Report on the Health Effects of the Asbestos Mines on the Population of Neighbouring Communities

MASTER FINAL COPY

Prepared for the
Ministry of Health in Cyprus

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Section 1

Executive Summary

We were commissioned by the Ministry of Health of the Government of Cyprus to carry out a study of the health effects of the asbestos mine on the communities of the villages of Kyperounda and Kato Amiandos. Following a number of site visits and several meeting with all the stakeholders as well as investigating all the sources of data the investigating team developed an agreed protocol for the study, which was broadly in line with the terms of reference set out by the Government. The components of the study included the following:

1. Literature review.
2. A census of Kyperounda and Kato Amiandos
3. Spirometry testing
4. A study on mortality
5. Survey of medical and social issues
6. Respiratory morbidity
7. Conclusions and recommendations

1. REVIEW OF THE LITERATURE

Our literature review confirmed that there are literally many thousands of scientific papers that deal with the health impact of asbestos. There is an on-going controversy regarding the health risk imposed by chrysotile asbestos. According to the Collegium Ramazzini, an international learned society in environmental and occupational medicine, there should be an immediate worldwide ban on all sales and uses of all forms of asbestos, including chrysotile.

At the turn of the 20th century, it was noted that those working with asbestos suffered lung disease. The first case of asbestosis was described in 1924 in a textile worker. In the 1930s and 1940s scientists recognised a casual link between asbestos exposure and asbestosis. In the 1950s and 1960s asbestos was recognised as a predisposing factor for lung cancer and malignant mesothelioma. In 1960 the link between asbestosis and mesothelioma was established in the Kimberley area of South Africa. Further studies in the 1970s and 1980s showed an alarming incidence of mesothelioma based on pathology reports.

The International Agency for Research on Cancer of the World Health Organisation has declared chrysotile asbestos a proven human carcinogen. Sales of chrysotile asbestos have virtually ended in Western Europe and North America, because of widespread recognition of its health hazards.

According to the Canadian review there is strong epidemiological and pathological evidence that the only association of asbestos exposure and lung cancer is the association of asbestosis and lung cancer. Thus, a lung cancer should only be attributed to asbestos exposure when asbestosis is present on clinical or pathological grounds.

Pleural disease is the most common disorder associated with asbestos exposure. Hyaline and calcified pleural plaques were found in the 1960s to be an index of exposure to asbestos. Shipyard workers were found to have a tenfold great incidence of pleural abnormalities than parenchymal disease.

The prevalence of asbestosis is strongly related to the length of the exposure. One of the early epidemiological studies analysed chest X-Rays of asbestos insulation workers and found that the prevalence of asbestosis was clearly related to the length of exposure.

The observation that mesothelioma resulted from occupational exposure to asbestos was first reported in Britain in 1935. In 1952, a Canadian industrial medical clinic reported a case series, which contained two cases of pleural tumours from among 8 respiratory cancers. In 1960, Wagner and colleagues reported the first case series of malignant mesothelioma.

In 1980 Peto reported on the incidence of pleural mesothelioma in asbestos textile workers in relation to age, time since first exposure, intensity of exposure and period of observation. His research suggested that the recent marked increase in recorded rates of mesothelioma is real and not merely a diagnostic artefact.

The mesothelioma risk from chrysotile is well established, although the relative risk is far less than the risk imposed by crocidolite asbestos (blue asbestos). Sophisticated cohort analysis of death rates by Professor Julian Peto predicts an epidemic of mesothelioma deaths in Europe that will peak sometime in the next decade.

There is clear evidence that asbestos dust is associated with pulmonary fibrosis and pleural plaques that produce a restrictive lung disorder, which can be measured by a reduction in the forced vital capacity (FVC) and forced expiratory volume in one second (FEV1).

2. A CENSUS OF THE POPULATION OF THE TWO VILLAGES

To ascertain the level of occupational and household exposure, we conducted a local census of the two villages. Information for the local census was gathered from the subset of the population who attended for spirometry. This data was supplemented with data from a telephone interview and local interviews with the populations of the two villages. From this were able to calculate the exposure rate of the villages. The response rate to our local census was 79%.

As expected, we identified a strong age effect on occupational exposure. Among men over 75 the vast majority (83%) worked on the mine, and among those in the 50-74 age group, over half (56.1%) were occupationally exposed. Among all ages 40.7% have been occupationally exposed.

Of the households that had experienced occupational exposure 24% had been exposed for over 20 years and a further 20% for between 10 and 19 years.

3. SPIROMETRY TESTING

The objective of the study is to investigate the respiratory health of those residents who have had an occupational or household exposure to asbestos. The underlying hypothesis is that prolonged exposure to asbestos would cause a significant decline in the respiratory health of the exposed population. The asbestos mine closed 16 years ago (1988), and, in that most people would have been at least 20 years of age when they started working on the mine, we concluded that the cohort aged 50 years and over would have experienced the highest levels of exposure. Spirometry therefore was targeted on residents in the age range 50 to 75 years.

Spirometry aims to measure the performance of the respiratory system by measuring expiratory volumes and flow rates. It is a test that requires maximum co-operation from a patient, as they must make a maximal inspiratory and expiratory effort. It is essential that a patient gives full effort, and failure to do so causes unreliable results. In other words, the test is heavily dependent on a resident's technique and effort.

All residents aged between 50 and 75 years were invited for spirometry by a letter from the village presidents of Kyperounda and Kato Amiandos. To encourage as many people as possible to attend the research team held two spirometry clinics per day, from 9 a.m. to 1p.m. and 4pm to 7 p.m. in Kyperounda for 5 days. Three sessions were held in Kato Amiandos. Two experienced operators used two calibrated spirometres, following a strict protocol. As a matter of policy spirometry was done on all who attended, including those aged under the age of 50 and those aged over the age of 75 years. In all 273 people attended for spirometry, 218 from Kyperounda and 55 from Kato Amiandos.

In this study we found clear evidence of significant restrictive patterns among those who were exposed to asbestos. Indeed there appeared to be a gradient according to the level of exposure. Highest rates of restrictive disorder were found among the occupationally exposed men in Kato Amiandos (41.7%), followed by occupationally exposed men in Kyperounda (28.3%). Women with a household exposure had higher rates (19.0%) than non-exposed women (4.0%). This finding shows that the spirometry was successful in measuring exposure to asbestos.

A history of cigarette smoking has a definite adverse impact on lung function tests. The greatest deficiency in lung function was found among men who had smoked and been occupationally exposed. Our findings suggest that occupational exposure to chrysotile asbestos dust has about the same impact as heavy cigarette smoking. This finding shows how important it is to encourage men who have worked on the mine to stop smoking. The poorer respiratory status of men is due to higher levels of exposure but also to the high rates of cigarette smoking. There is clear evidence that smoking aggravated the effect of asbestos exposure. It is therefore of especial importance that men who have experience occupational exposure should be encouraged to give up smoking.

We were intrigued by the finding that women had such high FVCs. Among the group with no exposure the average FVC was 112, which is 12% higher than expected. In our view the most likely explanation for this finding is that the body shape of Cypriot women living in the villages tend to be short and stocky. The implication is that the spirometer, which only standardises for height and mass, is under estimating the vital capacity of these women. We recommend that a study should be undertaken to investigate this very important question. It is important to standardise for body shape, and this can be done by measuring shoulder width.

4. STUDY OF MORTALITY

We used three sources of ascertainment, namely data on mortality registration, data from priest records and data from cemeteries to obtain an accurate count of the number of deaths that had occurred in Kyperounda and Kato Amiandos. Our evaluation of mortality data showed that the four-year period from 2001 to 2004 there was a large level of agreement between priest records and registration data.

We used three years of mortality data and population data from the 2001 census to calculate national age specific rates. While the calculation of SMRs for the index villages showed that there is no statistical difference at the 95% confidence level in the mortality experience of Kyperounda and Kato Amiandos and the other control villages, it should be noted that the SMR in Kato Amiandos was 46% higher than expected. It seems probable that the long-term exposure to asbestos has resulted in a small excess of deaths. It is important that the mortality rates of the exposed villages should be monitored over the next decade.

5. SURVEY OF MEDICAL AND SOCIAL ISSUES

A medical survey was undertaken to assess the respiratory health of the residents of Kyperounda and Kato Amiandos. A questionnaire was developed after holding a number of discussions with community leaders from the two villages. A major objective of the survey was to gather information on the views, opinions and perceptions of the villagers. Factors studied included smoking history, respiratory problems, previous medical problems, current symptoms and occupational details. Respiratory health was assessed using a modified version of the British Thoracic Society’s questionnaire.

The sampling frame for the survey was residents of the two villages aged 50 years and over who had been invited to have their lung function tested by spirometry. Two Greek-speaking interviewers gathered data prior to the respondent undergoing spirometry testing

The vast majority of respondents have lived in the villages for over 30 years, and only 2.1% for less than 20 years. Among the male respondents 70% were retired and 28% were in full-time employment. Among females 58% were retired, 25% were housewives and 16% in full-time employment.

Analysis by village of residence showed much higher exposure rates in Kato Amiandos. Among men in Kato Amiandos, 86.4% had worked on the mine compared to 72.4% of men living in Kyperounda. Among the women living is Kato Amiandos 48.4% had worked on the mine compared to only 8% of Kyperounda women.

Women living in Kato Amiandos had higher rates of household exposure than women living in Kyperounda did. Of the 31 females from Kato Amiandos, 80.6% lived in the same household as someone who worked on the mine, compared to 60.2% of the of the

133 women respondents in Kyperounda. There was no evidence of any other significant exposure to asbestos besides the mine

Occupational exposure was largely age dependent, with older people more likely to have worked on the mine. Three-quarters of men in the survey had worked on the mine and one quarter of females. The residents of Kato Amiandos had higher levels of occupational exposure than residents of Kyperounda.

Household exposure was largely a factor among women. Two-thirds of the women in the survey lived in a household with someone who worked on the mine. As with occupational exposure, household exposure was strongly age dependent. There was no evidence of any other significant source of asbestos exposure among the village populations.

There is evidence that the health of those who have worked on the mine has been adversely affected. A higher proportion of men who have been occupational exposed perceive their health to be poor compared to their non-exposed counterparts. Those who have occupational exposed have higher rates of heart disease and bronchitis. The occupationally exposed are more likely to cough in morning in winter months and more likely to bring up phlegm in the morning in winter than their non-exposed counterparts.

However, because of the relatively small numbers involved in our analysis none of these differences achieved statistical significance at the 95% confidence level. This does not mean that these are not real differences, but that the differences cannot be established by statistical tests that demand confidence at the 95% level. It seems highly likely that if more residents were examined that the reported difference would reach statistical difference. Moreover, it must be remembered that the failure to demonstrate a statistical difference does not necessarily mean that there is not a real difference.

There is some evidence that household exposure has adverse effects on respiratory symptoms. However, those with household exposure had similar rates of heart disease and bronchitis as their non-exposed counterparts. Rates of self-reported depression were twice as high among exposed women.

The level of smoking among older men appears to have declined as many have given up the smoking habit. However, it seems probable that many of the older men had smoked for many years before giving up, and therefore we included them in the group with a history of smoking for the purposes of analysis. We would recommend a health promotion campaign among the villages to encourage men to give up the habit.

Although the rate of self-reported cancers in the occupationally exposed group was not statistical different, it is of concern that those with an occupational exposure probably have a higher risk of developing cancer.

6. RESPIRATORY MORBIDITY

The findings of our analysis of hospital records confirm the findings of the spirometry. There is no doubt that the exposed populations in the villages of Kyperounda and Kato Amiandos have experienced significant respiratory morbidity that is due to their exposure to the asbestos mine.

The villages of Kyperounda and Kato Amiandos have an admission rate for chronic obstructive pulmonary disease, which is thirteen times higher than the national admissions rate. This is a highly statistically significant difference that cannot be explained by easy access to the hospital. Moreover proportion of hospital admissions for this diagnosis is seven times higher than that occurring elsewhere on the island.

The admissions to hospital ratio for the whole of the Lemesos district, excluding the villages of Kyperounda and Kato Amiandos is significantly higher than elsewhere in Cyprus. It is therefore important that the scope of the investigation is expanded to include other villages in the Lemesos district that have experienced significant levels of exposure to asbestos.

We found that over the whole of Cyprus there have been 48 hospital admissions for mesothelioma recorded over a five-year period from 1998 to 2002 and that the index villages of Kyperounda and Kato Amiandos have higher than expected rates. It is worth mentioning that the number of mesothelioma cases reported to the Cyprus Cancer Registry was 17 for the period 1998 to 2002. However the true incidence of mesothelioma can only be measured by a carefully designed study and this is included in the plans of the Ministry of Health for the final of a four-part study.

7. CONCLUSIONS AND RECOMENDATIONS

<u>The main conclusions of our study are summarised below:</u>

1. There was a significant health effect from both occupational and household exposure to asbestos. In this study we found clear evidence of significant restrictive lung disease patterns among those who were exposed to asbestos. Indeed there appeared to be gradient according to the level of exposure

2. Highest rates of restrictive lung disorder were found among the occupationally exposed men in Kato Amiandos (41.7%), followed by occupationally exposed men in Kyperounda (28.3%). Women with a household exposure had higher rates (19.0%) than non-exposed women (4.0%). This finding shows that the spirometry was successful in measuring exposure to asbestos.

3. The level of restrictive lung disease showed a gradient according to the type of exposure, with smoking having almost as great an impact as asbestos exposure. We believe that there is a clear message. While nothing can be done to reduce the impact of past asbestos exposure, the level of smoking among men remains a significant and important health hazard.

4. The spirometry tests showed that the force vital capacity (FVC) for non-exposed, non-smoking males and females were slightly higher than predicted values. We therefore concluded that this group had normal respiratory function, and that there is no evidence of an environmental exposure to asbestos in ambient air.

5. While there were more cancers among the exposed population, the difference did not reach statistical significance at the 95% confidence level. Moreover, a number of

residents were aware of family members who had died from lung cancer and mesothelioma.

6. The calculation of standardised mortality ratios (SMR) were based on 67 observed deaths in Kyperounda and 14 observed deaths in Kato Amiandos over the period 2001-2004. The SMR for Kyperounda was 99 (CI 78-129) and for Kato Amiandos 146 (CI 72-232). While the calculation of SMRs for the index villages showed that there is no statistical difference at the 95% confidence level in the mortality experience of Kyperounda and Kato Amiandos and the other control villages, it should be noted that the SMR in Kato Amiandos was 46% higher than expected. It seems probable that the long-term exposure to asbestos has resulted in a small excess of deaths. It is important that the mortality rates of the exposed villages should be monitored over the next decade.

7. The villages of Kyperounda and Kato Amiandos have an admission rate for chronic obstructive pulmonary disease, which is thirteen times higher than the national admissions rate. This is a highly statistically significant difference that cannot be explained by easy access to the hospital. Moreover proportion of hospital admissions for this diagnosis is seven times higher than that occurring elsewhere on the island

8. We found that over the whole of Cyprus there have been 48 hospital admissions for mesothelioma recorded over a five-year period from 1998 to 2002. However there were only 17 cases of mesothelioma reported to the Cancer Registry. For the same period. The statistical significance for Kyperounda and Kato Amiandos could not be established at this stage due to the fact that remaining communities near the asbestos mines have not yet been investigated.

<u>The most important recommendations of the study are shown below:</u>

1. It is recommended that the scope of any future investigation should be expanded to include other villages in the Lemesos district that have experienced significant levels of exposure to asbestos. The mortality rates of all the villages exposed to the asbestos mines should be assessed, and a study of morbidity should also be included in any subsequent study as there are good data that could be used for analysis.

2. It is recommended that the respiratory health of residents living in other villages that have been exposed to the asbestos mines should be included in any subsequent study

3. It is recommended that a subsequent stage of this study should concentrate on accurately describing the incidence of lung cancer and mesothelioma.

4. The researchers will provide a list of persons that would need to have their health monitored regularly (on an annual basis). It is recommended that the Ministry of Health should ensure that this monitoring is adhered to.

5. It is recommended that the Ministry of Health should immediately run anti smoking campaigns as a priority in the villages around the asbestos mines.

6. It is recommended that the true extent of the overweight/obesity prevalence should be measured by a properly designed study.

Section 2

Background to the study

1. INTRODUCTION

The Ministry of Health of the Government of Cyprus commissioned a group of consultants to work in collaboration with the Institute of Cancer Research (UK), to investigate the health effects of the asbestos mines for the villages of Kyperounda and Kato Amiandos. This is intended to be the first of a four-part study of all the villages that might have had adverse health effects from the asbestos mines. It is expected that on completion of this study the Ministry of Health will commission the second and then the third part of the study, which, while similar in nature to the present study, would place a great focus on studying the incidence and prevalence of cancer rates in the exposed populations. As we understand the current position, the fourth and final part of the study would be an overall case control study of all the cases of mesothelioma for the whole of Cyprus as well as bringing together the outcomes of the first three parts.

The Institute of Cancer Research (UK) has a specific academic interest in the study of mesothelioma and intends to publish the results of this important research on completion of the study, subject to the agreement and collaboration of the Ministry of Health.

2. BACKGROUND TO THE STUDY

The photograph below shows the abandoned asbestos mine that lies on the eastern side of Mount Olympus in the Troodos Mountains. Remedial landscaping is being done to stabilise the slopes and to lessen the dust that blows off the open face.
On the road down from the top of the Troodos Mountains there is a layby with a viewing platform of the workings and a display board detailing the history of the mine. The text reads as follows: -

"The area laying ahead of you is the Amiandos Mine which operated during the period 1904-1988 and is situated in the Troodos Mountain Range. The Troodos range geologically constitutes part of an ancient geological ocean floor and has been known as the Troodos Ophiolithic Complex. It consists of asbestos veins in the form of chrysotile veins scattered within serpentine (sepentinized charzburgite) appearing in the central part of the range at altitude of 1500 meters. The thickness of the veins ranges between just a few millimetres to 2 centimetres.

Cyprus is considered to be one of the oldest asbestos sources and until recently it has been one of the largest chrysotile asbestos producing areas in Europe. Mining and use of asbestos in Cyprus has been carried out since ancient times and in particular the Classical and Roman Ages. This fibrous mineral was used for making incineration plaques for the dead, shoes, wicks for lamps, and for other purposes.
The more recent history of the mine as well as the large scale exploitation of asbestos began when asbestos was being used for the manufacturing of asbestos slates, bricks,

heat insulation, pipes, motor vehicle brakes etc. The first mining lease in Cyprus was signed in 1904 in this area and included 600 hectares of land within the state forest of Troodos. Asbestos mining during the first decades of the twentieth century was carried out by primitive means, mainly simple tools and was done manually. This was the period when the largest number of personnel had been employed here. It is said that during the 1930s the number of people employed at the mine, including those manning various services exceeded 10,000! Around the mine, a small community was created, with people living in houses or temporary dwellings. It was a time when the mine provided more income to the economy than any other single industry or enterprise in the island.

Most people employed at the mine originated from the surrounding villages, there were however people from every corner of the island, in particular people coming from poor areas. The community provided a large and fully equipped hospital, a school, a police station, a cinema, grocery shops, butchery, and coffee shops and in general all commodities found in every small town

As the years went by, business began to become increasingly mechanised until 1949-1950, when a large-scale mechanisation in the mining and processing of asbestos was implemented. The annual production of asbestos fibres ranged between 20,000 to 40,000 tons.

The number of employees began to decrease and many houses and in particular the empty ones were dismantled. Until the end of the mine in 1988, mining of asbestos was carried out in an area covering 220 hectares. In this stretch the forest was cleared, the soil was removed and every form of natural life was destroyed, it is estimated that during this period a million tons of chrysotile asbestos fibres were mined and in order to carry out this task 130 million tons of rocks and soil were excavated and moved. It is worth noting that for the transportation of the asbestos to Limassol port an aerial ropeway 30 km long was established and operated until 1942. According to existing records, the asbestos fibres produced were exported and sold to European countries yielding approximately 75,000,000 pounds to the owner company Cyprus Asbestos Mines Ltd.

Following a decision by the Council of Ministers in 1992 the exploitation license was annulled and two years later the Council of Ministers determined that the mine should be closed down permanently. In addition, it was decided that environmental reclamation works should commence and that the area of the mine should be developed.

