

Prevention of lung cancer through the use of knowledge on asbestos and other work-related causes – Norwegian experiences

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LANGÅRD S. Prevention of lung cancer through the use of knowledge on asbestos and other work-related causes — Norwegian experiences. *Scand J Work Environ Health* 1994;20 special issue: 100—7. This review attempts to estimate the contribution of different known work-related causes of lung cancer in the Norwegian male population in order to predict the potential of prevention of work-related cases. The presented estimates are based on data from epidemiologic studies made in Norway, but may be of significance for other countries with a similar work-force structure. Over the past decade asbestos-related lung cancer appears to have contributed about two-thirds of the lung cancers that have been related to work exposure in Norway, for example, possibly 125—175 of the 1100 cases that occurred among Norwegian men in 1987. The potential for prevention is, however, greater due to synergism. To a less extent compounds of nickel and chromium have also contributed, along with exposure to polycyclic aromatic hydrocarbons, radon daughters, seafaring work, and other, less significant specific and nonspecific determinants of lung cancer.

KEY TERMS — attributable causal fraction, chromates, nickel, polycyclic aromatic hydrocarbons, radon daughters, review, seamen, work area dust.

Lung cancer incidence is high in Norway, and it results in a large number of deaths among men and an increasing number of deaths among women (1). Of the new cases of cancer among men in Norway in 1987, lung cancer contributed 1100 (1). The total number of new cases among men increased from 189 in 1955 to 1106 in 1989 (1, 2).

All Nordic countries have developed comprehensive cancer registers that have served as sources of research on the causation of lung cancer from the 1960s on (3). Early research on cancer causes focused mainly on the problem of “one cause and one effect” (4). To some extent that was also the case for research on possible relationships between environmental exposure and lung cancer in Norway (5, 6). However, as elucidated by Selikoff and his colleagues (7, 8), among others, it became increasingly clear during the 1960s that lung cancer had a multicausal etiology. Norwegian scientists have also carried out research that has contributed to the knowledge on this multicausal etiology (9, 10), as well as to the use of such knowledge in primary and early secondary prevention (11, 12).

As for other types of tumors, there are only two main categories of lung cancer determinants (ie, genetic and environmental). Therefore all lung cancers

that would not occur in the complete absence of exposure to an environmental determinant are preventable (13, 14). Thus, to generate a firm basis for prevention, the primary purpose of studies on the causality of lung cancer is to reveal and subsequently quantify the causes of the disease (12, 15).

Because of the significantly increased incidence of lung cancer during the past five to six decades (1, 2, 16), this tumor site appears to be a suitable source for research on tumor causes, as well as for research on the versatility of prevention. Results derived from such research are significant when approaches for intervention are being chosen (11, 12).

Lost opportunities for prevention

Except for some authors (9, 10, 17—21), Norwegian scientists may not have contributed significantly enough to the understanding of the causes of asbestos-related lung cancers, nor to the development of versatile methods for preventing these cancers. However, one early contribution to the understanding of asbestos-related lung cancer and other lung diseases was made by Wolff (22) in 1940. This radiologist worked at a rural hospital in the industrialized village of Rjukan in the county of Telemark. He became interested in asbestos-related diseases after having observed some cases of asbestosis in the local population (23).

Scientists at universities paid hardly any attention to Wolff's comprehensive literature study (22), nor did governmental agencies of the Nordic countries.

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This lack of interest may have contributed to the virtual absence of preventive actions against asbestos-related diseases in the Nordic countries during the subsequent two decades. One can only guess what the preventive outcome might have been had the authorities initiated prevention, as indicated by Wolff (22).

As underlined by Enterline (24), it took many decades also in other western countries between the generation of knowledge on the preventability of asbestos-related lung cancer and the use of this knowledge in prevention.

Asbestos-related lung cancers quantitatively

New cases of lung cancer are often attributable in part to past occupational exposure to carcinogenic substances (9, 14). It has been shown that asbestos contributes a major portion to the occurrence of work-related lung cancers (8–10, 14). In Norway about 45% of all the men developing lung cancer have been occupationally exposed to asbestos some time during their career (9, 25–27). It has also been shown that about 20–25% of the cases of lung cancer among men in the 1980s could have been prevented had the patients never been occupationally exposed to asbestos (9, 26).

