

## **Appendix**

# **Appendix**

## **The evidence for the passive smoking theory**

“There is overwhelming evidence, built up over decades,  
that passive smoking causes lung cancer”

- Vivienne Nathanson, British Medical Association

## Glossary of terms

### Case-control study

Epidemiological research which surveys a sample group (the cases) and compares them to a healthy sample group (the controls). In this instance, the cases are lung cancer sufferers. When the subject is no longer alive to answer questions, family members may be asked to provide information. Also known as a retrospective study.

### Cohort study

Epidemiological research which monitors a group of people (the cohort) over a period of time, usually several years. Typically, they are surveyed at the outset of the study, at its end and sometimes in between. In the field of secondhand smoke research, the cohort are healthy individuals at the outset and are monitored for lung cancer over time. Because they are healthy to begin with, the possibility of *recall bias* is eliminated. For this, and other reasons, cohort studies are considered of greater value than *case-control studies*. Also known as a prospective study.

### Confidence interval

The margin of error between the lower and upper end of the relative risk. Shown in brackets after the *relative risk*. In epidemiology, it is standard practice for there to be a confidence of 95% ie. only a one in twenty theoretical chance of the true risk falling outside the upper and lower ends of the interval. In practice, this confidence is often misplaced.

### Confounding factor

Any external factor that may influence the results of a study. In the field of lung cancer research, these particularly include age, occupation, income, asbestos exposure, infection, radiation, diet and smoking history.

### Data-dredging

A term used to describe the practice of asking subjects about a vast number of lifestyle factors in the hope of finding an association with one or more of them. Data-dredging is one of the reasons why the 95% confidence level is misleading. A researcher may ask his sample group about 100 different lifestyle factors. Chance dictates that 5 statistically significant findings will emerge, even if none of them are a genuine risk. The

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researcher is, however, free to publish these 5 statistically significant associations. Now consider that there are thousands of multi-factorial studies being conducted at any one time around the world. The sheer volume of findings guarantees that bogus associations will frequently be reported. They will be statistically significant, but far fewer than 95% of them will be real.

### Dose-response relationship

If A leads to B, any increase in A should lead to an increase in B. In the case of active smoking, it has been proven that heavier smokers have a greater risk than lighter smokers and that risk increases according to the number of years spent smoking. If secondhand smoke poses a risk to nonsmokers, one would also expect to see a linear relationship between lung cancer risk and length and intensity of exposure. If the reverse happens, it is an *inverse* dose-response relationship.

### Null hypothesis

The premise that no relationship exists between A and B.

### Null study

Any epidemiological result which does not achieve statistical significance and therefore supports the *null hypothesis*.

### Publication bias

There is a well-known, proven tendency for medical and scientific journals to favour publishing epidemiological studies which deliver *statistically significant* results. Although it is not necessarily the case, *null studies* are generally of less interest to their readers and the media. If *null studies* are not published, evidence for the null hypothesis will be under-reported. Publication bias is particularly common when results support the editorial stance or are topical.

### Recall bias

In case-control studies, where information is gathered retrospectively through interviews, there is a known tendency for some subjects to exaggerate or downplay their exposure to A as a result of what they have been told about B. In the field of secondhand smoke research, this usually means lung cancer cases overstating their past exposure to tobacco smoke because they see their condition as uniquely related to smoking.

### Relative risk

The term relative risk, which has particular pertinence to cohort study computations, is also commonly used in describing risk estimates from lifestyle epidemiology generally. The most common form of risk computation is specifically and properly called an odds ratio yet is more typically referred to as “relative risk” by general definition. The relative risk, however specifically computed, is the headline estimate - or what might be called the best guess - provided by epidemiologists to show the relationship between A and B. The relative risk falls between the low and high ends of the *confidence interval*.

### Smoker misclassification

When information about smoking behaviour is self-reported (as is usually the case), there is a known tendency for some smokers to classify themselves as nonsmokers (see chapter 6). Nonsmokers very rarely classify themselves as smokers, however, and this misclassification leads to a muddying of results. Since around 1990, some researchers have tested their subjects for cotinine - which is present at high levels in users of tobacco. This procedure helps to exclude current smokers from the sample group but because cotinine disappears from the body after several weeks, it does not eliminate former smokers. In case-control trials, this can be a significant problem, since many smokers quit their habit when diagnosed with lung cancer.

### Statistical significance

Meaning that the finding is probably not the result of chance. Significance is attained when the lower and upper confidence limits are both above (or, for negative associations, both below) 1.0. In epidemiology, significance is not an objective measure, as it is in common parlance. It is sometimes mistakenly said all relative risks below 2.0 (or 3.0) are statistically insignificant. This is not true. They may not be considered a substantial or meaningful in practical terms - and they may still be false findings - but they are statistically significant if they meet the test above.

### Wish bias

The researcher's desire to reach a preconceived conclusion can sway the results. The bias may be personal, financial, political or institutional. Wish bias manifests itself in confounding factors being overlooked, alternative explanations ignored, unfavourable data omitted or the study design being skewed to make a positive association more likely.

## A brief history of passive smoking

Takeshi Hirayama conducted the first epidemiological research into passive smoking by monitoring the health of nonsmoking women married to smoking husbands and this model remains the gold standard for research of this kind. In the 25 years since Hirayama's paper was published (1981), a further 63 similar reports have been published. Taken together they form a substantial body of evidence which, according to one Surgeon General, is "overwhelming" in supporting the hypothesis that nonsmokers exposed to secondhand smoke are more likely to suffer from lung cancer than those who generally avoid exposure. After reading all of these studies, I have not been able to endorse this interpretation.

There are only three possible outcomes in studies of this kind. The first is that the hypothesis is correct (ie. that passive exposure to tobacco smoke increases lung cancer risk). The second possibility is that there is a negative association (ie. that passive smoking reduces the risk of lung cancer). The third possibility is that there is no association either way; this is known as the 'null hypothesis'.

A relative risk (RR) of 1.0 represents no association either way. An RR below 1.0 represents a negative association and an RR above 1.0 represents a positive association. For example, 0.9 = 10% less risk, 1.35 = 35% greater risk and 2.0 = 100% greater risk.

In the studies listed below, researchers typically compare a group of married, nonsmoking women who have lung cancer (the cases) with a group of married, nonsmoking women who do not (the controls). Questions are asked of both groups regarding exposure to tobacco smoke and, to put it in simple terms, if marriage to a smoker is a more common trait amongst the lung cancer cases than amongst the controls, it might be inferred that marriage to a smoker increases lung cancer risk. If, for example, 60% of the lung cancer cases are married to smokers and only 40% of the controls are married to smokers, it might be inferred that marriage to a smoker increases lung cancer risk by half (RR = 1.5).

