

# Deaths in Canada from lung cancer due to involuntary smoking

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Recently published evidence indicates that involuntary smoking causes an increased risk of lung cancer among nonsmokers. Information was compiled on the proportion of people who had never smoked among victims of lung cancer, the risk of lung cancer for nonsmokers married to smokers and the prevalence of such exposure. On the basis of these data we estimate that 50 to 60 of the deaths from lung cancer in Canada in 1985 among people who had never smoked were caused by spousal smoking; about 90% occurred in women. The total number of deaths from lung cancer attributable to exposure to tobacco smoke from spouses and other sources (mainly the workplace) was derived by applying estimated age- and sex-specific rates of death from lung cancer attributable to such exposure to the population of Canadians who have never smoked; about 330 deaths from lung cancer annually are attributable to such exposure.

**Des données publiées récemment révèlent que l'exposition involontaire à la fumée du tabac aggrave le risque de cancer du poumon chez les non-fumeurs. On a compilé des renseignements sur la proportion de personnes n'ayant jamais fumé parmi les victimes de cancer du poumon, le risque de cancer du poumon chez les non-fumeurs mariés à des fumeurs et la prévalence d'une telle exposition. D'après ces renseigne-**

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ments, on estime que 50 à 60 décès par cancer du poumon survenus au Canada en 1985 chez des personnes n'ayant jamais fumé ont été causés par le fait de vivre avec un conjoint fumeur; dans environ 90% des cas il s'agit de femmes. Le nombre total de décès par cancer du poumon attribuables à la fumée des autres, tant celle du conjoint que celle d'autres sources (principalement les lieux de travail), a été obtenu de la façon suivante: on a appliqué à la population canadienne de personnes n'ayant jamais fumé les taux estimatifs de mortalité par cancer du poumon selon l'âge et le sexe attribuables à une telle exposition. Celle-ci causerait quelque 330 décès par an.

**I**n eight recent reviews of the literature on passive smoking and lung cancer the authors, using criteria for causation similar to those originally proposed by Hill<sup>1</sup> or those adopted from Hill by the International Agency for Research on Cancer,<sup>2</sup> concluded that prolonged exposure to environmental tobacco smoke increases the risk of lung cancer.<sup>3-10</sup>

Involuntary exposure to tobacco smoke is estimated to cause 2500 to 5200 deaths from lung cancer annually, 2.3% to 4.7% of the total, in the United States.<sup>3,11</sup> Voluntary smoking and occupational exposure are responsible for about 85%<sup>12</sup> and 10%<sup>13</sup> respectively of all such deaths. Thus, involuntary exposure to tobacco smoke is the third largest known cause of death due to lung cancer.

The urban population of the United States spends 88% of the time in just two environments, the home and the workplace,<sup>14</sup> in which the estimated average daily exposure to tobacco smoke particulate matter is about 1.4 mg per person.<sup>14</sup> Canadian exposure values are probably similar or higher, given the colder climate (and therefore greater time spent indoors) and higher rates of cigarette smoking than in the United States.<sup>15,16</sup>

Involuntary smoking has been assessed in

relation to cancers of the lung,<sup>17-41</sup> nasal sinuses,<sup>21-24</sup> brain,<sup>23,24,42,43</sup> breast, uterine cervix and endocrine glands (mainly the thyroid), leukemia and lymphoma.<sup>37,38,42</sup> Such exposure may cause other types of cancer, but there is not yet sufficient evidence to justify a similar risk estimate.

To date, the epidemiologic studies of involuntary smoking and lung cancer have defined exposure mainly in terms of the spouse's cigarette smoking habits; few have assessed exposure outside the home. Also, most of the studies have been restricted to cases of lung cancer in women or have included only small numbers of cases in men. Accordingly, we carried out a study to estimate the number of deaths from lung cancer attributable to spousal smoking among Canadian women who had never smoked. We also estimated the number of deaths from lung cancer attributable to spousal smoking among men who had never smoked and the overall number of such deaths attributable to involuntary smoking.