The potential of prevention in relation to a given cancer determinant is equal to the fraction of the total number of cases that would not have occurred in the complete absence of the determinant of concern. Thus the reduced exposure to asbestos fibers in Norway from the late 1970s on, combined with the general prohibition of its use during the 1980s, resulted in significantly reduced occupational exposure in the same period. Because of this reduction in exposure it has been predicted that the incidence of asbestos-related lung cancers among Norwegian men should start to level off by the late 1980s, followed by a decline in the absolute numbers of asbestos-related cases from 1992–1993 on (15).

Prevention of asbestos-related lung cancer

Data presented by Hammond et al (8) show that asbestos-exposed smokers who quit smoking can expect their risk of lung cancer to be reduced within 10–12 years to one-third of the risk among those who continue smoking. A study of my colleagues and I has also shown a reduction in lung cancer risk to one-third among asbestos-exposed subjects who had quit smoking more than 11 years ago, as compared with those who had not (21).

As of the mid-1980s it was suggested (15) that 125 to 175 yearly “weighted cases” of lung cancer among men, out of a total of about 1100 new cases among male Norwegians (1, 2), were attributable to asbes-

tos. By “attributable to” I mean an estimate of the total number of “weighted cases” as defined by the “sum” of the asbestos-related “causal weights” in each individual case in the national population. The “causal weight” is the fraction of the sum of all (known) weighed causes of a given case resulting from a given cancer determinant, after the effect of interaction has been partitioned between (two) determinants in proportion into the weighed contribution of each separate determinant, thus weight being added to each of the interacting determinants (15). This procedure implies, for asbestos and smoking combined, that the causal fraction that relates to the interaction between the two determinants is to be partitioned between asbestos and smoking in proportion to the causal weight of each of the two factors. The total number of weighted cases is thus generated by adding causal weight to all new cases to which asbestos exposure has contributed as a cancer determinant.

The documented multiplicative interaction between asbestos and smoking, as indicated by epidemiologic data (8), results in a significantly larger annual rate of lung cancer cases at the national level than those 125–175 weighted cases that are “caused” by exposure to asbestos. Among male Norwegians this situation implies that the number of preventable lung cancers in the hypothetical complete absence of asbestos exposure among the national male work force from the 1940s on would have been significantly higher in the 1980s and early 1990s than the corresponding number of weighted asbestos-related cases. As many as 300–350 annual cases of the 1100 (1, 2) could have been prevented (15, 25).

Consequently, when one projects two to three decades ahead, one must allow that the complete avoidance of asbestos exposure from the mid-1980s on may prevent 300–350 lung cancer cases annually from the year of about 2015 on, given that exposure to other lung cancer determinants is unchanged (11, 12, 15). Between 1992–1993 and 2015 the incidence of new asbestos-related lung cancer cases in Norway is likely to decline gradually to close to zero (15).

Given that these predictions are correct, complete avoidance of exposure to asbestos contributes a major portion to the total potential for preventing work-related lung cancer, for example, about 15 and 25% of all weighted and preventable cases, respectively, among men (table 1). For all lung cancer more than 90% of the new cases are likely to be preventable (9, 12, 15, 26).

This prediction implies that the potential of preventing asbestos-related lung cancer in Norway during the next two decades can be calculated in absolute figures as follows: If it is assumed that the hypothetical potential for prevention is 325 cases in 1995 (eg, the number of cases that would not have occurred had there been no asbestos exposure

Table 1. Estimated hypothetical potential of the prevention of work-related lung cancer in Norway as of 1994; the number of cases is given both as weighted cases and preventable fraction.

Determinant	Number of lung cancer cases	
	Weighted cases	Preventable fraction
Asbestos	125–175	300–350
Nickel compounds	7–8	—
Chromium compounds	3–4	—
Stainless steel welding	<2	—
Radon	3–5	—
Polycyclic aromatic hydrocarbons	4–6	—
Seafaring work	>25	—
Electromagnetic fields	1–2	—
Mineral oils	2–8	—
Man-made mineral fibers	1–2	—

during the four decades prior to 1985) and that this potential declines linearly to zero during the 20 years subsequent to 1995, the total potential for prevention is about 3250 cases for the entire period.

