructive pulmonary disease deaths. Tobacco smoking was responsible for an estimated 467,000 deaths, accounting for approximately one in five or six deaths in US adults in 2005 [38]. Other studies corroborate these numbers, demonstrating that approximately 270,000 US males and 174,000 US females die as a result of smoking each year. In US adults over 35 years of age, almost 50,000 deaths are caused by second-hand smoke exposure [39].

Should all smoking cease in the USA, an estimated 13.2 years of life would be saved for each male and 14.5 years of life for each female who currently smokes [40]. Most recent data indicate that this would amount to over 5 million years of potential life saved annually, excluding deaths from smoking-attributable residential fires and adult deaths from second-hand smoke [39]. Simply making all workplaces smoke-free would prevent 350 strokes and 130 deaths, and save US$11.64 million [41].

While lives lost by far represent the most serious consequence of smoking, tobacco consumption is costly to individuals for a number of other reasons. On 1 April 2009, the largest US federal cigarette excise tax increase in history went into effect. The combined federal and average state excise tax for cigarettes is US$2.21 per pack [42]. In most states, the new price for one pack of cigarettes is approximately US$6. New York City residents pay approximately US$10 [43].

Smokers also pay more for health insurance; based on an online search, the monthly premium for a health insurance plan with a US$1500 deductible for a 44-year-old male nonsmoker was US$292. The same policy for a smoker was US$338 per month. Life insurance rates double in premium for smokers. A 20-year term US$500,000 life insurance policy for a healthy 44-year-old male costs US$1140 per year; for a one pack per day smoker, this cost rises to US$2571 [105].

Homeowners insurance rates are approximately 10% greater for smokers, given that one-third of household fires are smoking related. Smokers also lose money on the resale value of their cars and homes as the smoking-related odors and aesthetic issues often lead to lower compensation. They spend more on dry cleaning and teeth cleaning. In the long term, studies indicate that smokers tend to earn less and receive less in pension and social security

benefits, as discussed later [105]. In short, among the numerous drawbacks of smoking, smokers risk life (via shorter life spans) and limb (via peripheral vascular disease) on a daily basis.

Cost of smoking to society

According to a study by the Society for Human Resource Management, 5% of employers prefer to hire nonsmokers and 1% do not hire smokers at all [105]. This may, in part, be secondary to higher health and life insurance costs and claims. However, lost productivity, absenteeism, maintenance costs, worker's compensation costs (an average cost of US$2189 cost per smoker compared with US$176 per nonsmoking employee), property damage, accidents and the effects of second-hand smoke on non-smokers also cause a financial burden to employers [106]. The Health Policy Institute of Ohio (HPIO) estimates that smokers miss an average of 6.2 days of work per year owing to illness compared with 3.9 days for nonsmokers, and employees who smoke have almost twice as much lost production time per week as nonsmokers. Businesses thus lose US$3400 annually for every employee who smokes.

The average medical cost of caring for patients with stroke during the first year is US $34,368. Average costs accrue through 6 years, with US$8150 in the second year, US$1915 in the third year, US$1753 in the fourth year, US$1408 in the fifth year and US$702 in the sixth year [41]. In 1999, it was estimated that smoking may account for 6–8% of all healthcare spending in the USA. From 1995 to 1999, smoking-related healthcare costs totaled US$157.7 billion each year. More than US$75 billion was attributable to direct medical costs including ambulatory care, hospital care, prescription drugs and nursing homes [107]. In Canada in 2002, it was estimated that 339,179 of all hospital diagnoses were attributable to smoking, accounting for 2,210,155 acute care hospital days (10.3% of total) [44].

Of 22 billion packs sold in the USA in 1999, US$3.45 per pack was spent on medical care attributable to smoking and US$3.73 per pack in productivity losses were incurred, for a total cost of US$7.18 per pack. The economic costs of smoking totaled US$3391 per smoker per year [40]. More recent numbers indicate a total economic burden of approximately US $193 billion per year. By comparison, investments in comprehensive, state-based tobacco prevention and control programs in 2007 totaled US$595 million – 325-times less than the smoking-attributable costs [39].

Some good news

While smoking definitively causes stroke, there are several important motivational facts that can be emphasized to patients to help them to stop smoking. First, a dose–response relationship exists. In short, medical practitioners can emphasize that "the more you smoke, the more you stroke", reiterating that a reduction in daily cigarette usage, while not ideal, has been demonstrated to reduce stroke risk.