## Methods

For exposure to spousal smoking the proportion of people who had never smoked among lung cancer victims was applied to the number of deaths in Canada during 1985 for which lung cancer was medically certified as the underlying cause.<sup>44</sup> We calculated the proportion of population attributable risk of lung cancer due to spousal smoking using the formula of Cole and MacMahon,<sup>45</sup> estimates of the prevalence of exposure to smoking by spouses<sup>28,41</sup> and the weighted average relative risk of lung cancer for exposed nonsmokers in 12 epidemiologic studies.<sup>6</sup>

For overall exposure the age- and sex-specific rates of death from lung cancer attributable to involuntary smoking among people who had never smoked that were estimated by Repace and Lowrey<sup>3</sup> were applied to the Canadian population

at risk, as determined from the 1983 survey on smoking habits of Canadians (unpublished tabulations, Statistics Canada).

## Results

### *Deaths from lung cancer attributable to spousal smoking*

Lung cancer was medically certified as the underlying cause of death for 11 442 Canadians in 1985 (Table I). Let us assume that involuntary smoking causes lung cancer only among people who have never smoked. In Canadian studies 7%<sup>46</sup> or 13% (unpublished data, Nutrition Canada Mortality Followup Study, D.T.W.) of deaths from lung cancer occurred among people who had never smoked. Combining the results of these two studies yielded values of 2.5% for men, 32.5% for women and 7.3% overall. Similarly, pooled results from four recent studies in the United States<sup>28,30,39,41</sup> indicated that the proportions of lung cancer victims who had never smoked were 1.5% for men, 11.5% for women and 4.0% overall. The lower values for US women were from larger, more recent studies. The current value for Canadian women likely lies between 32.5% and 11.5% because the risk of death from lung cancer among Canadian women has recently increased dramatically<sup>47</sup> and because most of this increase can probably be attributed to voluntary smoking. Pooling the Canadian and US data yielded estimates of 1.6% for men, 12.4% for women and 4.4% overall. Applying these values yielded estimates of about 130 and 390 deaths from lung cancer among men and women respectively who had never smoked (Table I).

The prevalence of exposure of people who had never smoked to smoking by spouses was estimated from data for the control groups in two large, recent case-control studies.<sup>28,41</sup> Dalager and

Table I — Estimated number of deaths from lung cancer in Canada in 1985 attributable to spousal cigarette smoking, by sex

Variable*	Men	Women	Total
Total no. of deaths from lung cancer	8278	3164	11 442
% of people who had never smoked	1.6	12.4	4.4
No. of deaths from lung cancer among people who had never smoked	132	392	524
Prevalence of exposure to spousal smoking <sup>28,41</sup> (and 95% confidence limits [CL])	0.18 (0.14, 0.22)	0.48 (0.44, 0.52)	0.37 (0.34, 0.41)
Relative risk of lung cancer (and 95% CL) <sup>6</sup>	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)	1.3 (1.1, 1.5)
% of deaths from lung cancer attributable to spousal smoking (and 95% CL)	5.1 (1.6, 8.6)	12.6 (5.2, 20.0)	10.6 (4.1, 17.1)
No. of deaths from lung cancer attributable to spousal smoking (and 95% CL)	7 (2, 11)	49 (20, 78)	56 (21, 90)

\*See results section for calculation of variables.

colleagues<sup>41</sup> observed that 48.0% of women in the control group and 18.2% of men in the control group who had never smoked had spouses who had ever smoked (female controls were hospital controls; male controls comprised almost equal numbers of hospital and general population controls). Garfinkel and associates<sup>28</sup> reported that 49.5% of women in the control group who had never smoked had husbands who were smokers; men were not included in this study. Pooling the results for female controls in these two studies yielded a prevalence rate of exposure of 0.48 for women (Table I).

Blot and Fraumeni<sup>6</sup> pooled the results of 12 epidemiologic studies (5 from the United States, 2 from Japan, 2 from Hong Kong and 1 each from Greece, Great Britain and Sweden) and obtained a weighted average relative risk of lung cancer of 1.3 (95% confidence limits [CL] 1.1 and 1.5) for women who had never smoked and who were married to men who had ever smoked.