The biggest environmental problem created was the huge crater in the area of the quarry, the extensive piles of debris placed on steep slopes and in valleys as well as the pollution of surface waters and dam catchment areas with asbestos fibres, with possible effect on public health and safety. Work on the restoration of the environment commenced in the year 1996 and included stabilisation and reclamation of the debris as well as re-vegetation and reforestation. Priority was given to the piles of waste, which could under the circumstances impose dangers to the properties situated below the mine. These works are continuing at a steady pace and it is expected that the whole area of the mine will be covered before 2010.

For reforestation purposes 30 different species of plants are being used including perennial herbs, shrubs and trees. The seed is collected from the surrounding forests the object being to create mixed forest plant communities similar to the vegetation of the surrounding area. For reforestation purposes fertile soil will be required to be transported and laid (around one million cubic meters for the whole mine area will be required) and this task is not only costly but it requires specialised techniques as well, and the plants require more care. Works are expected to cost many millions of pounds and the funds will be covered by annual state budget.

In addition to the reclamation works being carried out, the competent state services are considering ways of future development of the mine area for recreation purposes, for tourism and for environmental education. These plans are expected to start being developed when reclamation works are nearly completed."

3. HISTORY OF MINING

Between 1878 and 1904 the British government made several efforts to develop the industrial mining of the asbestos and sent several samples to England for analysis. All these efforts failed because the asbestos fibres were very short and their treatment and commercial use was not at all profitable.

The mining of asbestos in the Troodos Mountain started in 1904 when the industry began to produce asbestos leaves and from raw material with short fibres. The industry began production at very low levels and the methods used were of a very primitive nature. In 1905 a license to mine asbestos was granted by the Government to Cesar Trompeta for 50 years. He transferred the license to an Austrian Company named Compagnia Mineraria di Cipro. In 1919 it was pronounced hostile and the general manager together with other Germans and Austrian technicians were dismissed and exiled from Cyprus. The company changed hands several times and in 1947 it passed to a group of companies from four European countries (Sweden, Britain, Denmark and Ireland). The production gradually increased and the mine developed the capacity to mine 35000 tones of pure asbestos fibres per annum.

The method of mining was of an open cast type as the nature of the rock was such that it did not allow the creation and support of galleries. The mining was carried out with excavators that broke the rock at the side of mountain. This was transported in the two main rippers and from there it was moved by rail to a station where it was kept. Then there was a separation of the thin from the thick materials. The thin material went to a surface area for drying out or to a drying machine. The thick material, which contained very few asbestos fibres, went straight to the waste piles. The waste piles amounted from 3 to 5 million tones per annum.

Following the drying out process there was a separation of the asbestos fibres from the rock and the dust and then a separation into the main types of material (4T, (3S) SR (HSH), 6F, 7M according to an agreed prototype) and put in sacks ready for export.

The transportation of the asbestos fibres during the initial period was carried out by air railway that started from the site of the mine down the side of the mountain and all the way to the company's storage rooms in Limassol and the docks for loading onto the ships.

Our study of the background and history of the asbestos mine was of considerable help as we set about designing the study.

Section 3

Designing the Study

The first stage of our investigation was to design an agreed study protocol with the Ministry of Health. This involved a detailed search of the literature, which is presented in section 4, and a number of meetings with Dr Andreas Georgiou and Professor Julian Peto, a world authority on the health effects of asbestos, who visited Cyprus with the research team to inspect the site. Working within the terms of reference of the study, and taking account of the information we gathered from our preliminary visits to the index villages, we developed a protocol that was agreed by the Ministry of Health. It was agreed that the study should focus on examining differences in health status between those with an occupational or household exposure, compared with non-exposed residents of Kyperounda and Kato Amiandos. The analysis of mortality and hospital activity data would make appropriate geographical comparisons between the index villages and control areas.

1. The investigating team

Dr E S Williams, Consultant in Public Health Medicine and Occupational Medicine, lecturer in epidemiology at St George's Hospital Medical School, London, and Dr Andreas Georgiou, Chief Medical Officer, Consultant in Community Medicine & Hygiene, Occupational Medicine and General Medicine, of the Department of Medical and Public Health Services of the Ministry of Health of the Government of Cyprus, headed the investigating team. Mr Andy Leonidou Consultant in Human Resource Management was responsible for co-ordinating the study. Dr Kevin Carroll, Consultant in Public Health Medicine had specific responsibility for spirometry testing and other respiratory investigations. The investigating team included a Consultant Radiologist, a Specialist Statistician, a Data Manager, Occupational Health Advisor and other supporting Specialist Registrars in Public Health.

The investigating team had access to continuing advice and support from Professor Julian Peto of the Institute of Cancer Research (UK) as well as access to other resources as and when they were needed. Professor Peto is well known as an international expert in cancer epidemiology and has published over 150 research papers on various aspects of cancer epidemiology. He is recognised as a world authority on asbestos, and has published studies on the epidemiology of mesothelioma.

Dr David Furness, Director of the Electron Microscope Unit and Reader of the MacKay Institute of Communication and Neuroscience of Keele University (UK) developed the protocol for animal lung tissue sampling and analysis. It should be noted that Dr Furness formed a research group that build up a state of the art EM techniques and equipment and his department is integral part of the School of Life Sciences at Keele University.

The terms of reference of the study included reviewing the literature on the impact of asbestos fibres on the health of populations in the villages of Kato Amiandos and Kyperounda. Amongst other issues the team undertook to investigate and evaluate medical records that exist in hospitals, clinics, out patient departments, the Central Office of the Public Health Department of the Ministry of Health as well as all available records at the Department of Statistics of the Ministry of Finance such as the Census and Demographic Reports. The investigating team also obtained mortality records from the Ministry of the Interior for the last five years and all available records from the Cancer Registry.

The study would examine the differences in mortality between the local population and national figures, and carry out a comparative study of the health status using medical social questionnaires.

Dr Williams worked closely with Dr Andreas Georgiou, Chief Medical Officer in the Ministry of Health and Consultant in Community Medicine & Hygiene, Occupational Medicine and General Medicine, in designing the study of the health impact of asbestos fibres. In discussions with the Ministry of Health it was agreed that the investigating team needed the collection of preliminary data in designing the study protocol. It was also agreed that local factors should be taken into account in order to be sure that the study addressed the questions that were being investigated. Advanced medical research entails flexibility; therefore the objectives of the study were refined and developed according to the findings aiming at the disclosure of any public health problem.

2. SITE VISITS TO MEET STAKEHOLDERS

The first stage of the investigation was to make a number of site visits to meet all the stakeholders, which would help the investigating team understand the problem in more detail, and so design a more detailed protocol of the study, with the assistance and contribution from Dr A. Georgiou.

The team of research investigator visited Cyprus on a number of occasions for this purpose. The main aim of these visits was two-fold, firstly to find out and gather as much information as possible about potential health problems before designing the study in more detail and secondly to examine in more detail all the sources of available data such as hospital activity, mortality and cancer registry records as well as the latest census and demographic reports. Discussions were held with a wide range of stakeholders, including members of the Ministry of Health, officials from Kyperounda Hospital, local community leaders in the villages of Kyperounda and Kato Amiandos residents in the local area and other interested parties. The purpose of these discussions was to gather as much information as possible that was essential for the development of the protocol for the study.

2.1 Meeting Council leaders of Kyperounda and Kato Amiandos

We held separate meetings respectively with Mr Pelopidas Vasiliades, leader of Kyperounda Council and Mr Kriton Kyriakides, leader of Kato Amiandos Council. The purpose of those meetings was firstly to explain the terms of reference of the study and to seek their co-operation and support and secondly to investigate all the health concerns of the local communities of Kyperounda and Kato Amiandos and incorporate them, as far as possible, into the design of the study.

We explained that we proposed to investigate respiratory health in general and to offer spirometry testing in particular to all residents over the age of 50 and then make comparisons of the differences between those that had been occupationally exposed to the asbestos mines with the non-exposed population. Depending on the outcomes of the spirometry testing we proposed to select a sample and refer them for specific examinations such as X-Ray investigations and other sub clinical or occupational examinations as required.

Both Council Leaders were extremely helpful and supportive to this medical research study and offered us their full co-operation. They provided us with names and addresses of all residents over the age of 50, which enabled us to set up database systems and invite them to attend for spirometry testing.

We also explained that we needed to carry out a census of the local population, primarily to identity individuals who worked in the asbestos mines as well as households that had been exposed to asbestos fibres. In addition we wanted to secure help and support for the distribution and collection of questionnaires relating to medical and social issues.

We sought help from the Council Leaders to identify households in their respective communities who kept animals such as goats or sheep and ask for their permission for the collection and analysis of lung tissue samples for asbestos fibres. We had to explain that this procedure was included in our terms of reference and we proposed to send the samples in specially preserved bottles to a special laboratory in the UK.

2.2 Meeting priest to ascertain death records

We had meetings with the local priest in Kyperounda and were allowed to examine the death and burial records that he kept and match those to other sources of mortality data such as those collected from the Ministry of the Interior. The village of Kato Amiandos does not have their own priest, they have visiting priest instead to perform various church related functions, including burials. Priest records for Kato Amiandos were however collected from the Council Leader and made available to us. We were also able to carry out a census of the cemeteries in the two villages and compare the information collected to priest records.

2.3 Meeting local residents

We met with local residents on a few occasions in both villages to hear their stories of what life was like working in the mines and to explore any health concerns they had. By far the biggest problem described by the residents was related to the dust and the residual respiratory problems that resulted. The residents informed us that there had been a previous study on the health effects on the asbestos mines but they had not been given the results of the study. The local communities asked for assurances that they would be given information on the outcomes of our study and we indicated that we would work with officials from the Ministry of Health to ensure they receive feedback.

From 1956 onwards the company running the mining brought in machinery and the number of people working in the mine was gradually reduced to around 500. Shift working and much improved conditions were introduced from 1960 and by the time the mine closed down in 1988 the actual number of people working at the time was down to 250.

3. Investigating Sources of Data

The second stage of our study was to ascertain the sources of data that were available, and to establish a relationship with key professionals that would assist us by providing us with access to data. To this end we visited a number of key organizations. Our first action was to make a tour of the area around the mine. To gain an impression of the situation on the ground we did a tour of the local area around the asbestos mine to see the remains for ourselves and to assess if there was any current environmental risk from dust.

3.1 Kyperounda and Makarion Hospitals

We visited Kyperounda Hospital and had discussions with key personnel in order to examine the feasibility of obtaining data from their systems on the number of cancer incidents, admission records and examination of old x-rays and hospital heath records as applied to Kyperounda and Kato Amiandos villages. We also visited the Makarion Hospital as it has the main computer centre for the Island and had meetings with the Hospital Director and with Zena Socratous who operates the computer system.

3.2 District Office and Town Hall

We visited these departments to examine the possibility of obtaining information on the registration of deaths, and to investigate the availability of priest records for Kato Amiandos as they were kept there.

3.3 Cancer Registry

We were given information on how the Cancer Registry was set up in Cyprus, how information is collected and how the whole system is managed. The conclusion from this meeting was that it would be possible to make meaningful use of the Cancer Registry data that were collected from year 1998 onwards. The Cancer Registry provided us with an electronic copy of their records from 1998 to 2001 having first obtained permission for the use of the data from the Commissioner of the Data Protection in Cyprus.

3.4 The Ministry of the Interior

We met with officials from the Ministry of the Interior to discuss the system for collecting and collating mortality records. We were given to understand that the system of reporting deaths, recording and collating the information has been refined and it is now much improved. Death records are now fully computerised in the Information Technology Department of the Ministry of the Interior and they provided us with an electronic copy of their records from year 2000 onwards having obtained approval from the Commissioner of Data Protection.

3.5 The Department of Statistics

We held several meeting with officials from the Department of Statistics, situated within the Ministry of Finance. Mrs Chappa and members of her Department were very helpful and provided us with an electronic copy of data from the last census, which was completed in October in 2002, as well as an electronic copy of patient records for the years from 1998 to 2002. They also gave us copies of various statistical reports that were available and copies of demographic reports for the purposes of our study. The Ministry of Health obtained approval from the Commissioner of the Data Protection before the patient records data could be released for research purposes.

3.6 The Government Veterinary Service

We met with Mr Pavlos Tomazos, Veterinary Pathologist of the Public Veterinary Services and secured his help and co-operation in obtaining lung tissue samples from goats preserving them in formalin for transportation to the Electron Microscope Unit of Keele University UK for analysis, in accordance with the protocol developed by Dr David Furness.

3.7 Previous Ministry of Health study

The Ministry of Health carried out a study, which included number of medical examinations for people who worked in the asbestos mine during the period from 2nd April to 23rd June 2000. The number of people examined was 516 and the breakdown of the number in each village is shown in the table below:

Village	Number	Village	Number
Pelendri	175	Spilia	4
Kato Amiandos	56	Kannavia	15
Chandria	12	Potami	7
Agridia	16	Kato Milos	18
Dymes	20	Ayios Ioannis	8
Potamitissa	20	Ayios Theodoros	9
Kakopetria	8	Kaliana	1
Evrichou	4	Ayia Erini	2
Milikouri	4	Kyperounda	86
Agros	28	Limassol town and suburbs	17
Nicosia town and suburbs	6		

We have entered the details of the medical questionnaires into a statistical database system and plan to analyse the results of the questionnaires for the villages of Kato Amiandos and Kyperounda and integrate them into the present study. The results of the questionnaires from other villages would be analysed in subsequent parts of the overall study as and when necessary.

3.8 Cases of mesothelioma

As part of our overall investigation we would hope to identify all the cases of mesothelioma among the population of the two index villages. We would obtain data from the Cancer Registry and identify all the recorded cases of mesothelioma over the last few years. We propose to recruit all the cases of mesothelioma for a subsequent case control study of all mesothelioma cases.

3.9 New Soluble Mesothelin-Related Proteins (SMR) test

Researchers in Australia have developed a new blood test for early detection and diagnosis of mesothelioma. We have exchanged correspondence with Professor Bruce Robinson from the University of Western Australia who led the team of researchers. Professor Robinson indicated that he was hoping to be able to visit Cyprus during the course of our study and advise if we would be able to use the soluble mesothelin-related proteins (SMR) test for a sample of the population in the two villages of Kato Amiandos and Kyperounda. However, regrettably at the time of writing the report Professor Robinson has not been able to visit Cyprus as he had higher priorities in Spain and Turkey and had advised us that he hopes to visit Cyprus during 2005, perhaps around November 2005. Therefore we would propose to postpone this element of the study until such time as the visit from Professor Robinson takes place.

4. AN AGREED PROTOCOL

With the information collected from several site visits and following detailed discussions with Dr Andreas Georgiou, Chief Medical Officer, Consultant in Community Medicine & Hygiene, Occupational Medicine, and General Medicine we were able to produce an agreed protocol. Our initial assessment, following a review of the scientific literature, and an assessment of the environmental information, led us to conclude that the most important areas of investigation were as follows:

4.1 Population Census of Kato Amiandos and Kyperounda

A population census in the village of Kato Amiandos and Kyperounda will be carried out with the aim of identifying the occupational and household exposure history of residents. The basic concept of the study is to ascertain the exposure history and compare health status by exposure group. Therefore, the index population will be grouped according to occupational exposure and household exposure, and the level of asbestos related pathology ascertained in the different groups.

4. 2 Investigation of respiratory health

We agreed to carry out the spirometry testing on all people between the ages of 50 and 75 in Kato Amiandos and Kyperounda. These tests would be carried in morning and afternoon sessions to enable as many people as possible to attend.

4.3 Assessment of mortality

To compare the overall death rate in the population of the two index villages against selected control villages, Limassol district and Cyprus. National age specific death rates will be calculated in order to calculate SMRs in the exposed and control villages. In the subsequent stages of the study, as more village populations are investigated, we will examine the possibility of calculating the life expectancy of exposed and control villages.

4.4 Examination of morbidity using hospital records

Using medical records we plan to identify all respiratory diseases, including chronic obstructive pulmonary disease (COPD), asthma, lung cancers and mesothelioma. Depending on the quality of the data we plan to calculate age standardised admission ratios and indirectly age standardised proportional admission ratios in order to make geographical comparisons. This aspect of the study would be more meaningful as more village populations are included in the study.

4.5 Medical social survey

By undertaking a questionnaire survey and doing a rapid appraisal exercise, we will estimate the perceived health risk to the population. It is now widely recognised that perceived social and psychological risks are important components of any environmental health risk assessment.

4.6 X-ray investigations

A selected sample from the outcomes of the spirometry tests will be referred for X-ray investigations. Depending on the results of the X-ray investigations a number of people might also be referred for further investigations such as MRI, but only if that proves necessary.

4.7 Analysis of lung tissue samples

We aim to collect lung tissue samples from goats and send them to our specially selected laboratories at Keele University for analysis. The three possible techniques that may be used include Phase Contrast Optical Microscopy, Scanning Electron Microscopy and Transmission Electron Microscopy. Asbestos fibre counting and identification will be performed according to agreed European, American or International Standards.

4.8 Analysis of previous study

Data will be entered on a database from the study conducted in 2000 by the Ministry of Health, and we will consider how this data maybe incorporated into the future stages of the study.

4.9 Cases of mesothelioma

To identify the cases of mesothelioma for the subsequent case controlled study.

4.10 The study objective

The main objective of the study was to investigate the health of residents who have had an occupational or household exposure to asbestos, as well as those who have not been exposed to the asbestos mines, in the villages of Kyperounda and Kato Amiandos.

Section 4

Literature Review

1. INTRODUCTION

This chapter examines the scientific literature for evidence of the health effects of exposure to asbestos. As we have studied the literature two things became apparent. First, there are literally many thousands of scientific papers that deal with the health impact of asbestos. For this reason we have tended to focus on review articles which summaries the key research findings. Second, there is an on-going controversy regarding the health risk imposed by chrysotile asbestos. According to the Collegium Ramazzini, an international learned society in environmental and occupational medicine, there should be an immediate worldwide ban on all sales and uses of all forms of asbestos, including chrysotile.[1] However, a Canadian review argues that the weight of the evidence suggests that exposure of the general population to the very low levels of chrysotile that are found in some public buildings (levels not greatly different from ambient air) will never produce mesothelioma, asbestosis, or lung cancer because these diseases all appear to require quite high-level occupational chrysotile exposure.[2]

2. CHARACTERISTICS OF ASBESTOS

The term ‘asbestos’ is not a mineralogical definition but a commercial designation for mineral products that possess high tensile strength, flexibility, resistance to chemical and thermal degradation, and high electrical resistance and that can be woven. So asbestos is a generic name given to a variety of naturally occurring minerals.

Asbestos is a fibrous hydrated magnesium silicate with many commercial uses due to its indestructible nature and fire resistance. The word asbestos is derived from Greek and means inextinguishable. It has been used for many centuries as a wick for oil lamps and as napkins that can be cleansed by fire. The mining and manufacture of asbestos started in the late 19th century. As the commercial value of asbestos became more widely recognised, large deposits of white asbestos (chrysotile) in Canada and Russia, and blue asbestos (crocidolite) in South Africa, were developed. Blue asbestos was first discovered in South Africa in 1805 and within a few years was being mined extensively. Early in the 20th century brown asbestos, named amosite after the village Amosa, was discovered in South Africa. In addition to the crocidolite deposits of the northern Cape, South Africa also has large deposits of white asbestos (chrysotile) and brown asbestos (amosite) both of which have been mined extensively. Mining in South Africa reached its peak in 1977 with more than 380,000 tons being exported and 20,000 miners employed in the industry. Blue asbestos was found and mined in Western Australia in the 1950s. World production of asbestos peaked in 1973, with the largest producers being Russia, South Africa, Canada, China and Brazil. The production and use of asbestos increased greatly between 1877 and 1967. Due to health concerns, production fell by 50% in the 1990s.
At the turn of the 20th century, it was noted that those working with asbestos suffered lung disease. The first case of asbestosis was described in 1924 in a textile worker.[3] In the 1930s and 1940s scientists recognised a casual link between asbestos exposure and asbestosis. In the 1950s and 1960s asbestos was recognised as a predisposing

factor for lung cancer and malignant mesothelioma.[4] In 1960 the link between asbestosis and mesothelioma was established in the Kimberley area of South Africa. Further studies in the 1970s and 1980s showed an alarming incidence of mesothelioma based on pathology reports.[5]

3. Types of asbestos

The minerals that make up asbestos belong to two groups—serpentine (chrysotile) and amphibole (crocidolite, amosite, anthophyllite asbestos, tremolite asbestos and actinolite asbestos). The most common types of fibre are chrysotile (white asbestos), which accounts for 90% of asbestos in commercial use and is a member of the serpentine group. It is a magnesium silicate. Crocidolite, which is a member of the amphibole group, takes the form of blue straight fibres. It is a sodium iron magnesium silicate. Amosite, made up of brown or grey fibres, contains iron and magnesium. Tremolite is a calcium magnesium iron silicate which is white to greyish green and can be found in metamorphic rocks.