Regarding quitting (which would be ideal), several health-related benefits can be emphasized to occur over the following time frame. After quitting, the following has been demonstrated:

- Within 20 min blood pressure drops to the level it was before the last cigarette
- Within 8 h carbon monoxide levels in the blood return to normal
- Within 24 h the chance of a heart attack decreases
- Within 2 weeks to 3 months circulation improves and lung function increases

- Within 1–2 months smoking-related stroke risk due to hypercoagulability normalizes to that of nonsmokers
- Within 1–9 months lungs regain normal ciliary function, reducing infection risk
- At 1 year the risk of heart disease is cut in half
- At 5 years stroke risk is reduced to that of a nonsmoker in most cases
- By 10 years the risk of lung cancer is approximately half that of a smoker. The risks for cancers of the mouth, throat, esophagus, bladder, kidney and pancreas also decrease
- By 15 years the risk of heart disease is that of a nonsmoker

Smokers have more help than ever before to help them quit successfully. Working with their healthcare provider is the most effective way to quit smoking. Effective methods typically include a combination of medications, replacing unhealthy habits with healthy habits and emotional support. Convincing evidence indicates that nicotine replacement therapy, bupropion and varenicline are all effective treatments for both short- and long-term smoking cessation [45].

Expert commentary

A clear correlation between smoking and health risk has long been established. Nevertheless, the prevalence of smoking in our society remains at unacceptable levels. Smoke-free laws in certain areas have already been associated with declines in heart disease [46–50]. In California (USA), decreases in smoking have led to a reduction in lung cancer and heart disease death rates [51]. State tobacco control programs have been shown to be effective in reducing tobacco use and improving health outcomes [51–56], and there is considerable evidence that raising tobacco prices reduces tobacco use [47,108].

Certainly individuals have the right to choose whether they smoke or not in the privacy of their own homes; however, given the clear risk of second-hand smoke to others, all smoking in public areas needs to be banned. Taking this a step further might imply that given the clear evidence that intervention can lead to healthy change, society has little excuse as to why there should not or cannot be a smoke-free America sometime in the near future. In any case, adoption of restrictive smoke-free laws will not only reduce direct costs and lives lost to smokers by making them smoke less while in public, but will also act to protect nonsmokers from exposure to second-hand smoke. Over time, such efforts will act to create an environment in which smoking is unacceptable.

Five-year view

The national health promotion and disease prevention initiative, Healthy People 2010, outlines a goal to reduce the prevalence of cigarette smoking among US adults to less than 12% by 2010 [109]. Some population subgroups, such as Hispanics, Asian women, individuals with higher levels of education and older adults are already meeting this target. However, the majority of subgroups are unlikely to meet this target.

What then needs to be done to make such goals a more plausible reality?

First, there must be increased recognition nationwide (and worldwide) that smoking cessation should be made a priority. In the USA between 2000 and 2009, tobacco-generated funds amounted to US$79.2 billion from the tobacco Master Settlement Agreement (MSA) and US$124.3 billion from tobacco taxes. However, less than 3.0% of these tobacco-generated funds were dedicated to tobacco prevention and cessation programs in the USA.

In order to fully fund state tobacco control programs at CDC-recommended levels, only 15% of the MSA funds and annual state excise tax revenues would be required [57]. These recommended expenditure levels are primarily based on each state's current smoking prevalence, also taking into account other factors such as the proportion of individuals living at or below 200% of the poverty level, average wage rates for implementing public health programs, support infrastructure, geographic size, and so on [110]. Considering the copious tax revenues generated by smoking (as described previously) in conjunction with the lack of funding placed towards smoking cessation, one wonders if the potential loss of tax revenue somehow relates to the lack of smoking cessation efforts? A likely unwritten reason (until now) for the global lack of smoking cessation efforts.