According to the data already presented (8, 21), smoking cessation among smokers with prior exposure to asbestos would reduce the incidence to one-third in 10–12 years. If that decline does not extend beyond 10–12 years and all current smokers among the 150 000 Norwegians significantly exposed to asbestos in previous decades (15) were to quit smoking instantaneously, the number of preventable cases would be about 1000 if the value is uncorrected for those who have already quit smoking. If each of these persons were to gain 15 years of life, the corresponding number of saved person-years would be about 15 000.

However, many (36%) of the smokers had already followed advice to quit smoking 10 or more years ago, while 45% of the subjects with prior exposure to asbestos were still smoking as of 1982–1983 and were thus eligible for smoking intervention (21). Hence the total preventable outcome, for example, the number of cases prevented among asbestos-exposed subjects, resulting from both previous and future smoking cessation is likely to be greater than 1000 cases. Conversely, resulting from the fact that “only” 45% still smoke, the outcome of future smoking cessation only is likely to be slightly less than 1000 cases.

The estimates of the contribution of each separate work-related lung cancer determinant as the causal weight and “preventable fraction,” respectively, also yields the corresponding hypothetical potential for prevention in relation to each cancer determinant.

Lung cancers resulting from other types of exposure

Norwegian authors have performed several studies that can be used to help estimate the preventability of work-related lung cancers and contribute knowledge on a number of determinants of cancer in the respiratory organs. Some of the results can also serve for quantitative estimates of the casual weight of each individual determinant, thus indicating the corresponding potential for future prevention. Some of these studies are presented in the following discussion.

Nickel and its compounds

The first Norwegian scientist to publish a study on the carcinogenic action of nickel was Løken (28). He reported three cases of lung cancer among nickel refinery workers. The late head of The Cancer Registry of Norway, Pedersen, and his co-workers (5) added significant information to the knowledge on causal relations between exposure to nickel compounds and the occurrence of cancer in respiratory organs. Their study reported 48 and 14 cases of cancer in the lungs and the nasal cavities, respectively, among nickel refinery workers.

In a follow-up, by Magnus et al (29), of a different fraction of the same nickel refinery cohort, the total numbers were 82 and 21 of bronchial and nasal sinus cancers, respectively, between 1953 and 1979. After the cases occurring in the subsequent 14 years are added, the total number of lung cancers in that cohort amounts to 150 among workers with more than three years of employment, accounting for 10 years of latency (Berge S, personal communication), for example, five to six cases annually, uncorrected for the effects of other types of exposure. The number of weighted cases would be lower. Kreyberg (30) added information on the possible effects of interaction between nickel exposure and smoking on the occurrence of lung cancer.

The nickel refinery of concern is the only plant in Norway manufacturing nickel metal. Other sources of nickel-related lung cancers could occur in other exposure situations, for example, from exposure to nickel fumes in nickel plating and from exposure fumes from welding on stainless steel. However, the total number of weighted nickel-related cases is unlikely to exceed seven or eight annually.

Chromium and its compounds

Ferrochromium and chromium pigment manufacturing, both involving possible exposure to hexavalent chromium, has taken place for many decades at four different locations in Norway. The workers at two of these manufacturing plants have been studied for the occurrence of lung cancer (6, 31–33).

The first study (6) was also the first epidemiologic study to indicate that hexavalent chromium pigments

are probable human carcinogens. At the same time another study (34) appeared that scrutinized the mutagenic effects of hexavalent chromium. After a period of 12–15 years, with limited research on the untoward effects of hexavalent chromium, these studies (6, 34) seemed to initiate a wave of research on the causality between exposure to hexavalent chromium compounds and cancer in humans and in experimental systems (35, 36).

The total number of lung cancers resulting from exposure to hexavalent chromium was about one case annually in these two cohorts (6, 31–33). The other two ferrochromium production units were small. There are also other sources of occupational exposure to hexavalent chromium in Norway, for example, chromium plating, but the total number of additional chromium-related cases annually may not exceed one or two weighted cases (table 1). Welding on stainless steel could be another source of exposure to both hexavalent chromium and nickel compounds.