Because of its unique physical properties asbestos was extensively used in fireproof textiles and insulation for boilers and pipes. It was also used for yarn, felt, paper, millboard, paints, cloth, filters and wire insulation. More recently asbestos has been used in cement pipes for water, gaskets and brake linings, roofing and floor products.

4. Types of exposure

Primary occupational exposure to asbestos has occurred among those working in asbestos mines, with secondary occupational exposures in manufacturing plants producing textiles, friction materials, tiles and insulation materials. Significant exposure has occurred among asbestos insulators, referred to as laggers in the UK, who mixed asbestos cement on site. Household exposures occurred when asbestos workers returned home in clothes covered in asbestos dust. Wives who washed the dust-covered clothes of their husbands were at particular risk of household exposure. Evidence of domestic exposure among the household contacts of asbestos workers has been well documented. The occurrence of neighbourhood cases (environmental exposure) has also been described in the immediate vicinity of crocidolite mines in South Africa and Australia and of factories that used these fibres in the UK and Germany.[6]

As much as 50 per cent or of inhaled asbestos fibres remain lodged in the lungs, where it is almost impossible for the body to dispose of them. Asbestos fibres are extremely resistant to destruction in body fluids, and many of the fibres are too long to be engulfed and removed by the cells that normally scavenge and remove particles that happen to deposit in the lungs.[7] The International Program on Chemical Safety (IPCS) Task Group, in an evaluation of the health risks of exposure to chrysotile, noted that there is an exposure response relationship for all chrysotile-related diseases. Therefore the reduction of exposure through the introduction of control measures should significantly reduce risks.[8]

Important determinants of asbestos toxicity include exposure concentration, duration and frequency and fibre dimensions and durability. Long thin fibres reach the lower airways and alveolar regions of the lung and are more toxic than short and wide fibres or particles. Wide particles are expected to be deposited in the upper respiratory tract and not to reach the lung and pleura. However, short thin fibres may also play a role in asbestos pathogenesis. Fibres of amphibole asbestos such as tremolite asbestos, actinolite asbestos and crocidolite asbestos are retained longer in the lower respiratory tract than chrysotile fibres of similar dimensions.[9]

Between 1930 and 1959, eight studies were conducted in which friction product manufacturing workers were part of the study population. These studies found evidence of asbestosis among highly exposed workers, but provided little information on the magnitude of exposure. The U.S. Public Health Service proposed the first occupational guidelines for asbestos exposure in 1938. Between 1960 and 1974, a further five epidemiological studies of friction product manufacturing workers were conducted. During this same time period, the initial studies of brake lining wear (dust or debris) emissions reached the conclusion that automobile braking was not a substantial contributor of asbestos fibres greater than 5 microm in length to ambient air.[10]

The causal relationship between asbestos exposure and lung cancer was confirmed in 1955 in asbestos textile workers in the United Kingdom, and later, in 1960, in South Africa, mesothelioma was attributed to asbestos exposure to even relatively low airborne concentrations of crocidolite. A more difficult question is whether cases of mesothelioma are caused by general urban air pollution with asbestos fibres in the industrialised world. McDonald in his review of the epidemiology of mesothelioma in a historical context concludes that there is no direct evidence one way or the other for this hypothetical risk. He argues that exposure response findings in chrysotile miners and millers, and the fact that mortality from mesothelioma in females in the USA and Western Europe has shown no increase during the last three decades, suggests that the risk is probably small and beyond the limits of detection.[11]

5. Health Effects of Exposure to Asbestos

Chronic exposure to asbestos may increase the risk of lung cancer, mesothelioma and non-malignant lung and pleural disorders. Evidence in humans comes from epidemiological studies as well as a number of studies of workers exposed to asbestos in a variety of occupational settings. According to the Agency for Toxic Substances and Disease Registry (ATSDR), diseases from asbestos exposure take a long time to develop. Most cases of asbestosis or lung cancer in asbestos workers occur 15 or 20 years after initial exposure to asbestos.

According to a review by the Unit of Environmental Cancer Epidemiology, International Agency for Research on Cancer, Lyon, France, asbestos causes four diseases in humans: Lung fibrosis (asbestosis) follows heavy exposure and, in industrialised countries, is mainly a relic of past working conditions. The risk of pleural fibrosis and plaques is likely to be linearly dependent from time since first exposure and is present for all types of asbestos fibres. The diagnostic uncertainties regarding pleural plaques and the substantial degree of misclassification make it difficult to precisely estimate the shape of the dose-response relationship. The risk of lung cancer seems to be linearly related to cumulative asbestos exposure, with an estimated increase in risk of 1% for each fibre/ml-year of exposure. All fibre types seem to exert a similar effect on lung cancer risk; a multiplicative interaction with tobacco smoking has been suggested. Pleural mesothelioma is a malignant neoplasm which is specifically associated with asbestos exposure: the risk is linked with the cubic power of time since first exposure, after allowing for a latency period of 10 years, and depends on the fibre type, as the risk is about three times higher for amphiboles as compared to chrysotile. Environmental exposure to asbestos is also associated with mesothelioma risk.[12]

A critical review by the Department of Preventive Medicine in Mount Sinai School of Medicine concluded that chrysotile, which accounts for 99% of current world asbestos production of 2 million tonnes, is an extremely hazardous material. According to the review, clinical and epidemiological studies have established incontrovertibly that chrysotile causes cancer of the lung, malignant mesothelioma of the pleura and peritoneum, cancer of the larynx and certain gastrointestinal cancers. Chrysotile also causes asbestosis, a progressive fibrous disease of the lungs. Risk of these diseases increases with cumulative lifetime exposure to chrysotile and rises also with increasing time interval (latency) since first exposure. Comparative analyses have established that chrysotile is 2 to 4 times less potent than crocidolite asbestos in its ability to cause malignant mesothelioma, but of equal potency of causation of lung cancer.[13]

The International Agency for Research on Cancer of the World Health Organisation has declared chrysotile asbestos a proven human carcinogen. Sales of chrysotile asbestos have virtually ended in Western Europe and North America, because of widespread recognition of its health hazards. However, asbestos sales remain strong in Japan, across Asia and in developing nations worldwide. The claim has been made that chrysotile asbestos can be used safely under certain conditions in those nations. According to the reviewers, that claim is not accurate. The Collegium Ramazzini, an international learned society in environmental and occupational medicine, has called for an immediate worldwide ban on all sales and uses of all forms of asbestos, including chrysotile. The rationale for this ban is threefold: (1) that safer substitute materials are readily available, (2) that controlled use of asbestos is not possible, and (3) that the health risks of asbestos are not acceptable in either the industrialised or the newly industrialising nations.[14]

A Canadian review of asbestos-related disease in the workplace and the environment makes the point that despite the large number of studies into the health effects of asbestos-related diseases, it continues to be sources of controversy for epidemiologist, clinician, and pathologist. A thorough review of over a hundred studies shows that most investigators are agreed that the different fibre types behave differently in the lung, with chrysotile being rapidly removed, and amphibole persisting. These differences in biological behaviour probably account for the much greater disease potential of amphibole (amosite and crocidolite) compared with chrysotile asbestos, particularly in regard to mesothelioma induction in man. Asbestosis is defined as diffuse interstitial fibrosis of the lung caused by asbestos exposure, and this is the only condition to which the term asbestosis should be applied. The classical pathological diagnostic criteria for asbestosis, namely the presence of diffuse interstitial fibrosis resembling usual interstitial pneumonia, and asbestos bodies visible in ordinary tissue sections, have proved to withstand the test of time.[15]

According to the Canadian review there is strong epidemiological and pathological evidence that the only association of asbestos exposure and lung cancer is the association of asbestosis and lung cancer. Thus, a lung cancer should only be attributed to asbestos exposure when asbestosis is present on clinical or pathological grounds. Analytical electron microscopy indicates that chrysotile asbestos does induce mesothelioma in man, but that extremely high levels of retained fibres, levels as high as those seen in cases of asbestosis, are required for this event to occur. The weight of the evidence suggests that exposure of the general population to the very low levels of chrysotile that are found in some public buildings (levels not greatly different from ambient air) will never produce mesothelioma, asbestosis, or lung cancer because these diseases all appear to require quite high-level occupational chrysotile exposure. Even if one accepts the ideas (probably wrong) that any level of asbestos exposure carries a risk of cancer, and that mathematical extrapolation of risk from high-level occupational exposure to low-level building exposure is scientifically valid, the calculated risks are much smaller than real everyday risks such as driving to work. Thus, exposure to asbestos at environmental levels appears to produce no real dangers to health.[16]

According to Becklake, writing in the Annals of Occupational Hygiene, the non-malignant respiratory conditions associated with exposure to environments contaminated by chrysotile asbestos dust includes pulmonary parenchymal and pleural fibrosis, small airway abnormality and conditions affecting the large airways such as chronic bronchitis and chronic airflow limitation. The first two are attributed to the specific biological effects of asbestos dust, the latter two to non-specific effects of exposure to mineral dusts and/or other airborne pollutants in workplaces contaminated by asbestos dust.[17]

Prevalence rates for all the clinical markers of morbidity (radiographic change, lung function deficit and symptoms) have been shown to increase with increasing exposure to chrysotile but more steeply when exposure is in textile and other manufacturing plants than in mining and milling. The presence of amphiboles such as tremolite in the airborne dust may also result in steeper exposure-response relationships, while exposure in crocidolite mining results in very much steeper exposure-response relationships. Clinical asbestosis, though less frequent and less severe than previously, is still associated with increased morbidity, while localized pleural fibrosis in the form of plaques with minimal or no parenchymal fibrosis, currently the most frequently encountered non-malignant asbestos related condition encountered in clinical practice, may also be associated with morbidity, including lung function deficit. Progression of asbestos-related airway disease, documented as lung function loss over time, may, under the influence of continued exposure, be comparable to the progression observed under the influence of continued smoking.[18]

5.1 Pleural disease

Pleural disease is the most common disorder associated with asbestos exposure. Hyaline and calcified pleural plaques were found in the 1960s to be an index of exposure to asbestos. Shipyard workers were found to have a tenfold great incidence of pleural abnormalities than parenchymal disease.[19] Among British shipyard workers, 36% of the laggers with continuous exposure developed pleural plaques, extensive pleural thickening (5%) or pulmonary fibrosis (7%). Among those who were continuously exposed for 30 years, 70% has pleural plagues. A study of shipyard workers in Connecticut showed that 17% those with pleural changes (without other signs of lung disease) had reduced forced vital capacity (FCV<80% of predicted).[20] Other epidemiological studies have shown that the forced expiratory volume and the forced vital capacity are reduced in non-smoking asbestos workers with pleural plaques.[21,22]

Asbestos-induced pleural fibrosis is the most common radiographic abnormality among asbestos-exposed persons. Circumscribed pleural plaques and diffuse pleural thickening account for more than 90% of the asbestos-induced chest wall abnormalities, and their prevalence is expected to increase for the next 15 to 20 years. Several investigators have recently found that pleural plaques and diffuse pleural thickening independently contribute to the development of restrictive lung function. Asbestos-induced pleural fibrosis is also associated with evidence of interstitial lung abnormalities, even among those with normal parenchyma on chest X-ray film. However, neither a lymphocytic alveolitis nor an interstitial parenchymal fibrosis influenced the relationship between pleural fibrosis and restrictive lung function. The above findings suggest that asbestos-induced pleural disease contributes to the development of restrictive lung function.[23]

A study of over a thousand sheet metal workers occupationally exposed to asbestos reported pleural fibrosis in around 30%. After controlling for a number of confounding factors, a multivariate regression found that both plaques and diffuse pleural thickening were independently associated with a decrease in FVC, but not with a decrease in the FEV1/FVC ratio.[24] A study of a group of construction insulators exposed to asbestos showed that those who had pleural plaques with diffuse pleural fibrosis had a significantly decreases in FEV1 and FVC.[25]

The pathogenesis of asbestos-induced pleural diseases has been subject to extensive investigation. Asbestos fibres can provoke pleural inflammation from direct toxicity to mesothelial cells. Inhaled asbestos fibres can also elicit pleural injury indirectly via the release of growth factors and inflammatory cytokines from within the lung. Although progress has been made in the understanding of the mechanisms of asbestos pleural injury, many important questions remain unanswered. The role of genetic factors and possible environmental co-factors in the pathogenesis of benign asbestos pleural diseases requires further research.[26]

5.2 Asbestosis

Asbestosis is a serious, progressive, long-term disease of the lungs. According to the American Thoracic Society it is defined as parenchymal fibrosis with or without pleural thickening and is usually associated with dyspnoea, bibasilar crackles and pulmonary function changes.[27] Because the development of asbestosis is dose dependent, symptoms appear only after a latent period of 20 years or longer, although the latent period may be shorter after intense exposure.[28] Inhaling asbestos fibres irritates and inflames lung tissues. Inhaled asbestos fibres deposit at airway junctions and respiratory bronchioles. Asbestosis tends to be patchy in that the fibrosis tends to affect the lower lobes and sub-pleural regions of the lungs. Early lesions are characterised by discrete areas of fibrosis in the walls of respiratory bronchioles, which sometimes are accompanied by asbestos bodies. In addition to peri-bronchiolar fibrosis, there is an intense cellular reaction that may narrow and obstruct the airway lumen.

Asbestos bodies are characteristically observed in tissue sections of the lung. The number of bodies per gram dry lung tissue in the general population is generally fewer than 500, but twice as many are found in the lungs of blue-collar workers. Persons with pleural plaques have 10,000 to 20,000 bodies per gram and persons with parenchymal asbestosis more than 100,000.[29]

The prevalence of asbestosis is strongly related to the length of the exposure. One of the early epidemiological studies analysed chest X-Rays of asbestos insulation workers and found asbestosis in 10% of those who worked 0-9 years, 44% of those who worked 10-19 years and 73% of who worked 20-29 years, and around 90% of those who worked over 30 years.[30] A British study showed that both current smokers and ex-smokers had a higher prevalence of asbestos related radiological changes than non-smokers in shipyard workers.[31]

A large study evaluated radiographic changes among sheet-metal workers who were occupationally exposed to asbestos for at least 20 years. An overall prevalence of asbestos-related changes on X-ray was found in 31% of workers, 19% with pleural abnormalities and 12% with parenchymal abnormalities. Among those with 40 or more years' exposure, 41.5% had radiographic signs of asbestos-related disease.[32]

The characteristic pulmonary function changes of asbestosis are a restrictive impairment with a reduction in lung volumes, especially the FVC. Large airway function, as reflected in the FEV1/FVC ratio, is generally well preserved.

5.3 Mesothelioma

The observation that mesothelioma resulted from occupational exposure to asbestos was first reported in Britain in 1935.[33] In 1952, a Canadian industrial medical clinic reported a case series which contained two cases of pleural tumours from among 8 respiratory cancers. In 1960, Wagner and colleagues reported the first case series of malignant mesothelioma.[34] Their series consisted of 33 cases, 28 who were exposed in the crocidolite-mining region in the Northern Cape and 4 who were exposed in asbestos factories. They reported that mesothelioma occurred 20 to 40 years after exposure to asbestos dust.[35] Wagner was of the opinion that crocidolite asbestos was the major asbestos type that could cause mesothelioma.

In the USA Selikoff and colleagues investigated the question whether other types of asbestos were also a cause of mesothelioma. They examined over 2,000 autopsies between 1953 and 1964 and found 26 cases of asbestosis and 7 cases of malignant mesothelioma. Studying the mortality records of asbestos insulators over a 20-year period, they also found 10 cases of mesothelioma as the cause of death among 307 consecutive asbestos insulator deaths. They concluded that malignant mesothelioma was a risk for asbestos exposure in general, and confirmed that indirect exposure could also be important, and claimed that chrysotile/amosite asbestos could also be a major risk factor for mesothelioma.[36]

In 1965 a Working Group under the auspices of the Internal Union against Cancer reviewed a number of case control studies which showed a link between asbestos and mesothelioma and emphasised the need for more extensive epidemiological studies on the importance of the type of asbestos fibre.[37] As fibre of more than one type of asbestos was almost always used in manufacture it was suggested that research should concentrate on countries where it was mined or milled as the problem of mixed exposures might be less serious.[38]

A Canadian study examined 30,000 current and previous employees of the extensive chrysotile mines and mills of Quebec who had worked for at least one month in the industry. Mortality was investigated in a cohort born 1891-1920. Among 2,413 male deaths in the cohort to the end of 1966, there was a modest, exposure-related excess of lung cancer but only three deaths were from mesothelioma.[39] The implication of this study was that the risk of mesothelioma from exposure to chrysotile was relatively small.

