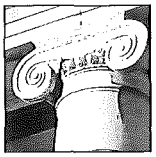

Lung Cancer without Asbestosis: Isn't It Actually the Smoking That Did It?

A Commentary by Mark G. Zellmer of Husch Blackwell LLP
Author bio on page 12

A pathologic finding of asbestosis is — almost without contradiction in the medical and scientific literature — clear evidence that asbestos, at least, contributed to the development of lung cancer.[1] Many medical experts regard the presence of asbestosis as a necessary prerequisite to any finding that asbestos caused any lung cancer.[2] In order to opine that asbestos caused lung cancer, other medical experts will look for evidence of sufficient exposure to cause asbestosis, even if asbestosis is not evident from radiology or pathology.[3] Still, other experts take a position contrary to both of these views. Those who testify for plaintiffs, as well as those invested in the "ban asbestos" movement, have engaged in a long effort to show that lesser exposures than needed to cause asbestosis will nonetheless cause or contribute to cause lung cancer.

The basis of such opinions should be the subject of careful scrutiny. Whether under *Frye* or *Daubert*, without appropriate basis, such opinions should not be admissible evidence.[4]

Too little attention has been paid to how plaintiffs' experts control for the increased risk of lung cancer from cigarette smoking. Without appropriate controls for all aspects of cigarette smoking which affect the risk of lung cancer, the increased risk from asbestos exposure is actually an increased risk from cigarette smoking. Any inquiry into this matter involves several questions: what factors affect the risk of lung cancer from smoking for which a researcher must account when trying to determine the risk from asbestos exposure; what is the methodology of studies and its reliability; what are the findings on asbestos, smoking and the risk of lung cancer; and which of these factors have not been taken into account and what is the effect on the studies.

Lung Cancer Without Asbestosis — What Factors That Influence Smoking Habits Must Be Controlled?

Admittedly, the accurate calculation of the risk of lung cancer from cigarette smoking is complicated; however, any study attempting to determine the risk of lung cancer attributable to asbestos exposure must control appropriately for various characteristics among the control group that would increase the risk of lung cancer. To analyze it otherwise will confound the conclusions. In other words, the study will erroneously conclude that asbestos exposure created the excess risk, when in fact it was cigarette smoking that created the excess risk.

Gender

The gender differences in smoking habits between men and women are well known. Greater percentages of men smoke more frequently and more heavily than women.[5] Blue-collar occupations are male-dominated. Calculation of lung cancer risk by comparison of the blue-collar workers to the general population, without adjustment for gender, will lead to erroneous findings of an excess risk of lung cancer that are actually due to the greater smoking habits of males. On the other hand, as gender differences are well understood and male-only control groups are widely available for comparison, gender differences are rather easily controlled in most studies.

Age

As expected, age is associated with cigarette smoking habits. The likelihood that someone will have ever smoked increases with age:

Age (Years)	RR (95% CI) *Likelihood of ever smoking*
18-24	0.53
25-34	0.75
35-44	0.74
45-54	0.89
55-64	1.00

The likelihood that someone is a current smoker also increases with age until the 55-64 age range, presumably, at least in part, because sickness intervenes in the upper age group, leading those older individuals to cease smoking:

Age (Years)	Percent Current Smokers *(95 Percent CI)*
18-24	14.0
25-34	22.7
35-44	25.0
45-54	24.5
55-64	13.7[6]

Smoking Among Blue Collar Occupations, Particularly Construction Workers

Any study that involves smoking as a possible confounder and uses the general population as a control group in comparison to blue-collar workers fails to consider that blue-collar workers "smoke more heavily, initiate smoking at a younger age, and are less likely to quit."[7] However, even distinguishing blue-collar workers from other classifications of workers is not enough. Certain blue-collar occupations, particularly construction workers, are more likely to be ever smokers, current daily smokers and persistent smokers. Construction workers have the highest rate of current smoking, 1.5 times greater than the rate reported for all smokers.[8] *See Chart 1 Below.*

Canadian statistics provide further and similar insights. Among occupational classifications of daily smoking rates of Canadian workers, the highest rate is the male-dominated blue-collar occupations.[10] Among blue-collar occupations, workers in the outdoor occupations classified as construction/transportation/mining have the highest daily smoking rate and have the highest proportion of heavy smokers, by a relatively substantial margin, over other classifications of blue-collar occupations.[11] *See Chart 2 Below.*

Chart 1

Occupation	Percent Ever Smoker	Percent Current Daily Smoker	Percent Persistent Smoker
Construction/Extraction	48.4	25.6	53.3
Installation/Maintenance/Repair	47.9	24.6	51.4
Production	44.3	22.7	51.2
Transportation/Material Moving	45.4	23.1	50.8
All Occupations	37.0	15.8	42.7[9]

Chart 2

Occupation	Percent Daily Smoker *(males)*	Percent Heavy Smoker *(25+ cigarettes/day)*
Blue-Collar Indoor	34	40
Manufacturing	33	40
Materials Handling/Crafts	39	40
Blue-Collar Outdoor	40	45
Forestry/Farming/Fishing	30	34
Construction/Transportation/Mining	43	49
All Occupations	29	35[12]

Finally, construction workers studied in 1977-1978 who are older and have worked longer in the profession, i.e. 20+ years, are more likely to be heavy smokers (greater than 1 pack per day) than younger workers in the same occupation for a lesser time, i.e. less than 5 and 5-19 years in the profession.[13] Specifically, the percent of construction workers who smoke more than one pack per day are as follows:[14]

Percent of construction workers who smoke more than one pack per day

<5 Years	5-19 Years	20+ Years
30	26	37

Comparing a specific subset of blue-collars workers to the general population, or even to a general group of blue-collar workers, simply cannot adjust appropriately for the risk of smoking since certain blue-collar workers start smoking earlier, smoke longer and more heavily than either the general population or even blue-collar workers in general.