Mild steel and stainless steel welding

In Norway the welding trade is large due to the number of welders in shipbuilding in previous years and the exploitation of crude oil and natural gas in the North Sea. Extrapolating from data presented by Stern (37) indicates that as many as 4000–5000 Norwegian welders could have welded stainless steel for more than five years during the past two to three decades, thus possibly contributing a small number of lung cancer cases.

The possible relationship between exposure to welding fumes generated from mild steel and, to some extent, stainless steel welding has been studied extensively during the past four decades (37, 38). However, as of today, no firm conclusion has been reached on the possible causal relationship between such exposure and lung cancer, nor as to the possible dose-response relationships between exposure to fumes and the presumed additional risk of lung cancer (38).

My colleagues and I have attempted to add to the information on this matter by carrying out a series of cohort studies among shipyard welders and workers. Two of the studies have been published (39, 40). One (39) revealed an excess incidence of lung cancer. There were 53 observed cases in the whole cohort versus 31.3 expected. Among the welders there was an excess of lung cancer (7 observed versus 3.2 expected). However, an inverse relationship between exposure time and response existed that could indicate that other lung cancer determinants contributed to the excess. Two malignant mesotheliomas had also occurred (0.7 expected), indicating that asbestos could have contributed to the excess of lung cancer. Smoking was also a possible confounder. This cohort also contributed to a study by the International Agency for Research on

Cancer (IARC) (41) that comprised more than 11 000 mild steel and stainless steel welders and gave evidence of a relationship between exposure to hexavalent chromium from stainless steel welding and an excess of lung cancer close to a relative risk of 1.7, as compared with the respective national figures expected for men.

The other study (40) scrutinized the incidence of cancers among 4571 shipyard workers and welders first employed at a shipyard between January 1940 and December 1979. There were 65 observed cases among all of the shipyard workers versus the 46.3 expected from the national rates for men. For the welders there was an elevated incidence of lung cancer (9 observed, 3.5 expected) that was related to the duration of employment and time since first employment. The results indicated a relationship between exposure to welding fumes and lung cancer risk. There were four pleural mesotheliomas versus 1.2 expected, all among nonwelders. Thus exposure to asbestos and possibly also smoking were possible confounders.

In a case-referent study (42) carried out among 176 incident lung cancer cases among men, 28 of the men had welded for more than three years [odds ratio (OR) 1.9]. Of them 16 had welded stainless steel for more than three years (OR 3.3). These results seemed to indicate a higher lung cancer risk among stainless steel welders than among mild steel welders. There are two more studies in progress that may add information to the issue — whether and to what extent nickel and hexavalent chromium in welding fumes may add to the risk of lung cancer among stainless steel welders (43).

These three studies (39, 40, 42) do not confirm that exposure to welding fumes add much to the occurrence of lung cancer in Norway, possibly less than five annual cases for mild steel and stainless steel welding combined. If the excess lung cancer presented in the IARC study (41) is considered as the true figure for stainless steel welders in Norway, the total number of new cases is not likely to exceed two weighted cases annually (table 1).

Polycyclic aromatic hydrocarbons in primary aluminum manufacturing

Norway is a major manufacturer of primary aluminum, and a series of studies among workers has taken place or is in progress (44, Rønneberg & Andersen, unpublished manuscript). One of these studies included 7410 male workers of the industry and yielded 57 lung cancer cases, which was 21 cases more than expected (44). It was, however, indicated that the cases could, to some extent, have resulted from exposure to asbestos, thus cases being added from exposure to asbestos rather than from exposure to polycyclic aromatic hydrocarbons (PAH). In another study (Rønneberg & Andersen, unpublished manuscript) no more than 15 of 39 lung cancer cases (39

observed, 24 expected) could have been attributed to PAH, and it is likely that asbestos had also contributed.

All in all, there seems to be only a few lung cancer cases attributable to PAH exposure, probably less than three cases annually. There are also other sources of PAH exposure, for example, coke ovens and foundries, but no studies have been made in these industries. Thus hardly more than four to six weighted cases seem to be attributable to PAH annually (table 1).