A motivating factor that may encourage officials to allocate these funds towards cessation is the projected cost of stroke to our society should these cessation goals not be met. The estimated direct and indirect cost of stroke in the USA for 2009 is US$68.9 billion [58]. Figure 1 shows the per-patient costs for stroke care by time period as determined in a recent review of 71 studies worldwide (mean costs upon hospital discharge: US$17,250; 3–6 months: US$10,216; 6–12 months: US$16,973; 12 months: US$28,525; >12 months: US $36,213) [59]. The average total cost per patient for all kinds of stroke in this review ranged from US$468 to US$146,149. According to the American Heart Association, the estimated lifetime cost for ischemic stroke in the USA 10 years ago was at the upper end of this range: US$140,048. From 2005 to 2050, the cost of stroke, in 2005 US$, is projected to be US $1.52 trillion for non-Hispanic white individuals, US$313 billion for Hispanic individuals and US$379 billion for black individuals. Loss of earnings is expected to be the highest cost contributor [58].

Second, stroke risk should be a routine part of education programs and targeted efforts should be made to educate the highest-risk groups first. It has been shown that adults with education levels at or below the equivalent of a high-school diploma make up approximately half of current smokers. Furthermore, it is this group that has the lowest quit ratios – 39.9 compared with 48.8% in 2008. Thus, some education programs should be tailored towards groups with lower education [57]. Similarly, aggressive action needs to be taken to assist young smokers between the ages of 16 and 24 years to quit or never to start smoking. A total of 70% of adolescent smokers regret their decision to start smoking and more than 54% of current US high-school cigarette smokers tried to quit smoking within the preceding year. Unfortunately, rates for failed quit attempts among younger smokers are at least 10% higher than those for adults. The reason for this high percentage of cessation failure is likely secondary to a propensity for young smokers to make unassisted attempts. Thus, providers need to become more involved using cognitive–behavioral interventions, which have shown promise in this population in the past, as well as considering pharmaceutical approaches, to help our youth quit smoking [111]. Last, and most importantly, programs aimed at preventing smoking in younger age groups (middle-school years [grades 6–9] and arguably even younger) need to be instituted; it is easier to never start smoking than it is to quit.

Healthcare providers owe it to patients across all ages to assist them with smoking cessation. Smoking cessation, or choosing never to smoke, is one of the single most important events in a patient's life. This decision dictates their future lifetime health, their lifetime productivity and influences the life of their friends and family through second-hand smoke exposure. Healthcare providers must not be afraid to be aggressive with patients regarding smoking; state the facts, but emphasize support in all cessation efforts.

Limitations of this article

While a large number of studies pertaining to smoking and stroke risk have been reviewed in this article, the study literature on this topic is expansive; as such, this article does not include every possible study on the subject. In addition, we frankly acknowledge that our personal belief regarding the global deficiency in smoking prevention and cessation efforts has undoubtedly colored the tone of our article. However, we believe that the breadth of studies represented in this paper provides a fair overview of the impact that smoking has on our society. Our hope is that after reading this article healthcare providers and patients do not become discouraged, but rather become inspired to rouse the fight against smoking.

Key issues

- Cigarette smoking is the single most preventable cause of mortality in society today, attributable for 140,000 strokes and over 5 million years of potential life lost in the USA annually.
- Smoking increases the risk of stroke by three to fourfold, and exposure to environmental smoke in the home increases the risk of stroke by 1.5 to twofold.
- Aside from the health risk, smoking is also financially costly to individuals in the form of increased taxes and insurance rates, and lost wages.
- Smoking is costly to society, causing an economic burden of approximately US $193 billion per year in the USA; the cost of stroke alone amounted to US$68.9 billion last year.
- In the USA, the prevalence of smoking adults remains approximately 20% and has remained virtually stable over the past 25 years. Smoking is more common in males, adults 18–44 years of age, and those who are of lower socioeconomic status and uninsured.
- Smoking prevention and education efforts need to start early in life (middle-school years [grades 6–9] or earlier). Never smoking is ideal for the individual and acts to minimize the burden of smoking-related healthcare costs to society as a whole.
- There is clear evidence that smoking cessation and reduction has a beneficial effect on health. A dose–response relationship exists between cigarette smoking and stroke risk: “the more you smoke, the more you stroke”. Smoking cessation reduces stroke risk.
- Quit ratios are only approximately 50% in the general population and even lower in less educated individuals and younger age groups.
- Healthcare providers need to take an active role in providing behavioral and pharmaceutical interventions to help all patients to quit smoking.
- Increasing funding for smoking prevention and cessation programs makes fiscal sense and will help achieve goals towards establishing a healthier American and worldwide population.