Or it might not. In this example, can we be sure that it was the husband's smoking habits that made the difference? Can we be sure that the women were not smokers themselves? What if the women all lived in a city or all worked in the asbestos industry? What if they were older than the controls and therefore had a higher risk of

cancer anyway? Are their diets comparable? Did they used to be smokers? All these are confounding factors and need to be identified and avoided. If they are unavoidable, the figures must be adjusted to take them into account.

The numbers involved are crucial if we are to draw any conclusions from a study of this kind. In the example above, the women married to smokers appear to have a relative risk of lung cancer of 1.5; a 50% increase. That is based on 40% of the healthy controls being married to smokers. But what if there were only 5 women in each group? That would mean two of the controls were married to smokers and three were not. Among the cases, this ratio is reversed. Technically, 40% of the controls were married to smokers but the difference between the two groups comes down to one woman in each group saying that she is or is not married to a smoker. The study is vulnerable because of its small size and may not be - indeed, probably *is* not - representative of the population at large. If, on the other hand, 1,000 women are in each group and the percentages remain the same we can say with rather more confidence that marriage to a smoker increases lung cancer risk and that this lies somewhere around 1.5.

Clearly, we must exercise caution before drawing conclusions from small sample groups but as the number of participants increases, the margin for error is reduced and our estimates should become more accurate. As discussed in chapter 7, epidemiologists distinguish between chance results and genuine associations by using a standard of statistical significance. In our example of 5 lung cancer patients, the RR is 1.5 but this does not tell the whole story. The full RR is 1.5 (0.4-5.5) with the figures in brackets being the lower and upper limit. Because of the small number of cases, the confidence interval (or the margin of error) is very wide and we can only surmise that the risk to the nonsmokers falls between a 60% reduction and a six-fold increase - not very useful.

In the second example, there are 500 cases and so the margin of error is much narrower and the RR is 1.5 (1.3-1.7). This tells us that risk is increased by at least 10% and may be as high as 100%. This association is statistically significant because the lower limit of the confidence interval is above one. If it was 1.0 or lower it would not be significant, since the RR includes the null hypothesis and the negative hypothesis. And if an RR is not statistically significant, it tells us nothing. It does not matter whether the headline figure is higher or lower than 1.0, it supports neither the positive or negative hypothesis.

The null hypothesis itself cannot be proven even in the unlikely event of the RR landing exactly on 1.0. However, if enough studies show nonsignificant findings, one might reasonably infer that there is no association to investigate.

Of the epidemiological papers that studied the effect of secondhand smoke on nonsmoking wives, 9 found a statistically significant positive association, 3 found a statistically significant negative association and the remaining 52 found no statistically significant association either way. Some within the tobacco control movement have

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claimed that the risk from passive smoking is too small to be demonstrated conclusively in small and medium sized studies. Only very large studies, they say, have the statistical power to meet the criteria for significance but these studies are difficult to carry out thanks, in part, to the relative scarcity of lung cancer patients who have never smoked. There is some truth in this, although it is worth pointing to the 12 findings below that have achieved statistical significance (albeit with 3 of them going in the 'wrong' direction).

Since the mid-1980s, it has become clear that early reports from Hirayama and Trichopoulos showing a doubling of lung cancer risk were erroneous and that if a risk exists at all, it falls at a level well below 1.5 and that if risk exists at all, it is realistically imperceptible. In the past twenty years, very few statistically significant associations have come to light and so those who have put their faith in the passive smoking theory have used the nonsignificant findings found in the bulk of studies to make their case. They have claimed that although the majority of epidemiological papers do not show significant associations, the weight of evidence points towards a positive association and that, taken together, they show a risk of around 1.20.

While it is unusual to infer anything from relative risks that do not meet the minimum standard of statistical significance, it has been claimed in this sphere that it is not completely unreasonable to draw conclusions if they all point in the same direction and show a similar relative risk. However, that is not the case here.

Of the 52 statistically insignificant results, 18 (35%) have a relative risk of 1.0 or below and 34 (65%) have a relative risk above 1.0. The best that can therefore be said of this data is that there are a few more studies pointing up than down. This is feeble stuff. No one is claiming that secondhand smoke *protects* people from lung cancer but if the 18 studies that point in that direction are not to be trusted, why trust the 34 that point the opposite way?

If we accept that secondhand smoke causes lung cancer in nonsmoking women because a slim majority of the nonsignificant results lean that way then we must also accept that women who are exposed to secondhand smoke in childhood are less likely to suffer from lung cancer (a majority of the studies regarding passive smoking in childhood have shown a negative correlation).

If the majority of studies showed relative risks that were closely grouped between 1.20 and 1.30 then one might be more inclined to accept the plausibility of the passive smoking hypothesis. Britain's SCOTH committee and anti-smoking groups around the world have now settled on a relative risk for secondhand smoke and lung cancer of 1.24 but not one of the 64 studies below shows a risk of that magnitude. Even if one allows a generous margin of error and settles for any risk between 1.20 and 1.29, there are only five studies that fit the bill.

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For every study that shows a statistically significant positive association, there are six that do not. This is hardly overwhelming evidence in support of the passive smoking theory and yet these nine significant associations do exist, compared to 'only' three in the opposite direction. Are they suggestive? The reader should not infer that it is difficult or unusual for a random result to achieve statistical significance. Most, if not all, of the transient health scares that appear in the daily newspapers achieve this minimum scientific criteria. Any epidemiologist who asks questions about enough aspects of their subjects' lifestyle will chance upon plenty of apparent associations and although passive smoking may seem a limited field there is plenty of scope for data-dredging.

In the studies below, patients were asked about everything from the length of their menstrual cycle to whether they owned a black and white television. Findings can be made for those with heavy smoking husbands, light smoking husbands and ex-smoking husbands. Results can be divided by age, occupation, diet and social status. They can be split according to the major types of lung cancer the cases are suffering from (there are four), as well as other cancers, heart disease, stroke and overall mortality. They can be rearranged according to the type of exposure (childhood, adulthood, spousal, mother, father, sibling, social, workplace) and, finally, the risks can be adjusted as the author sees fit in order to account for confounding variables. A study of one case group can, therefore, produce over a hundred individual risk ratios and the chances of finding a significant association becomes far more likely.

There is a natural tendency for epidemiologists to want to show a positive result if only because null studies are of little interest and are less likely to be published. This tendency is particularly strong when the issue relates to secondhand smoke and when the researcher has a personal or financial bias. From the very outset, there was a hope and expectation that passive smoking was indeed linked to lung cancer in nonsmokers. This prevailing bias has led to studies being written up in such a way that emphasised the results that supported the passive smoking theory and ignored the vast majority that did not.