Mortality studies show a steep rise in mortality from mesothelioma, which began in the 1940s and is well explained as reflecting a parallel increase in the industrial use of asbestos from about 1910, assuming a 30 to 40 year latency period.[40] As a result of this increase, mesothelioma is currently estimated to be responsible for 20 deaths per million male population in Western Europe and the USA. This compares with an estimated death rate of 1 or 2 per million 30 years ago. As the epidemic has unfolded in the UK, the overall distribution of occupations which have been responsible has remained the same but there is evidence that the contribution of work in shipyards has fallen while work in construction has increased.[41]

In 1980 Peto reported on the incidence of pleural mesothelioma in asbestos textile workers in relation to age, time since first exposure, intensity of exposure and period of observation. His research suggested that the recent marked increase in recorded rates of mesothelioma is real and not merely a diagnostic artefact. The risk did not appear to have been much higher among men who were initially very heavily exposed. One possible explanation of this surprising observation is that chrysotile is eliminated, or ceases to be biologically active, more quickly than other types of asbestos.[42]

A review of the carcinogenicity of mineral fibres, notably asbestos, reported in Environmental Health Perspectives (1986) concluded the mineral fibres represent the greatest cause—after cigarette smoke—of respiratory cancer due to air pollutants. Past asbestos exposure may currently account for 2000 mesothelioma deaths per year and 4000 to 6000 lung cancer deaths per year. All major commercial types of asbestos (crocidolite, amosite, and chrysotile) can cause each of the major asbestos-related respiratory diseases.[43]

A cohort mortality study of chrysotile miners employed since 1946 in Balangero, northern Italy was updated to the end of 1987, giving a total of 427 deaths out of 27,010 man-years at risk. A substantial excess mortality for all causes (standardised mortality ratio (SMR) = 149) was found, mainly because of high rates for some alcohol related deaths (hepatic cirrhosis, accidents). For mortality from cancer, however, the number of observed deaths (82) was close to that expected (76.2). Although part of the excess mortality from laryngeal cancer is probably attributable to high alcohol consumption in this group of workers, the data suggest that exposure to chrysotile asbestos (or to the fibre balangeroite that accounts for 0.2-0.5% of total mass in the mine) is associated with some, however moderate, excess risk of laryngeal cancer and pleural mesothelioma. The absence of excess mortality from lung cancer in this cohort is difficult to interpret.[44]

Peto et al, of the Institute of Cancer Research (UK), analysed mesothelioma mortality since 1968 to assess the state of the mesothelioma epidemic, and to predict its future course. They found that rates of mesothelioma in men formed a clear pattern defined by age and date of birth. Rates rose steeply with age showing a very similar pattern in all five-year birth cohorts. Combining projections for all cohorts resulted in a peak of annual male mesothelioma deaths in about the year 2020 of between 2,700 and 3,300 deaths. If diagnostic trend is responsible for a 20% growth in recorded cases every 5 years, an extreme but arguable case, and if this trend has now ceased, the peak of annual male deaths will be reduced to 1300, reached around the year 2010. Analysis of occupations recorded on death certificates indicated that building workers, especially plumbers and gas fitters, carpenters and electricians are the largest high-risk group. These data indicate that mesothelioma deaths will continue to increase for at least 15 and more likely 25 years. For the worst affected cohorts, that is men born in the 1940s, mesothelioma may account for around 1% of all deaths. Asbestos exposure at work in construction and building maintenance will account for a large proportion of these deaths, and it is important that such workers should be aware of the risks and take appropriate precautions.[45]

In 1999 Peto commented again on the European mesothelioma epidemic, revising upward previous projected death rates. Projections for the period 1995-2029 suggest that the number of men dying from mesothelioma in Western Europe each year will almost double over the next 20 years, from 5,000 in 1998 to about 9,000 around 2018, and then decline, with a total of about a quarter of a million deaths over the next 35 years. The highest risk will be suffered by men born around 1945-50, of whom about 1 in 150 will die of mesothelioma. Asbestos use in Western Europe remained high until 1980, and substantial quantities are still used in several European countries. These projections are based on the fit of a simple age and birth cohort model to male pleural cancer mortality from 1970 to 1989 for six countries (Britain, France, Germany, Italy, The Netherlands and Switzerland) which together account for three-quarters of the population of Western Europe.[46]

A cohort analysis of pleural cancer mortality in Europe used death certification data from eight European countries over the period 1970-1994. Cohort effects were steadily and appreciably upwards in all countries up to the generations born in 1940 or 1945, and levelled off for the 1950 cohort, except in Hungary, where persistent rises were observed. Thus, most rises in pleural cancer mortality in Europe were on a cohort of birth basis. Since most pleural cases were asbestos-related mesothelioma, and since asbestos has an early-stage effect on subsequent mesothelioma risk, exposure early in life is important for determining the subsequent mesothelioma risk of each generation. Consequently, the data indicate that the peak mortality from pleural cancer in most western European countries will be reached in the first decades of the 21st century, that is around 2010-2020, when the generations born between 1940 and 1950 will reach the peak age for mesothelioma incidence and mortality. This contrasts with US data, where the peak of pleural cancer incidence has been reached at the end of the 20th century, and reflects a delay in adopting adequate prevention measures since the 1940-1945 generations entered the workforce in the 1960s, when cancer risk from asbestos exposure was already recognized.[47]

An important question remains how long the epidemic can be expected to last? From estimates of the industrial use of asbestos it seems possible that the peak in the USA might have already been reached in 2000, with an expected gradual decline over the next 40 years.[48] However, as we have seen above the more sophisticated analysis by Prof. Julian Peto, the expert who is providing advice to our research team, suggests that the peak in Europe may not be reached until 2010-2020.[49]

5.4 Mesothelioma in South Africa

To estimate incidence of mesothelioma in the Republic of South Africa (RSA), a case register was compiled for the period 1976-84 by contacting all medical practitioners and institutions likely to have seen cases in this period. Demographic, diagnostic and exposure details were sought and cases were accepted if they were histologically confirmed. Of the of 1347 cases ascertained, 52% were white, 31% black African, 16% mixed race and 1% Asian. Almost three-quarter (73%) were males. The ratio of only pleural to only peritoneal mesothelioma was 11:1, although there were differences by race. A large majority of males (85%), with an exposure history, had prior exposure to asbestos, mostly occupational. A similar proportion of women had contact with asbestos but mostly through other types of exposure.

Standardised incidence rates per million population aged 15 years and over, calculated for sex-race subgroups, were highest in white males (32.9 per million per year, 95% CI 22.7-46.4), mixed race males (24.8 per million per year, 95% CI 6.2-36.9) and mixed race females (13.9 per million per year, 95% CI 7.7-23.5). These incidence rates are amongst the highest ever reported for a national population. Age-specific standardised incidence rates were highest in white males (over 100 per million, per year, in men over 55 years). Reasons for the differing rates by population group are likely to include differential access to health services. More rigorous control of asbestos exposure in the RSA is recommended.[50]

A multi-centred case-control study described the exposure experiences of South African mesothelioma cases, with emphasis on the contribution made to the caseload by different fibre types, the proportion of subjects with no recall of asbestos exposure and only environmental contact, and the importance of putative causes other than asbestos. Interviews were conducted with 123 patients with mesothelioma by trained interviewers in study centres established in Johannesburg, Kimberley, Pretoria, Bloemfontein, Cape Town and Port Elizabeth.

Results showed a convincing history of asbestos exposure in the overwhelming majority of cases (only 5 cases had unlikely asbestos exposure). Twenty-three subjects had worked on Cape crocidolite mines, 3 at Penge (an amosite mine), 3 on mines producing amosite and Transvaal crocidolite and 1 on a Transvaal crocidolite mine. Exclusively environmental exposure accounted for at least 18% of cases, the large majority of whom (20/22 subjects) had had contact with Cape crocidolite. There was a relative paucity of cases linked to amosite and no convincing chrysotile case. Non-asbestos causes occur rarely, if at all, in South Africa. The researchers concluded that the preponderance of crocidolite cases, followed by amosite and then chrysotile cases, is consistent with the view that there is a fibre gradient for mesothelioma risk potential for South African asbestos (crocidolite > amosite > chrysotile).[51]

5.5 Mesothelioma in Cyprus and other countries

A previous epidemiological survey has shown that several forms of asbestos occurred naturally. In Cyprus a research study into mesothelioma identified that both chrysotile and tremolite in domestic and environmental samples throughout the mountain region. The study of mesothelioma showed that 5 of 13 had no known contact with the asbestos mine. The authors concluded that evidence was accumulating which suggests that naturally occurring tremolite may be causing disease in the Troodos region of Cyprus.[52] The most recent records of the Cyprus Cancer Registry revealed that there have been 17 mesothelioma cases during the period 1998 to 2002.

A review of research in New Zealand by the National Centre for Epidemiology and Population Health concluded that there was a big asbestos disease problem. The lack of action on warnings in the 1960s and 1970s has led to epidemics of mesothelioma and asbestosis, which can be clearly documented via the death and cancer registers. In addition, an uncertain number of lung cancers due to asbestos exposure have occurred. The epidemic started in the 1980s, and it is estimated that it eventually has cost the lives of at least 2000 to 3000 workers.[53]

A paper on asbestos related disease and compensation in the Netherlands reported that the number of asbestos-related diseases is increasing. An age-cohort model predicts a steep rise in pleural mesothelioma deaths up to 490 cases per year among men; with a total death toll close over 12,000 cases during 2000-2028. In the past decade the number of compensation claims for asbestos-related diseases has more than doubled, with increasing verdicts in favour of claimants.[54]

5.6 Lung Cancer

A British review of the relationship between asbestos exposure, lung cancer and asbestosis, examined 45 research papers. The evidence showed that the risk of lung cancer was raised in asbestos-exposed workers whether asbestosis is present or not. Although increasing exposure increases the risk of disease, variability in estimation of fibre levels and in subject susceptibility should be borne in mind. Consensus opinion recommends that attribution of lung cancer to asbestos exposure should be based on clinical and occupational histories. According to the evidence the risk of lung cancer in those who both smoke and are exposed to asbestos is increased in a multiplicative way, putting subjects at very great risk.[55]

A Swedish review of over a hundred studies concluded that the inhalation of asbestos fibres increases the risk of bronchial carcinoma. It has been claimed that asbestosis is a necessary prerequisite for the malignancy, but epidemiological studies usually do not have enough statistical strength to prove that asbestos-exposed patients without asbestosis are without risk. Several recent studies do actually indicate that there is a risk for such patients. In addition, case-referent studies of patients with lung cancer show an attributable risk for asbestos of 6% to 23%, which is much higher than the actual occurrence of asbestosis among these patients. Thus there is an increasing body of evidence that, at low exposure levels, asbestos produces a slight increase in the relative risk of lung cancer even in the absence of asbestosis. Consequently, the authors conclude that all exposure to asbestos must be minimized.[56]

A large number of cohort studies have reported on the relative risk of acquiring lung cancer and mesothelioma from different fibres types. The table is derived from McDonald’s historical review of mesothelioma. The large Canadian cohort study, which first reported in 1971, had been followed up and recent data showed that almost 80% of the cohort had died. The lung cancer SMR suggests that the risk for chrysotile exposure is relatively small.

From a total of around 8,000 deaths, only 38 were due to mesothelioma – a proportional mortality of only 0.5%. Proportional mortality rates (PMRs) are a very crude indicator of risk since they do not take levels of exposure or competing causes of death into account. The South African and Australian data shows high proportional mortality rates associated with crocidolite. (Note that these rates are derived from a relatively small percentage of deaths in the cohort.) Nevertheless the data in Table 1 (over page) leaves little doubt that crocidolite carries a much higher risk than chrysotile, with amosite and tremolite somewhere in between.

The School of Public Health of the University of Sydney examined the ratio of the relative risk of lung cancer due to asbestos exposure in smokers and non-smokers. The researchers concluded that the excess relative risk of lung cancer from asbestos exposure is about three times higher in non-smokers than in smokers. The modified measure has been placed within a more versatile model of interaction. If interaction is present the relative risk from asbestos exposure changes only slightly between light and heavy smokers, but is higher in very light smokers and non-smokers. The relative risk estimated from epidemiological studies of a mixed population of non-smokers and smokers applies to smokers.[57]

Table 1 Cohort studies of male asbestos miners and millers:
Standardised mortality rates and proportional mortality per 1000

Year	Country	Subjects	Fibre	Deaths					
				All cause		Lung cancer		Mesothelioma	
				N	%	N	SMR	N	PMR/1000
1993	Canada	10918	Chrysotile	7312	67	545	1.33	33	4.5
1990	Italy	952	Chrysotile	427	45	22	1.11	2	4.7
1992	RSA	3212	Amosite	648	20	26	1.33	4	6.2
	RSA	3430	Crocidolite	423	12	27	2.03	20	47.3
1988	Australia	6505	Crocidolite	820	13	91	2.64	32	39.0
1986	USA	406	Tremolite	165	41	21	2.45	4	24.2

Airborne fibres of tremolite have been shown to constitute an environmental hazard in Libby, Montana, northern California. The Imperial College School of Medicine, London set up a study to determine excess risk from lung cancer, mesothelioma, and all-cause mortality in a cohort of men exposed to tremolite, but no other form of asbestos. Mortality by certified cause and various measures of exposure to tremolite and related amphibole fibres was assessed in a cohort of 406 vermiculite mineworkers in Libby, Montana, employed before 1963 and followed up until 1999. The results were as follows. There were a total of 285 all cause deaths (SMR 1.27). There were 44 lung cancer deaths (SMR 2.40), 51 non-malignant respiratory disease (SMR 3.09) and 12 deaths ascribed to mesothelioma (4.21% of all deaths). The study concluded that the all-cause linear model would imply a 14% increase in mortality for mine workers exposed occupationally to 100 fibres per ml per year or about 3.2% for a general population exposed for 50 years to an ambient concentration of 0.1 fibres per ml. The study concludes that amphibole fibres, tremolite in particular, are likely to be disproportionately responsible for cancer mortality in persons exposed to commercial chrysotile, but to what extent cannot be readily assessed.[58]

5.7 Asbestos hazard

All forms of asbestos may cause pulmonary fibrosis, lung cancer and mesothelioma, but the degree of hazard depends on fibre type (greater with amphiboles than with chrysotile) and on the fibre size distribution (long fibres more hazardous than short). From this it is apparent that meaningful comparisons of the incidence of disease

observed in different occupational cohorts should take careful account of differences not just in fibre type, but also in the airborne fibre size distributions.
There appears to be an association between pulmonary fibrosis and lung cancer in that both diseases show a similar dose-response relationship with respect to asbestos exposure, show similar latent periods for development, show a similar dependence on fibre type and size, and both diseases emanate from the same underlying chronic inflammatory condition. These observations suggest that asbestos-induced lung cancer, like fibrosis, is a threshold phenomenon. It can be concluded that exposures which are insufficient to elicit chronic inflammation/cell proliferation (manifest for example, as alveolar Type II cell hyperplasia or fibrosis) will not incur any increased risk of lung cancer.

Very few cases of mesothelioma can be reliably attributed to chrysotile despite the many thousands of workers who have had massive and prolonged exposures to this type of asbestos. In contrast, mesothelioma has been observed among some workers who experienced only brief exposures to amphiboles. These differences are most likely explained by the limited durability of chrysotile in the lungs, in contrast to the amphiboles which are more persistent. It would appear that for a fixed level of exposure, the risk of developing mesothelioma is much greater for amphiboles than for chrysotile.

Evidence from human studies suggests that amphibole asbestos may lead to the development of mesothelioma at lower levels of cumulative exposure than would be required to cause lung cancer. However, no reliable exposure-response curve can be constructed for asbestos-induced mesothelioma either in animals or in humans, and although a threshold could be postulated on theoretical grounds, the available data do not allow the identification of a threshold level of exposure below which there would be no risk.

6. COMMENTS

1. While the health impact of asbestos is well documented, there is still a controversy over the extent of the carcinogenic risk imposed by chrysotile. One view is that all asbestos, including chrysotile, is so dangerous that its commercial use should be banned. Another view is that carcinogenic risk from chrysotile is similar to that of cigarette smoking.

2. The mesothelioma risk from chrysotile is well established, although the relative risk is far less than the risk imposed by crocidolite asbestos (blue asbestos). Sophisticated cohort analysis of death rates by Professor Julian Peto predicts an epidemic of mesothelioma deaths in Europe that will peak sometime in the next decade.

3. There is clear evidence that asbestos dust is associated with pulmonary fibrosis and pleural plaques that produce a restrictive lung disorder which can be measured by a reduction in the forced vital capacity (FVC) and forced expiratory volume in one second (FEV1).

4. Cigarette smoking increases the risk of respiratory problems among those exposed to asbestos. Some research suggests that the effect is multiplicative, while others argue that the effect is summative.

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Section 5

Census of Kyperounda and Kato Amiandos

The 2001 national census recorded the number of households in Kyperounda as 456 and the population as 1,497. In Kato Amiandos there were 80 households with a population of 219. Table 1 shows the age-sex breakdown of Kypertounda.

Table 1 Age sex structure of Kyperounda: 2001 Census

	Males		Females		Persons	
Age group	n	(%)	n	(%)	n	(%)
0-4 years	70	(9.6)	46	(6.0)	116	(7.7)
5-14 years	107	(14.6)	123	(16.0)	230	(15.4)
15-24 years	101	(13.8)	107	(14.0)	208	(13.9)
25-34 years	80	(10.9)	99	(12.9)	179	(12.0)
35-44 years	102	(13.9)	85	(11.1)	187	(12.5)
45-54 years	84	(11.5)	78	(10.2)	162	(10.8)
55-64 years	73	(10.0)	90	(11.8)	163	(10.9)
65-74 years	64	(8.7)	79	(10.3)	143	(9.6)
75- and over	51	(7.0)	58	(7.6)	109	(7.3)
All years	732	(100)	765	(100)	1497	(100)

In Kyperounda the number of people aged 50 and over were 224 men and 263 women, giving a total of 487 persons, that is 32.5% of the population. The proportion of children under 14 was 23.1%, that is just under a quarter of the population. Table 2 shows the age-sex structure of Kato Amiandos as recorded in the 2001 national census. In Kato Amiandos the number of people aged 50 and over were men 51 and women 57, giving a total number of 108 persons, or 49% of the population. The proportion of children under 14 was 15.5%.

Table 2 Age sex structure of Kato Amiandos: 2001 Census

Age group	Males		Females		Persons	
	n	(%)	n	(%)	n	(%)
0-4 years	3	(2.8)	5	(4.4)	8	(3.6)
5-14 years	12	(11.3)	14	(12.4)	26	(11.9)
15-24 years	8	(7.5)	14	(12.4)	22	(10.0)
25-34 years	12	(11.3)	10	(8.8)	22	(10.0)
35-44 years	13	(12.3)	8	(7.1)	21	(9.6)
45-54 years	16	15.1)	14	(12.4)	30	(13.7)
55-64 years	18	(17.0)	20	(17.7)	38	(17.4)
65-74 years	15	(14.2)	18	(15.9)	33	(15.1)
75-and over	9	(8.4)	10	(8.8)	19	(8.7)
All years	106	(100)	113	(100)	219	(100)

A local census of households

To ascertain the level of occupational exposure by household, we conducted a local census of the two villages. Information for the local census was gathered from a subset of the population who attended for spirometry. This data was supplemented with data from a telephone interview of households and local interviews with the residents of the two villages. From this data we were able to calculate the proportion of households that had been occupationally exposed within the two villages. The response rate to our local census was 79%.

Occupational exposure

Table 3 shows occupational exposure of households in Kyperounda.

Table 3 Occupational exposure of households in Kyperounda

	Exposed		Non-exposed		All households	
Age group of head of household	(%)	n	(%)	n	(%)	n
20-49 yrs	12.7	21	87.3	144	100	165
50-74 yrs	56.1	96	43.9	75	100	171
75 and over	83.0	39	17.0	8	100	47
All ages	40.7	156	59.3	227	100	383

As expected there is a strong age effect on occupational exposure. In households with a head aged 75 and over, the vast majority (83%) reported that they had worked on the mine, and among those in the 50-74 age group, over half (56.1%) had been occupationally exposed. Among all ages, 40.7% of households in Kyperounda have been occupationally exposed. Table 4 shows occupational exposure for households in Kato Amiandos. The proportion of households with an exposure to the asbestos mine in Kato Amiandos is 67.1% compared to 40.7% in Kyperounda. This is undoubtedly explained by the nearer proximity of Kato Amiandos to the mine. Of the households that had experienced occupational exposure 24% had been exposed for over 20 years and a further 20% for between 10 and 19 years.

Table 4 Occupational exposure of households in Kato Amiandos

	Exposed		Non-exposed		All households	
Age group of head of household	(%)	n	(%)	n	(%)	n
20-49 yrs	0	0	100	3	100	3
50-74 yrs	72.7	40	27.3	15	100	55
75 and over	61.1	11	38.9	7	100	18
All ages	67.1	51	32.9	25	100	76

Section 6

Spirometry in Kyperounda and Kato Amiandos

1. INTRODUCTION

There is a large body of evidence which shows that exposure to chrysotile asbestos is associated with non-malignant respiratory conditions, including pulmonary parenchymal and pleural fibrosis, small airways abnormality and conditions affecting the large airways, such as chronic bronchitis and chronic airflow limitation. Prevalence rates for respiratory symptoms have been shown to increase with increasing exposure to chrysotile.