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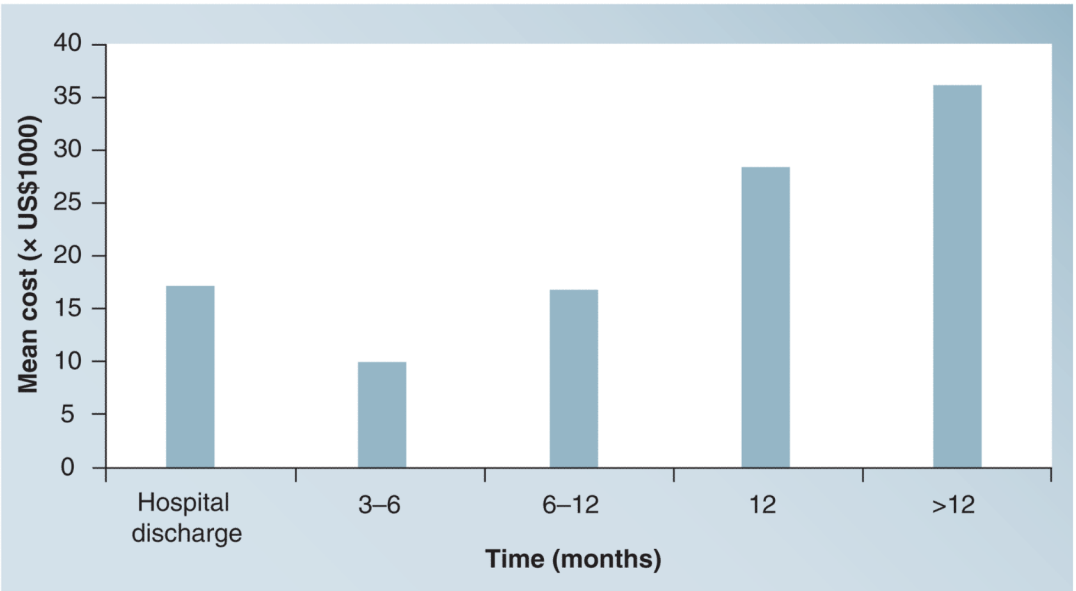

Figure 1. Stroke care cost estimates per patient by time period post-stroke onset
Evaluates 71 studies reporting costs for stroke care.
Adapted from [58].

Table 1

The association between smoking and stroke.

Study	Title	Population	Results	Risk	Ref.
Asplund *et al.*	Relative risks for stroke by age, sex, and population based on follow-up of 18 European populations in the MORGAM Project	Eight European countries 93,695 men and women	Smoking confers an increased risk of stroke	HR: Men: 1.82 Women: 2.84	[60]
Putaala *et al.*	Silent brain infarcts and leukoaraiosis in young adults with first-ever ischemic stroke	Finland 669 young adults	Smoking is an independent risk factor for silent brain infarcts	OR: 1.69 (95% CI: 1.05–2.72)	[61]
Myint *et al.*	Risk factors for first-ever stroke in the EPIC-Norfolk prospective population-based study	UK 25,000 individuals	There is an increased risk of stroke among current smokers compared with never-smokers Ex-smokers did not have increased risk of stroke compared with nonsmokers Excess stroke risk seems to decline after smoking cessation	RR: 1.70 (95% CI: 1.29–2.23)	[62]
Zhang *et al.*	Incidence and risk factors for stroke in American Indians: the Strong Heart study	USA: Native American tribes/communities 7252 individuals	Current smokers had significantly higher stroke incidence than past smokers and nonsmokers	HR: Current smokers: 2.38 Past smokers: 1.6	[63]
Song *et al.*	Risk of stroke and myocardial infarction after reduction or cessation of cigarette smoking: a cohort study in Korean men	Korea 475,734 men	Sustained ex-smokers and never-smokers had lower risks of all stroke	HR: 0.66 (95% CI: 0.55–0.79)	[29]
Assmann *et al.*	Assessing risk of myocardial infarction and stroke: new data from the Prospective Cardiovascular Munster (PROCAM) study	Germany 26,975 individuals	Cigarette smoking was found to be independently predictive of stroke risk	HR: 2.34 (95% CI: 1.52–3.60)	[64]
Weikert *et al.*	Joint effects of risk factors for stroke and transient ischemic attack in a German population: the EPIC Potsdam study	Germany 25,538 individuals	There is a stronger association between the risk factor of smoking with ischemic stroke than TIA The attributable risk of smoking for ischemic stroke is 8.1%	RR: TIA: 1.13 (95% CI: 0.69–1.84) Ischemic stroke: 1.49 (95% CI: 0.89–2.50)	[65]
Harmsen *et al.*	Long-term risk factors for stroke: twenty-eight years of follow-up of 7457 middle-aged men in Goteborg	Sweden 7457 individuals	Smoking increased the risk of stroke during the follow-up period of 16–21 years	HR: 0–15-year follow-up: 1.27 (95% CI: 0.97–1.67) 16–21-year follow-up: 1.78 (95% CI: 1.34–2.36) 22–28-year follow-up: 1.15 (95% CI: 0.92–1.42)	[66]
Dagenais *et al.*	Impact of cigarette smoking in high-risk patients participating in a clinical trial. A substudy from the Heart Outcomes Prevention Evaluation (HOPE) trial	Canada, USA, Mexico, Brazil, Argentina and 14 Western European countries 9541 individuals	Smokers had an increased risk of stroke compared with never-smokers The rates of stroke among former smokers were not different from those of never-smokers	RR: 1.42	[67]
Feigin *et al.*	Risk factors for SAH: an updated systematic review of epidemiological studies	Various countries around the world; 14 longitudinal and 23 case–control studies 3936 individuals	Smoking is one of the most important risk factors of stroke	Current smoking: RR: 2.2 (95% CI: 1.3–3.6) OR: 3.1 (95% CI: 2.7–3.5)	[68]