The risk of lung cancer from smoking based upon how heavily a group may smoke can be estimated. Reflecting that doubling the amount of smoking doubles the risk of lung cancer, the lifetime risk of lung cancer among moderate smokers is approximately 10 percent, while the risk among heavy smokers is 20 percent.[15]

Effect of Education

The level of education is strongly associated with smoking habits. Since blue-collar workers tend to have less formal education, there is an obvious overlap in the differences in smoking habits correlated to differences in occupation and differences in attainment of formal education.[16]

Level of education still needs to be considered when comparing smoking habits of a control group to the subjects under study. Simply stated, people with only some high school education when compared to people with 16 or more years of education (essentially an undergraduate college degree) are 4.2 times more likely to be current smokers, 2.6 times more likely to be ever smokers, 1.6 times more likely to be heavy smokers and 0.3 times less likely to cease smoking.[18] Calculating the risk of lung cancer by comparison of two groups with differing educational attainment will provide misleading results about what may be causing differences in the risk of lung cancer.

Cancer Prevention Study-II (CPS-II): Selection Bias

The CPS-II "is a volunteer-organized and volunteer-selected population" in which the "subjects are friends, neighbors, and relatives of CPS-II volunteers and, therefore, reflect the social and ethnic backgrounds of people who volunteer their services to the American Cancer Society."[19] There are all sorts of socio-economic and demographic factors that differentiate the CPS-II participants from the general population.[20] Some of the distinctions between the CPS-II group and the general populations or specific occupational groups include the following:[21]

- Those in CPS-II have a higher average level of educational achievement;
- Those in CPS-II are older adults with a median age of 57; and
- Those in CPS-II are known to be healthier and experience significantly lower deaths than the general population.

In CPS-II, more than 36 percent of men and 25 percent of women were college graduates.[22] Failure to adjust for the occupations and the overall health of the control group compared to the subjects under study will mean that any finding of increased risk of lung cancer will be due to the lesser smoking rates among the control group.

Duration of Cigarette Smoking

The risk of lung cancer increases much more rapidly from an increase in the duration of smoking than from an increase in the number of cigarettes smoked per day.[23] In fact, the risk of lung cancer increases by the fourth or fifth power from increased duration of smoking, while risk increases only to the second power from an increase in the number of cigarettes smoked per day.[24] Hence, because the risk of lung cancer increases "so rapidly" with the duration of cigarette smoking, researchers must control for this factor.[25] To reach appropriate and reliable conclusions, researchers cannot just

Occupation	Number of People	Percent of High School Education or Higher
Farming/Fishing/Forestry	639	55.4
Construction/Extraction	6,670	74.8
Installation/Maintenance/Repair	4,268	89.7
Production	8,224	77.5
Transportation/Material Moving	6,593	78.7[17]

control whether subjects are non-smokers, present, or former smokers. It is also not sufficient simply to control for the number of cigarettes smoked per day.[26]

Statistics from the Institute of Medicine indicate the following averages:[27]

- Average age at which people become daily smokers: 17.7 years
- The percentage of persons of all daily smokers who did so before age 18: 71 percent

This occurs even though forty-four states and the District of Columbia have prohibited the sale of cigarettes to minors since 1920.[28] The effect of duration of cigarette smoking on the risk of lung cancer is so profound that the inclusion of just a few more long term smokers in the subject group will falsely amplify the apparent effect of asbestos on the risk of lung cancer, especially if the number of subjects in the study is small.[29]

Studies on Lung Cancer, Asbestosis and Cumulative Exposures to Asbestos

Any number of studies has attempted to show that asbestos-related lung cancer will occur without the occurrence of asbestosis or without sufficient exposure to cause asbestosis. An inquiry into these studies raises questions about methodology, particularly whether the risk of lung cancer from cigarette smoking confounded the results of the studies.

Gustavsson Study

In 2002, Gustavsson, et al. studied 1,039 subjects with lung cancer compared with 2,359 referents, all from Stockholm County, Sweden.[30] The researchers used postal questionnaires and follow-up interviews to determine smoking habits and asbestos exposure.[31] The authors classified as never smokers, former smokers, and current smokers in categories of 1-10, 11-20 and 20+ cigarettes per day. A "senior" industrial hygienist "blinded" to the study and using a survey of Swedish work places from 1969-1973 classified asbestos exposure as 0, >0-0.99, 1.0-2.49 and >2.5 f/cc-years.[32] Originally, the authors had categories for cigarette smoking of 30 or more cigarettes per day and >4.5 f/cc-years; however, the numbers of subjects in these categories, as well as the categories of 20-30 cigarettes per day and 2.5-4.5 f/cc-years, were so small that the authors combined these two sets of categories.[33] They also controlled for age, year of inclusion, radon, nitrogen dioxide, diesel exhaust and combustion products.[34] *The results are below.*

It is important to note that the relative risk for asbestos exposure without cigarette smoking in the categories of >0-0.99 and 1.0-2.49 f/cc-years is not statistically significant.[35] Other 95 percent confidence intervals are very wide.[36] Lung cancer is a dose-response disease both relating to asbestos and smoking. With one minor exception, the risks calculated by Gustavsson increased with greater doses of cigarette smoking; however, in five instances charted by Gustavsson, the risk declined with increasing doses of asbestos exposure. For a known dose-response disease, lung cancer from asbestos exposure, relative risks that do not increase with increasing dose should be viewed with substantial skepticism.

