Occupational Cancer Research in the Nordic Countries

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Occupational cancer research in the Nordic countries benefits from certain structural advantages, including the existence of computerized population registries, national cancer registries with high-quality data on cancer incidence, and a personal identification number for each inhabitant. This article outlines the utilization of this research infrastructure in Denmark, Finland, Iceland, Norway, and Sweden, together with research examples from the different countries. Future research on occupational cancer in this region requires that national legislation on electronic handling of sensitive personal information should not be stricter than the European Union Directive on individual protection with regard to personal data. A personal identification number is essential both for keeping up the high quality of data of the registers and for the high quality of the process of linking the different data sources together. Although previous occupational research has focused on male workers, a broader approach is needed in the future, including a study of how cancer risk in women may be affected by occupational activity and the question of possible cancer risk in offspring of men and women exposed to workplace carcinogens. — *Environ Health Perspect* 107(Suppl 2):233–238 (1999). *http://ehpnet1.niehs.nih.gov/docs/1999/Suppl-2/233-238kjaerheim/abstract.html*

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Certain features of the Nordic countries are valuable for occupational cancer research in this region. These features include national cancer registries with high-quality outcome data, existence of a personal identification number for each individual, and population registries on electronic media with daily updates on births, deaths, immigration, and emigration. The national cancer registries were established in 1943 in Denmark, 1953 in Finland, Norway, and Iceland, and 1958 in Sweden. Personal identification numbers have been used since 1948 in Sweden, 1953 in Iceland, 1964 in Norway, 1967 in Finland, and 1968 in Denmark. All Nordic countries can thus deliver cancer incidence data collected from the whole populations. Studies on cancer etiology, therefore, usually have cancer incidence rather than mortality as outcome. Each country may contribute a small numeric basis for epidemiologic studies when rare cancer sites or rare exposures are investigated, but in such instances research cooperation between the countries has proved beneficial.

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Abbreviations used: EMF, electromagnetic fields; IARC, International Agency for Research on Cancer; SIR, standardized incidence ratio.

Linkages

By linkages between national cancer registries, population registries, and censuses, information on cancer incidence by occupation or industry has been obtained. Thus, occupational groups can be identified from national data rather than from individual employers. In Sweden, the Cancer–Environment Registry links the incidence of cancer with the 1960 census data on industry and occupation (*1*). In Norway, Finland, and Denmark, cancer incidence has generally been linked with the 1970 census, but double linkages with both the 1960 and 1970 censuses have also been done (*2–4*). In Denmark, additional linkage has also been done with the Registry of Supplementary Pension Funds, giving the whole occupational history of each individual (*5,6*). These data sources have been extensively used in studies of occupation and cancer, both at the national (*7–9*) and the Nordic levels, in the general population (*10*), and for specific occupations (*11–15*). However, one major limitation of the data is that generally the occupational information is limited to one or two points in time. All Nordic countries have undergone a marked industrialization during the 20th century, with a concomitant reduction of the number of persons employed in farming, fishing, and forestry. More recent trends show an increase in the number of persons employed in the tertiary sector, including a large proportion of women (*16*). With such major changes in occupational structure during the last decades, it is clear that the occupational activity in 1970 and/or 1960 for some persons will not be representative for their entire working lives. Comparisons between the 1960 and 1970 censuses in Norway show that occupational mobility differs between groups, and although it is rather low among skilled workers and persons with more education, it is much higher among the unskilled, who tend to stay within the industrial sector (*17*). When a longer time span is taken into account, however, a greater mobility would most probably appear. In Denmark in 1970, for instance, at least one out of four men working in manufacturing, construction, and transport had a background in agriculture (*18*). The census data are based on the compulsory reporting for all household members on questionnaires self-administered by all heads of households. Shortly after the 1970 census in Norway, a sample of the population was interviewed regarding the census questions. A high correlation was found between the occupational information given in the two situations for all groups except female farmers, who were often classified as housewives in the census questionnaire (*17*).

Numerous linkages have also been done with individually established occupational cohorts based on personnel lists from one plant or industry, union membership lists, membership in pension funds, etc. These kinds of studies are facilitated by the tradition of a mostly cooperative climate in the relations between employers and unions and the development of workplace democracy. When a company or a plant is being investigated for cancer risk, more comprehensive information on duration of employment, exposures, and possible confounders are often available than in the pure register linkage studies. The occupational safety and health departments established in the industry are often important partners in the task of collecting these additional data, as they usually have expertise both in occupational medicine and hygiene.

The quality of the linkage is ensured by the personal identification numbers being used in most formal transactions in the Nordic countries. The Swedish

Cancer–Environment Registry has been validated regarding the linkage, and an extremely low proportion of false hits was found (*19*). On the basis of this research infrastructure, which ensures high-quality incidence data at reasonable costs, a large number of studies, especially occupational cohort studies and case–control studies nested in a cohort, have been performed.

