PROGRAMME FOR INTERVENTION AGAINST ASBESTOS RELATED DISEASES IN THE COUNTY OF TELEMARK, NORWAY

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INTRODUCTION

Although the relationship between exposure to asbestos and pneumoconiosis and lung cancer was revealed some 85 and 60 years ago respectively, scientists are still preoccupied with quantification of these relationships. Much work has been carried out both to remove asbestos and to minimize exposure in work places. Quite little has been done to reduce disease risk among the great number previously exposed subjects.

Attempts have been made to quantify the public health significance of past exposure to asbestos.[5,9] In Norway it has been estimated that 125–150,000 people have been exposed during the past four-five decades to an extent which is detectable in population based studies.[8] In our country no one has carried out intervention among people at high asbestos related risk. In fact, only few scientists have been willing to indulge in the task of stimulating risk reduction and assisting the high risk people to reduce their individual risk.

Our department, which is located in the county of Telemark, Norway, has diagnosed about 700 cases of asbestos-related illnesses during the past 10 years. The cases are mainly lung cancers, mesotheliomas, asbestosis, and pleural plaques. A number of cohort studies and case-control studies carried out among the county population has confirmed that past asbestos exposure has contributed 40 to 45 percent of the environmental causes of lung cancer among the local male population.[4,6,7,8] This high contribution to the "causal weight" is calculated by using etiologic fraction estimation.[7,8] Based on these and other local studies it has been estimated that 11–12,000 asbestos exposed persons are living in the county. We have collected exposure information on about 5,500 of these, mainly males. The lung cancer incidence in males in this county is about 30% higher than in the country as a whole.[1] The total male population in the county is about 80,000, of whom 33,400 are over 39 years old.[4]

These findings have inspired us to start an intervention study of determinants for increased asbestos related disease risk among males in the county. The purpose of the study is to reduce asbestos related disease risk and to prevent illnesses which otherwise would be caused by asbestos or by previous exposure to both asbestos and tobacco smoke. Methods

We have designed a programme in which these 5,500 subjects serve as base for recruitment of subjects assigned for intervention. As a large proportion of these subjects have been identified through a screening programme,[4] where age exceeding 39 years was one of the inclusion criteria, the majority of the subjects are over 40. Most of the other subjects, who have been identified as asbestos exposed through other epidemiologic studies or through clinical surveys, are also above 40 years of age.

We have decided to intervene only against those determinants which give high risk for development of asbestos related lung cancer in males as the primary activity in the early phase. The intervention is planned to comprise two elements;,

a) Information intervention among previously asbestos exposed present smokers, by doctor or nurse, counselling on the potential great lung cancer risk reduction among these combined exposed subjects; and

b) A programme for intensive screening for lung cancer among previously asbestos exposed previous and present smokers.

Evaluation of the results is planned to measure the effect on the smoking prevalence in the intervention group, and the long term effect on lung cancer incidence and mortality, mortality all causes, and mortality due to other asbestos related diseases.

We intend to estimate each participants a priori risk of developing lung cancer and subsequently to use this risk as criterion for determining to which of the two intervention groups the subject is to be assigned. For estimation of the individual a priori lung cancer risk, one needs to know; a) each subjects individual exposure history to lung cancer determinants, and b) to have a set of information from the literature which makes it possible to assess each subjects risk, when the accurate exposure history is known. At present it is not possible to take genetic disease determinants into account in the risk estimation.

For each participant we need to obtain accurate information on the duration and the intensity of past exposure to all major lung cancer determinants. By taking a detailed, individual occupational history, as well as history of exposure to tobacco smoke and alcohol, we have already obtained sufficiently detailed exposure information from about 2,000 subjects. From another 3,500 subjects we have obtained information on exposure to asbestos and tobacco smoke, but supplementary information is needed to be able to carry out assessment

of the lung cancer risk. It is also intended to continue collection of exposure information in another 22,000 subjects in whom we have obtained only that exposure information which has been needed to assign these subjects to job categories in previous epidemiologic studies.

From the data on cancer incidence in the total Norwegian population, which have been collected by the Norwegian Cancer Registry since 1953, it is known that the present average a posterior risk for lung cancer in the Norwegian male population increases from about 1×10^{-4} at the age of 40–44 to 15×10^{-4} and even higher at the age of 65–69 (Figure 1, line a).