Epidemiological research has demonstrated that the presence of amphiboles, such as tremolite in the airborne dust, may also result in steeper exposure-response relationships, while exposure in crocidolite mining results in very much steeper exposure-response relationships. Clinical asbestosis is associated with increased morbidity, while localised pleural plaques may also be associated with morbidity, including lung function deficit. There is evidence to suggest that the progression of asbestos-related airways disease, may, under the influence of continued exposure, be comparable to the progression observed under the influence of continued smoking.[1]

A Taiwan study conducted a cross-sectional health survey of 459 workers in 33 asbestos-related factories to determine the prevalence of asbestos-related lung disease and the impairment of lung function among asbestos workers. Similar to our study, each worker was asked about his medical and occupational history and was given a medical examination, chest X-ray and pulmonary function test. An analysis of the pulmonary function test showed that both forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) decreased significantly with an increasing cumulative dose of exposure after controlling for age, height and smoking effects during analysis. However, the FEV1/FVC ratio and FEF 25-75% were not affected by exposure dose. The authors concluded that among workers in Taiwan, there is a significant effect on the respiratory system, especially pulmonary function, due to asbestos exposure.[2]

There is evidence that asbestos-induced pleural disease contributes to the development of restrictive lung function which helps to identify exposed individuals who are at excess risk of asbestosis.[3]

A study to assess the contribution of smoking to functional abnormalities in a group of asbestos-exposed shipyard workers compared 73 workers who never smoked with 73 current smokers. Pulmonary function was compared between the 2 groups. Non-smokers had significantly higher FVC, FEV1, and FEV1/FVC than did smokers. The researchers conclude that cigarette smoking was the major contributing factor to the obstructive lung disease observed in asbestos workers, and it also had a strong influence on the occurrence, nature, and magnitude of exercise limitation. The researchers concluded that the history of cigarette smoking has an important effect on the assessment of impairment from asbestos.[4]

A study conducted by the University of Southern California School of Medicine, Environmental Sciences Laboratory, Los Angeles set out to define the apparent steps in developing airways obstruction and restrictive lung disease in men exposed to asbestos for more than 20 years. Workers who had never smoked were compared with cigarette smokers. Spirometry was used to measure the FVC, FEV1, FEF25-75, and FEF75-85. The study compared mean expiratory flows and lung volumes in 1,146 men with pulmonary asbestosis age matched to 1,146 men without asbestosis who had a similar duration of asbestos exposure, and to 370 men without asbestos exposure. The study concluded that asbestos exposure reduced flows and produced air trapping after 20 years in workers who never smoked. Smoking increased these abnormalities.[5]

A study conducted by the Occupational and Environmental Medicine Program, University of Washington had the objective of determining whether respiratory symptoms are associated with diminished pulmonary function. Symptoms reported on the American Thoracic Society (ATS-DLD-78A) questionnaire were correlated with measured spirometric volumes in 816 asbestos-exposed workers. Cough, phlegm, wheeze, and dyspnoea were inversely related to pulmonary function. Cough, phlegm, and chronic bronchitis were associated with a 2% to 8% reduction in predicted values for forced vital capacity (FVC) and forced expiratory volume (FEV1); wheeze and dyspnoea were clinically more significant, with an 11% to 17% reduction. Wheeze, dyspnoea, and fibrosis were all significant independent predictors of risk for restrictive impairment. The results support the validity of the ATS questionnaire as an epidemiological tool and emphasise the importance of clinical history in assessing respiratory status.[6]

2. THE TARGET POPULATION

The objective of the study is to investigate the respiratory health of those residents who have had an occupational or household exposure to asbestos. The underlying hypothesis is that prolonged exposure to asbestos would cause to a significant decline in the respiratory health of the exposed population. The asbestos mine closed 16 years ago (1988), and, in that most people would have been at least 20 years of age when they started working on the mine, we concluded that the cohort aged 50 years and over would have experienced the highest levels of exposure. Spirometry therefore was targeted on residents in the age range 50 to 75 years.

3. THE AIM OF THE STUDY

The aim of the investigation was to determine if occupational and household exposures to asbestos have had a measurable effect on the respiratory function of the population living in the villages of Kyperounda and Kato Amiandos. To this end it was necessary to ascertain the exposure rate of residents in the two villages. The study was designed, therefore, to compare the lung function of the exposed population with non-exposed controls.

4. MEASURING RESPIRATORY FUNCTION

Spirometry aims to measure the performance of the respiratory system by measuring expiratory volumes and flow rates. It is a test that requires maximum co-operation from a patient, as they must make a maximal inspiratory and expiratory effort. It is essential that a patient gives full effort, and failure to do so causes unreliable results. In other words, the test is heavily dependent on a resident's technique and effort.

Spirometry is usually reported in both absolute values and as a predicted percentage of normal. Normal values vary according to sex, age, and size.

The two most common spirometry measures are:

1. The forced vital capacity (FVC). This is the maximum volume of air that can be forcibly and rapidly exhaled following a maximum inspiration. It is the basic manoeuvre in spirometry testing.
2. The forced expiratory volume in one second (FEV1). This is the total amount of air that can be forcibly exhaled within one second starting from a full inspiration. With normal lungs and airways a healthy person can normally blow out most of the air from their lungs within one second. This is a useful measure of how quickly the lung can be emptied.

A further measure is the ratio between the FEV1 and the FVC (FEV1/FVC) to estimate the proportion of air that can be expelled in one second.

Spirometry readings, of course, vary, depending on age, size, race and sex. However, a formula has been devised to standardise for these differences, and so it is possible to calculate predicted values for the average health person of a particular age, size and sex. These are known as the predicted values and are indexed to 100. The spirometer automatically compares an individual's measurement against their predicted value. This is usually expressed as a percentage of the predicted value.

4.1 Obstructive respiratory function

An obstructive disorder refers to any disease that affects the lumen of the respiratory airways, and can be caused by inflammation or bronchospasm. Asthma and bronchitis are common examples of obstructive airways disease. An obstructive pattern presents itself as a reduced flow rate and normal lung volumes. This means that the FEV1 is reduced while the FVC remains within normal limits.

4.2 Restrictive respiratory function

A restrictive lung disorder is one that affects the lung tissue itself or the capacity of the lungs to expand fully and hold predicted volumes of air. This can result from lung fibrosis and scarring, or a deformity that restricts the expansion of the lungs. Fibrosis of lung tissue, such as asbestosis would show a restrictive pattern on spirometry. In restrictive lung disease both the FEV1 and FVC are reduced proportionately. In asbestosis total lung capacity is reduced, as in other restrictive lung disorders. Using spirometry, vital capacity typically appears reduced, without a reduction in the ratio of forced expiratory volume in 1 second to forced vital capacity (FEV1 to FVC).

4.3 Combined respiratory function

This is a lung disorder that exhibits the features of both an obstructive and restrictive respiratory deficit. Examples would be a lung condition that damages lung tissue and also causes bronchospasm, such as cystic fibrosis.

5. SPIROMETRY TESTING

All residents aged between 50 and 75 years were invited for spirometry by a letter from the village presidents of Kyperounda and Kato Amiandos. To encourage as many people as possible to attend the research team held two spirometry clinics per day, from 9am to 1pm and 4pm to 7pm in Kyperounda for 5 days. Three sessions were held in Kato Amiandos. Two experienced operators used two calibrated spirometres, following a strict protocol. As a matter of policy spirometry was done on all who attended, including those aged under 50 and those aged over 75 years. In all 273 people attended for spirometry, 218 from Kyperounda and 55 from Kato Amiandos.

The age sex breakdown on those who reported for spirometry is shown in Table 1. Although the invitation for spirometry, as mentioned above, was addressed to the over 50s, a number of residents aged under 50 wanted to have their lung function tested. Just over half (52.4%) of the respondents were men. Most were in the 60 to 75 age group; slightly more men aged 76 and over (15.4%) attended than women (6.9%).

Table 1 Age sex breakdown of spirometry respondents

	Men		Women		Persons	
	n	(%)	n	(%	n	(%)
30-59 years	36	(25.2)	44	(33.8)	80	(29.3)
60-75 years	85	(59.4)	77	(59.2)	162	(59.3)
76 and over	22	(15.4)	9	(6.9)	31	(11.4)
All ages	143	(100)	130	(100)	273	(100)

5.1 Height, weight and body mass index

One of the variables needed for calculating predictive values is the body mass index. This meant that height and weight were measured on all respondents. The mean height of men was 168.04 cms and women 153.73 cms, and the mean weight 79.73kgs and 69.53kgs respectively. Body mass index is shown in Table 2. According to British and European standards almost eighty percent (78.4%) of the respondents are overweight with over a third (37.0%) being classified as obese. We believe that the BMI tends to overestimate the proportion of obesity, particularly among people who are short.

Table 2 Body mass index for respondent of Kyperounda and Kato Amiandos

	Frequency	Percent	Cumulative %	Diagnosis
BMI 24.9 or less	59	21.6	21.6	Normal weight
BMI 25 to 29.9	113	41.4	63.0	Over weight
BMI 30 and over	101	37.0	100	Obese
Total	273	100		

6. RESULTS

6.1 Spirometry diagnosis by sex

Table 3 shows diagnosis as generated by the spirometer. The diagnoses that we are most interested in are obstructive disorders, usually associated with bronchospasm, and restrictive or combined disorders, which are indicative of damage to lung tissue, such as occurs with pulmonary fibrosis and asbestosis. For convenience of presentation normal and early obstructive diagnoses and restrictive and combined diagnoses have been aggregated.

Table 3	Diagnosis provided by spirometer in by sex			
	Males		Females	
	n	(%)	n	(%)
Normal/early obstruction	84	(57.7)	104	(80.0)
Moderate/severe obstruction	21	(14.7)	7	(5.4)
Restrictive/combined	38	(26.6)	19	(14.6)
All	143	(100)	130	(100)

Pearson’s chi-squared = 14.88 P=0.0006

An examination of the table shows a significant difference in lung function between men and women, with 26.6% of men having obstructive and combined disease compared to 14.6% of women. The difference in the pattern of diagnosis between men and women is highly significant (P=0.0006). This finding is consistent with the fact that men had much higher levels of occupational exposure to asbestos dust and higher rates of cigarette smoking.

6.2 Spirometry diagnosis by occupational exposure

Table 4 compares the spirometer-generated diagnosis among men who worked on the mine with those who did not. There is a difference in lung function with those who have been occupationally exposed having far higher rates of restrictive/combined lung function (31.4%) than their non-exposed (12.1%) counterparts. Three-quarters (75.8%) of the non-exposed men had relatively normal lung functions. Note that the difference between the two groups just fails to reach statistical significance (p=0.0547).

Table 4	Diagnosis provided by spirometer by occupational exposure: Males			
	Occupationally Exposed		Non-occupationally exposed	
	n	(%)	n	(%)
Normal/early obstruction	56	(53.3)	25	(75.8)
Mild/moderate obstruction	16	(15.2)	4	(12.1)
Restrictive/combined	33	(31.4)	4	(12.1)
All	105	(100)	33	(100)

Chi-squared = 5.81 p=0.0547

Table 5 presents data for occupational exposure controlled by smoking for males. Those who smoke and have an occupational exposure have the highest rate of restrictive disease (36.1%), followed by the occupationally exposed non-smoker

(24.3%), the non-exposed smoker (17.4%) and the non-exposed non-smoker (0%). This is a statistically significant difference (p=0.0499).

Table 5 — Diagnosis provided by spirometer by occupational exposure by smoking history: Males

	Occupationally Exposed		Non-occupationally exposed	
	Smoker n=72	Never smoked N=33	Smoker n=23	Never smoked n=10
	Percentage			
Normal/early obstruction	50.0	60.5	69.6	90.0
Mild/moderate obstruction	13.9	15.2	13.0	10.0
Restrictive/combined	36.1	24.3	17.4	0
All	100	100	100	100

Occupationally exposed: Chi-squared = 0.82 p=0.664,
Non-occupationally exposed: Chi-squared = 2.18 p=0.337

6.3 Household exposure

Table 6 examines those who lived in the same household as someone who worked on the mine with non-household exposed controls. Once again there is a statistically significant difference (p=0.0073) in the pattern of spirometer generated respiratory disease, with females who experienced household exposed having four times higher rates (19.0%) of restrictive/combined lung disease than the non-exposed controls (4.3%).

Table 6 — Diagnosis provided by spirometer by household exposure: Females

	Household exposure		Non-household exposure	
	n	(%)	n	(%)
Normal/early obstruction	58	(73.4)	44	(95.6)
Mild/moderate obstruction	6	(7.6)	0	(0)
Restrictive/combined	15	(19.0)	2	(4.3)
All	79	(100)	46	(100)

Chi-squared = 9.84 p=0.0073, caution because of small numbers

Table 7 compares spirometer-generated respiratory diagnoses of the occupationally exposed men in the two villages. Once again there is a difference in the pattern of disease, with 41.7% of the men in Kato Amiandos having restrictive/combined disorder compared to 28.3% of Kyperounda men, although the difference just fails to reach statistical significance (p=0.17). Note, the proportion of smokers in Kato Amiandos (40.8%) was not statistically different from that in Kyperounda (35.8%) chi squared p=0.516.

Table 7	Diagnosis provided by spirometer by village for those occupationally exposure: Males			
	Kyperounda		Kato Amiandos	
	n	(%)	n	(%)
Normal/early obstruction	43	(53.0)	13	(54.2)
Mild/moderate obstruction	15	(18.5)	1	(4.2)
Restrictive/combined	23	(28.3)	10	(41.7)
All	81	(100)	24	(100)

Chi-squared = 3.54 p=0.17

6.4 Lung function tests FVC and FEV1

The forced vital capacity (FVC) and the forced expiratory volume in one second (FEV1) were recorded on all spirometry tests. An obstructive pattern, such as asthma, presents itself as a reduced flow rate and normal lung volumes. This means that the FEV1 is reduced while the FVC remains within normal limits. Fibrosis of lung tissue, such as asbestosis shows a restrictive pattern on spirometry. In restrictive lung disease both the FEV1 and FVC are reduced proportionately.

In theory, all people with normal lung function for their age, sex and body mass index should have a predicted FVC and predicted FEV1 of 100. It is therefore reasonable to compare groups that have a different age sex structure. The spirometry results have been aggregated into exposure groups in order to compare patterns of exposure. Table 8 compares the FVC by the occupational exposure of men, and Table 9 controls for smoking history. The figures on pages 45 to 49 show the ranked frequency distribution of the FVC and FEV1 by various exposure groups.

Table 8	Comparing the spirometry results for Forced Vital Capacity (FVC) by occupationally exposure groups: Males	
	Occupationally Exposed	Occupationally not exposed
Number	105	33
FVC mean	87.498	94.703
95% CI	83.061- 91.935	87.866-101.540
Standard error	2.237	3.357
Group median	88.667	93.900

The FVC among the occupationally exposed group is reduced by 12.5% while the FVC of the non-exposed group is 5.3% below the expected predicted value. The confidence intervals, which overlap, show that the difference does not reach statistical significance at the 95% level. Table 9 shows the impact of smoking. The FVC of those with an occupational exposure who smoke is reduced by about 15%. The FVC is reduced by roughly the same amount in non-exposed smoker (9%) and exposed non-smokers (8%). This suggests that the impact of occupational exposure is more or less equivalent to the impact of cigarette smoking.

Table 9	Comparing the spirometry results for Forced Vital Capacity (FVC) by occupationally exposure groups by smoking experience: Males			
	Occupationally exposed		Not exposed occupationally	
Smoking history	Smoker	Non-smoker	Smoker	Non-smoker
FVC mean	85.22	92.47	90.51	104.35
95% CI	79.92 – 90.52	84.20 – 100.74	82.23 – 98.79	92.43 – 116.27
Standard error	2.65	4.06	3.99	5.27
Group median	86.7	95.6	89.1	101.45

There is little doubt that this failure to demonstrate statistical difference is due to the small numbers involved, particularly among the non-exposed group.

6.5 Force expiratory volume in one second (FEV1)

Table 10 shows the impact of occupational exposure on the FEV1. The occupationally exposed group is almost 19% below the expected value of 100, compared to the non-exposed group which is 12% below the expected value. Yet the confidence limits overlap and therefore the values do not reach statistical difference at the 95% confidence level. Moreover, we know that cigarette smoking also has an impact of the FEV1.

Table 10	Comparing the spirometry results for Forced Expiratory Volume in One Second (FEV1) by occupationally exposure groups: Males	
	Occupationally exposed	Occupationally not exposed
Number	105	33
FEV1 mean	81.085	87.848
95% CI	76.580-85.589	81.223-94.474
Standard error	2.271	3.252
Median	80.900	90.700

Table 11 shows the FEV1 by exposure group after controlling for smoking history. This analysis shows a gradient between the groups with the occupationally exposed smokers having the lowest FEV1, and the non-exposed, non-smokers the highest FEV1. What is most interesting is that the FEV1 value for the exposed non-smoker and non-exposed smoker were rather similar. This suggests that, as we saw with the FVC, exposure to asbestos dust has a more or less similar impact as cigarette smoking on the FEV1.

Table 11	Comparing the spirometry results for Forced Expiratory Volume in One Second (FEV1) by occupationally exposure groups by smoking experience: Males			
	Occupationally exposed		Not exposed occupationally	
Smoking history	Smoker	Non-smoker	Smoker	Non-smoker
FEV1 mean	78.70	86.27	84.99	94.41
95% CI	72.94 – 84.47	79.31 – 93.23	76.27 – 93.72	84.87 – 103.94
Standard error	2.89	3.41	4.21	4.21
Median	79.7	84.70	89.5	93.45

6.6 Household Exposure

Tables 12 and 13 compare the FVC and FEV1 respectively, for females by their household exposure. The group with household exposure has a FVC that is lower than the non-exposed group. The fact that the non-exposed group has a value of 112 may be due to small numbers or it may suggest that the spirometry machine over estimate the FVC in Cypriot women. This may be because the women in our sample tend to be of shorter than expected, although their stocky body shape suggests that they have a large lung capacity than the spirometer is anticipating. It is interesting to note that overall females have higher values for the FVC and FEV1 than men. This suggests that men in general have poorer respiratory health than women. Undoubtedly the high rate of cigarette smoking among men is the main factor for this difference.

Table 12	Comparing the spirometry results for Forced Vital Capacity (FVC) by household exposure groups: Females	
	Household exposed	Not exposed
Number	79	46
FVC mean	100.334	112.113
95% CI	93.646 – 107.023	105.008 – 119.218
Standard error	3.359	3.527
Median	100.00	110.10

While the difference between the exposure groups for FVC is just below significance at the 95% confidence level, the difference in the FEV1 is statistically significantly different between the two groups.

Table 13	Comparing the spirometry results for Forced Expiratory Volume in One (FEV1) second by household exposure groups: Females	
	Household exposed	Not exposed
Number	79	46
FEV1 mean	93.146	105.435
95% CI	87.683 – 98.608	98.943 – 111.926
Standard error	2.743	3.223
Median	95.800	99.867

7. Respiratory symptoms

The next section reports on the relationship between respiratory symptoms as measured by the British Thoracic Society questionnaire and spirometry results.

7.1 Cough

Table 14 shows the respiratory function of those men who reported a winter cough. It is important to note that for both the FVC and the FEV1 there is a significant difference between those with winter cough and those who do not cough in winter.

Table 14 — Comparing the spirometry results for Forced Vital Capacity (FVC) and Forced Expiratory Volume (FEV1) by winter cough: Males

	Cough in winter			
	Yes, n = 70		No, n = 70	
	Mean	95% CI	Mean	95% CI
FVC	83.44	77.92-88.96	95.42	90.42-100.08
FEV1	74.38	68.91-79.85	91.04	86.72-95.37

This suggests that among men, winter cough is a good indicator of poor respiratory function. Among the female population we see a different pattern (Table 15). Winter cough was not related to the spirometry results of the FVC and FEV1. Indeed, the respiratory functions of female with a winter cough were no different from those who did not report a winter cough.

Table 15 — Comparing the spirometry results for Forced Vital Capacity (FVC) and Forced Expiratory Volume (FEV1) by winter cough: Females

	Cough in winter			
	Yes, n = 57		No, n = 68	
	Mean	95% CI	Mean	95% CI
FVC	109.16	101.04-117.20	100.90	94.63-107.16
FEV1	99.44	93.41-105.46	96.18	90.04-102.32

7.2 Phlegm

For men there was a statistically significant relationship (p=0.009) between bringing up phlegm from the chest in the morning in the winter months and the FEV1, but not the FCV (p=0.75).

8. Health status and spirometry

Table 16 examines the relationship between perceived health status and the forced vital capacity (FVC). What is most interesting is that among the male population there is a consistent and significant relationship, whereas among the female population there is no relationship at all. It appears that men are more objective at assessing their health status than women.

Table 16 Health status and FVC for men and women

	Men		Women	
	Forced Vital Capacity (FVC)			
	Mean	95% CI	Mean	95% CI
Good	95.96	90.58-101.33	104.03	93.48-114.58
Fair	86.60	81.56-91.64	104.77	98.85-110.70
Poor	78.28	60.41-93.14	106.08	63.22-148.93

8.1 Mine years

A linear regression showed that there was no relationship between the length of time worked on the mine in years and the FVC and FEV1. The length worked on the mine was aggregated into three groups to see if there was a relationship with lung functions as measured by the FVC and FEV1. Table 17 shows the results of this analysis. The FVC of men who had worked on the mine for over 20 years was only 2% less than men who had worked on the mine for less than 10 years. There is no detectable relationship between the length of occupational exposure and the FEV1.

Table 17 Respiratory functions by length of occupational exposure: Males

Length of time on mine	FVC		FEV1	
	Mean	95% CI	Mean	95% CI
1-9 years	88.35	80.48-96.22	80.65	72.75-88.54
10-19 years	87.69	78.13-97.24	80.96	72.17-89.76
20 years and more	85.45	78.38-92.53	80.14	72.16-88.13

9. Chest X-rays of a selected population

We selected a sample of residents with severe signs of restrictive lung disease for a screening radiological examination of their lungs. Twenty-four residents were invited to have an anterior posterior lung X-ray at Kyperounda hospital. Dr Robin Evans, consultant radiologist, reported on the X-rays. Calcified pleural plaques consistent with previous asbestos exposure were found in 5 cases. One resident had extensive bilateral asbestos related pleural disease. The radiologist recommended a CT scan in order to make a more definitive diagnosis. There were no cases of lung cancer or mesothelioma. A list of the residents affected would be given to the Ministry of Health for on going monitoring of their health for the next 5 to 10 years.