Confidentiality

Concerns about medical confidentiality are not new (*20,21*), but the discussion has intensified in recent years (*22,23*), partly because of the wish of the European Union to coordinate regulations on data handling and security in its member countries. Restrictions on the use of the personal identification number to combine information from different sources have been proposed, and the question of informed consent has been much debated. In the Nordic countries, informed consent has not been required when data are used for research and statistical purposes, and the consent to linkage studies has been given by the data inspectorates in the respective countries. A European Union directive on protection of the individual with regard to processing of personal data (*24*) confirms informed consent as the fundamental principle in the handling of sensitive information on individuals, but provides for exceptions when data are used for certain statistical and research purposes and have no direct consequences for the individual. It is therefore important that none of the Nordic countries pass laws that will place more restrictions on epidemiologic research than this directive requires. The use of the personal identification number is essential both for maintaining high-quality data of the registers and for the high quality of the linking process itself.

Both scientifically and economically, the requirement of an active, informed consent from all study subjects would render the performing of future occupational cancer research in the Nordic countries virtually impossible.

Compensation

The reporting of occupational diseases is compulsory in all Nordic countries. Because of complex disease etiologies and sometimes inadequate attention to occupation as a possibly important factor, it can be assumed that a large proportion of occupational diseases are never reported or compensated. In spite of its close association with occupational exposure, even mesothelioma is underreported as an occupational disease in most of the Nordic countries (*25–27*). In Finland, however, an asbestos program has been developed and the proportion of mesotheliomas recorded as occupational diseases was recently reported to be very high (*28*). A Norwegian study has indicated that from 1991 to 1993 only 4.6% of all male lung cancer cases were reported as possibly occupational diseases, although approximately 20% would have been expected according to usual estimations of attributable risk (*29*). There is reason to believe that underreporting is a general problem and that a proportion of workers do not receive the compensations intended by legislation.

Research Examples

The program of evaluations of carcinogenic risks to humans performed by the International Agency for Research on Cancer (IARC) gives rise to a list of Group 1 (definitely carcinogenic) substances, mixtures, and exposure situations. Most of these substances, mixtures, and exposure situations also have been investigated in Nordic studies. The following brief presentation of selected studies of Nordic occupational cancer epidemiology has been based mainly on this list.

Asbestos

Asbestos was classified as a Group 1 carcinogen in 1977 (*30*), with an update of the evidence in 1987 (*31*). Risk of pleural mesothelioma has increased among workers in specific occupations (*32–34*). Elevated risk of lung cancer has been found among asbestos-exposed workers in general (*35*), especially among exposed heavy smokers (*36*). In a Norwegian case–control study, the smoking-adjusted odds ratio of lung cancer increased from 1.2 in those with light asbestos exposure, to 2.7 in those with moderate exposure, and to 4.3 in subjects with heavy exposure (*37*). A Finnish cohort study on workers in two anthophyllite mines found a risk of lung cancer almost 3 times higher than that in the general population and showed increased risk from intensity and duration of exposure (*38*). The study concluded that anthophyllite, a mineral mined only in Finland, gave a high risk of lung cancer but a lower risk of pleural mesothelioma compared with other types of asbestos. A recent Danish study found that all histologic types of lung cancer were elevated during the first 25 years after start of employment in an asbestos cement factory but that after this time the risk of adenocarcinomas was especially high (*39*).

Large proportions of the population have had some exposure to asbestos. From a survey of an industrialized county of Norway, 18% of the men over 40 years of age were reported to have had some exposure (*40*). In Finland, a screening of current and retired workers in housebuilding, shipyard, and asbestos industries revealed that 22% had pleural and parenchymal changes (*41*). Mesothelioma trends may serve as indicators of previous asbestos exposure, although changes in diagnostic and coding practices may compromise their interpretability. Several investigations of time trends have been published from Nordic countries, indicating an increased incidence among men at least through the 1980s, with a stable, age-adjusted incidence in Finland from 1990 (*4,28,42,43*).

Polyaromatic Hydrocarbons

IARC classified coal tars and derived products, shale oil, and soots as Group 1 carcinogens in 1985 (*44*), with an update of the evidence in 1987 (*31*). In an early study of workers from four aluminum plants in Norway, an elevated risk of lung cancer was found (*45*). A more recent investigation found an elevated risk of both bladder cancer and lung cancer related to exposure to coal tar pitch volatiles 40 years and 35 to 50 years or more before observation, respectively, among men employed for 3 years or more in an aluminum plant (*46*). Cancer risk has been shown to be elevated in occupational groups such as chimney sweeps (*47,48*) and asphalt workers (*49*), thought to be at least partly due to exposure to polycyclic aromatic hydrocarbons.