Study	Title	Population	Results	Risk	Ref.
Li *et al.*	Risk factors for stroke in subjects with normal blood pressure: a prospective cohort study	Sweden 28,449 individuals	Besides age, smoking was the risk factor that accounted for most strokes. The population-attributable risk was 39%	RR: 3.21	[69]
Mannami *et al.*	Cigarette smoking and risk of stroke and its subtypes among middle-aged Japanese men and women: the JPHC Study Cohort I	Japan 41,282 individuals	Smoking raises risks of total stroke and SAH for men and women, and the risk of ischemic stroke, either lacunar or large-artery occlusive infarction, for men	Total stroke: 1.27 Ischemic stroke: 1.66	[70]
Rodgers *et al.*	Risk factors for first-ever stroke in older people in the North East of England: a population-based study	UK 4440 individuals	Smoking is a risk factor for first stroke in individuals >65 years of age	1.72	[34]
Yamagishi *et al.*	Smoking raises the risk of total and ischemic strokes in hypertensive men	Japan 3626 individuals	Smoking >20 cigarettes per day increases the risk of stroke in men, especially in hypertensives	RR: 1.6 (95% CI: 1.1–2.4) In hypertensives: RR: 2.3 (95% CI: 1.2–4.4)	[71]
Tanizaki *et al.*	Incidence and risk factors for subtypes of cerebral infarction in a general population: the Hisayama study	Japan 1621 individuals	Smoking is a risk for lacunar stroke in men	RR: 2.2 (95% CI: 1.3–3.9; $p < 0.01$)	[72]
Hart *et al.*	Comparison of risk factors for stroke incidence and stroke mortality in 20 years of follow-up in men and women in the Renfrew/Paisley Study in Scotland	Scotland 15,406 individuals	Smoking is a strong predictor of stroke mortality and incidence	≥20 cigarettes/day: Men: 1.47 Women: 1.64	[73]
Nakayama *et al.*	Population attributable fraction of stroke incidence in middle-aged and elderly people: contributions of hypertension, smoking and atrial fibrillation	Japan 2302 individuals	Smoking increases the risk of stroke in individuals 40–64 years of age. The risk was not statistically significant in those over the age of 65 years	RR: 1.84 (p-value not accessible, but noted to be statistically significant)	[74]
Jacobs *et al.*	Cigarette smoking and mortality risk: twenty-five-year follow-up of the Seven Countries Study	Europe, USA, Japan 12,763 individuals	Compared with never-smokers, smokers smoking ≥10 cigarettes/day had an increased risk of death from stroke at 25 years	HR ≥10 cigarettes/day: 1.5 (95% CI: 1.24–1.82)	[75]
You *et al.*	Risk factors for stroke due to cerebral infarction in young adults	Melbourne, Australia 201 individuals	Current smoking is a risk factor for stroke in adults aged 15–55 years	OR: 2.5	[76]
Whisnant *et al.*	A population-based model of risk factors for ischemic stroke: Rochester, Minnesota	USA 1444 individuals Rochester Epidemiology Project	The risk of ischemic stroke at younger ages was greatly increased by current cigarette smoking. At older ages, risk was increased but by a lesser amount	Ever-vs never-smoker: 1.7 (95% CI: 1.31–2.23) Current vs never-/past smoker: 2.3 (95% CI: 1.67–3.12)	[77]
Rohr *et al.*	Traditional risk factors and ischemic stroke in young adults: the Baltimore– Washington Cooperative Young Stroke study	USA (Baltimore–Washington) 1516 individuals	Cigarette smoking is an important modifiable cause of stroke in young adults, particularly in black individuals	OR: Men: White: 2.0; black: 3.3 Women: White: 2.1; black: 2.2	[78]
You *et al.*	Risk factors for lacunar infarction syndromes	Australia 203 individuals	Current smoking increases the risk of lacunar stroke	Current smoking: OR: 6.6 (95% CI: 2.9–14.8)	[79]
Lindenstrom *et al.*	Lifestyle factors and risk of cerebrovascular diseases in women. The Copenhagen City Heart Study	Denmark 7060 individuals	Cigarette smoking increases the risk of cerebrovascular disease	RR: 1.4 (95% CI: 1.02–1.94)	[80]