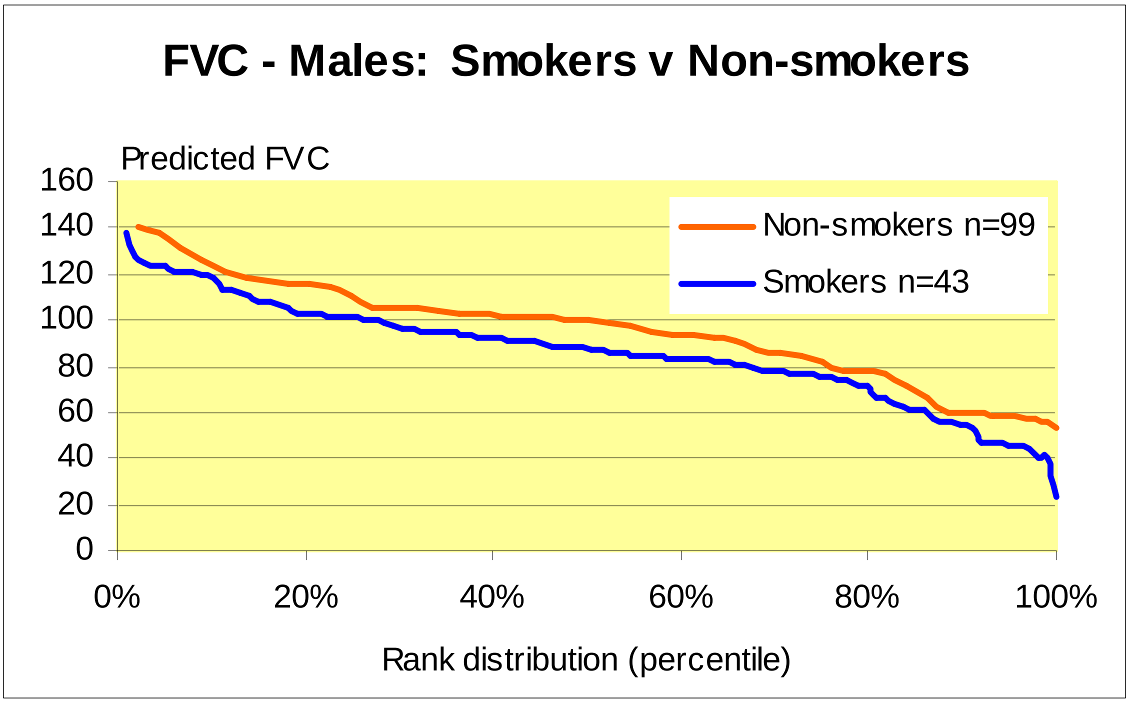
9. COMMENTS

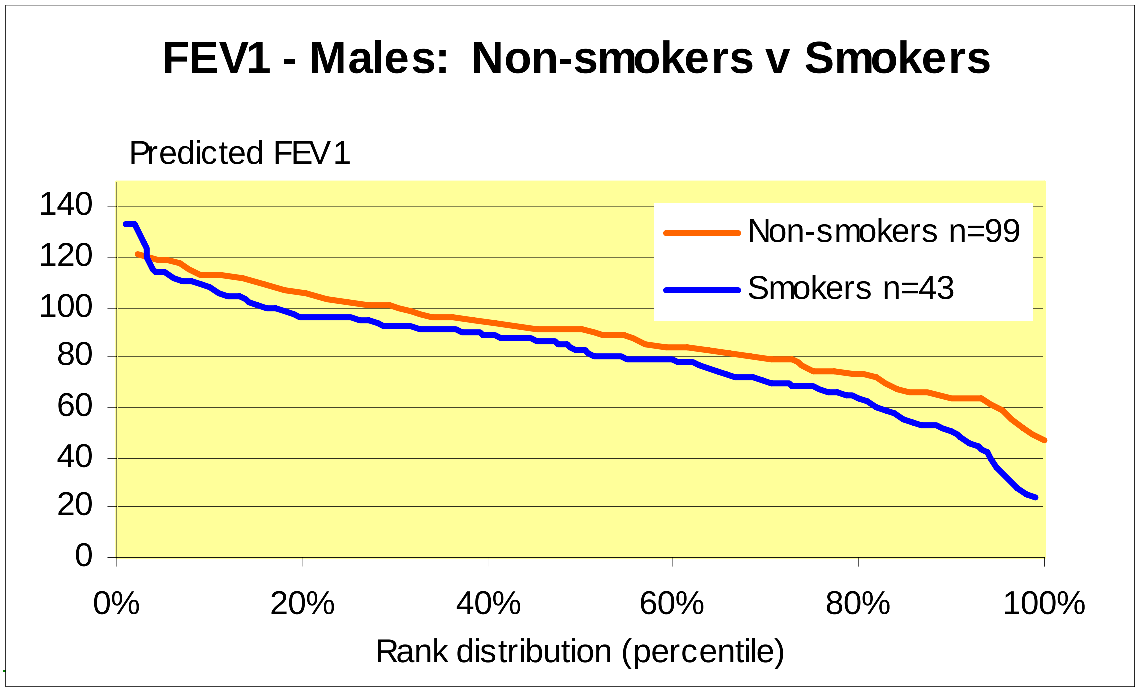
1. The scientific literature shows that asbestosis effects respiratory function and is usually associated with restrictive disorder on spirometry.
2. In this study we found clear evidence of significant restrictive patterns among those who were exposed to asbestos. Indeed there appeared to be a gradient according to the level of exposure. Highest rates of restrictive disorder were found among the occupationally exposed men in Kato Amiandos (41.7%), followed by occupationally exposed men in Kyperounda (28.3%). Women with a household exposure had higher rates (19.0%) than non-exposed women (4.0%). This finding shows that the spirometry was successful in measuring exposure to asbestos.
3. A history of cigarette smoking has a definite adverse impact on lung function tests. The greatest deficiency in lung function was found among men who had smoked and been occupationally exposed. Our findings suggest that occupational exposure to chrysotile asbestos dust has about the same impact as heavy cigarette smoking. This finding shows how important it is to encourage men who have worked on the mine to stop smoking.
4. In men the symptoms of the British Thoracic Questionnaire were closely associated with the spirometry results. Winter cough and a cough that produced phlegm were the most predictive of poor respiratory function. This finding highlights the importance of attacks of bronchitis being properly treated.
5. The poorer respiratory status of men is due to higher levels of exposure but also to the high rates of cigarette smoking. There is clear evidence that smoking aggravated the effect of asbestos exposure. It is therefore of especial importance that men who have experience occupational exposure should be encouraged to give up smoking.
6. We were intrigued by the finding that women had such high FVCs. Among the group with no exposure the FVC was 112, which is 12% higher than expected. In our view the most likely explanation for this finding is that the body shape of Cypriot women living in the villages tend to be short and stocky. The implication is that the spirometer, which only standardises for height and mass, is under estimating the vital capacity of these women. We recommend that a study should be undertaken to investigate this very important question. It is important to standardise for body shape, and this can be done by measuring shoulder width.
7. The force vital capacity (FVC) for non-exposed, non-smoking males (see table 9) and females (see table 12) were slightly higher than predicted values (100). We therefore concluded that this group had normal respiratory function, and that there is no evidence of an environmental exposure to asbestos in ambient air.
8. We believe that there is a similar problem in the measurement of the body mass index (BMI). The body mass index showed very high rates of obesity among the village populations. It seems likely that the current method of calculating BMI is flawed in that it does not take account of a person's body shape. It seems highly likely that the current measure is over diagnosing

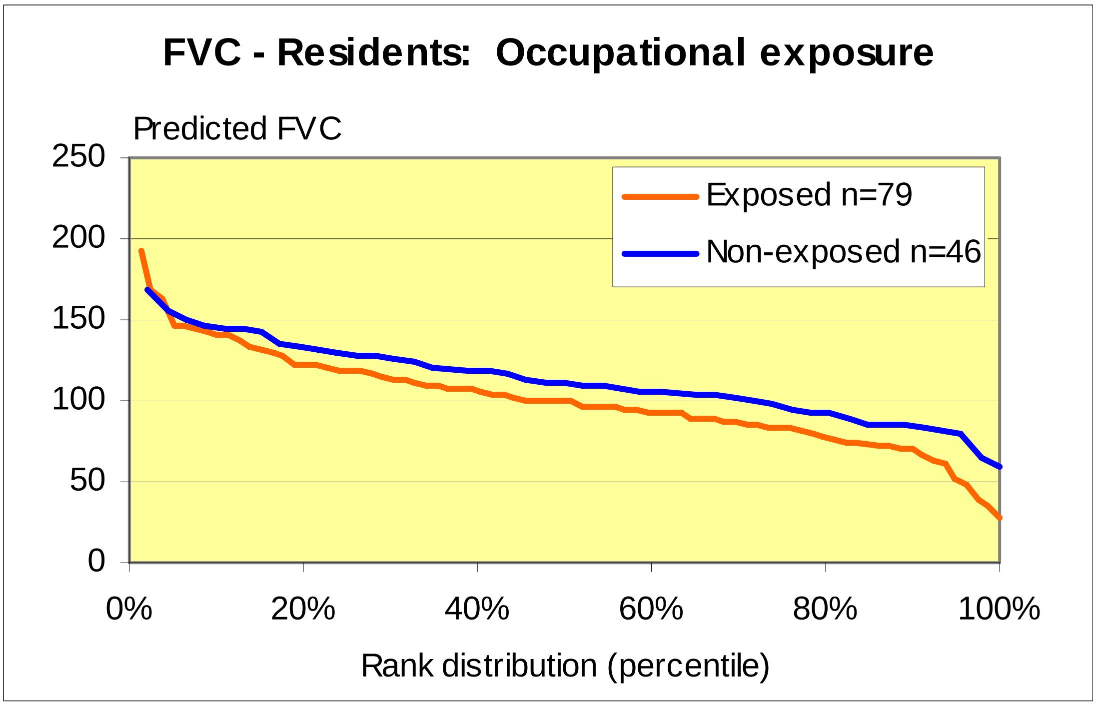
obesity in the Cyprus population. Nevertheless, it still seems probable that there is a problem with overweight and obesity in this population, and it is important that there is a further study of this problem.

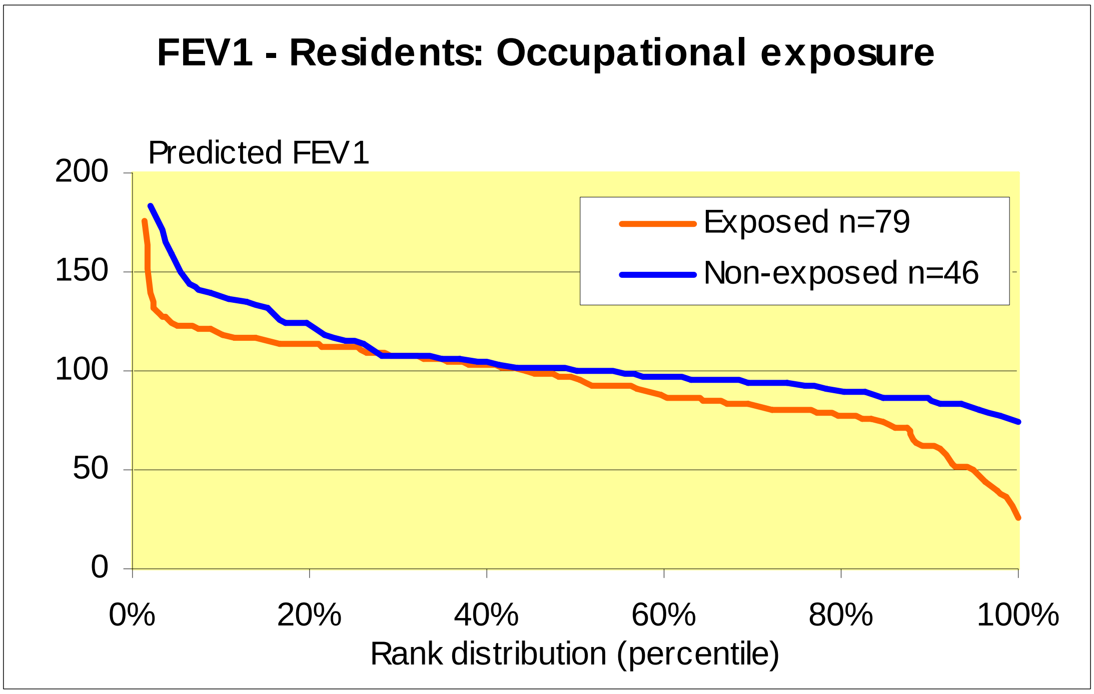
ILLUSTRATIVE GRAPHS

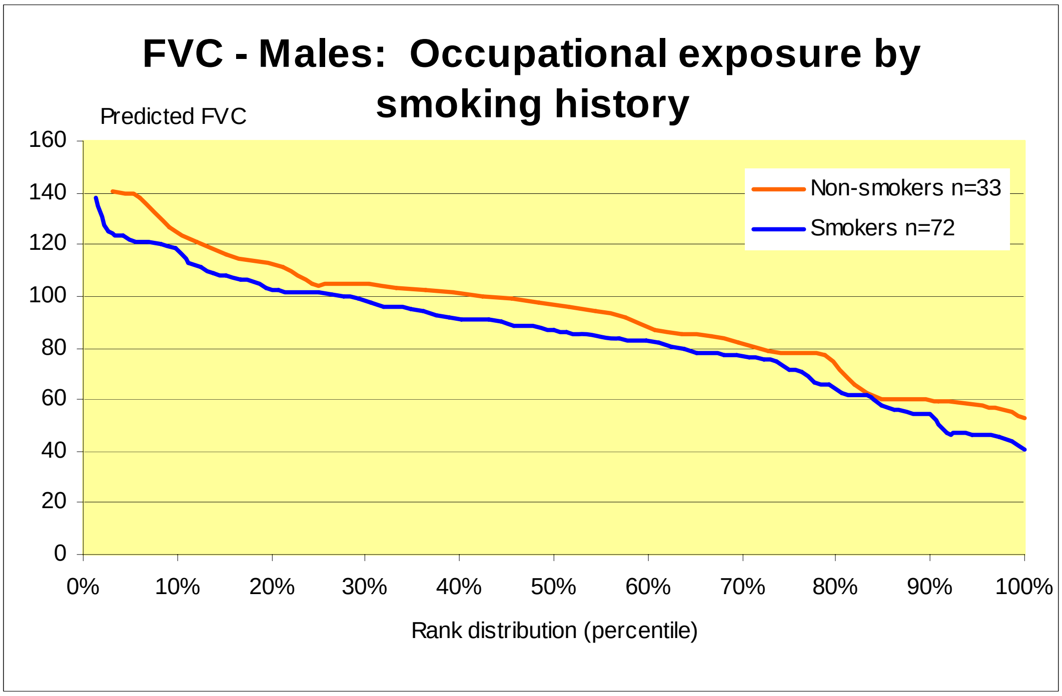
The following graphs are illustrative of the analysis described above. The percentage rank order distributions of the FVC and FEV1 for various exposure groups are compared.