Chromium

Chromium and chromium compounds were evaluated by IARC in 1990, and chromium [VI] was classified as a Group I carcinogen (*50*). In a small plant producing chromium pigment, an elevated risk of lung cancer was found (*51*), and in a cohort of ferrochromium and ferrosilicon workers the risk of lung cancer was elevated in the subgroup employed in ferrochromium production before 1965 (*52*). Results from a cohort study of masons in Iceland suggested an elevated risk of lung cancer associated with hexavalent chromium (*53*). A case–control study with data from Sweden, Denmark, and Finland suggested that an elevated risk of nasal cancer might be associated with exposure to chromium (*54*), but nickel exposure was a common exposure among the cases.

Nickel

Nickel and nickel compounds were evaluated by IARC in 1990, and nickel compounds were classified as Group 1 carcinogens (*50*). An excess risk of lung cancer and nasal cancer was observed in a cohort study published in 1973 of nickel refinery workers in Norway (*55*). Subsequent follow-up of the cohort has indicated a persistent risk of lung cancer also among persons employed around 1960 (*56,57*), and has suggested a multiplicative effect of smoking and nickel exposure on lung cancer risk (*57*). The elevated risk of nasal cancer in nickel refinery workers was supported in a recent publication from Finland, where a small cohort from a nickel refinery opened in 1960 was studied (*58*).

Arsenic

Arsenic and arsenic compounds were classified as Group 1 carcinogens in (*59*). An update was made in 1987 (*31*). Studies on lung cancer among Swedish copper smelter workers have shown 3- to 5-fold elevations in standardized mortality rates and a positive dose–response relationship with exposure to arsenic (*60–62*).

Wood Dust

Wood dust was evaluated and classified as a Group 1 carcinogen by IARC in 1995 (*63*), but the furniture and cabinet-making industry was already classified in 1981 (*64*) with an update in 1987 (*31*). Wood dust and especially dust from hardwood trees have been associated with nasal cancer. In a Danish–Finnish–Swedish collaborative case–control study, an elevated risk of nasal cancer was associated with exposure to hardwood or mixed wood dust and with exposure to softwood dust alone (*54*). The study showed that hardwood exposure was associated with adenocarcinoma, but there was also some indication that softwood exposure alone might be associated with epidermoid and anaplastic carcinomas. In a Danish study, a 4-fold elevation of risk of nasal cancer was seen among workers exposed to wood dust (*65*). For lung cancer and upper respiratory cancer, no association with exposure to wood dust, mainly from pine, spruce, and birch, was found in a Finnish study (*66*).

Benzene

Benzene has been classified as a Group 1 carcinogen since 1981 (*67*). An elevated risk of acute myeloid leukemia was found in a cohort of Swedish petrol station attendants, hypothesized to be associated with benzene that was previously contained in petrol (*68*). A Nordic study of gas station attendants, however, did not repeat this finding but found an increased incidence of cancers of the kidney, pharynx, larynx, lung, and nasal sinuses (*15*).

Silica

Crystalline silica, inhaled in the form of quartz or cristobalite from occupational sources, was classified by IARC as a Group 1 carcinogen in 1997 (*69*). In a Nordic study of men in occupations with possible exposure of silica dust, an excess risk of lung cancer was found among foundry workers in all countries and among miners in Sweden (*11*). In a follow-up study of Finnish granite workers relative risk of lung cancer was between 2 and 5, allowing for 20 years or more of latency (*70*). In this study the cytotoxicity of different granite fractions and their capacity to induce reactive oxygen species in human leukocytes were also investigated.

Radon and Its Progeny

Radon and its decay products were evaluated as Group 1 carcinogens by IARC in 1988 (*71*). In a study on cancer incidence among workers exposed to radon and thoron daughters in a niobium mine in Norway, a standardized incidence ratio (SIR) of 11.1 for lung cancer was found for the miners, whereas the SIR for the total cohort was four (*72*). A Finnish cohort study among sulfide ore miners showed an elevated mortality of lung cancer interpreted to be due to exposure to radon daughters and silica dust (*73*). In Sweden, a study on lung cancer and occupation showed an excess risk among underground miners (*35*).

Alcohol

Alcoholic beverages were classified as Group 1 carcinogens by IARC in 1988 (*74*). Although consumption of alcoholic beverages is not an occupational exposure in the strict sense, high alcohol consumption may be viewed as work related in occupational groups that produce, handle, or serve alcohol (*75*). Elevated incidence of cancer at sites that have been associated with consumption of alcohol was found in studies of brewery workers in Denmark (*76*) and Sweden (*77*) and among male waiters and cooks in Norway (*78*).

Herbicides

Two early case–control studies from Sweden suggested an association between exposure to phenoxy herbicides and risk of soft tissue sarcoma (*79*) and malignant lymphoma (*80*).