These risk levels are average levels for experienced lung cancer risk in the general male population. The levels are outcomes from exposure to a range of disease determinants that characterize the past exposure situation for the general population. The individual risk levels, which have lead to these population based risk levels, ranges from low levels among subjects with hardly any exposure to high levels in subjects with previous exposure to a multitude of strong disease determinants.

It would be preferable to have access to reference levels for lung cancer which were uninfluenced by external disease determinants. However, such reference entities are not available. We have therefore decided to apply the national age standardized lung cancer incidence as reference entity for estimation of those risk levels which should serve as criteria for assignment to either of the two intervention groups.

We have chosen to assign those subjects to the subgroup for information intervention who, between five and 25 years from the date of enrollment, are extrapolated to have an a priori lung cancer risk five times or more higher than the national age adjusted background level (Figure 1, line b). Those subjects who are estimated to be at 10 times or higher lung cancer risk than the reference level at the time of enrollment, or who reach this risk level during the study, are to be enrolled into the lung cancer screening group (Figure 1, line c).

The means of intervention have been planned as follows:

a) The information intervention is designed with the purpose to reduce the a priori lung cancer risk by means of providing individually designed oral and risk-determined written information to the study subjects. The content of the information will be different for each subject, and is to be designed to meet each persons needs. These "needs" are determined on basis of the available information on the relevant disease determinants which has been collected beforehand hy means of individual work histories an individual information on the non-occupational disease determinants. The magnitude of the a priori lung cancer risk is to be estimated by comparing each subjects past exposure with comparable group based exposure information in published literature. This literature information on relative rate ratios at given past exposures, is to be multiplied by the absolute a posteriori risk at the given ages in the cancer registry data. This approach also enables us to extrapolate the individual a priori lung cancer risk to different points in time in the future. These extrapolated risk estimates are also to be taken into account for the content of the information designed for each participant.

b) The lung cancer screening is planned to be based on two-angle pulmonary X-rays every four months and on yearly three-day exfoliative cytology examination among the members of the high risk groups aged 50 to 69, as these are defined above. Only those participants who exceed an estimated yearly a priori lung cancer risk of 80×10^{-4} will be assigned to triannual screening, as indicated by the broken line c in Figure 1. Those high risk members who do not exceed an estimated risk of 80×10^{-4}, will be screened biannually by two-angle pulmonary X-rays. (The risk among heavy smokers rarely exceeds 60×10^{-4}).

In order to make interpretation and evaluation of the study outcome possible, the study is in need of a kind of "unit" which is applicable both in presence and in absence of intervention. We consider "gained healthy years" among the members of the study group to be an adequate unit for judging the results. Reduced number of exposure-related lost years of life in the study cohort is assumed to be a natural consequence of increased number of healthy man-years. Therefore, gained years of life could also serve as a "unit" for measurement of the outcome of the two strategies for intervention.

DISCUSSION

The choice of frequent X-rays and the less frequent cytology examinations is based on recommendations from the Early Lung Cancer Cooperative Study,[1] which indicated that two-angle lung X-rays are about four times as efficient in detecting early lung cancer as is exfoliative cytology examinations.

We have also considered to chose fixed a priori levels for lung cancer risk as enrollment criteria for each of the two intervention groups. By doing that, assignment to either of the two intervention groups would have taken place when the estimated individual a priori risk exceeds either of these two fixed levels. However, as the experienced a posteriori risk for lung cancer increases with age, (Figure 1, line a) fixed a priori risk levels would have given older people preference before young subjects. It seems likely that individual information intervention may lead to a greater risk reduction when given to high risk groups at young age, than when given to older subjects with a comparable high a priori risk. Therefore, fixed risk level across the age groups might lead to reduced efficiency.

For interpretation and evaluation of the results, we are faced with the same difficulties as other researchers who have indulged in the problem of prospective health assessment.[10] A "controlled" study, in the sense that half of those subjects who are eligible for the study were assigned to the study group and the other half to the reference group, is one possible way to get a reference group. In the present study, however, where a positive outcome of the intervention seems likely, it is difficult to leave half of the group without intervention.