How these results are presented is entirely down to the authors, and their interpretation invariably moulds the report's summary and the accompanying press release. They may choose to publish only the results that appear to support the hypothesis or, if they tabulate the rest of the findings, write up their paper in such a way as to stress positive associations and downplay the null findings. If 99 results support the null hypothesis and one supports the a priori hypothesis, it is the single positive association that makes the headlines. The early 1990s studies of Janerich, Brownson and Stockwell are fine examples of this tendency.

What follows is every peer-reviewed study of nonsmoking wives ever published with the editorialising stripped away to reveal the data in its pure form. Doctoral theses and dissertations are not included unless they have subsequently been published in a

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book or scientific journal. When results have been published more than once (eg. Hirayama, Fontham), the most recent version has been reviewed. Where confounding factors have been accounted for, the adjusted odds ratios have been used.

The studies are listed in order of size, with the studies with the largest sample group listed first. The order of the studies is important since those with the largest sample group are likely to offer the most accurate results. The reader will notice that the higher relative risks appear towards the bottom, where the smallest and least reliable studies lie. If one examines the results from the ten largest studies it is very difficult to view them as anything other than a random assortment of numbers hovering either side of 1.0. In order, they appear: 1.29, 1.11, 0.70, 1.03, 1.53, 1.10, 0.89, 1.10, 0.90 and 0.96. Between them, they give an average relative risk of 1.06 which is so close to a zero risk that if it were not so political, the issue of passive smoking would have been quietly shelved years ago. The smaller studies lift the average slightly higher - as the EPA found to its benefit - but some of these involve just 8 or 9 women and, with apologies to their authors, they are meaningless.

The results of studies that have investigated childhood exposure, workplace exposure, the effect on men or the association with other diseases are no more consistent or compelling than those involving nonsmoking wives and lung cancer (and the reader is encouraged to seek them out) but there are fewer of them and so the studies listed below provide the largest body of evidence regarding the passive smoking theory.

The number of subjects is based on the total number of female lung cancer cases involved in the study. The relative risks are taken from the tabulated evidence given in the original study in most cases. In a small minority of cases, relative risks are not shown in the original papers and in these instances the risks have been calculated from the available data. Statistically nonsignificant risks that exceed 1.0 are marked "(null)" and those that fall below 1.0 are marked "(negative)". Statistically significant findings are marked with an asterisk.

## The studies

**Fontham (1994) 651 subjects: RR = 1.29\* (significant - positive)**

As the largest cohort study of its kind, Elizabeth Fontham's 1994 study provides the strongest evidence for a slim association between passive smoking and lung cancer in nonsmokers. In 1991, she released preliminary results, just in time for them to be included in the EPA report and her final paper (1994) produced much the same findings. For those with husbands who smoked cigarettes, cigars or pipe tobacco, relative risk narrowly achieved significance at 1.29 (1.04-1.60).

Exposure in occupational and social settings also showed a significant risk of 1.39 and 1.50 respectively but there was no association with exposure in childhood (0.89). Generally, there was evidence of a dose-response relationship and the results were adjusted for diet, race, age and occupation. Although slight in every instance, the associations were consistently more compelling for adenocarcinoma than for other types of lung cancer. This was surprising since, of the four major types of cancer (the others are small cell, large cell and squamous cell), adenocarcinoma is least associated with smoking.

**Boffetta et al (1998) 508 subjects: RR = 1.11 (null)**

The World Health Organisation commissioned the International Agency for Research on Cancer to carry out this European study of 650 never-smoking lung cancer patients, of whom 508 were married women. When compared against a control group of 1,008 healthy women, no statistically significant link was found between a husband's smoking habits and lung cancer: RR = 1.11 (0.88-1.39). The only statistically significant finding in the paper was an apparent protective effect from exposure to secondhand smoke during childhood of 0.77 (0.61-0.98).

**Wu-Williams (1987) 417 subjects: RR = 0.7\* (significant - negative)**

By 1987, several papers had provided the unlikely and, to many, unwelcome suggestion that exposure to tobacco smoke actually protected nonsmokers from lung cancer but it was not until the publication of Anna Wu-Williams' study that such an association achieved statistical significance. Wu-Williams was working in UCSF's Department of Preventive Medicine when her study into lung cancer risks for women in China appeared in the *British Journal of Cancer* showing a statistically significant 0.7 (0.6-0.9) negative association between secondhand smoke and lung cancer.

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### **Wang (2000) 407 subjects: RR = 1.03 (null)**

This large Chinese study apparently demonstrated that lung cancer risk was doubled by owning a colour TV and trebled by owning a refrigerator but came up empty-handed with regard to secondhand smoke. The RR of 1.03 (0.6-1.7) for passive smoke exposure in adult life was highly supportive of the null hypothesis.

### **Zaridze (1998) 358 subjects: RR = 1.53\* (significant - positive)**

This study from Moscow found an association between passive smoking and lung cancer although there was an inverse dose-response relationship; ie. the women's lung cancer risk dropped as the husband's cigarette consumption rose. Risk also fell as the duration of exposure rose. Zaridze's relative risk for women married to smokers was positive and statistically significant (1.53 (1.06-2.21)). Strangely, a similar association was found with marriage to a smoker even when the husband did not smoke in her presence (1.48 (0.86-2.53)) and exposure in childhood or from any other family member yielded statistically nonsignificant negative results of 0.92 and 0.91 respectively.

### **Zhong (1999) 322 subjects: RR = 1.10 (null)**

This large Chinese study sought to find the causes of the recent rise in lung cancer in Shanghai and identified statistically significant associations with low vitamin C consumption, genetic susceptibility, high risk occupations and cooking fumes but not secondhand smoke. After comparing 322 lung cancer cases with 377 controls, the relative risk supported the null hypothesis with an RR of 1.1 (0.8-1.5). The RR for those exposed in childhood was similar, albeit in the other direction, at 0.9 (0.5-1.6).

### **Wen (2006) 294 subjects: RR = 0.89 (negative)**

This Chinese cohort study had a sample group of 64,881 nonsmoking, married women who were interviewed between 1997 and 2004. In direct contrast to Stockwell (1992), it found some evidence that secondhand smoke exposure in the workplace was a risk factor for lung cancer but found no risk when that exposure was in the home. Like Stockwell, the author wrote at length about the positive association while skimming over the more plentiful evidence that showed no link between passive smoking and lung cancer.

The relative risk to a woman exposed to smoke by her husband was 0.89 (0.42-1.92) and the risk from exposure in childhood was 0.21 (0.03-1.61). This very low latter association was compensated by a higher, positive association with workplace exposure of 2.25 (0.95-5.27). None of these results were statistically significant. When all three sources of exposure were taken together, the RR in this sizeable study was effectively zero: 1.03 (0.57-1.87). As is often the case in these studies, there was scant evidence of a

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dose-response relationship between length or intensity of exposure and risk. Indeed, the wives who had the most exposure had the lowest risk (0.79 (0.48-1.31)).