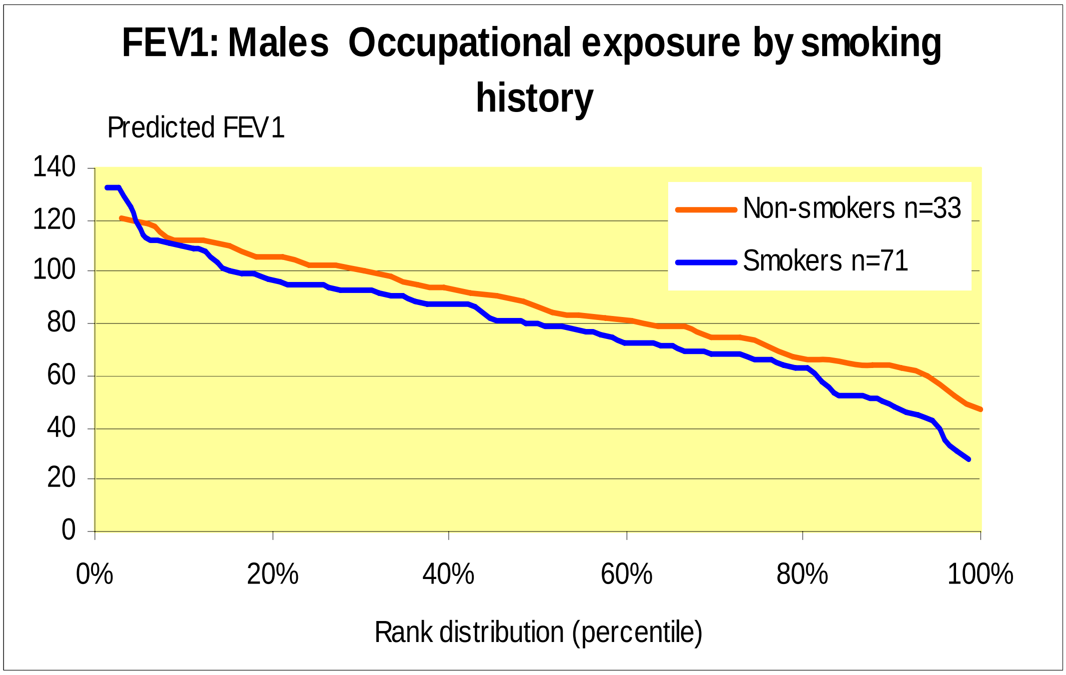


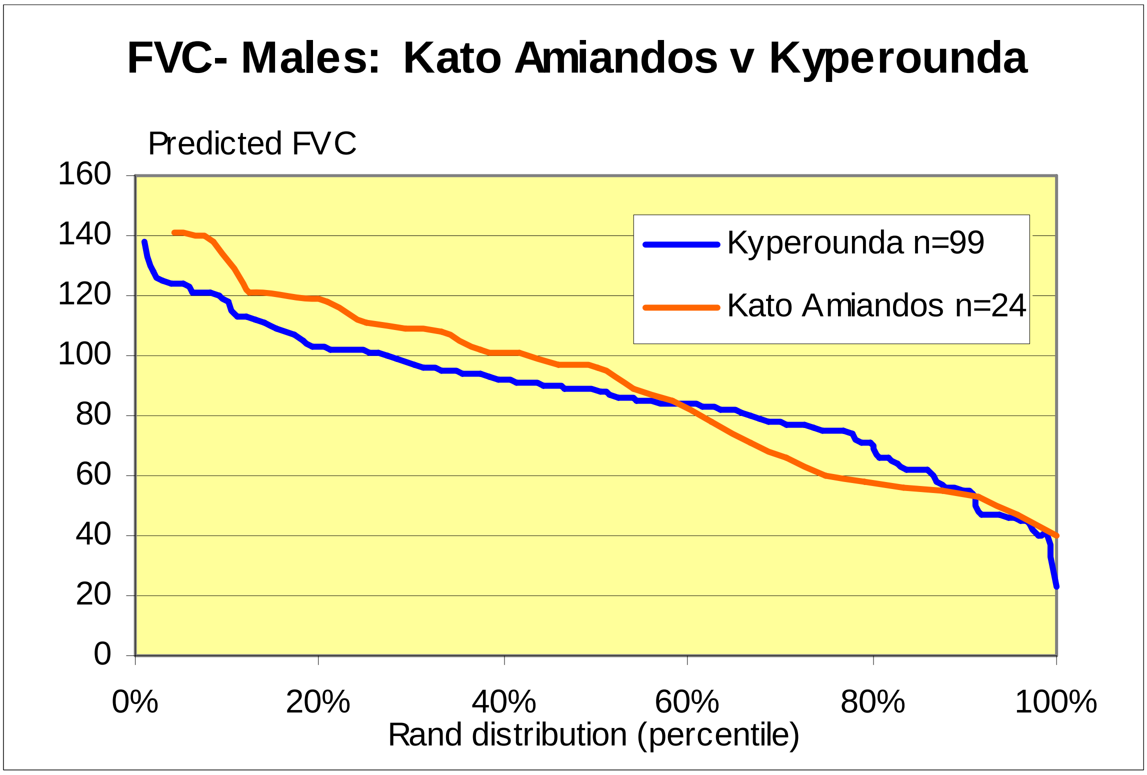


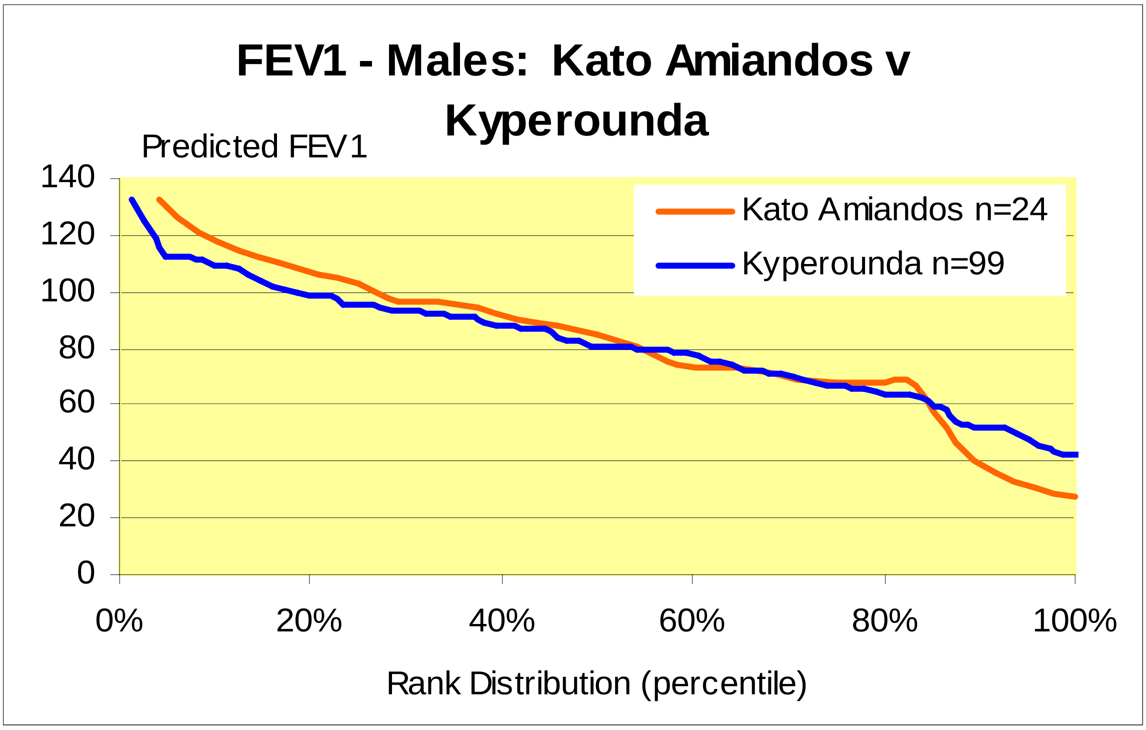

FVC - Residents: Occupational exposure
Predicted FVC
250
200
150
100
50
0
0%
20%
40%
60%
80%
100%
Rank distribution (percentile)
Exposed n=79
Non-exposed n=46

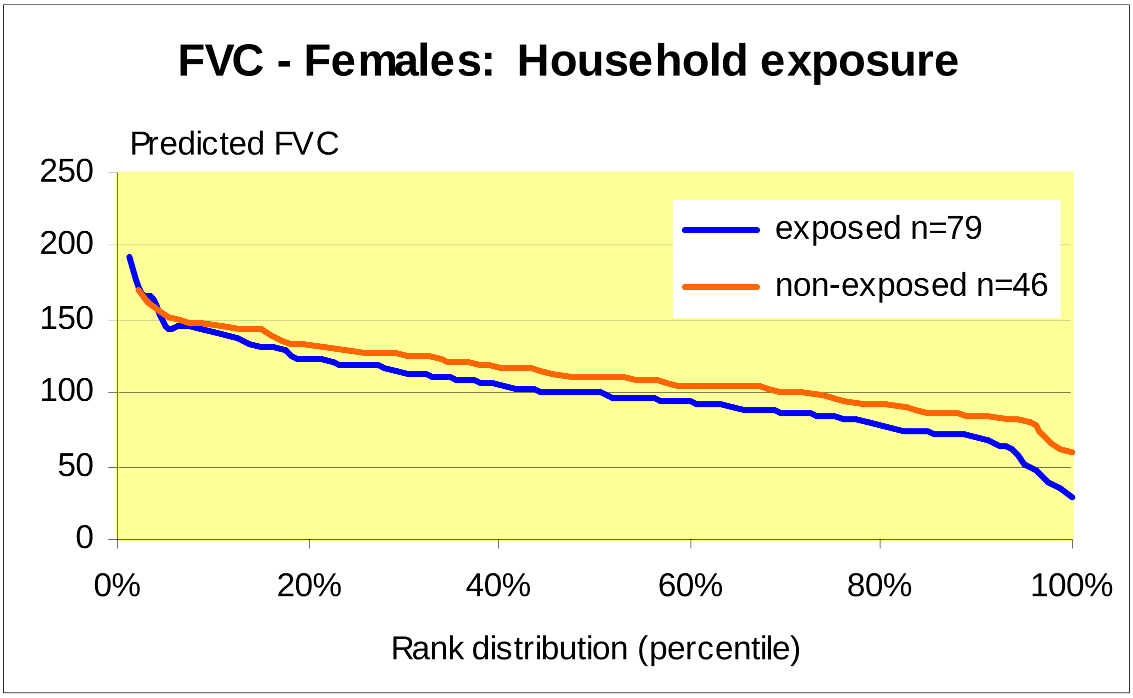

FEV1 - Residents: Occupational exposure
Predicted FEV1
200
150
100
50
0
0%
20%
40%
60%
80%
100%
Rank distribution (percentile)
Exposed n=79
Non-exposed n=46

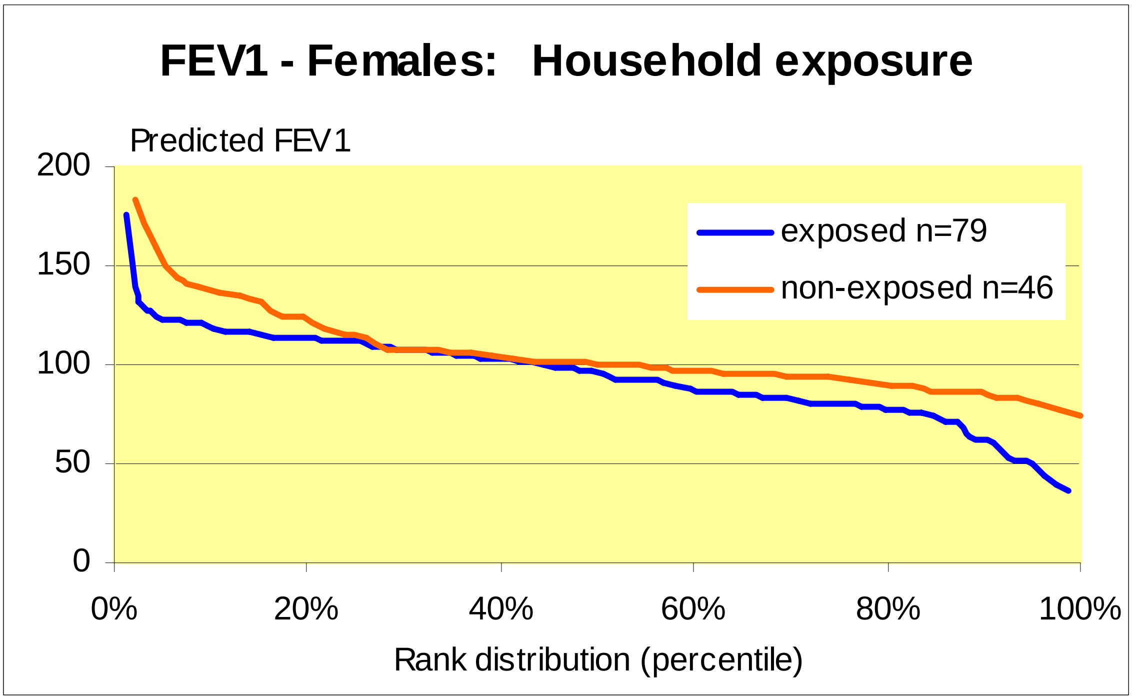

FVC - Males: Occupational exposure by smoking history
Predicted FVC
160
140
120
100
80
60
40
20
0
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
Rank distribution (percentile)
Non-smokers n=33
Smokers n=72


FEV1: Males Occupational exposure by smoking history
Predicted FEV1
140
120
100
80
60
40
20
0
0%
20%
40%
60%
80%
100%
Rank distribution (percentile)
Non-smokers n=33
Smokers n=71

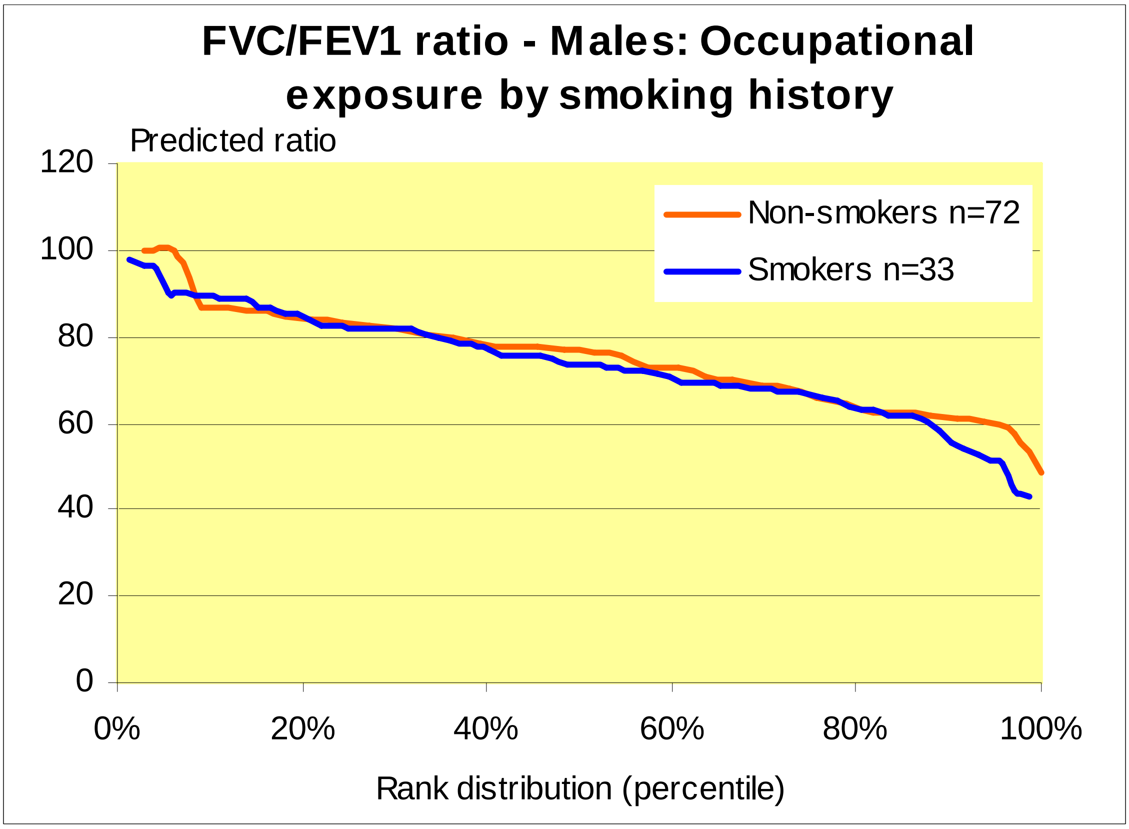

FVC- Males: Kato Amiandos v Kyperounda
Predicted FVC
160
140
120
100
80
60
40
20
0
Kyperounda n=99
Kato Amiandos n=24
0%
20%
40%
60%
80%
100%
Rand distribution (percentile)


FEV1 - Males: Kato Amiandos v Kyperounda
Predicted FEV1
140
120
100
80
60
40
20
0
Kato Amiandos n=24
Kyperounda n=99
0%
20%
40%
60%
80%
100%
Rank Distribution (percentile)


FVC - Females: Household exposure
Predicted FVC
250
200
150
100
50
0
exposed n=79
non-exposed n=46
0%
20%
40%
60%
80%
100%
Rank distribution (percentile)


FEV1 - Females: Household exposure
Predicted FEV1
200
150
100
50
0
exposed n=79
non-exposed n=46
0%
20%
40%
60%
80%
100%
Rank distribution (percentile)

As reported above, both the FEV1 and FVC are reduced proportionately in restrictive lung diseases, such as asbestosis. The chart below shows that the occupationally exposed groups, of both smokers and non-smokers, have pattern on spirometry that is consistent with restrictive lung disease.



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Section 7

Respiratory morbidity in Kyperounda and Kato Amiandos

1. INTRODUCTION

One of the greatest challenges in epidemiology is to obtain accurate morbidity data. Some epidemiologists are now exploring the possibilities of using hospital inpatient data to describe the morbidity of people who are treated in hospital. While hospital data is problematic in that it only provides information on those who attend for treatment, and therefore can say nothing about those who do not attend, it is nevertheless proving to be a useful source of morbidity for those conditions that usually required hospital treatment. Another potential source of bias is that the distance that people need to travel to get hospital treatment influences admission rates. It is well known that areas with easy access to hospital services tend to have higher admission rates than areas that are remote from hospitals. Despite these potential difficulties hospital admissions, when carefully analysed to take account of these problems, are proving to be an extremely valuable source of morbidity data for conditions that usually require hospital treatment.

2. OBTAINING HOSPITAL RECORDS

With these difficulties in mind we visited Kyperounda Hospital and had discussions with key personnel to examine the feasibility of obtaining data from their data systems. We also visited the Makarion Hospital as it has the main computer centre for the Island. We had very useful meetings with both the Hospital Director and with Zena Socratous who operates the computer system. She explained the hospital system in some detail, focusing on the way the data was collected and coded.

Having investigated the variables that were gathered on each admission we concluded that it was possible to use in-patient data to compare the incidence of admissions between the index villages of Kyperounda and Kato Amiandos with other geographic areas.

We visited the Department of Statistics and were able to obtain an anonymous abstract of hospital data for Cyprus for the five-year period 1998 to 2002.

3. METHOD OF ANALYSIS

The abstract of hospital admissions data was entered into a computer statistical database, cleaned, grouped and prepared for analysis.

Each patient record contained an ICD 10 diagnostic code, age, sex, the four-digit area of residence code and the hospital treatment code. We assessed the quality of approximately 250,00 records by searching for missing values. The data was of good quality, with only 2% missing codes in the age, sex or area of residence variables. Every single record had a diagnostic code. The small number of records with missing codes was excluded from subsequent analysis. Table 1 describes missing codes by hospital.

For purposes of comparison we calculated directly aged standardised admission rates, indirectly age standardised admission ratios (SARs), and indirectly age standardised proportional admission ratios (PARs). Direct rates were calculated using the European standard population. The indirect ratios were calculated using the overall rates for Cyprus as the standard (Cyprus = 100). Population denominators were taken from the 2001 national (Cyprus) census. Standardisation was done using 10-year age bands.

To make geographic comparisons Cyprus was used as the standard, and therefore its standardised admission ratio (SAR), and its age standardised proportional admission ratio (PAR) = 100. We aggregated the hospital records of Kato Amiandos and Kyperounda because the number of records from the villages was too small to be analysed separately in a meaningful way. Ratios were calculated for Lemesos district and the other four districts of Cyprus. We also calculated ratios for Lemesos district excluding the index villages. This allowed us to use the rest of Lemesos district as a control area to compare with the exposed index villages.

As a measure of morbidity we have concentrated on overall admissions and respiratory diseases. The respiratory diseases were grouped as follows using ICD 10 codes: All respiratory diseases (ICD code J00-J99) and chronic lower respiratory diseases (ICD J40-J49) as a subset. Chronic lower respiratory diseases were then subdivided into chronic obstructive pulmonary disease (COPD) (ICD J40-J44) and asthma (ICD J45-J46).

3.1 Missing records

As mentioned above, the first step in our analysis was to examine the number of records with missing data. Table 1 shows a breakdown of records with missing data by the hospital of treatment. The completeness of the data was excellent, with just 2% of records containing missing data. There is no significant variation between the hospitals, with the exception of Paralamni that had 6.8% of missing values.

Table 1 All Cyprus in-patient hospital admission records for the five-year period 1998 to 2002 by hospital

	Hospital	All Records	Inpatient Records With Missing Age, Sex or Area	
		N	N	%
Code				
H1	Nicosia General Hospital	49,366	227	0.5%
H2	Archbishop Makarios III Hospital	46,726	573	1.2%
H5	Larnaka District Hospital	34,916	543	1.6%
H6	Limassol District Hospital	80,829	2,538	3.1%
H7	Paphos District Hospital	27,208	673	2.5%
R1	Kyperounta	3,137	63	2.0%
R2	Paralimni	2,694	184	6.8%
R3	Polis Chrysochous	1,269	5	0.4%
S1	Athalassa Psychiatric Institution	1,411	45	3.2%
	CYPRUS	247556	4851	2.0%

4. RESULTS OF ANALYSIS

The next step in our analysis was to compare the overall hospital admission rate for Cyprus, the districts and the index villages. We found that the directly standardised rates produced the same pattern of admission as the indirectly standardised ratios, and so we are presenting only the indirectly standardised ratios, which are easier to interpret. Table 2 shows the overall SAR for Cyprus, the districts of Cyprus and for the index area of Kyperounda and Kato Amiandos with upper and lower confidence intervals.

Table 2

All Diagnoses: Indirect age standardised admission ratio
Cyprus hospital admission records 1998 to 2002
Comparing Kyperounda/Kato Amiandos with Cyprus and districts

	Number of admissions	Ratio	Lower CI	Upper CI
Cyprus	242,718	100	99.6	100.4
Lefkosia district	79,953	83.2	82.6	83.8
Ammochostos district	8,074	63.1	61.7	64.5
Larnaka district	36,678	90.7	89.8	91.6
Lemesos district	86,968	130.8	129.9	131.7
Pafos district	31,045	128.9	127.5	130.3
Kyperounda and Kato Amiandos	1,280	187.0	176.9	197.5
Lemesos excluding K and K. A.	85,688	130.2	129.3	131.1

The admission ratio of Lemesos district (130.8) and Pafos district (128.9) is higher than the national figure, as is the rate for the index villages (187.0). In interpreting this data it is important to take account of the supply of hospital services between the different areas. This is because it is well known that hospital supply has a strong influence on the overall hospitalisation rate. Communities that live near to a hospital are likely to have higher rates than those who need to travel greater distances to get hospital treatment. Therefore, we cannot exclude the possibility that the higher rate observed in Kyperounda/Kato Amiandos is because it has a nearby hospital.

4.1 Analysing respiratory morbidity

The next step in our analysis was to examine variations in admission for respiratory disease. We started by looking at rates for all respiratory disease (ICD 10 J00-J99) and the results are shown in Table 3.

The SAR for Kyperounda / Kato Amiandos (194.4) is just slightly higher than the SAR for all diagnoses (187). Moreover, the proportional admission ratio (118) is only slightly above the national ratio. This suggests the excess of all respiratory disease may simply be a factor of the overall higher hospitalisation rate of the index villages. Our hypothesis is that exposure to asbestos has caused specific types of lung disease. To test this idea we examined respiratory diseases in more detail. First we examine chronic lower respiratory disease ICD 10 (J40-49).