Study	Title	Population	Results	Risk	Ref.
Shaper *et al.*	Risk factors for stroke in middle aged British men	UK 7735 individuals	Current smokers had >two times the risk of stroke compared with men who have never smoked, but the increasing trend with the amount smoked was not significant	RR: <20 cigarettes/day: 2.4 (95% CI: 1.6–3.6) 20 cigarettes/day: 2.6 (95% CI: 1.7–4.2) >20 cigarettes/day: 3.5 (95% CI: 2.4–4.9)	[81]
Boysen *et al.*	Stroke incidence and risk factors for stroke in middle-aged men in Copenhagen, Denmark	Denmark 13,088 individuals	Smokers have three times the risk of stroke than nonsmokers at age 35 years. The risk decreases with age	RR of smokers at age 35 years: 3	[82]
Abbott *et al.*	Risk of stroke in male cigarette smokers	Honolulu 8006 individuals	Compared with nonsmokers, cigarette smokers had two to three times the risk of thromboembolic or hemorrhagic stroke	RR: 2–3 ($p < 0.001$)	[83]

CI: Confidence interval (given if stated in original article); HR: Hazard ratio; OR: Odds ratio; RR: Relative risk; TIA: Transient ischemic attack.

Table 2

The dose–response relationship between cigarette smoking and stroke.