Furthermore, compared to other studies, the risk numbers in Gustavsson are extraordinarily high. In Chen's study, the risk of lung cancer among workers with asbestosis was associated with a relative risk of 7.44. When adjusted for the risk of cigarette smoking, the relative risk fell to 3.15.[37] These are workers with asbestosis, workers for which everyone would attribute their lung cancer, at least in part, to their asbestos exposure. Yet, the risk numbers of Gustavsson even for those without asbestosis were many multiples higher. Even the Helsinki criteria argued that the risk of lung cancer doubled at 25 f/cc-years.[38] Gustavsson found risk numbers that were much higher than two times at exposures substantially below 25 f/cc-years. "[I]nvestigators have viewed large and highly significant effects with excitement, as signs of important discoveries. Too large and too highly significant effects may actually be more likely . . . signs of large bias. . ."[39]

Asbestos Exposure *(fiber years)*	**Never Smokers**		**Current Smokers** (no. of cigarettes smoked/day)					
			1-10		11-20		>20	
	RR	*95% CI †*	*RR*	*95% CI*	*RR*	*95% CI*	*RR*	*95% CI*
Unexposed	**1**		**10.5**	**6.7, 16.6**	**23.3**	**15.2, 35.8**	**45.4**	**28.6, 71.9**
0> - 0.99	**1.8**	**0.6, 5.5**	**18.1**	**8.2, 40.4**	**17.0**	**8.8, 32.7**	**38.5**	**17.7, 83.4**
1 - 2.49	**2.7**	**0.7, 9.5**	**12.1**	**5.1, 29.3**	**29.8**	**15.1, 58.6**	**36.8**	**11.9, 113.7**
≥ 2.5	**10.2**	**2.5, 41.2**	**13.56**	**4.6, 40.0**	**86.2**	**28.8, 258.2**	**80.6**	**20.2, 322.0**

Anyone would be forgiven for asking the obvious question why the relative risks determined by Gustavsson were inordinately high. The control group was comprised of people selected from computerized registers of the population of Stockholm County, Sweden. The authors "frequency matched" the control group to the subjects on the basis of five-year age groups and year of inclusion in the study. The control group was in separated into two parts: the "population referents" selected without restriction and the "mortality-matched referents" selected based on vital status on December 31, 1990 and being alive at the beginning of each inclusion year.

Gustavsson, et al. provided no indication that the control groups were selected and matched with any concern for education, occupation, or smoking habits. As Swedes in Stockholm should not be different from Americans and Canadians, those in the subject group under study and exposed to asbestos are likely to be concentrated in blue-collar occupations and have less formal education and, consistent with such demographics, smoke more heavily, start smoking earlier and smoke longer during their lives. Failure to account for the lesser smoking habits of the Stockholm control group when compared to the subjects, could have created the appearance, but not the fact, of a higher excess risk from asbestos exposure.

The problem is even greater considering the small numbers in the various categories, creating the likelihood that a major difference in the smoking habits of a few people would make major changes in the relative risk numbers.

Markowitz Study

Markowitz, et al. tracked 2,377 North American insulators for lung cancer from 1981 through 2003.[40] Between 1981 and 1983, the researchers administered chest radiographs to all participants read by B-readers. They also took smoking histories as well as occupational histories, focusing on time of participants spent in the insulator trade. The authors did not estimate cumulative dose, noting that the exposure of all insulators in the study was relatively similar in type and dose.[41] *The results are above.*

For all groups, the average duration of work in the insulator trade ranged from 32 to 34 years.[42]

The study by Markowitz, et al. is perhaps most interesting because there is some misunderstanding within portions of the defense bar about the limits of what the authors concluded. They made no suggestion that high cumulative doses of asbestos exposure are unnecessary to cause an asbestos-related lung cancer, i.e. that low dose exposures will cause lung cancer. They understood that the insulators in their study were highly exposed workers with an average duration in the trade of 32 to 34 years.[43] In fact, no one would argue that these workers have not been exposed at levels that are sufficient to cause asbestosis. The authors merely attempt to prove that such high doses of exposure will cause or materially contribute to cause lung cancer, even without radiographic evidence of asbestosis.

Variable *All Insulators (n= 2,377)*						**Poisson Regression**	
	No. of People	*No. of Lung Cancer Deaths*	*No. of Person -Years*	*No. Lung Cancer Deaths /Person -Years x 10*	*Rate Ratio*	*Age-Adjusted Rate Ratio*	*Age-Adjusted Rate Ratio 95% CI*
Insulators without Asbestosis, nonsmokers	**253**	**7**	**5,205**	**13.45**	**3.36**	**3.55**	**1.66-7.58**
Insulators without Asbestosis, smokers	**665**	**62**	**12,057**	**51.42**	**12.85**	**14.44**	**10.74-19.43**

The basis for this conclusion in the Markowitz study centered on two groups of insulators without radiographic signs of asbestosis: first, a group 253 insulators who did not smoke and experienced seven deaths from lung cancer (age-adjusted risk ratio of 3.55, compared to a ratio of 1.0 for the control group); and, second, a group of 665 insulators who smoked and experienced 62 deaths from lung cancer (age-adjusted risk ratio of 14.44, compared to a ratio of 10.31 for the control group). Since conclusions about the first group are based on seven lung cancer deaths, changes in the absolute number of those in this group with findings of asbestosis would have a major effect on the conclusions.