There have been few studies of lung cancer among men who have never smoked, and the number of cases in all studies except that by Hirayama<sup>23</sup> was less than 25.<sup>7</sup> In a group of 64 men who died from lung cancer and who had never smoked, Hirayama<sup>23</sup> observed a relative risk of lung cancer of 2.25 (90% CL 1.19 and 4.22) for those whose wives smoked at the start of the 15-year follow-up period.

Given that tobacco smoke concentrations in homes with one or more smokers may be higher in Japan than in Canada or the United States,<sup>24</sup> we applied the lower pooled relative risk estimate for women to men (Table I).

The proportions of deaths from lung cancer attributable to spousal smoking among people who had never smoked were estimated to be 5.1% and 12.6% for men and women respectively. Applying these rates to the number of deaths from lung cancer among people who had never smoked yielded estimates of 7 and 49 deaths attributable to spousal smoking among men and women respectively.

### Deaths from lung cancer attributable to overall involuntary exposure to tobacco smoke

Applying the rates of death from lung cancer attributable to overall involuntary smoking (i.e., in home, at work or elsewhere) derived by Repace and Lowrey<sup>3</sup> to the population of Canadians who had never smoked yielded an estimate of about 330 deaths attributable to such exposure annually (Table II). The negative age-specific estimates in Table II may be attributed to sampling errors within relatively small subgroups.

### Discussion

The estimate of the annual number of deaths from lung cancer attributable to overall involuntary smoking, 330, may be considered an upper limit since it is based on the assumption that all of the difference in lung cancer risk found between Seventh-Day Adventists (SDAs) who had never smoked and non-SDAs who had never smoked<sup>48,49</sup> was due to differential involuntary smoking. SDAs have much less involuntary exposure to tobacco smoke than non-SDAs because most of their family and social contacts do not smoke. SDAs may also be less exposed to other lung carcinogens or more exposed to protective factors than non-SDAs. Repace and Lowrey<sup>3</sup> argued that the SDA and non-SDA groups were demographically and educationally similar and were thus likely to have similar occupational distributions; however, there is no direct information on this point. They also felt that there is no reason to suspect differential exposure to domestic radon (a lung carcinogen). Furthermore, any dietary differences between the groups are unlikely to account for more than 30% of the difference in risk (nonsmoking women in the study by Hirayama<sup>22</sup> who ate green and yellow vegetables daily had a relative risk of lung cancer of 0.71 compared with women who consumed such vegetables less often), whereas the relative risk of lung cancer for SDAs compared with

Table II — Estimated number of deaths from lung cancer attributable to overall involuntary smoking, by age and sex

Age, yr	Men			Women		
	Rate of death from lung cancer <sup>3</sup>	Population at risk (in 1000s)	Expected no. of deaths	Rate of death from lung cancer <sup>3</sup>	Population at risk (in 1000s)	Expected no. of deaths
40-44	0.0	213	0.0	6.0731	298	18.10
45-49	0.0	155	0.0	5.2193	296	15.45
50-54	5.1779	137	7.09	1.9803	288	5.70
55-59	-2.4152	87	-2.10	7.1737	284	20.37
60-64	9.0651	102	9.25	6.1823	333	20.59
65-69	10.6740	86	9.18	2.2710	288	6.54
70-74	-17.5301	61	-10.69	20.3400	250	50.85
75-79	30.5764	39	11.92	28.8750	177	51.11
80-84	84.8475	37	31.39	-18.6560	130	-24.25
≥ 85	48.9612	18	8.81	104.1890	99	103.15
Total			64.85			267.61

non-SDAs is 2.4 (a difference of 140%). Finally, they argued that the 60% of SDAs who do not work for church-run organizations must have some exposure to tobacco smoke in the workplace and that this would tend to offset any overestimation of the risk of lung cancer attributed to involuntary smoking by this approach. Furthermore, the increased risk of lung cancer associated with involuntary smoking found in the recent study by Dalager and colleagues<sup>41</sup> was not accounted for by race, employment in a high-risk industry, exposure to asbestos, parental smoking or dietary intake of vitamin A or carotene.