[The paper does not make it clear exactly how many of the subjects succumbed to lung cancer. However, the author showed that 106 of the lung cancer cases were married to smokers, and that 36% of the wives were married to smokers. The above figure is a calculation based on these two figures.]

### **Schwartz (1996) 257 subjects: 1.1 (null)**

This study of lung cancer patients in Detroit examined various possible causes of the disease but failed to support the passive smoking theory. The sample group included a minority of men and the authors did not provide relative risks for either gender, but the overall figure for people 'exposed in the home' supported the null hypothesis with an RR of 1.1 (0.8-1.6).

### **Gao (1987) 246 subjects: RR = 0.9 (negative)**

Another large Chinese case-control study found no association between lung cancer and exposure to secondhand smoke in adulthood; RR 0.9 (0.6-1.4). There was, however, a dose-response relationship between years spent married to a smoker and increased lung cancer risk (1.1, 1.3 and 1.7 for 20-29 years, 30-39 years and 40+ years). None of the findings achieved statistical significance, except for the relationship with the stir-frying of food (2.6 (1.3-5.0)).

### **Kreuzer (2000) 234 subjects: RR: 0.96 (negative)**

This substantial study from Germany included 234 female lung cancer patients who had never smoked matched against a control group of 535 healthy women. There was no association between lung cancer and secondhand smoke exposure from a spouse (0.96 (0.7-1.33)) or in childhood (0.78 (0.56-1.08)). Both results were negative and neither were statistically significant.

### **Sun (1996) 230 subjects: RR = 1.16 (null)**

This obscure Chinese study reported an association between secondhand smoke and lung cancer for those exposed in childhood and for those exposed both at home and at work but there was no association with smoking by the husband (1.16 (0.86-1.69)). As insignificant as that risk was, it fell still further if the wife was exposed for more than 35 years to 0.86 (0.45-1.65). It is not clear whether the paper was subject to the peer-review process.

### **Lee (2000) 228 subjects: RR = 2.2\* (significant - positive)**

This study of lung cancer patients from Taiwan is the only retrospective (case-

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control) study that fully supports the passive smoking theory. The authors apparently adjusted for all the important confounding factors and there was a linear dose-response relationship. The researchers asked their subjects whether or not their husbands smoked in their presence; those who answered yes were found to have a statistically significant relative risk for lung cancer of 2.2 (1.5-3.1).

### **Wu (1985) 220 subjects: RR = 1.2 (null)**

Anna Wu and her colleagues surveyed 220 female lung cancer patients in Los Angeles between 1981 and 1982. As they reported: “We did not observe any elevated risk associated with passive smoke exposure from either parents (RR=0.6; 95% CI= 0.2,1.7) [or] from spouse(s) (RR=1.2; 95% CI= 0.5,3.3).”

### **Brownson (1992) 218 subjects: 1.0 (exactly zero)**

As discussed in Chapter 7, the authors of this study drew conclusions that were at odds with the statistics they presented. According to Brownson, his study “suggests a small but consistent elevation in the risk of lung cancer in nonsmokers due to passive smoking” before adding: “The proliferation of federal, state, and local regulations that restrict smoking in public places and work sites are well founded.” These words formed the basis of the media reports that covered the study and few journalists would have delved further. Had they done so they would have found a relative risk for wives married to smokers of 1.0 (0.8-1.2). For squamous cell carcinoma - the type of lung cancer that was most strongly associated with cigarette smoking - the risk was just 0.5 (0.3-1.3) and when the study was extended to cover 431 female lung cancer patients who recalled exposure from all family members, the relative fell to 0.8 (0.6-1.1).

### **Hirayama (1984) 200 subjects: RR = 1.45\* (significant - positive)**

Although sometimes treated as a separate entity, Hirayama's 1984 study was an expanded version of his pioneering paper of 1981 (discussed in Chapter 6). Hirayama's methodology has much to commend it since the time-scale was lengthy and the number of participants fairly large. Furthermore, it was a cohort study and, as such, eliminated recall bias. The sample group of 142,857 women was assembled in 1965 and, by 1979, 427 had contracted lung cancer. 269 were married and, of these, 200 were nonsmokers. Of these, 163 had been married to a smoker or an ex-smoker and it was they who became the focus of Hirayama's research.

The Japanese paper was noteworthy for not only finding a statistically significant association between marriage to a smoker and lung cancer but for showing a dose-response relationship. When their husbands smoked less than a pack a day, the association was 1.45 (1.04-2.02) and when they smoked more than a pack a day, the association rose to 1.91 (1.34-2.71). Both these figures were lower when Hirayama published his final

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study in 1984 by which time he was now using the lowered confidence interval of 90% to make his estimates, effectively doubling his chances of finding a significant relationship. The overall relative risk was 1.45 (1.02-2.08).

### **Lam (1987) 199 subjects: RR = 1.65\* (significant - positive)**

This study from Hong Kong found a positive association of 1.65 (1.16-2.35) between secondhand smoke exposure and lung cancer, based on 199 nonsmoking wives against a control group of 335. As the EPA noted, upon reviewing the study in 1993, confounding factors may have been at work. Lam did not ask questions about diet, air pollution, cooking fumes, occupation, age, class or any other factors that might confound the data. Since the only attempt to tackle smoker misclassification was to ask subjects if they had a history of tobacco use, it is likely that some ex-smokers and smokers were mistakenly classified as nonsmokers. Additionally, there was an inverse dose-response relationship between the amount smoked by the spouse and risk. According to Lam, the women married to the lightest smokers were at greatest risk of lung cancer.

### **Janerich (1990) 191 subjects: RR = 0.93 (negative)**

No fewer than nine authors put their name to this report which strived to draw some evidence against secondhand smoke after Luis Varela had studied the same data and found none (see Chapter 7). Varela had found no association between secondhand smoke and lung cancer and it took a good deal of statistical conjuring for Janerich to suggest otherwise. The most newsworthy finding was a relative risk of 2.07 (1.16-3.68) for the 52 subjects who recalled at least 25 'smoker-years' of exposure to passive smoke in childhood ('smoker years' were calculated by multiplying the years of exposure by the number of smokers in the home) but there was no association with those who had less than 25 'smoker years'. This finding contradicted the weight of evidence that showed childhood exposure to smoke to have no effect on lung cancer risk in later life.

More pertinently, there was a nonsignificant negative risk ratio for the lung cancer patients who had been married to smokers: RR = 0.93 (0.55-1.57).