What is the reliability of the finding that these workers do not have asbestosis? The authors admitted one limitation in the study: that the subjects were evaluated for asbestosis only once between 1981 and 1983. The authors suggested this limitation

"Those who testify for plaintiffs, as well as those invested in the 'ban asbestos' movement, have engaged in a long effort to show that lesser exposures than needed to cause asbestosis will nonetheless cause or contribute to cause lung cancer. The basis of such opinions should be the subject of careful scrutiny. Whether under Frye or Daubert, without appropriate basis, such opinions should not be admissible evidence.

was not significant to the findings because the work force under study had already been in the trade for an average of 32 to 34 years. This explanation falls short. Citing an "average" means that some workers are in the trade longer, but some are in the trade for a lesser time. Although latency for asbestosis can be as short as 15 years, latency can be 40 years or longer.[44] Reflecting this latency, 61.4 percent of the insulators in the Markowitz study had asbestosis while, in other studies, 94.2 percent of insulators had asbestosis after 40 years from onset of exposure.[45]

The authors admitted another possible limitation: that asbestosis was missed on the X-rays. Indeed, chest radiographs miss 10-18 percent of biopsy-proven asbestosis.[46] Furthermore, poor quality of the film, mistakes by X-ray readers, and other factors ultimately reduce to 40 percent the positive predictive power of X-ray films for asbestosis.[47] CT scans, not used in the Markowitz study, are much more accurate.[48] The authors suggested that this limitation is not meaningful, as so few in the study group died from asbestosis. Similarly, this explanation also misses the mark. Of 2,377 insulators with asbestosis, 1,125 were Category 1, which means they are most unlikely to die of the disease. Even among the heavily-exposed insulation trade, the percentage of insulators who die of asbestosis is in the low, single-digit percentages.[49]

Markowitz, et al. used a control group of approximately 54,000 people from CPS-II. Despite the use of blue-collar workers as a control group, the authors did not document fully appropriate adjustments for differences between the controls and the subjects under study.[50]

- Although the article mentioned that data was available on the age of initiation of smoking, the authors mention no use of this data, other than possibly a calculation of pack-years; however, the concept of pack-years includes but is not the same as duration of smoking.[51] If the CPS-II group initiates smoking later than the insulators, any apparent increased risk of lung cancer among the insulators is actually due to the difference in the age of initiation of the smoking habit.

- There is no apparent adjustment for the healthier status of people in CPS-II compared to the general population. Although it is not certain, if healthier status means less lung cancer, the apparent increased risk of lung cancer among the subject group may actually come from the better health of the CPS-II group, not asbestos exposure.

Those in the CPS-II, on average, have higher educational achievement than the general population and, hence, have more moderate smoking habits. In addition, those in the CPS-II blue-collar cohort, on average, will smoke less heavily than those in the construction trades, including insulators. Markowitz, et al. tracked pack-years for both the insulators and the CPS-II group. To the extent that the authors controlled for heavier smoking in the insulator cohort, differences in education and blue-collar occupation should not have an effect the risk calculations. If not controlled, all or part of the increased risk is not from asbestos exposure, but rather from heavier smoking.[52]

Finally, Markowitz, et al. made a relatively common error overestimating the positive effects of cessation of smoking. They note, for example, that lung cancer risk among former smoking insulators (5.8) was similar to the risk of never-smoking insulators (5.3).[53] These numbers do not reflect a decline in the risk of lung cancer following the cessation of smoking but, rather, reflect the reverse effect of the duration of cigarette smoking. Smokers who ceased smoking 30 years ago simply did not smoke long enough to accumulate a substantially higher risk than non-smokers.[54] A person's risk of lung cancer after cessation of smoking will not decline but, on an age-adjusted basis, remains constant. In other words, smoking will increase the risk of lung cancer, but cessation of smoking cuts off further increases in risk (other than increases due to age or other factors).

That the risk of lung cancer declines after cessation of smoking is a myth based on a simple mathematical error. The risk of lung cancer increases with age, even among people who have never smoked. When researchers attempt to calculate risk after cessation of smoking in comparison to the non-smoking population, they divide the former smokers' risk by the increasing risk

of lung cancer in the non-smoking population. When they divide a constant risk by an increasing risk, the result is an apparent but erroneous decline in risk.[55] Markowitz et al appear to fall prey to this simple error, stating "lung cancer death rate ratios [are calculated] using the CPS-II non-smokers as a reference. The lung cancer mortality rate ratio dropped steeply. . . "[56]

Finkelstein Study

Finkelstein tracked the condition of workers in a cement plant in Canada owned and operated by Johns Manville.[57] These production employees worked at the plant starting before 1960, worked for at least 9 years and had at least 12 months of asbestos exposure.[58] The 30 workers with radiographic evidence of asbestosis had average cumulative exposure of 137 f/cc-years, while those 117 workers without radiographic evidence of asbestosis had average exposure of 101 f/cc-years.[59]

The findings regarding lung cancer were as follows:

Subjects with Lung Cancer	Asbestosis	Expected Cases of Lung Cancer	SMR	95% Confidence Interval
17	No	4.43	3.84	2.24 - 6.14
4	Yes	0.58	6.84	1.88 - 18[60]

Finkelstein concluded that exposure to asbestos increased the risk of lung cancer "at doses below which fibrosis becomes apparent on plain film X-rays."[61]

The numbers in this study are small; if only a few subjects contracted lung cancer because they smoked more or smoked longer, the calculations of risk from asbestos exposure would decline radically.