Since 1981, 14 investigations of the relation between involuntary smoking and lung cancer have been reported.<sup>17-41</sup> All but one<sup>31</sup> have shown increased risks of lung cancer in exposed populations or subgroups. In eight studies significantly increased risks for one or more subgroups were observed.<sup>17-26,28-30,37,40,41</sup>

Rothman<sup>50</sup> recently reviewed Hill's criteria for causal inference in epidemiology.<sup>1</sup> Both authors contend that there are no hard-and-fast rules for causal inference. Nevertheless, Hill's criteria or variations thereof have been used by various authorities, including the US surgeon general<sup>12</sup> and the International Agency for Research on Cancer.<sup>5</sup> These criteria can be applied to the available epidemiologic evidence on the relation between involuntary smoking and lung cancer.

#### *Strength of association*

There is no sharp definition of a "strong" association. Relative risk estimates for lung cancer (i.e., the incidence rate of lung cancer among people who have never smoked and who are exposed to tobacco smoke divided by that for people who have never smoked and have not had such exposure) range from 0.8 to 2.1.<sup>6</sup> Values of 1.1 to 3.5 have been observed for nonsmoking women whose husbands were "heavy smokers" (various definitions used).<sup>6</sup> Pooled data from 12 epidemiologic studies gave a weighted relative risk estimate of 1.3 (95% CL 1.1 and 1.5) for lung cancer among nonsmoking women whose husbands smoked.<sup>6</sup> Similarly, pooled dose-response data from seven epidemiologic studies gave a weighted relative risk estimate of 1.7 (95% CL 1.4 and 2.1) for nonsmoking women whose husbands were heavy smokers.

Compared with the relation between active smoking and lung cancer, for which relative risk values of up to 14 have been reported for average smokers,<sup>12</sup> the observed association between involuntary smoking and lung cancer is relatively modest. However, as noted by Rothman,<sup>50</sup> "the strength of an association is not a biologically consistent feature but rather a characteristic that depends on the relative prevalence of other causes". Weak associations do not eliminate a causal relation, but they are, in principle, more

likely than stronger associations to be explained by undetected biases or confounding.

#### *Consistency*

A positive association between lung cancer and involuntary smoking by nonsmoking women whose husbands smoke has been reported from 13 epidemiologic studies conducted in 6 countries.<sup>17-30,32-41</sup> A weakly negative association was observed in a poorly described study conducted in Hong Kong.<sup>31</sup> Significantly increased risks among groups or subgroups were observed in eight studies<sup>17-26,28-30,37,40,41</sup> and significant exposure-risk gradients in five.<sup>23,26,28,29,41</sup> Conclusions could not be drawn in two of the studies because of inadequate information<sup>35</sup> or insufficient numbers of nonsmoking subjects with lung cancer.<sup>36,38</sup> The first study by Garfinkel<sup>27</sup> revealed a weakly positive but not significant association, possibly owing to substantial misclassification of exposure status.<sup>27,28</sup> Koo and coworkers<sup>34</sup> reported a relative risk of 1.48 for women whose husbands were smokers and 1.75 when cases were restricted to squamous cell carcinoma. Wu and collaborators<sup>39</sup> reported a relative risk of 1.2 for adenocarcinoma among women married to smokers as well as an exposure-risk relation (the relative risk was 2.0 for women with 31 or more years of exposure at home or work). Thus, although significant risks were not reported in all the studies, the overall evidence is consistent and strongly supportive of a causal relation.

#### *Specificity*

This criterion requires that a given cause lead to a single effect. There is not sufficient evidence that involuntary smoking causes cancers other than lung cancer, but it does cause other adverse health effects.<sup>8,10,51,52</sup> However, there is no logical basis for inferring that a given cause can produce only one effect. Rothman<sup>50</sup> rejected this criterion as "useless and misleading".

#### *Temporality*

The onset of involuntary exposure to tobacco smoke occurs many years before the diagnosis of lung cancer or death. For example, of the 16 subjects with lung cancer whose spouses smoked in the study by Correa and colleagues<sup>29</sup> 9 had 41 or more pack-years of exposure. Furthermore, the relative risk increased with increasing duration of exposure and, for men, when there was exposure early in life to smoking by the mothers.<sup>29</sup>

#### *Biologic gradient (dose response)*

The relative risk of lung cancer among non-

smokers was found to increase as involuntary exposure to tobacco smoke increased in six studies.<sup>23,26,28,29,40,41</sup> Trends were formally significant in five of the studies and approached such significance in the other. These trends were apparent for men, women or both sexes combined (depending on the study).