### **Wang T. (1996) 181 subjects: RR = 1.11 (null)**

Another Chinese study and another study full of null associations. A husband's smoking resulted in a risk ratio of 1.11 (0.65-1.88), exposure in childhood showed 0.91 (0.55-1.49) and workplace exposure showed 0.89 (0.45-1.77). Once again, lung cancer was significantly associated with exposure to cooking oil vapours (3.79 (2.29-6.77)).

### **McGhee (2005) 179 subjects: RR = 1.38 (null)**

This cohort study was published in the *BMJ* in the run up to England's smoking ban and was brief and to the point. It showed a nonsignificant relative risk of 1.38

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(0.94-2.04) with lung cancer. Only subjects aged 60 or over were included and there was no adjustment for diet, occupation or air pollution.

### **Enstrom & Kabat (2003) 177 subjects: RR = 0.97 (negative)**

Of the 118,094 Californians who enrolled in the ACS's Cancer Prevention Study in 1959, 25,942 were nonsmoking women married to a smoker and it was they who became the focus of Enstrom and Kabat's prospective study (discussed in Chapter 10). Monitored through to 1998, the authors found no statistical link between passive smoke and lung cancer and the relative risk of 0.97 (0.90-1.05) strongly supported the null hypothesis.

### **Neuberger (2006) 160 subjects: RR = 0.37\* (significant - negative)**

160 women with lung cancer from the state of Iowa answered questions about their exposure to various suspected carcinogens, as did 542 controls. As expected, asbestos, urban living and a personal history of lung disease were found to be statistically significant factors but passive exposure to tobacco smoke was not. Only 37% of the cases recalled exposure in adulthood, against 62% of the healthy controls, and this led to a statistically significant *negative* relationship between passive smoking and lung cancer of 0.37 (0.26-0.54).

### **Garfinkel (1981) 153 subjects: RR = 1.17 (null)**

Garfinkel's paper was the first in a series of failed attempts to use the vast American Cancer Society national database to produce evidence for the passive smoking theory (see Enstrom & Kabat and Cardenas). Started by Cuyler Hammond in 1959, this survey was carried out by ACS volunteers across the United States and included 375,000 nonsmoking women. By 1981, 203 of them had contracted lung cancer. 153 had been married, 88 of them to smokers.

Comparing these rates to those expected in wives married to nonsmokers, Garfinkel found no statistically significant relationship between secondhand smoke exposure and any cancer except, perversely, that women married to smokers were less likely to suffer from cancer of the uterus.

The wives were grouped between those whose husbands smoked less than a pack and more than a pack of cigarettes a day. The former had an RR of 1.27 (0.88-1.89), the latter - those more heavily exposed to smoke - had an RR of just 1.10 (0.77-1.61). When the figures were adjusted for confounding factors, the former rose to 1.37 and the latter fell to 1.04. The overall risk ratio was 1.17 (0.85-1.61). None of these figures came close to statistical significance and Garfinkel did not pretend otherwise. His own assessment was that women married to smokers had "very little, if any, increased risk of lung cancer" and that "even if the estimates from this analysis are in error and there was a slight

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increase in lung cancer trends in nonsmokers, it did not appear to be an important problem.”

### **Cardenas et al. (1997) 150 subjects: RR = 1.2 (null)**

The American Cancer Society's million person study also provided the data for this study. When Garfinkel used the database in 1981 (above), he found no association between secondhand smoke and lung cancer, nor did Enstrom & Kabat (2003). The Cardenas study had a slightly smaller sample group of lung cancer patients but it also supported the null hypothesis, albeit with a slightly different RR of 1.2 (0.8-1.6) for women. For men, the RR was 1.0, although this was raised to 1.1 after the authors made adjustments. As with Garfinkel's paper, there was an implausible reverse dose-response relationship between years spent living with a smoker and lung cancer risk. And again, none of the RRs were statistically significant.

### **Lan (1993) 139 subjects: RR = 1.15 (null)**

Another Chinese study and another strong correlation between indoor air pollution and lung cancer. Lung cancer was strongly associated with coal burning with a risk ratio of 7.53 (3.31-17.17) but, alas, there was no association with passive smoking. The crude data showed a risk of 0.84 but after (unexplained) adjustments were made, this rose to 1.15 (0.43-21.82), which, as the very broad confidence interval suggested, was anything but statistically significant.

### **Garfinkel (1985) 134 subjects: RR = 1.31 (null)**

As in his earlier prospective study, Garfinkel's 1985 retrospective study found no significant association between secondhand smoke and lung cancer. The relative risk here was 1.31 (0.94-1.83), although there was a stronger risk ratio for those who were most heavily exposed. Exposure during childhood also supported the null hypothesis with 0.91 (0.74-1.12). Perhaps the most intriguing aspect of the paper was the insight it gave into the misclassification of nonsmokers. Of the 283 female, nonsmoking lung cancer patients enrolled, 113 were later revealed to be smokers and 36 turned out not to have lung cancer.

### **Sobue (1990) 120 subjects: RR = 0.94 (negative)**

This Japanese study surveyed 120 nonsmoking, female lung cancer patients and found no association between marriage to a smoker and lung cancer: RR = 0.94 (0.62-1.40). The only statistically significant associations that came to light in this report were a protective effect if the subject's father smoked - 0.60 (0.4-0.91) - and a link between lung cancer and cooking with wood and straw - 1.90 (1.09-3.30)

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### **Kurahashi (2007) 109 subjects: RR = 1.34 (null)**

Another Japanese study and another statistically insignificant positive association: 1.34(0.81-2.21). Co-authors of the study included Liu, Sobue and Inoue, all of whom had previously conducted passive smoking studies with mixed results. 80% of the cases had adenocarcinoma.

### **Stockwell (1992) 108 subjects: RR = 1.6 (null)**

This American study retrospectively interviewed 210 female lung cancer patients, of whom 108 were married. Results were adjusted for age, race and education but not for diet and occupation. The relative risk for spousal exposure was a nonsignificant 1.6 (0.8-3.0). There was no association with exposure in social settings.

### **Chang-Yeung (2003) 106 subjects: RR = 1.01 (null)**

This study examined various possible carcinogens but found few relationships, particularly with regard to passive smoking. Funded by Hong Kong's Anti-Cancer Society, the authors made much of an apparent association between exposure to secondhand smoke and lung cancer in men but the statistical significance disappeared once the figures were adjusted for confounders. No amount of cherry-picking could mask the fact that the relative risk for wives married to smokers was zero: 1.01 (0.47-2.18).