Study	Title	Population	Conclusion	Risk	Ref.
Bhat *et al.*	Dose–response relationship between cigarette smoking and risk of ischemic stroke in young women	US case–control study of 18–49-year-old females Cases (n = 466) Controls (n = 604)	Strong dose–response relationship between cigarette smoking and ischemic stroke risk in young women	OR (vs never-smokers): Overall: 2.6 ($p < 0.0001$) 1–10 cigarettes/day: 2.2 11–20 cigarettes/day: 2.5 21–39 cigarettes/day: 4.3 ≥40 cigarettes/day: 9.1	[33]
Chiuve *et al.*	Primary prevention of stroke by healthy lifestyle	US cohort study among 43,685 men from the Health Professionals Follow-up Study and 71,243 women from the Nurses' Health Study	Smoking is an independent predictor of total stroke among men and women	RR (vs never-smokers): Men: 1–14 cigarettes/day: 1.32 (95% CI: 0.90–1.95) 15–24 cigarettes/day: 2.01 (95% CI: 1.43–2.81) ≥25 cigarettes/day: 2.72 (95% CI: 1.95–3.79) Women: 1–14 cigarettes/day: 1.85 (95% CI: 1.52–2.25) 15–24 cigarettes/day: 2.59 (95% CI: 2.16–3.11) ≥25 cigarettes/day: 2.39 (95% CI: 1.86–3.07)	[84]
Kelly *et al.*	Cigarette smoking and risk of stroke in the chinese adult population	China Prospective cohort study of 169,871 men and women aged ≥40 years	Positive dose–response relationship between cigarette smoking and risk of stroke	RR (vs never-smokers): 1–9 cigarettes/day: 1.21 10–19 cigarettes/day: 1.21 ≥20 cigarettes/day: 1.36 ($p < 0.0001$)	[85]
Woodward *et al.*	Smoking, quitting, and the risk of cardiovascular disease among women and men in the Asia–Pacific region	Australian and Asian analyses of participants from 40 cohorts, involving 463,674 Asians and 98,664 Australasians	Positive dose–response relationship between cigarette smoking and risk of stroke The percentage of hemorrhagic stroke attributable to smoking was 4–12% in males and <1–9% in females For ischemic stroke, corresponding figures were 11–27% and <1–22%	HR (vs nonsmokers): Hemorrhagic stroke: 1.19 (95% CI: 1.06–1.33) Ischemic stroke: 1.38 (95% CI: 1.24–1.54) Exact HRs for positive dose–response relationship not given	[31]
Ueshima *et al.*	Cigarette smoking as a risk factor for stroke death in Japan: NIPPON DATA80	Japanese cohort study of 9638 men and women aged ≥30 years	Smoking is an independent risk factor for stroke death in Japanese individuals with moderate cholesterol levels	RR for all stroke (vs never-smokers) Men: 1–20 cigarettes/day: 1.60 (95% CI: 0.91–2.79) ≥21 cigarettes/day: 2.17 (95% CI: 1.09–4.30) Women: 1–20 cigarettes/day: 1.42 (95% CI: 0.72–2.78) ≥21 cigarettes/day: 3.91 (95% CI: 1.18–12.90)	[86]
Kurth *et al.*	Smoking and risk of hemorrhagic stroke in women	US prospective cohort study among 39,783 women participating in the Women's Health Study	Current women smokers have an increased risk of total hemorrhagic stroke, ICH and SAH Positive dose–response relationship between cigarette smoking and risk of stroke	RR (vs never-smokers): <15 cigarettes/day: Total: 1.93 ICH: 2.15 SAH: 1.70 ≥15 cigarettes/day: Total: 3.29 ICH: 2.67 SAH: 4.02	[19]