The concluding statement that the risk of lung cancer from asbestos exposure increased "at doses below which fibrosis becomes apparent on plain film X-rays" is curious, if not misleading. If the author is trying to opine that asbestos-related lung cancer will occur without asbestosis, his conclusion may not have a sound scientific basis but, at least, his conclusion would be clear. On the other hand, his concluding statement referred to "doses." If he is claiming that asbestos exposure will cause lung cancer at doses lower than what will cause asbestosis, his study proved nothing of the sort. Since the average doses of the factory workers in the study exceeded 101 f/cc-years, these doses were well in excess of the doses that have been generally regarded as sufficient to cause asbestosis.[62]

Additionally, the efforts of Finkelstein are subject to the same problem as Markowitz. Cement workers who died of lung cancer allegedly without asbestosis could have developed asbestosis between the time of their last radiography and the time that they contracted lung cancer.[63]

Finkelstein used Canadian men in the general population as a control group. He concluded that the "difference between the proportion of ever-smokers in the cohort and proportion of ever-smokers in the general population [was] quite small . . . [meaning that] 'smoking alone' could not explain the elevated lung cancer risk found among the cement workers." *Finkelstein at 1067-1068.* This analysis failed to reflect fully the differences between the smoking habits of the asbestos worker cohort and the general population:

- The blue-collar cohorts smoke more heavily than the general population.
- The blue-collar cohorts initiate smoking earlier than the general population.

Failure to control for these factors means that the excess risk identified by Finkelstein comes not from the asbestos exposure, but rather from the more serious smoking habits of his asbestos-exposed cohort.

If we assume that, based upon the Gaudette research, blue-collar factory workers are 14.29 percent more likely to smoke heavily than all occupations (35 percent for all occupations versus 40 percent for factory workers, so 5 percent /35 percent =14.29 percent), and that, based on the Peto research, heavy smokers are 10 percent more likely to contract lung cancer, then for the 117 workers without asbestosis, they should be expected to have an additional 1.67 cases of lung cancer based on heavier smoking habits (117 x 14.29 percent x 10 percent = 1.67). Additionally, if, on average blue-collar workers start smoking earlier, increasing their risk of lung cancer by 6.378 percent , another 7.46 cases of lung cancer would be expected among the 117 workers without asbestosis (117 x 6.378 percent = 7.46). This is a total of 13.56 expected cases out of 117 workers (7.46 + 1.67 + 4.43 = 13.56). The relative risk calculated by Finkelstein is too high, it should be 1.25 (17/13.56=1.25). The corrected relative risk is 32.6 percent of the relative risk calculated by Finkelstein. With the lower end of the 95 percent confidence interval at 2.24, as calculated by Finkelstein, the corrected lower end of that confidence interval is 0.728 (2.24 x 32.6 percent = 0.728) and, hence, no longer statistically significant.

Hein/Dement Study

Hein, et al., studied a cohort of 3,022 white and non-white male and white female production workers in a South Carolina textile mill that used mainly chrysotile, but on occasion used some crocidolite.[64] The authors utilized work histories with a job exposure matrix to estimate the cumulative exposure to asbestos. They tracked the workers for lung cancer as well as other diseases and conditions. The results were numerous and included the following:

The calculations of relative risk were intended, in part, to account for smoking because the authors thought that smoking habits should not vary between those exposed and those not exposed to asbestos.[66] This is not necessarily true. Since males are more likely to smoke than females, and smoking increases with age, if the non-exposed cohort was younger or had more females or both, the relative risk would reflect falsely higher numbers for the danger of lung cancer from asbestos exposure.

lung conditions among the cohort, including asbestosis. They present their calculations of SMR and relative risk for asbestosis commingled with asthma (one case), COPD (29 cases) and pneumoconiosis and respiratory diseases other than asbestosis (41 cases).[68] Hence, it is not possible to determine from this study at what level of cumulative exposure asbestosis was occurring. In the end, Hein, et al., did not relate any of these non-malignant conditions to the occurrence of lung cancer.

Group	Lag (years)	Cumulative Exposure (fibre-years/ml)*						
			<1.5	1.5 - <5	5 - <15	15 - <60	60 - <120	≥120
Overall	**10**	**O/E**	**34/22.1**	**33/25.3**	**34/21.7**	**35/18.8**	**37/9.2**	**25/4.7**
		SMR	**1.54** (1.07-2.15)	**1.3** (0.90-1.83)	**1.57** (1.08-2.19)	**1.86** (1.30-2.59)	**4.02** (2.83-5.53)	**5.36** (3.47-7.92)
		RR	**1**	**1.00** (0.62-1.62)	**1.37** (.85-2.21)	**1.61** (1.00-2.59)	**3.20** (1.99-5.14)	**4.91** (2.88-8.35)
Long-Term	**0**	**O/E**	**2/0.56**	**7/5.2**	**26/15.9**	**31/16.7**	**32/9.4**	**33/5.8**
		SMR	**3.56** (0.43-12.9)	**1.34** (0.54-2.75)	**1.64** (1.07-2.40)	**1.85** (1.26-2.63)	**3.41** (2.33-4.81)	**5.68** (3.91-7.98)
		RR	**1****	**1****	**1.14** (0.53-2.44)	**1.39** (0.66-2.95)	**2.39** (1.13-5.06)	**4.62** (2.17-9.84)

*1** reference groups with less than 5 f/cc-years exposure.*

The 10 lag years meant that the 10 years of exposure prior to contracting lung cancer was excluded from the cumulative dose. The reference to "long term" referred to workers who had one or more years of exposures.