### **Ko (1997) 105 subjects: RR = 1.3 (null)**

This was another study designed to identify why the lung cancer rate was so high amongst nonsmoking women in Asia. 105 female patients were retrospectively surveyed and significant associations were found with low vegetable consumption, frying food and kitchen ventilation but not with secondhand smoke. Relative risk for women married to smokers was a nonsignificant 1.3 (0.7-2.5) and childhood exposure gave a nonsignificant 0.8 (0.4-1.6).

### **Dalager (1986) 99 subjects: RR = 0.86 (negative)**

This paper from the US - co-authored by Elizabeth Fontham - drew together three studies from Texas, Louisiana and New Jersey. The overall lung cancer risk for nonsmokers living with smokers was exactly in line with the null hypothesis with an RR of 1.0 (0.64-1.56). When the figure was adjusted for gender, race, age, asbestos exposure, diet and employment, the RR fell to 0.86 (0.52-1.34). This was based on male and female subjects combined since the authors did not split the findings by gender. In their own assessment of risk to women, the authors excluded the Texas study (which was the largest) and since the New Jersey study only included men, this limited them to the 28 women from Louisiana. Here the authors reported nonsignificant risks of 1.96 (0.82-4.7) for women and 0.93 (0.3-2.9) for men.

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### **Kabat (1984) 97 subjects: RR = 0.79 (negative)**

In their study of 749 females with lung cancer, Geoffrey Kabat and Ernst Wynder identified 97 cases who were nonsmokers and found no association between secondhand smoke exposure and their disease either in the home or in the workplace. The authors did not assign relative risks to their statistics but when the EPA assessed the study in 1992, they found the association to be 0.79 (0.25-2.45) ie. a nonsignificant protective effect. The only significant positive association that emerged from the paper was a link with those who “worked in a textile-related job” (3.1 (1.11-8.64)).

### **Kalandidi (1990) 91 subjects: RR = 2.1\* (significant - positive)**

Along with the Fontham study, Kalandidi's paper provides perhaps the best evidence of secondhand smoke being a carcinogen to nonsmokers. 91 nonsmoking women with lung cancer were surveyed and a positive association of 2.1 (1.1-4.1) was found. This association did not vary significantly whether adenocarcinoma or other forms of lung cancer were under scrutiny.

### **Shimizu (1988) 90 subjects: RR = 1.10 (null)**

The authors of this Japanese study were quick to emphasise that their statistics showed a four-fold increase in lung cancer risk for those exposed to tobacco smoke by their mother. Closer examination showed that this finding was based on the experiences of just three individuals. More reliable was their finding that “no association was observed between the risk of lung cancer and smoking of husbands or passive smoke exposure at work.”

### **Nyberg (1998) 89 subjects: RR = 0.94 (negative)**

Another null study with a slender tendency towards the negative. Using data from a Swedish sample group, a relative risk of 0.94 (0.53-1.67) was found for wives and risks of 0.76 and 0.29 for those exposed to smoke by their father and mother respectively.

### **Koo (1987) 86 subjects: RR = 1.64 (null)**

This retrospective study of 86 female, never-smoking lung cancer cases found a statistically nonsignificant relative risk from a husband's smoking of 1.64 (0.87-3.09). Adjustments were made for age, education and (for some reason) number of children, but more important confounding factors such as diet, pollution and cooking methods went unmentioned. The subjects who had the heaviest smoking husbands, and those who recalled the most frequent exposure, had the lowest lung cancer risks and, as the author reported: “The lack of a dose-response pattern, and an almost consistent drop in the RR at the highest doses of exposure would seem to lend little, or only weak support for the passive smoking linkage with lung cancer.”

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### **Chan (1982) 84 subjects: RR = 0.75 (negative)**

This retrospective study from Hong Kong focused on 189 female lung cancer cases, of whom 84 were nonsmokers. Of those who were married, 40% recalled being exposed to secondhand smoke. 60% did not. This left a relative risk of 0.75, thereby implying that exposure to tobacco smoke reduced the chances of suffering lung cancer in later life by 25%.

### **Zatloukal (2003) 84 subjects: RR = 0.43\* (significant - negative)**

This retrospective study from the Czech Republic had a sample group of 366 female lung cancer cases, of whom 84 were life-long nonsmokers. Various possible causes of lung cancer were investigated, and statistically significant associations were found with high red meat consumption, low fish consumption and a family history of lung disease.

Of the 84 subjects, only 7 had been exposed to secondhand smoke in adulthood (defined as 3 or more hours a day). Zatloukal broke down the results by adenocarcinoma (0.36 (0.11-1.22)) and other types of lung cancer (0.66 (0.22-1.96)), thereby disguising the fact that when the figures were combined to show all lung cancer cases, the negative relationship with secondhand smoke becomes statistically significant: (0.43 (0.19-0.95)).

### **Wang, S (1996) Up to 83 subjects: RR = 2.5\* (significant - positive)**

The tabulation of results makes it hard to ascertain how many female, nonsmoking lung cancer patients were married in this study but it is evident that there were no more than 83. The source of exposure is also vague and, critically, the sample group appears to include smokers. The authors gave a risk ratio of 2.5 (1.3-5.1) for women, falling to 1.02 for men. As with Sun (1996), the standard of the peer review process - if any - is unclear.

### **Du (1996) 75 subjects: RRs = 1.09 (null)**

This Chinese study found statistically significant associations between lung cancer and both indoor air pollution and cooking fumes, but once again found no such link with secondhand smoke exposure. A sample group of 75 nonsmoking women was compared to two control groups. Against one group there was a nonsignificant RR of 1.19 (0.66-2.16); against the other the RR was precisely 1.0 - a valuable reminder that picking the right control group is as important as selecting the case group. There was no dose-relationship, indeed the RR for those who lived with a smoker for more than 30 years was below 1.0.

### **Akiba (1986) 72 subjects: RR = 1.5 (null)**

The focus of this Japanese study was 72 female nonsmoking wives of smokers. All the women were, in a unique twist, atom bomb survivors from Hiroshima and Nagasaki.

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Although various factors were considered, only those women who actively smoked were found to be at greater risk of lung cancer than those who were unexposed. The lone exception was women from blue collar families who lived with a heavy smoker, but only 6 of the subjects fell into this category.

While these findings were not statistically significant, the authors emphasised that there was a dose-response relationship between the amount smoked by the husbands and the lung cancer risk of the wives. This was true. What was also true was that the risk declined as the years of exposure rose. If the husband smoked for 1-19 years, the risk to the wife was 2.1 (0.7-2.1) but if he smoked for more than 40 years the risk fell dramatically, to 1.3 (0.7-2.3).

### **Zhou (2000) 72 subjects: RR = 0.94 (negative)**

Another Chinese study, this time surveying 72 nonsmoking wives married to smoking husbands with a negative, statistically nonsignificant relative risk of 0.94 (0.41-1.97). Women exposed in childhood also showed an inverse risk of 0.89.