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Study	Title	Population	Conclusion	Risk	Ref.
Broderick *et al.* (Hemorrhagic Stroke Project Investigators)	Major risk factors for aneurysmal subarachnoid hemorrhage in the young are modifiable	US case–control study of men and women aged 18–49 years Cases (n = 312) Controls (n = 618)	Smoking is the most important preventable cause of aneurysmal SAH	OR (vs never-smokers): <1 pack/day: 3.32 ≥1 pack/day: 6.13	[87]
Lam *et al.*	Mortality and smoking in Hong Kong: a case–control study of all adult deaths in 1998	Hong Kong case–control study: 27,507 deceased cases and 13,054 live controls	Smoking increases the risk of death from stroke in middle-aged men There is a positive dose–response relationship	RRs for stroke death in men aged 35–69 years (vs nonsmokers): 1–14 cigarettes/day: 1.58 15–24 cigarettes/day: 1.79 ≥25 cigarettes/day: 2.20 (trend $p < 0.001$) Not statistically significant cause of stroke death in men aged ≥70 years or women of any age	[88]
Wang *et al.* (Hypertension in China [Syst-China] Trial Collaborative Group)	Risks of smoking in treated and untreated older Chinese patients with isolated systolic hypertension	Chinese cohort study of 2284 elderly men and women aged ≥60 years	Smoking is a risk factor for all-cause, noncardiovascular and cancer mortality, as well as fatal and nonfatal stroke The potential benefits of antihypertensive treatment and quitting smoking are approximately similar	HRs (vs never-smokers): Total stroke: 1–9 cigarettes/day: 1.3 (95% CI: 0.7–2) 10–20 cigarettes/day: 1.8 (95% CI: 0.9–2.1) >20 cigarettes/day: 2.2 (95% CI: 1.1–4.6)	[89]
Tanne *et al.*	Risk profile and prediction of long-term ischemic stroke mortality: a 21-year follow-up in the Israeli Ischemic Heart Disease (IIHD) Project	Israeli cohort study of 9734 men aged ≥40 years	Smoking >20 cigarettes per day was associated with 80% excess risk of ischemic stroke mortality	HR (vs nonsmokers): 1–10 cigarettes/day: 1.57 (95% CI: 1.08–2.27) 11–20 cigarettes/day: 1.37 (95% CI: 0.93–2.03) >20 cigarettes/day: 1.79 (95% CI: 1.17–2.74)	[90]
Prescott *et al.*	Mortality in women and men in relation to smoking	European pooled data from three prospective population studies of 30,917 adult men and women aged ≥20 years	Smoking increases the risk of mortality from stroke in females Positive dose–response relationship between cigarette smoking and risk of stroke	RR (vs never-smokers): Female: Ex-smoker: 1.2 <15 cigarettes/day: 1.8 ≥15 cigarettes/day: 2.5 (trend $p < 0.001$)	[91]
Haheim *et al.*	Smoking habits and risk of fatal stroke: 18-years follow-up of the Oslo Study	Norwegian cohort study of 16,209 men aged 40–49 years	Cigarette smoking increases the risk of stroke	RRs (vs never-smokers or former smokers): Cigarette and cigar/pipe smokers: 6.1 (95% CI: 3.0–12.5) Cigarettes only: 4.1 (95% CI: 2.3–7.4) Pipe and/or cigars only: 2.2 (95% CI: 0.9–5.5) RR increased by 30% with an increase in consumption of five cigarettes	[92]
Lee *et al.*	Impact of alcohol consumption and cigarette smoking on stroke among the elderly in Taiwan	Taiwan Observational survey of 2600 men and women aged ≥65 years	Smoking >20 cigarettes/day was associated with a significant risk of cerebral infarction	POR: Current smokers: 1.53 Heavy smoking: 1.96 (≥20 cigarettes/day)	[93]
Wannamethee *et al.*	Smoking cessation and the risk of stroke in middle-aged men	UK-based prospective study in 7735 men aged 40–59 years	Smoking cessation decreases the risk of stroke, particularly in light smokers A complete loss of risk is not seen in heavy smokers	RR (vs never-smokers): 3.7 (95% CI: 2.0–6.9) Upon quitting, within 5 years light smokers (<20 cigarettes/day) reverted to the risk level of those who had never smoked. Heavy smokers retained >two times risk compared with never-smokers (RR: 2.2; 95% CI: 1.1–4.3)	[94]
Robbins *et al.*	Cigarette smoking and stroke in a cohort of US male physicians	US Physicians' Health Study – cohort study of 22,071 men 40–84 years of age	Current, but not former, cigarette smoking was significantly associated with an increased risk for nonfatal stroke	RR (vs never-smokers): Former smokers: 1.20 (95% CI: 0.94–1.53)	[95]

Study	Title	Population	Conclusion	Risk	Ref.
				Current smoker <20 cigarettes/day: 2.02 (95% CI: 1.23–3.31) Current smoker ≥20 cigarettes/day: 2.52 (95% CI: 1.75–3.61) (p-trend < 0.0001)	
Colditz *et al*.	Cigarette smoking and risk of stroke in middle-aged women	US prospective cohort study of 118,539 women 30–55 years of age	Positive dose–response relationship between cigarette smoking and risk of stroke	RR (vs never-smokers): 1–14 cigarettes/day: 2.2 (95% CI: 1.5–3.3) ≥25 cigarettes/day: 3.7 (95% CI: 2.7–5.1)	[96]
Wolf *et al*.	Cigarette smoking as a risk factor for stroke. The Framingham Study	US Framingham Heart Study Cohort of 4255 men and women 36–68 years of age	Smoking is an independent risk factor for stroke Positive dose–response relationship between cigarette smoking and risk of stroke	RR: Male: 10 cigarettes/day: 1.7 20 cigarettes/day: 1.38 30 cigarettes/day: 1.62 40 cigarettes/day: 1.90 Female: 10 cigarettes/day: 1.19 20 cigarettes/day: 1.40 30 cigarettes/day: 1.6 40 cigarettes/day: 1.97	[97]

HR: Hazard ratio; ICH: Intracerebral hemorrhage; NIPPON DATA80: National Integrated Project for Prospective Observation of Non-Communicable Disease and its Trends in the Aged, 1980; OR: Odds ratio; POR: Prevalence odds ratio; RR: Risk ratio; SAH: Subarachnoid hemorrhage.