Lung cancer among seamen

Although Norway has had a great number of seamen over the past five to six decades, and many of them have been exposed in the engine room to, for example, asbestos, oil mist and fumes, organic solvents, and, to some extent, PAH, only a few studies have concerned the occurrence of lung cancer in this population (45, 46). The study that we carried out showed a very high excess of lung cancer — up to 47 times the expected figures — among those who smoked more than 25 cigarettes daily in 1963, as compared with those smoking less than 5 cigarettes daily (45). In terms of absolute risk (about 1.4 per 100 cases yearly), this is one of the highest lung cancer risks ever observed. Another study (46) on the occurrence of cancer among captains and mates on Norwegian tankers did not reveal any excess lung cancer.

Between 1955 and 1965 the number of Norwegian seamen averaged 50 000. In subsequent years the number declined to about 20 000 as of 1986, after which the total has risen to about 30 000. Hence, currently, there may be 120 000 or more current and previous seamen living in Norway, thus contributing a significant number of lung cancer cases. It is, however, possible that many of the persons with heavy exposure to lung cancer determinants are already deceased.

Given that the excess lung cancer in our study (45), which apparently was primarily related to smoking, was confounded by the work-related exposure factors already mentioned, the very high incidence of lung cancer could in part result from occupational exposure. The total number of cases in the whole cohort was 3 per 1000 cases annually during the 12 years of follow-up. If it is assumed that one-fourth of the cases was caused by occupational exposure, as much as 50 weighted cases in the whole population of seamen could result annually from work-related exposure (table 1). However, dust from asbestos insulation used to be one of the prime work-related exposure factors influencing lung cancer risk among engine room workers (45). Thus, for this population, it is difficult to estimate the number of weighted cases that are related to work at sea but are unrelated to asbestos exposure, possibly up to 25 cases. Additional studies are needed.

Electromagnetic fields

Norway is a major manufacturer of ferroalloys, primary aluminum, and magnesium, as well as a producer of hydroelectric power. Workers in these industries and those dealing with transporting electricity are potentially exposed to electromagnetic fields. As of today, none of the studies performed in these industries have confirmed that electromagnetic fields are major determinants of lung cancer (4, 29, 33, 47, 48). Welders are also exposed to electromagnetic fields (39, 40). Norwegian data cannot be used to quantify the number of weighted lung cancer cases caused by exposure to electromagnetic fields.

Radon daughters in mining and tunnel work

In Norway only two cohorts have been scrutinized for lung cancer among miners exposed to radon and its daughters (49–51). One of the studies (50) was nonpositive, while the other yielded a highly positive result for lung cancer (49, 51). Among the workers in the second study there was a clear dose-response relationship between the estimated dose and the incidence of lung cancer, which was 19 cases. This relation was more pronounced than that for smoking and lung cancer (51). In fact, the dose-response relationship indicated that radon daughters could be a stronger determinant of lung cancer than has been reported in any other study at comparable “doses” of radon daughters. This particular cohort of miners (51) contributes less than one case annually.

There are only a few current and previous miners in Norway, and mining appears not to have taken place in areas with high levels of radon daughters. Tunnel construction is a large trade, and the tunnels are constructed through all types of rock. Thus many tunnel workers may be exposed to low levels of radon daughters and may possibly contribute one to three weighted cases of lung cancer annually (table 1).

Vinyl chloride

Norwegian scientists have contributed to some extent to knowledge on the possible relationship between exposure to vinyl chloride and the occurrence of cancer (52, 53). However, the excess lung cancer in the study group of concern was marginal. In a large European study by Simonato et al (41) the causality between exposure to vinyl chloride and lung cancer was not confirmed. As of today, no firm evidence has been presented that exposure to vinyl chloride results in an excess risk of this cancer. The Norwegian study (52, 53) also revealed a possible link between exposure to vinyl chloride and the occurrence of melanomas of the skin. The IARC study (41) did not, however, confirm a such causal relationship.

Mineral oils

Only one study in a cohort of only a few hundred subjects has been performed in Norway on exposure

to mineral oils (54). There was a significant excess incidence of lung cancer, but the total number was only 10 (3.9 expected) in the critical group, equivalent to 7.2 cases per 1000 subjects annually. Thus the total number was far less than one case annually. Seamen, however, form another group that can be exposed to mineral oil aerosols, and this exposure could, to some extent, explain the very high lung cancer incidence for seamen (45). Thus the total number of new weighted cases to appear annually in the entire Norwegian population could amount to two to eight cases. However, some of these cases should be subtracted from those related to seafaring.