### *Biologic plausibility*

Whole tobacco smoke is a known human carcinogen.<sup>5,12</sup> There are at least 38 known or probable carcinogens in the particulate phase of mainstream tobacco smoke (that inhaled by a smoker while puffing) and another 16 in the volatile phase.<sup>51</sup> Air contaminated by tobacco smoke contains these carcinogens, but the main source of tobacco smoke contaminants in indoor air is sidestream smoke (that emitted by the burning tip of an idling cigarette, cigar or pipe), which contains higher concentrations of many toxic and cancer-causing chemicals than does mainstream smoke.<sup>12</sup> Painting the skin with sidestream smoke condensate produced carcinomas in 33% of mice, compared with 6% of those painted with mainstream smoke condensate.<sup>53</sup>

Nicotine and cotinine (the major metabolite of nicotine) have been detected in saliva, blood and urine samples from nonsmokers at concentrations related to the level of exposure to environmental tobacco smoke.<sup>54</sup> Nonsmokers heavily exposed at home to environmental tobacco smoke had urine cotinine levels similar to those of people who smoked less than three cigarettes per day. Given that there is an increased risk of lung cancer due to active smoking with only a few cigarettes per day,<sup>12</sup> exposure of nonsmokers to environmental tobacco smoke could reasonably be expected to cause some risk of lung cancer. Linear interpolation between the values for the relative risk of lung cancer for people who smoke 1 to 9 or 1 to 14 cigarettes per day in three large cohort studies and a value of 1 for nonsmokers yields an estimated relative risk of 1.5 to 2 for people who smoke a few cigarettes per day, similar to that for heavily exposed involuntary smokers.<sup>6</sup>

### *Coherence*

This criterion implies that a postulated causal relation does not conflict with what is known about the natural history and biology of the disease. As such, it is similar to biologic plausibility and will not be further discussed.

### *Experimental evidence*

There have been no randomized trials of exposure to or removal of exposure to environmental tobacco smoke (nor are there likely to be). Such

evidence is seldom available for any type of exposure in human populations.

### *Analogy*

It can be argued that a causal relation between lung cancer and involuntary smoking is analogous to the accepted causal relation between mesothelioma or lung cancer and nonoccupational exposure to environmental asbestos.<sup>55</sup>

Tobacco smoke contains many carcinogens, and the epidemiologic evidence that involuntary smoking causes lung cancer has stood up to critical review.<sup>3-10</sup> However, some investigators have questioned the evidence in part on the belief that involuntary smokers are exposed to a far smaller amount of tobacco smoke than are active smokers.<sup>56,57</sup>

It is misleading to measure one or even a few tobacco smoke contaminants in specimens from nonsmokers and then express the results as "cigarette equivalents". In a recent study the urine cotinine level among involuntary smokers averaged 0.7  $\mu\text{g}$  per milligram of creatinine and ranged from 0.3 to 1.6  $\mu\text{g}/\text{mg}$ , depending on the number of cigarettes smoked per day by other household members.<sup>54</sup> Active smokers had an average cotinine level of 8.6  $\mu\text{g}/\text{mg}$ ; among those who smoked less than three cigarettes per day the level was 1.6  $\mu\text{g}/\text{mg}$ . Thus, one might conclude that involuntary smokers are exposed to the equivalent of up to one or two cigarettes per day. However, the ratio of the amount of nicotine (the precursor of cotinine) in sidestream smoke to that in mainstream smoke is only about 3.<sup>12</sup> In contrast, the corresponding ratios for several of the carcinogens in tobacco smoke are much higher (e.g., *N*-nitrosodimethylamine, 20 to 100; 2-naphthylamine, 30; and 4-aminodiphenyl, 31).<sup>8</sup> Since sidestream smoke is the main source of involuntary exposure, the cancer risk may be greater than the equivalent of one or two cigarettes per day.