In distinction from the Markowitz article, Hein, et al. made no effort to determine whether asbestosis was a necessary prerequisite to the causation of lung cancer by asbestos exposure. They calculated the statistical mortality ratios (SMR) using NIOSH life tables. The relative risk numbers were calculated using workers from the same cohort who were either unexposed or exposed below 5.0 f/cc-years. The smoking information on the cohort was limited.[65]

Without any control for the confounding of cigarette smoking, the SMRs will improperly reflect higher risk numbers for asbestos. The authors note that the prevalence of cigarette smoking among white males in the cohort is similar to the general population.[67] The authors did not consider that a blue-collar factory population will also smoke more heavily and will initiate smoking earlier than the general population. Whether the calculation of SMRs or relative risk, the findings are not uniformly statistically significant until the range of exposure reaches 60-120 f/cc-years. Although the exposures are chrysotile, if long fibers were used, the exposures are at a level that may be expected to cause asbestosis. Hein, et al. noted and analyzed the occurrence of non-malignant

A 2016 study from Pierce, et al. determined that the no-effect level below which chrysotile is most unlikely to cause lung cancer is 89 to 168 f/cc-years.[69] Adjusted for cigarette smoking, the SMRs from Hein, et al. would almost certainly be comparable to this no effect level.

Conclusion

The lesson is simple: defense counsel should question a plaintiff's expert about which studies support his contention that the asbestos exposure at issue caused plaintiff's disease. Those studies should be subject to scrutiny regarding control for cigarette smoking and any other weaknesses with methodology. Plaintiff's expert should be questioned regarding any such issues with

the studies upon which he relies. The deposition testimony can then be used as the basis to strike the expert's opinions on causation of plaintiff's lung cancer.

Footnotes

[1] Mollo, F. et al. "The Attribution of Lung Cancers to Asbestos Exposure: A Pathologic Study of 924 Unselected Cases." *American Journal of Clinical Pathology.* Vol. 117 (2012) at 90.

[2] Cagle, P. "Criteria for Attributing Lung Cancer to Asbestos Exposure." *American Journal of Clinical Pathology.* Vol. 117 (2002) at 9, 14.

[3] Roggli, V.L. in *Pathology of Asbestos-Associated Disease.* (Springer, New York: 2014) at 160.

[4] *McClain v. Metabolife International,* 401 F.3d 1233, 1245 (11th Cir. 2005) ("[an expert's] conclusions [must be] supported by good grounds for each step in the scientific analysis...any step that renders the analysis unreliable under the Daubert factors renders the expert's testimony inadmissible."); *General Motors Corp. v. Grenier,* 981 A.2d 524 (Del. 2009) ("an expert's methodology must not only be intrinsically reliable but also reliably applied to the facts of the specific case..."); Boudreaux v. Bollinger Shipyard, 2016 La. App. LEXIS 1229 (La. App. 4th Cir. 2016) (expert testimony with insufficient grounds to link man's asbestos exposure to his fatal lung cancer is properly excluded); *State Board of Registration for the Healing Arts v. McDonagh,* 123 S.W.3d 146, 156 (Mo. 2003)(rule for expert testimony "expressly requires a showing that the facts and data are of a type reasonably relied on by experts in the field in forming opinions or inferences upon the subject of the expert's testimony").

[5] Ham, D.C. et al. "Occupation and Workplace Policies Predict Smoking Behaviors: Analysis of National Data from the Current Population Survey." *Journal of Occupational and Environmental Medicine.* Vol. 53:11 (Nov 2011) at 1337 (Tables 1 and 2; 1997-2004 smoking rates); Gaudette, L.A. et al. "Which Workers Smoke?" *Health Reports.* Vol. 10:3 (1998) at 35 (for 1994-1995 smoking rates).

[6] Ham, D.C. et al. "Occupation and Workplace Policies Predict Smoking Behaviors: Analysis of National Data from the Current Population Survey." *Journal of Occupational and Environmental Medicine.* Vol. 53:11 (Nov 2011) at 1337 (Tables 1 and 2; 1997-2004 smoking rates).

[7] Ham, D.C. et al. "Occupation and Workplace Policies Predict Smoking Behaviors: Analysis of National Data from the Current Population Survey." *Journal of Occupational and Environmental Medicine.* Vol. 53:11 (Nov 2011) at 1337, 1338 (1997-2004 smoking rates).

[8] *Id.*

[9] *Id.* (Table 3)

[10] Gaudette, L.A. et al. "Which Workers Smoke?" *Health Reports.* Vol. 10:3 (1998) at 35, 38 (1994-1995 smoking rates).

[11] *Id.* at 39.

[12] *Id.* at 39, 42.

[13] Levin, L.I. et al. "Smoking Patterns by Occupation and Duration of Employment." *American Journal of Industrial Medicine.* Vol. 17 (1990) at 711, 718.

[14] *Id.*

[15] Peto, R. "Influence of Dose and Duration of Smoking on Lung Cancer Rates." Tobacco: A Major International Health Hazard. (*International Agency for Research on Cancer*: 1986) at 24, Table 1, footnote b.