### **Kabat (1995) 69 subjects: RR = 1.08 (null)**

The second in Geoffrey Kabat's trio of studies retrospectively surveyed 69 female nonsmokers with lung cancer and found no association with secondhand smoke exposure.

### **Vineis (2005) 69 subjects: RR = 0.82 (negative)**

A strange one, this. No fewer than 26 people put their name to it and as a prospective study of 123,479 individuals (from 10 European countries), it stood every chance of making a valuable contribution. It spanned seven years and asked questions about diet, physical activity, age and various other confounding factors before falling at the final hurdle by including over 20,000 ex-smokers. Almost every other reputable study had made sure only never-smokers were included and with good reason: some of these women had been smoking for forty years or more before they quit and for many the damage had been done. It was well-known that ex-smokers had a greater risk of lung cancer than never-smokers.

Sure enough, the study showed that ex-smokers died of the disease at a greater rate than never-smokers and yet the authors appeared genuinely bewildered. "The fact that the association is stronger in former smokers is difficult to understand," they wrote, before hazarding the guess that former smokers "are more susceptible to low levels of environmental tobacco smoke."

Ultimately, it had little effect on the outcome of the study. Of the 69 women who contracted lung cancer, only 20 had been exposed to smoke in the home, leaving a risk ratio of 0.82 (0.37-1.82). More surprising was a statistically significant association

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between childhood exposure and lung cancer; an association that appeared to rise in relation to the level of tobacco exposure. As the authors admitted, this was the first time such an association had emerged from an epidemiological study. After 25 years of searching, it was unlikely to be representative of a genuine phenomenon.

### **Pershagen (1987) 67 subjects: RR = 1.2 (null)**

This cohort study enrolled 27,409 nonsmoking women in Sweden in the early 1960s. When they were followed up in 1984, just 77 of them had contracted lung cancer. There was no significant association with smoke exposure and the risk ratio was 1.2 (0.7-2.1). The authors made much of a stronger association with squamous and small cell carcinoma where the relative risk was 3.3 (1.1-11.4). By contrast, there was a negative RR of 0.8 (0.4-1.5) for all other types of cancer. At the time of publication, this appeared to be a suggestive finding since squamous and small cell carcinomas were strongly associated with smoking and Dalager had recently found a similar association, albeit weaker. If the passive smoking theory were true, it seemed logical that smokers and passive smokers would suffer from the same types of cancer. But subsequent studies (notably Fontham's) have not replicated these findings and adenocarcinoma has been found to be the prevalent form of the disease in nonsmokers.

### **Brownson (1987) 66 subjects: RR = 1.68 (null)**

Ross Brownson's first study into passive smoking retrospectively surveyed female, nonsmoking lung cancer patients in Colorado. He found no association between any form of secondhand smoke exposure and lung cancer. The study was confined to adenocarcinoma, a form of lung cancer least associated with smoking but more closely linked with women, and claimed a statistically nonsignificant relative risk of 1.68 (0.39-2.97) for those exposed to more than three hours of smoke per day (those with less than 3 hours exposure were taken as the controls. Only ten women fell into the case group, however, hence the very wide confidence interval. Other than active smoking, the only statistically significant association with lung cancer was found to be a low income.

### **Wang F. (1994) 55 subjects: RR = 0.78 (negative)**

This Chinese study of 114 women with lung cancer included 55 life-long nonsmokers. Unfortunately, smokers were not excluded from the sample group and so the findings should be treated with caution. The author found a negative association with secondhand smoke in adulthood and a positive association with exposure in childhood, with the latter achieving statistical significance. Since smokers were not excluded, the latter result is most likely due to the known tendency of the offspring of smokers to become smokers themselves.

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### **Joekel (1998) Fewer than 55 subjects: RR = 1.12 (null)**

This German study had a sample group of 55 men and women and found no association between passive smoke and lung cancer: 1.12 (0.54-2.32). Results were not broken down by gender.

### **Geng (1988) 54 subjects: RR = 2.16\* (significant - positive)**

In 1988, a book published to commemorate the recent 'Smoking and Health' conference provided a dumping ground for a number of studies and theses that did not make it into the mainstream medical journals and which, therefore, did not have to undergo the normal peer-review process. Inoue's study (see below) and Guan-Yi Geng's typewritten paper were two of them. The latter's presentation was amateurish and its origins uncertain but it is included here because (like Wang, 1996) it is a rare example of a study finding a statistically significant association between secondhand smoke and lung cancer.

The data came from Tianjin, a city which, according to the authors, had the highest rate of female smoking prevalence in China and - unsurprisingly - also the highest incidence of female lung cancer. Not enough data was presented to allow much analysis although the author concluded that nonsmoking women married to smokers had a lung cancer risk of 2.16 (1.03-4.53). This narrowly achieved statistical significance and, as with the Hirayama study, a dose-response relationship was evident. Also in line with the Hirayama study, the apparent risk was peculiarly high. The 2.16 risk ratio given here for nonsmokers living with smokers was very close to the 2.61 (1.4-4.6) risk found for (female) smokers living with nonsmokers.

### **Liu (1991) 54 subjects: RR = 0.77 (negative)**

The authors of this Chinese study found that those with a family history of lung disease, and those who cooked with coal, had a significantly increased lung cancer risk but there was no association with passive smoking. The 54 female lung cancer patients had not been exposed to secondhand smoke any more than the 202 controls and their relative risk was 0.77 (0.30-1.96).

### **Jee (1999) 51 subjects: RR = 1.9 (null)**

The relative risk found in this Korean cohort study was not statistically significant but it came close with an RR of 1.9 (1.0-3.5). If this seemed suggestive, the inverse dose-response relationship suggested otherwise. According to this paper, those who lived with a heavy smoker were substantially less likely to suffer lung cancer as those married to a light smoker (2.0 and 1.5 respectively).

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### **Shen (1998) 50 subjects: RR = 0.75 (negative)**

In keeping with most other studies, this retrospective Chinese study found lung cancer to be strongly associated with a family history of lung disease (4.36) and with exposure to cooking fumes (2.45) but not with passive smoke exposure.

### **Rapiti (1999) 41 subjects: 1.2 (null)**

This study from India threw up a remarkably high relative risk for exposure to ETS in childhood of 12.0 (4.3-32.0), something that has not been supported by any other study. For women who had smoking husbands, however, there was no statistically significant relationship with lung cancer incidence (RR = 1.2 (0.5-2.9)) and there was a negative dose-response relationship; the risk ratio fell below 1.0 for the women who had been most heavily exposed for the longest time.