A later analysis of cancer incidence in a Danish cohort of phenoxy herbicide production workers was suggestive of an association with soft tissue sarcoma but not with malignant lymphoma in three subsequent follow-up periods (*81–83*). Cohort studies of pesticide applicators in Finland and Sweden found no elevated risk of soft tissue sarcoma or malignant lymphoma (*84–87*). In a Swedish cohort of agricultural and forestry workers identified by the 1960 census and followed from 1961 to 1979 there was no elevated incidence of soft tissue sarcoma or non-Hodgkin lymphoma (*88,89*); and in a cohort study of more than 140,000 male farmers followed from 1971 to 1987, only lip cancer and multiple myeloma showed significant increases (*90*).

Solvents and Paints

Solvents and paints are widely used in industrial settings and have been included in several IARC evaluations (*31,67,91*). Benzene has been classified as a Group 1 carcinogen, whereas tri- and tetrachloroethylene have been classified as having limited evidence of human carcinogenicity. Recent cohort studies from Sweden (*92*) and Finland (*93*) of workers biologically monitored for trichloroethylene exposure indicated an elevated mortality from non-Hodgkin lymphoma and liver and biliary cancer. The Finnish cohort study also indicated that workers exposed to tetrachloroethylene had elevated risks of non-Hodgkin lymphoma, kidney cancer, and bladder cancer (*93*). Due to the common mixture and combination of different solvents, it is often not possible to study the effect of one specific solvent; occupations or industries may in such cases be the focus of study. Studies from Denmark (*12*) and Finland (*8*) have supported earlier findings of elevated incidence of cancer of the lung and urinary organs among painters. An international cohort study of workers in the reinforced plastics industry from Denmark, Finland, Italy, Norway, Sweden, and the United Kingdom suggested an increasing mortality by average exposure and time since first exposure for all lymphohematopoietic malignancies and for lymphomas (*94*). However, no consistent association with duration of exposure or cumulative exposure was found in this study. In a Danish incidence study, elevated risk of leukemia was found among the group exposed in the early production phase (*95*).

Electromagnetic Fields

The question of exposure to electromagnetic fields (EMF) and possible cancer risk has received much research attention in the last decade, although no consensus has been reached on the subject. Although three cohort studies on railway workers gave some support to the hypothesis of an association between EMF and leukemia risk (*3,96,97*), a nested case–control study with more refined exposure estimates was negative (*98*). A cohort study gave support to an association between work as a radio and telegraph operator at sea and breast cancer in women, also after adjustment for reproductive factors (*99*).

Cancer Risk in Children and the Role of Parental Occupation

The possible role of parental exposure in relation to childhood cancer has so far been investigated only in a few studies from the Nordic countries. In an early case–control study, no association between incidence of cancer during childhood and hydrocarbon-related occupations was found (*100*). Two studies have indicated elevated cancer risk among children with mothers or fathers who were healthcare workers (*101,102*). No association was found with parental lead exposure in printers (*103*), with stainless steel welding (*104*), or with exposure to electromagnetic fields (*105*).

Some studies have found elevated cancer risk among the offspring of farmers (*106–108*). Two Norwegian studies based on a large cohort established by multistep record linkage showed indications of an association between parental use of fertilizer and later testicular cancer in offspring (*108*) and between horticulture and pesticide use and all cancers at 0 to 4 years of age (*107*). However, a Danish case–control study did not find any elevated risk of testicular cancer in the group with a father who was a farmer or among those who grew up on a farm (*109*).

Future Priorities

For the continued development of occupational cancer research in the Nordic countries, the use of the personal identification number for ensuring the quality and completeness of the cancer registries and the linking process is essential. This technical framework will also support the cost efficiency and quality of studies utilizing biomarkers from serum banks.

After a few decades with a major focus on male workers in traditional production industries, other areas are now awaiting research attention. In the Nordic countries women entered the workforce in large numbers and at an early period in time. This makes these countries well suited to study the question of how cancer risk in women may be affected by occupational activity. Such studies will often have an additional focus on how occupational activity may influence lifestyle factors such as smoking or drinking and reproductive patterns such as parity and age at first birth. Some studies of women workers have been undertaken, such as studies of Icelandic nurses (*110*), Finnish health care personnel (*111*), Danish hairdressers (*14*), and Norwegian radio and telegraph operators (*99*) and waitresses (*112*). Also, several linkage studies based on occupational information from censuses have given data on cancer incidence in women (*8,10,113*). Results from these studies should form the basis for further etiologic studies among woman workers. The question of possible cancer risk in offspring of men and women exposed to workplace carcinogens has been briefly mentioned, but this research field is in its beginning. The method of establishing cohorts based on record linkages to study cancer incidence can be expected to prove both efficient and informative in this area of research.

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