Man-made mineral fibers

Workers in Norwegian glass and mineral fiber manufacturing were included in the IARC study on fibers and contributed 16 lung cancer cases versus 10.3 expected (55, 56). The excess was confined to those workers for whom 20 years or more of latency was accounted for (11 observed, 5.5 expected). No studies have been carried out on the user side. Hence, no exact data can be reported on the total yearly cases of lung cancer related to exposure to man-made mineral fibers; however, the number is very likely less than two cases.

Dusty trades

"Polluted" air (dusty trades) is another exposure "factor" that could influence the risk of lung cancer among exposed persons. In a study (57) performed 15 years ago, there was an excess (odds ratio) of up to 4.2 and 4.6 for those with 15–24 years and >25 years of exposure, respectively, in polluted work. Whether that excess was related to dust and general air pollution as such, to specific carcinogens, or to reduced bronchial clearance resulting in enhanced retention of other carcinogens or other causes, the fact that "polluted" air enhances the development of lung cancer should be explored further. This exposure could possibly contribute to the occurrence of lung cancer cases.

Methods for preventing work-related lung cancer

By the mid-1980s a new interventive method was proposed that uses the cumulative individual risk of disease as a tool for preventing cancer and other environmentally induced diseases (14), and the method has been further refined (11, 12, 58). It is based on the fact that, at any given time in life, each subject carries an absolute risk of a given disease that is equivalent to the sum of all risk fractions that are induced by individual determinants of the given disease — for example, the absolute risks related to genetic determinants and the risks of disease resulting from exposure to disease determinants during the whole previous life (figure 1).

Interrupting any current exposure to environmental disease determinants helps avoid further risk increase, and the future risk of the disease can thus be significantly reduced as compared with the risk that the subject would have had 10 to 40 years later had he or she not interrupted the exposure. Continued exposure to determinants remaining in the body, for example, asbestos fibers in the lung, cannot be avoided.

The effect of interrupting exposure to determinants of lung cancer may be greater and also take place quicker in situations with synergetic interaction between determinants. The results from at least two studies (8, 21) seem to support the view that multiplicative interaction between asbestos and smoking enhances the speed of the risk reduction resulting from smoking cessation. In addition, risk reduction appears to be quicker than expected from the experienced "latency period" for lung cancer for the same combined exposure (4, 7). Given that these results are confirmed in intervention studies, one might expect an enhanced effect of intervention, in gained healthy years, than what would be expected on the basis of a presumed "effect time" if it were equivalent to the latency period for the same individual or combined disease determinant.

Stimulated by this observation, a proposal has been put forward for organizing such risk-based intervention in communities (58, 59).

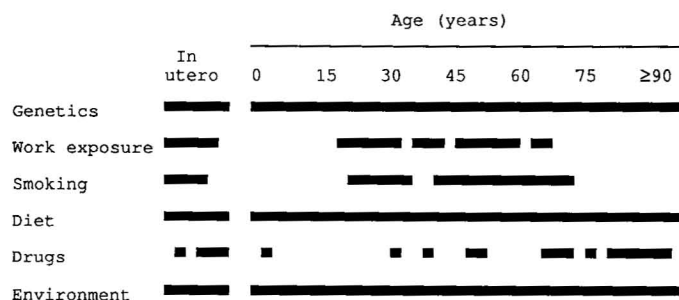


Figure 1. Periods in life when genetic determinants for lung cancer and potential exposure to lung cancer determinants exert their "action" on humans. Genetic determinants and dietary factors are always present, while other determinants act during various periods of life.

Need for future research on work-related cancer

The research in Norway on possible relationships between work-related exposure and lung cancer during the past two decades has concentrated on causality studies. This priority may have been well chosen. However, currently, there is a vast amount of available knowledge that is not being applied to the systematic prevention of lung cancer. Most of the major causes are already known for this disease. Therefore, at present, it seems appropriate to shift priorities from research on cancer causes to systematic preventive programs among high-risk groups for work-related lung cancers and the evaluation of their outcomes.

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