### **Trichopoulos (1981) 40 subjects: RR = 2.4\* (significant - positive)**

This paper (discussed in Chapter 6), surveyed 40 nonsmoking women with lung cancer in an Athens hospital between 1978 and 1980. Trichopoulos found that wives married to husbands who smoked 20 cigarettes or fewer each day had an elevated lung cancer risk of 2.4. This rose to 3.4 for those who had husbands who smoked more than 20 cigarettes a day. Since the study also showed that female smokers had an RR of 2.9, this meant that being married to a heavy smoker was more dangerous than being a heavy smoker. This was a far-fetched idea that Trichopoulos admitted sounded “strange.” Nonetheless, the findings were statistically significant and there was a dose-response relationship.

### **Liu (1993) 38 subjects: 1.72 (null)**

Unlike most other Chinese studies, Liu did not find a clear association between cooking fumes or a family history of lung disease with lung cancer. The association with secondhand smoke was unclear. The author split the subjects between those whose husbands smoked less than a pack a day and more than a pack a day. Taken together, there was no significant relationship (1.72 (0.77-7.3)) but there was some evidence of a dose-response relationship; those whose husbands smoked less than a pack had a risk ratio of 0.7 (0.23-2.2) and those living with heavier smokers had a risk ratio of 2.9 (1.2-7.3).

### **Buffler (1984) 33 subjects: RR = 0.78 (negative)**

Conducted on lung cancer patients in Texas, this study found no association between secondhand smoke and lung cancer. The relative risk for the 33 nonsmoking women in the study was 0.78 (0.34-1.81); a result that was both nonsignificant and negative. For men, the findings were even less compelling, with an RR of 0.52 (0.15-1.74).

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### **Lee (1986) 32 subjects: RR = 1.0 (exactly zero)**

This English study found a relative risk of 1.0 (0.37-2.71) for 32 nonsmoking wives married to smokers compared to 66 controls. As a small study, it was unexceptional in its format and methodology apart from being funded by the Tobacco Research Council which, in turn, was funded by the tobacco industry.

### **Inoue (1988) 29 subjects: 2.25 (null)**

Co-authored by Takeshi Hirayama, this retrospective study focused on 18 married women with lung cancer and claimed an RR of 2.25 (CI 90%: 0.91-7.10). There were a number of peculiarities, not least the way in which the authors doubled their chances of achieving statistical significance by using the lowered 90% confidence interval. They excluded women from the study if their husband smoked fewer than 5 cigarettes a day on the basis that these men never smoked in the house. This assumption was based on a separate questionnaire of 133 men which showed that those smoking 1 to 3 cigarettes a day never smoked at home. It was odd that the researchers went to the lengths of surveying a group of men who were not involved in the study when they could have simply asked the subjects if their husband smoked at home.

The numbers were very small and although it is slightly unclear from the paper, it seems that the 18 exposed cases were compared with just 2 unexposed cases, thereby making it impossible to draw any conclusions. The numbers were so small that statistical significance eluded the authors despite lowering the confidence interval, and they were not even able to show a strong link between active smoking and lung cancer. Stranger still, their RR for active smoking (1.66 (0.73-3.76)) was lower than that shown for passive smoking. As with Trichopoulos (above), it is hard to take any study seriously when it suggests that being a smoker is a healthier option than marrying one.

These shortcomings, and the probable lack of a peer-review (see Geng above), casts serious doubts over the value of this paper, as does the obvious bias of the authors. Their conclusion was that “smoking at home should (sic) therefore be restricted strictly in order (sic) to prevent nonsmoking family members from suffering unnecessarily from lung cancer and other selected diseases.”

### **Kubik (2001) 24 subjects: RR = 1.17 (null)**

In this paper from the Czech Republic, smokers were found to be ten times more likely to develop lung cancer, in line with countless previous studies, but of the 24 female, nonsmoking lung cancer cases involved, only 2 had been around a smoker for 3 or more hours a day. The raw data showed a relative risk of 0.91 but, as often happened with these studies, the authors' unexplained adjustments increased the figure slightly, to 1.17, with a very wide confidence interval of 0.2-5.6. For those exposed to tobacco smoke in childhood, the risk was smaller still: 0.85 (0.5-1.5).

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### **Nishino (2001) 24 subjects: RR = 1.8 (null)**

This Japanese study examined the possible effect of passive smoking on a huge variety of cancers. After adjustments, the RR for lung cancer was a nonsignificant 1.8 (0.67-4.6). The wide confidence interval was a reflection of the small number of participants; 11 of the women had a husband who smoked, 13 did not, and clearly it was impossible to make any firm conclusions from such a statistic. The limitations of the study are underlined when one considers that the only statistically significant finding was that exposure to secondhand smoke *reduced* breast cancer risk by 42%; RR 0.58 (0.34-0.99)

### **Johnson (2001) 23 subject: RR = 1.20 (null)**

This small, retrospective Canadian study found a slim majority of controls reporting exposure to tobacco smoke in adulthood and a slim majority of the lung cancer cases reporting the same, leaving an insignificant risk ratio of 1.20 (0.5-3.0).

### **Correa (1983) 22 subjects: RR = 2.07 (null)**

This retrospective study identified 22 married, nonsmoking women with lung cancer, of whom 14 recalled exposure to passive smoke. The numbers were small and the authors (including Elizabeth Fontham, in her first foray into this area of research) found a nonsignificant RR of 2.07 (0.81-5.25).

The authors found an association between a parent smoking and the development of lung cancer later in life but this finding was substantially undermined when it became clear that this only applied to those who went on to become smokers themselves and, even then, only for males with a mother who smoked. Women were not affected at all by childhood exposure and, oddly, having a father who smoked had no effect on either gender. The authors admitted that this was “puzzling.”

### **Humble (1987) 20 subjects: RR = 1.8 (null)**

The data for this study came from New Mexico and the small numbers involved meant the margin for error was wide. The authors employed a 90% confidence interval, rather than the more conventional 95%, but the findings still fell well short of achieving statistical significance; RR 1.8 (0.6-5.4).

### **Hole (1989) 9 subjects: RR = 1.37 (null)**

This masterpiece of extrapolation is discussed in Chapter 7. As the result of a single additional lung cancer case, the risk from passive smoking rose from zero to 1.37 (0.29-6.61). The extraordinarily broad confidence interval is a fair indicator of how unreliable this finding is.

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When the EPA assessed this study, its members increased the supposed risk by arbitrarily excluding three women who had lung cancer but who had not yet died of the disease. It must be assumed that two of these women had been married to nonsmokers, since their exclusion led to the EPA's RR rising to 1.99, with an even wider confidence interval of 0.24-16.72. The exclusion of these lung cancer cases is a further example of the EPA's manipulation of the data to strengthen the case against secondhand smoke.