[16] Stoops, N. et al. Educational Attainment in

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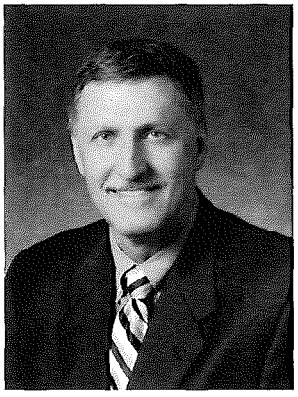

Zellmer speaks and writes extensively on products liability law and asbestos litigation. Such writing and presentation on asbestos litigation include subjects such as premises liability, application of statutes of limitations, medical causation, the litigation in historical context, and exclusivity of remedies under workers' compensation.

Zellmer defends toxic tort cases, particularly relating to asbestos, as well as other substances and chemicals. Zellmer also defends various defendants in product liability regarding vehicular and industrial equipment. Zellmer's trial practice is active in state and federal courts from coast to coast, and he has acted as national counsel in asbestos litigation.

"The lesson is simple: defense counsel should question a plaintiff's expert about which studies support his contention that the asbestos exposure at issue caused plaintiff's disease. Those studies should be subject to scrutiny regarding control for cigarette smoking and any other weaknesses with methodology. Plaintiff's expert should be questioned regarding any such issues with the studies upon which he relies.

the United States: 2003 Population Characteristics (June 2003) http://www.census.gov/prod/2004pubs/p20-550.pdf. Blue-collar workers have lower attainment of formal education than other workers. In fact construction workers have the second lowest formal educational attainment among all blue-collar workers.

[17] *Id.* Although people in farming, fishing, and forestry have the lowest percent of formal educational attainment, their relative numbers in the population, even compared to other blue-collar occupations, is low; hence, their impact on any risk assessment is also low.

[18] Zhu, B.P. et al. "The Relationship between Cigarette Smoking and Education Revisited: Implications for Categorizing Persons' Educational Status." *American Journal of Public Health.* Vol. 87:2 (February 1997) at 1583, 1586.

[19] Stellman, S.D. et al. "Smoking Habits of 800,000 American Men and Women in Relation to Their Occupations." *American Journal of Industrial Medicine.* Vol. 13 (1988) at 13, 14.

[20] Stellman, S.D. et al. "Smoking Habits and Tar Levels in a New American Cancer Society Prospective Study of 1.2 Million Men and Women." *Journal of the National Cancer Institute.* Vol. 76: 6 (June 1986) at 1057, 1061.

[21] Stellman (1988).

[22] Stellman (1986) at 1058). The CPS-II studies adjust for educational differences in various age groups but do not note such adjustment for occupational groups. Id. at 1061.

[23] Thun, M.J. et al. "Epidemiological Research at the American Cancer Society." *Cancer Epidemiology, Biomarkers and Prevention.* Vol. 9 (Sept 2000) at 861, 863.

[24] *Id.* at 863-864. For further information regarding how such statistics are determined, see Flanders, W.D. et al. "Lung Cancer Mortality in Relation to Age, Duration of Smoking, and Daily Cigarette Consumption." *Cancer Research.* Vol. 63:19 (October 2003) at 6556.

[25] Thun at 863.

[26] *Id.*

[27] Institute of Medicine. Growing Up Tobacco Free: Preventing Nicotine Addiction in Children and Youths. (*National Academies Press*, Washington, D.C.: 1994) at 1.

[28] Office of Inspector General. *Youth Access to Cigarettes.* (May, 1990) at 1.

[29] The significant effect from smoking earlier and smoking longer can be illustrated. Statistics regarding how early and how long different occupational groups smoke cigarettes are available, but not widely so. For example, one Italian study shows that the blue collar "workman" commenced smoking six-tenths of a year earlier than the average of the entire population under study. Verlato, G. et al. "Socioecomonic Inequalities in Smoking Habits Are Still Increasing in Italy." *BMC Public Health.* Vol. 14 (2014) at 879. If that is similar to the United States and Canada, the effect of that extra six-tenths of a year smoking can be calculated. Men, ages 70-79, who smoke seven years longer than men, ages 60-69, are at 2.16 times or 116 percent greater risk of lung cancer. Flanders, *supra.* at 6557, Table 1 (the men in the younger age group smoked approximately 15 percent more heavily than those in the older group). That is an increase of 16.57 percent for each additional year of smoking. The average likelihood that someone age 60-80 will contract lung cancer at some point in his or her lifetime is 5.94 percent. National Cancer Institute, Sureveillance, Epidemiolgy, End Results Program, SEER Cancer Statistics Review (1975-2012) https://seer.cancer.gov/archive/csr/19752012/browse_csr.php?sectionSEL=15&pageSEL=sect_15_table.19.html. Deducting the 5.94 percent from the expected increased risk per year leaves 10.63 percent increased risk. Starting smoking a mere six-tenths of a year earlier than others increases the expected lifetime risk of lung cancer by 6.378 percent.

[30] Gustavsson, P. et al. "Low-Dose Exposure to Asbestos and Lung Cancer: Dose-Response Relations and Interaction with Smoking in a Population-based Case-Referent Study in Stockholm, Sweden." *American Journal of Epidemiology.* Vol . 155:11 (2002) at 1018.

[31] *Id.* at 1019.

[32] *Id.* at 1018, 1020.

[33] *Id.* at 1018.

[34] *Id.* at 1020.

[35] *Id.*

[36] *Id.*

[37] Chen, M. et al. "Mesothelioma and Lung Cancer Mortality: A Historical Cohort Study among Asbestosis Workers in Hong Kong." *Lung Cancer.* Vol. 76 (2012) at 165, 167, 168.

[38] Wolff, H. et al. "Asbestos, Asbestosis, and Cancer, the Helsinki Criteria for Diagnosis and Attribution 2014: Recommendations." *Scandinavian Journal of Work, Environment and Health.* Vol. 41:1 (2015) at 5, 8.