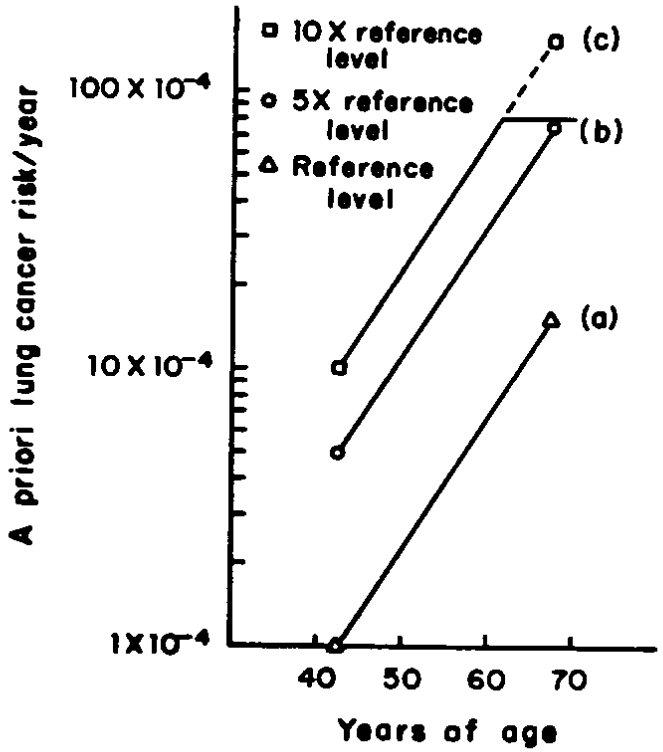

Figure 1. The figure illustrates the a posteriori experienced lung cancer risk (line a) and the a priori lung cancer risk criteria for assignment to the groups for information intervention (line b) and X-ray screening (line c), respectively. Those subjects with risk exceeding the horizontal part of line c are assigned to triannual screening.

We have decided to deal with the problem of evaluation in a similar way as was done in a New York study on the effect of smoking cessation in asbestos workers.[10] In this study the lung cancer mortality was compared among those who had stopped smoking and those who had not. As the numbers are likely to be small in the present study, such a method would allow us to apply intervention on the whole identified population, and subsequently use those who do not participate as reference entity.

In groups which have been heavily exposed to one or two major disease determinant, we consider screening for lung cancer useful only after a presumed development time ("latency period") of 15 to 20 years has elapsed from the first significant exposure. When applying this view, lung cancer screening has biological meaning in relation to the disease determinants at issue only after this presumed development time. When the past exposure has been low, screening only has biological meaning even later.

Depending on the obtained results, in the first place in terms of reduced smoking prevalence in the target group, and later in terms of reduced incidence of lung cancer, the study is intended to carry on as long as past asbestos exposure is considered to be a significant disease determinant in the target population. As reduction in smoking prevalence in the intervention group is to be a prime effect in the present study, one might also expect reduction in smoking related disease incidence and mortality. It is the intention to expand the study to include other major disease determinants in the local population. Such expanded intervention will be performed in close cooperation with the local general practitioners, occupational health physicians, and the hospital.

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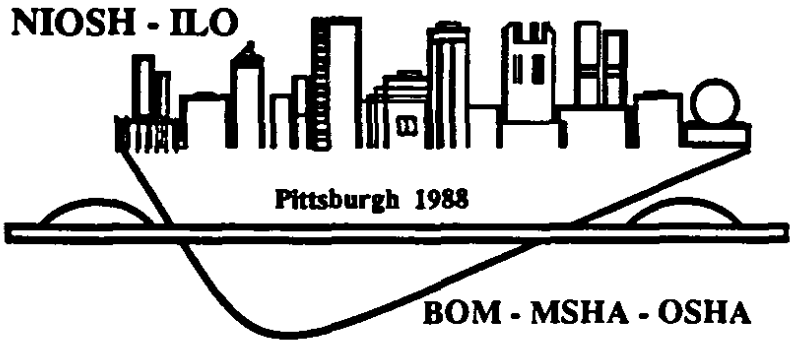

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