Active smoking is clearly hazardous, and an exposure equivalent to one or two cigarettes per day still results in substantial risk. In his 1981 report the US surgeon general concluded that "there is no safe cigarette and no safe level of consumption".<sup>58</sup> The lifetime risk of lung cancer for men in western Canada is 6.5%.<sup>59</sup> Over 90% of deaths from lung cancer occur among former or current cigarette smokers<sup>46</sup> who smoke an average of 27 cigarettes per day.<sup>13</sup> About 61% of the male population aged 20 years or older are current or former cigarette smokers.<sup>60</sup> Their lifetime risk of lung cancer is therefore about 10%.

Linear extrapolation indicates that a person who smokes one cigarette per day would have a lifetime lung cancer risk of about 0.4%. If one accepts the standards for lifetime involuntary carcinogenic risk to the public normally used by the US

Food and Drug Administration and the US Environmental Protection Agency with respect to carcinogens in air, water and food (i.e.,  $10^{-5}$  to  $10^{-7}$ ), even one cigarette per day results in a lung cancer risk that is about 400 times the highest definition of acceptable risk.<sup>61</sup>

In homes with infiltration of radon from building materials and the ground, the concentration of airborne radon daughters, radioactive elements known to cause lung cancer in occupationally exposed humans, was found to be increased by the presence of cigarette smoke.<sup>62</sup> If smoke particles are present, radon daughters adhere to them instead of adsorbing to other surfaces, and the radioactive particles are deposited in the lungs, whereas unbound radon gas is exhaled. Thus, average nonsmokers living in homes with smokers tend to have higher levels of exposure to radon daughters, which may explain part of their elevated risk of lung cancer.

Although we have focused on lung cancer, involuntary smoking has been associated with an increased risk of several other cancers, including those of the nasal sinuses,<sup>21-24</sup> brain,<sup>23,24,42,43</sup> breast, uterine cervix and thyroid, leukemia and lymphoma.<sup>37,38,42</sup> Sandler and associates<sup>38</sup> observed an increased risk of cancer among people aged 15 to 59 years who were exposed as children to household tobacco smoke. There were statistically significant trends of increasing risk of any type of cancer and of several specific cancers (those of aggregated smoking-related sites, the breast and uterine cervix, and leukemia and lymphoma) in relation to the number of household smokers. The risk of any type of cancer was greater for people with household exposure to tobacco smoke during both childhood and adulthood than for those with one or the other. The trends in risk were found for smokers and nonsmokers and persisted after adjustment for age, sex and education. Further research is required to clarify the role of involuntary smoking in the development of cancers other than lung cancer.

We conclude that in Canada about 50 to 60 deaths from lung cancer annually result from exposure to spousal smoking. Overall involuntary exposure to tobacco smoke (at home, work or elsewhere) may cause about 330 such deaths annually. To obtain a more precise estimate, research is required to determine the distribution of exposure levels in the Canadian population, and epidemiologic studies are needed to assess the risk of lung cancer in relation to better exposure data.

The levels of exposure of nonsmokers to environmental tobacco smoke outside the home may approach or exceed those at home. Among British men the average duration of exposure for nonsmokers married to nonsmokers was found to be 11 hours per week, of which 10 occurred outside the home; the corresponding values for nonsmokers married to smokers were 23 and 16 hours per week.<sup>63</sup> Repace and Lowrey<sup>14</sup> estimated that about 80% of the average daily amount of

exposure of nonsmokers to tobacco smoke particulate matter in the United States occurs at work. Friedman and coworkers<sup>64</sup> observed that in the San Francisco/Oakland region the average duration of exposure for nonsmoking women married to nonsmokers was 5.6 hours per week, of which 4.6 occurred outside the home; the corresponding values for nonsmoking women married to smokers were 20.5 and 7.8 hours per week. Similar results were obtained for men.

The evidence that substantial exposure to environmental tobacco smoke occurs outside the home, together with evidence that the true relative risk due to spousal smoking is probably about 1.5,<sup>7,11</sup> suggests that our estimate of about 330 deaths from lung cancer due to overall exposure is not unreasonable.

With the current scientific consensus that involuntary smoking causes some risk of lung cancer and the estimates of numbers of attributable deaths that we have presented, the public health implications are clear: involuntary exposure to tobacco smoke should be eliminated in indoor public areas, and educational programs to eliminate household exposure should be intensified.

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