[39] Ioannidis, J. "Why Most Published Research Findings Are False." *PLos Medicine.* Vol. 2, part 8: e124 (2005).

[40] Markowitz, S.B. et al, "Asbestos, Asbestosis, Lung Cancer and Smoking." *American Journal of Respiratory and Critical Care Medicine.* Vol. 188 (2013) at 90.

[41] *Id.* at 91.

[42] *Id.* at 91.

[43] *Id.*

[44] Selikoff, I.J. et al. "Latency of Asbestos Disease among Insulation Workers in the United States and Canada." *Cancer.* Vol. 46:12 (December 1980) at 2736, 2740.

[45] Selikoff, I. et al. "The Occurrence of Asbestosis among Insulation Workers in the United States." *Annals of the New York Academy of Sciences.* Vol. 132 (1965) at 139, 147.

[46] Roggli, V. et al. "Pathology of Asbestosis—An Update of the Diagnostic Criteria." *Archives of Pathology and Laboratory Medicine.* Vol. 134 (March 2010) at 462, 469.

[47] *Id.*

[48] *Id.*

[49] Selikoff, V. et al. "Asbestos-Associated Deaths among Insulation Workers in the United States and Canada, 1967-1987." *Annals of the New York Academy of Sciences.* Vol. 643 (1991) at 1, 7 (2.4 percent of 17,800 insulators died of asbestosis). For further analysis of the work by Markowitz et al, see Ross, R. Comment on "Asbestosis, Not Asbestos Exposure, Is the Primary Risk Factor for Lung Cancer." *American Journal of Respiratory and Critical Care Medicine.* Vol. 89:1 (January, 2014) at 114.

[50] Markowitz et al noted that the insulators are younger and smoke more frequently. *Id.* at 91.

[51] For example, person A smokes 2 pack per day for 15 years while person B smokes 1 pack per day for 30 years. While they both have a 30 pack-year smoking history, the lung cancer risk of person B is substantially higher than person A. According to Markowitz, et al. the American Cancer Society provided aggregate data for the CPS-II group on the number of people, person years, smoking status, pack-years, years since quitting and number of lung cancer deaths. Aggregate data on the length of cigarette smoking is not included. Id. at 91.

[52] On February 13, 2017, the author sent a letter to the American Cancer Society to obtain data in order to check the results of the Markowitz article. The letter stated, in part: "As I expressed to you when we first discussed this matter, my thought was that the carcinogenic effect of asbestos was overstated, and the carcinogenic effect of cigarette smoking was understated, in the article, Markowitz, S.B. et al, "Asbestos, Asbestosis, Lung Cancer and Smoking." *American Journal of Respiratory and Critical Care Medicine.* Vol. 188 (2013) at 90. To substantiate that determination, I made a request for access to the data on the blue collar subcohort of CPS-II that was used as the control group in the Markowitz article." On February 22, 2017, the American Cancer Society responded, declining to provide the requested data and suggesting that the author should file a request to undertake a collaborative project with the Society. The result of such an application is a foregone conclusion, as the Society only grants access to "well-qualified researchers" who have the "requisite knowledge, qualifications and experience to conduct the analysis." What is the likelihood that a lawyer will meet the Society's standards? In any event, should not data on which scientific conclusions are based be open to review to protect the integrity of the scientific conclusions and the scientific process?

[53] Markowitz at 92.

[54] Halpern, M.T. et al. "Patterns of Absolute Risk of Lung Cancer Mortality in Former Smokers." *Journal of the National Cancer Institute.* Vol. 85:6 (March 17, 1993) at 457, 461.

[55] Peto, J. "That Lung Cancer Incidence Falls in Ex-Smokers: Misconception 2." *British Journal of Cancer.* Vol. 104:3 (February, 2011) at 369.

[56] Markowitz at 92.

[57] Finkelstein, M.M. "Absence of Radiographic Asbestosis and the Risk of Lung Cancer Among Asbestos-Cement Workers: Extended Follow-Up of a Cohort." *American Journal of Industrial Medicine.* Vol. 53 (2010) at 1065, 1066.

[58] *Id.*

[59] *Id.* at 1067.

[60] *Id.* at 1068.

[61] *Id.* at 1069.

[62] Consensus Report. "Asbestos, Asbestosis, and Cancer: the Helsinki Criteria for Diagnosis and Attribution." *Scandinavian Journal of Work, Environment and Health.* Vol. 23 (1997) at 311, 314. For further commentary on this article, see Ross, R. "Regarding 'Absence of Radiographic Asbestosis and the Risk of Lung Cancer among Asbestos-Cement Workers: Extended Follow-up of a Cohort' by Murray Finkelstein." *American Journal of Industrial Medicine.* Vol. 54:6 (June, 2011) at 495.

[63] Id.

[64] Hein, M.J. et al. "Follow-up Study of Chrysotile Textile Workers: Cohort Mortality and Exposure Response." *Occupational and Environmental Medicine.* Vol. 64:9 (Sept 2007) at 616.

[65] *Id.* at 8.

[66] *Id.*

[67] *Id.*

[68] *Id.* at 7.

[69] Pierce, J. et al. "An Updated Evaluation of Reported No-Observed Effect Level for Chrysotile Asbestos for Lung Cancer and Mesothelioma." *Critical Reviews in Toxicology.* http://dx.doi.org/10.3109/10408444.2016.1150960 (2016) at 1. 14.