Table 3

All Respiratory Disease (ICD 10 J00-J99)
Indirectly age standardised admission and proportional ratios
Cyprus hospital admission records 1998 to 2002
Comparing Kyperounda/Kato Amiandos with Cyprus and districts

	Number of Admissions	Age standardised admissions ratio			Age standardised proportional ratio
	N	Ratio	Lower CI	Upper CI	Ratio
Cyprus	25622	100.0	98.8	101.2	100.0
Lefkosia district	7522	75.3	73.6	77.0	90.7
Ammochostos district	853	60.2	56.2	64.4	97.9
Larnaka district	3863	88.5	85.7	91.4	100.0
Lemesos district	9571	138.5	135.8	141.3	102.7
Pafos district	3813	147.7	143.1	152.5	116.6
Kyperounda/Kato Amiandos	145	194.4	164.0	228.7	118.0
Lemesos, excluding Kyper. & Kato Am.	9426	137.9	135.2	140.7	102.5

Table 4 shows that the SAR for chronic lower respiratory diseases is significantly higher in Lemesos district (170.1) than the other districts. And the SAR for the index villages (480.9) is nearly five times higher than the national rate (100). Moreover, the proportional admission ratio for the index villages is three times (281.6) the expected level. This shows that there is a markedly different pattern of hospital admissions in the index villages, with a three-fold higher than expected proportion of patients with chronic lower respiratory diseases being admitted to hospital. This finding shows that there is a clear, statistically significant increase in respiratory morbidity in the index villages. And the higher than expected proportional ratio provides clear evidence that the increase in admissions for lower chronic respiratory disease cannot be explained by an overall increase in hospitalisation.

Table 4

Chronic Lower Respiratory Disease (ICD 10 J40-J49)
Indirect age standardised admission and proportional ratios
Cyprus hospital admission records 1998 to 2002
Comparing Kyperounda/Kato Amiandos with Cyprus and districts

	Number of Admissions	Age standardised admissions ratio			Age standardised proportional ratio
	N	Ratio	Lower CI	Upper CI	Ratio
Cyprus	3075	100.0	96.5	103.6	100.0
Lefkosia district	782	65.2	60.7	69.9	77.6
Ammochostos district	147	89.7	75.8	105.5	138.1
Larnaka district	341	65.8	59.0	73.2	74.1
Lemesos district	1403	170.1	161.3	179.2	125.1
Pafos district	402	127.8	115.6	140.9	105.8
Kyperounda/Kato Amiandos	46	480.9	352.0	641.5	281.6
Lemesos excluding K and K & A	1357	166.4	157.7	175.5	122.8

The next stage of our analysis was to examine the even more specific diagnosis of chronic obstructive pulmonary disease (ICD 10 J40-J44), a condition that is known to be associated with exposure to asbestos. The result is shown in Table 5.

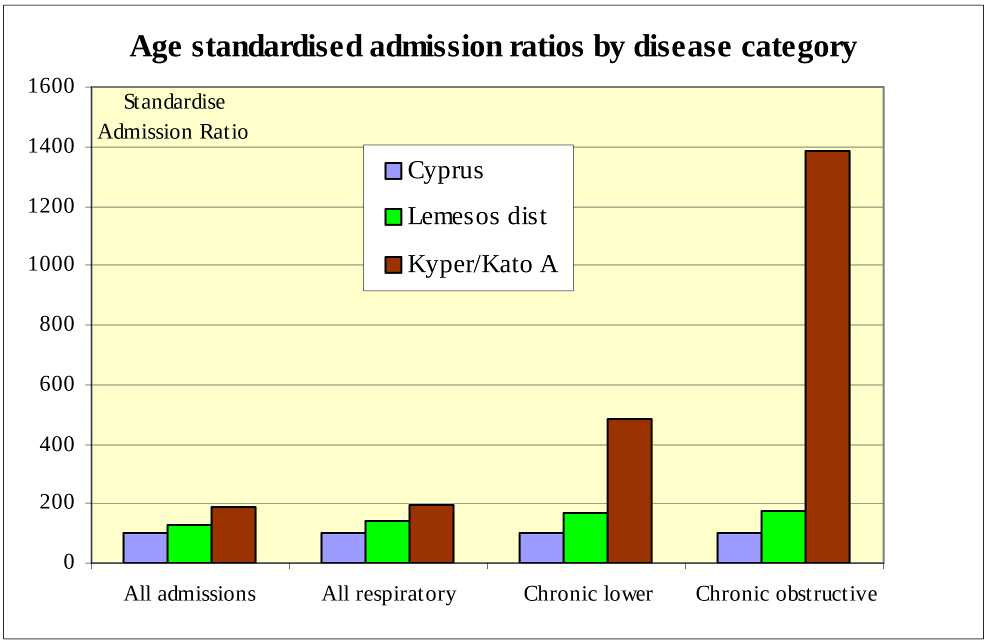
Table 5	**Chronic Obstructive Pulmonary Disease (ICD 10 J40-J44)** Indirectly age standardised admission and proportional ratios Cyprus hospital admission records 1998 to 2002 Comparing Kyperounda/Kato Amiandos with Cyprus and districts				
	Number of Admissions	Age standardised admissions ratio			Age standardised proportional ratio
	N	Ratio	Lower CI	Upper CI	Ratio
Cyprus	928	100.0	93.7	106.6	100.0
Lefkosia district	364	98.9	89.0	109.6	119.3
Ammochostos district	27	61.4	40.5	89.3	82.5
Larnaka district	28	18.3	12.2	26.5	21.0
Lemesos district	447	189.6	172.4	208.0	132.1
Pafos district	62	64.1	49.1	82.1	52.3
Kyperounda/Kato Amiandos	43	1384.0	1001.5	1864.3	723.0
Lemesos, excluding Kyper. & Kato Am.	404	173.6	157.1	191.4	121.6

There is now a dramatic, thirteen-fold increase in hospital admissions for chronic obstructive pulmonary disease in the index area of Kyperounda/Kato Amiandos compared to the national average. This is a highly statistical significant difference that certainly can not be explained by easy access to hospital. Moreover, the proportion of hospital admission for this diagnosis is seven times higher (720) than that occurring elsewhere on the island. It is interesting to observe that in Lemesos district, excluding the index area, the admission ratio is significantly higher than elsewhere in Cyprus. This suggests those villages other than those in the index area probably also have high rates of chronic obstructive pulmonary disease. This finding could be confirmed by a study of other exposed villages.

We examined the hospitalisation ratio of asthma and found that the numbers in the index area were very small. The small numbers make any analysis difficult to interpret, and therefore we advise caution in drawing too many conclusions from this data. Nevertheless, the asthma SAR for the index villages, based on only 3 admissions, was only 46.6 (CI 3-136), which suggests that the incidence of asthma is probably similar to the national average. The SAR for lung cancer in the index villages, based on 4 admissions, was 104 (CI 25-265) which is similar to the national rate.

Across Cyprus there were 48 hospital admissions for mesothelioma (but only 17 registered cases) recorded over the five-year period. The SAR for Lemesos district was 97 (CI 52-166) and for Lefkosia district, 164 (CI 111-233). The SAR for the index villages, based on 2 admissions, was 1130 (CI 127-4030). This may suggest an excess (not statistically significant) of mesothelioma in the index villages, but the true incidence can only be measured by a carefully designed epidemiological study.

The graph shows the large difference in hospital morbidity between the index area and the other districts of Cyprus.



5. COMMENTS

1. It is most gratifying to see that the quality of hospital data is of good quality that epidemiological investigations can be undertaken. The diagnostic coding was 100% complete and this is a reflection of the quality of data.
2. The findings of our analysis of hospital records confirm the findings of the spirometry. There is no doubt that the exposed populations in the villages of Kyperounda and Kato Amiandos have experienced significant respiratory morbidity that is due to their exposure to the asbestos mine.
3. The villages of Kyperounda and Kato Amiandos have an admission rate for chronic obstructive pulmonary disease which is thirteen times higher than the national admissions rate. This is a highly statistically significant difference that cannot be explained by easy access to the hospital. Moreover proportion of hospital admissions for this diagnosis is seven times higher than that occurring elsewhere on the island.
4. The admissions to hospital ratio for the whole of the Lemesos district, excluding the villages of Kyperounda and Kato Amiandos is significantly higher than elsewhere in Cyprus. It is therefore important that the scope of the investigation is expanded to include other villages in the Lemesos district that have experienced significant levels of exposure to asbestos.
5. We found that over the whole of Cyprus there have been 48 hospital admissions for mesothelioma recorded over a five-year period from 1998 to 2002 and that the index villages of Kyperounda and Kato Amiandos have higher than expected rates, although not statistically significant. However the true incidence of mesothelioma can only be measured by a carefully designed study and this is included in the plans of the Ministry of Health for the final of a four-part study. We believe that the hospital admissions records we examined and those that would be available in subsequent years should make a real to contribution to a study of the prevalence of mesothelioma.

Section 8

Mortality in Kyperounda and Kato Amiandos

One of the most widely used measures of the health status of a community is the death rate. An improvement in the general wellbeing of a community is usually accompanied by a decrease in mortality, while deterioration in health status is associated with an increase. In the UK, and most other countries of the European Union, mortality data is used to describe variations in health between small geographic areas.

In the literature review we saw that the exposure to asbestos is associated with a number of serious, potentially fatal diseases such as asbestosis, mesothelioma and lung cancer. We have also seen that both occupational exposure and household exposure to asbestos has a significant impact on respiratory function. A key question is whether the index villages of Kyperounda and Kato Amiandos have a higher than expected mortality rate.

The Imperial College School of Medicine, London examined the mortality experience in a cohort of vermiculite miners exposed to fibrous amphibole in Libby, Montana. Mortality by certified cause was assessed in a cohort of 406 vermiculite mineworkers in Libby, Montana, employed before 1963 and followed until 1999. They found 44 deaths from lung cancer (SMR 2.40), 51 from non-malignant respiratory disease (SMR 3.09), and 285 deaths from all causes (SMR 1.27). Included among the total were 12 deaths ascribed to mesothelioma (4.21% of all deaths). The study concluded that amphibole fibres, tremolite in particular, are likely to be disproportionately responsible for cancer mortality in persons exposed to commercial chrysotile, but to what extent cannot be readily assessed.[1]

A review by the Department of Respiratory Medicine in Ashford and St Peter's Hospitals in the UK showed that mortality from mesothelioma continues to rise steeply (5% to 10% per year) in most industrialized countries. They conclude that even with widespread asbestos abatement efforts, this increase is likely to continue in Western Europe and the United State well into the next century, at least until 2020. Unregulated use of asbestos in less industrialized countries may cause the epidemic to continue throughout the next century in those regions.[2]

Both cigarette smoking and inhaled asbestos fibres can cause lung cancer, but the assessment of how these agents act in combination is a matter of great difficulty. A Canadian study concluded that although case-referent studies seemed to support the multiplicative hypothesis, the information from them is essentially unreliable. They argue that the multiplicative hypothesis is untenable and that the relative risk of lung cancer from asbestos exposure is about twice as high in non-smokers as in smokers; the best estimate of the relative asbestos effect (RAE) is 2.04, with 95% confidence interval 1.28-3.25. This finding is not only of high statistical significance but also of great social and scientific importance.[3]

In view of the high levels of exposure, both occupational and household, experienced by the residents of Kyperounda and Kato Amiandos it is important to assess whether the all cause mortality in these villages is usually high. At this stage of our investigation it is not possible to study the mortality rates from lung cancer and mesothelioma.

To study the mortality experience of the residents of Kyperounda and Kato Amiandos we decided to compare the morality experience with the district of Lemesos, and with a number of control villages such as Klirou, Ormedia and Kiti, using the national rate as the standard. The villages controls are places we used in previous studies and we believe provide effective comparisons.

1. INFORMATION SOURCES

The calculation of SMRs requires three pieces of data. First, accurate data on the age structure of the populations under study; second, accurate data on the number of observed deaths that occur in the areas under examination, and, third, a standard age specific death rate.

Our previous research showed that death certification in Cyprus was incomplete. Recent discussions with the Department of Statistics suggest that there has been a great improvement in the completeness of death certification over the last three or four years. Moreover, the Department collects a national sample of priests' death records that are used to estimate the degree of under reporting. On the basis of the priests records an adjustment is made to the national mortality figures to correct for under reporting. Latest data suggest that death certification is now around 95% complete. To evaluate the completeness of national mortality data from the national database we examined priest records in the index villages.

1.1. Death certificates from the village priest

The priest in Kyperounda had complete lists of deaths since the early 1990s to date. A death register, which included the name of the deceased, address, date of death, age and sex, and details of next of kin, was meticulously maintained by the priest. There was information on the cause of death in more than half of the cases. We obtained a copy of the priest's death register and abstracted the details into a computer spreadsheet. We obtained records from the early 1990s until the present. These records were used to evaluate the completeness of national data. There was also data on a number of deaths that were caused by mesothelioma. With regard to Kato Amiandos the village does not have its own priest but a visiting priest to conduct a funeral service as and when the need arises. However we did manage to check priest records as report from the District Office in Lemesos.

1.2. Cemetery data

In an attempt to validate the priest records we undertook a census of the cemeteries in Kyperounda and Kato Amiandos, to ascertain burials that had occurred in the last five years. Deaths on the priest list were checked against the gravestones, and we found a high degree of correlation, but there were a small number of cases in which we could find no gravestone. On further discussion, we learned that in a few cases burial took place in the village cemetery, particularly in cases where the person was born in the village but lived in town during the latter years of his or her life. As we could not control for this potential bias, we decided that there was little to be gained from cemetery data that was not on the priest's list.

1.3. Ministry of the Interior, Mortality Register

We obtained a record of deaths that had occurred in the index villages from the Mortality Register of the Information Technology Department of the Ministry of the Interior, for the five-year period 2000 – 2004. From the three sources of data mentioned above we were able to construct Table 1, which shows the number of deaths, ascertained from each source.

A careful inspection of the table shows that data from registration was relatively incomplete in 2000. Our evaluation of the national registration system showed that the deaths recorded in 2000 were only about 65% of those recorded in subsequent years. In Kyperounda, for example only 10 deaths were registered compared to 16 recorded by the priest's records. For the period 2001 – 2004 the match between the three sources is extremely close, and so we decided to base our SMR calculations on this period. We therefore decided to exclude the data from the year 2000 from our analysis.

Table 1 — Annual number of deaths on priest register for the five-year period: 2000 - 2004

Year	Kyperounda			Kato Amiandos		
	Priest records	Registration	Cemetery	Priest records	Registration	Cemetery
2000	16	10	16	1	0	1
2001	14	11	14	4	3	4
2002	18	18	18	5	4	5
2003	14	13	14	1	1	1
2004	15	15	15	6	6	5
All years	77	67	77	17	14	16

2. Observed deaths

The number of observed deaths for Kyperounda and Kato Amiandos was derived from the national database, held at the Ministry of the Interior mortality register.

Because of the small size of the populations that are being compared, the observed deaths per year are relatively small, and subject to wide random variation. Small numbers present difficulties in making comparisons because they give wide confidence limits. To overcome these problems it is necessary to aggregate observed deaths for a number of years to obtain a larger number. As mentioned above, we decided to use data from the villages for the 4-year period 2001 to 2004 to calculate the annual number of observed deaths.

3. Age specific national mortality rates

To calculate the standardised mortality ratio (SMR) it is necessary to have the age structure of the areas under consideration, the total number of observed deaths for each area, and the age specific death rates of the standard population. Table 2 shows that data we used to calculate national age specific death rates per 1000 population. Because of the relatively small number of deaths in the younger age bands we have used deaths for a three-year period to calculate national age specific rates. Effectively using a three-year rolling average to estimate the annual number of deaths. Dividing by three then annualises these rates.

The Cyprus age specific death rate was used as the standard, and so the SMR for Cyprus = 100. An SMR greater than 100 indicates a less favourable mortality experience than the standard population and a ratio more than 100 indicates a more favourable experience.

Table 2 Cyprus national age specific death rates: 2001

Age group	Population from 2001 Census	Deaths for 3 years period 2001-2003	Annualised age specific death rates per 1000
0-4	42582	143	1.12
5-9	51718	19	0.12
10-14	53178	15	0.09
15-19	54603	74	0.45
20-24	51803	92	0.59
25-29	48272	84	0.58
30-34	48233	98	0.68
35-39	51561	111	0.71
40-44	52289	143	0.91
45-49	45580	221	1.62
50-54	42587	364	2.85
55-59	34554	516	4.98
60-64	30747	714	7.74
65-69	25445	1100	14.41
70-74	20965	1561	24.83
75-79	15974	2156	44.99
80+	18089	6733	124.07

4. EXPECTED DEATHS

To calculate the number of expected deaths in the index villages we used the population age structure from the 2001 census. The national age specific death rates, calculated above, were then applied to the village populations to calculate the number of deaths that would occur in each village if they experience the national death rate. This is known as the expected number of deaths. The calculation of the expected number of deaths for the villages of Kyperounda and Kato Amiandos are shown in Table 3. The annual number of expected deaths, if national age specific death rates applied, in Kyperounda was 14.34, and in Kato Amiandos 2.39.

Table 3 — Calculating the annual expected number of deaths for Kyperounda and Kato Amiandos, if the Cyprus age specific death rates applied to each village population

Age group		Kyperounda		Kato Amiandos	
	National age specific death rates per 1000	Population census 2001	Expected deaths	Population census 2001	Expected deaths
0-4	1.12	116	0.13	8	0.01
5-9	0.12	117	0.01	9	0.00
10-14	0.09	113	0.01	17	0.00
15-19	0.45	123	0.06	11	0.00
20-24	0.59	85	0.05	11	0.01
25-29	0.58	90	0.05	11	0.01
30-34	0.68	89	0.06	11	0.01
35-39	0.71	94	0.07	12	0.01
40-44	0.91	93	0.08	9	0.01
45-49	1.62	90	0.15	13	0.02
50-54	2.85	72	0.21	17	0.05
55-59	4.98	67	0.33	13	0.06
60-64	7.74	96	0.75	25	0.19
65-69	14.41	75	1.08	17	0.24
70-74	24.83	68	1.68	16	0.40
75-79	44.99	40	1.80	11	0.49
80+	124.07	63	7.82	7	0.87
Annual expected number of deaths			14.34		2.39

5. CALCULATING SMRS

The calculations of the standardised mortality ratios are shown in Table 4. The annual number of observed deaths is divided by the annual number of expected deaths, to give the ratio between observed and expected. The result multiplied by 100 to give the SMR.

Table 4 — Calculating SMRs for Kyperounda and Kato Amiandos with 95% Confidence Intervals

	Annualised observed deaths for the 4-year period 2001-2004	Annualised expected deaths	SMR (95% CI)
Kyperounda	14.25	14.34	99.4 (75.3 – 128.7)
Kato Amiandos	3.5	2.39	146.4 (80.1 – 245.7)

The wide confidence intervals are because of the small numbers on which the calculations are based. The confidence interval shows that we can be 95% sure that the true result lies within that range. It helps us to decide whether there is a statistical difference between SMRs—if the confidence interval overlaps 100, that means that the result is not statistical different from the national rate. However, there is a question about the wisdom to using 95% confidence intervals when comparing death rates.

The SMR for Kyperounda is very near to the national rate, while the SMR in Kato Amiandos, while not statistical different at the 95%, level is 46% higher than the national rate. The fact that the exposure to asbestos has caused a significant increase in respiratory disease suggests that the SMR in Kato Amiandos may be a reflection of higher than expected mortality in the village. This question can only be answered by following mortality rates in the village over a longer period of time.

5.1 Comparing SMRs across control villages

In Table 5 we compare SMRs across a number of villages that we have investigated in previous studies. Again we have aggregated four years data to derive an annual estimate of observed deaths. Expected deaths have been calculated by applying national age specific rates to the village populations from the recent census.

Table 5 Comparing SMRs across control villages

	Observed deaths					Calculating SMRs			
	2001	2002	2003	2004	Total	Annual observed	Annual expected	SMR	
Kyperounda	11	18	13	15	57	14.25	14.34	99	(75-129)
Kato Amiandos	3	4	1	6	14	3.5	2.39	146	(80-247)
Kiti	15	20	22	25	82	20.5	17.97	114	(91-142)
Ergates	24	14	7	8	54	13.5	6.07	222	(167-290)
Klirou	13	7	9	12	41	10.25	13.75	75	(54-101)
Ormedia	14	33	17	25	89	22.25	21.53	103	(83-127)
Lemesos district	1147	1259	1280	1584	5270	1317.5	1350.87	98	(95-100)

It is interesting to observe that the village of Ergates, which was exposed to significant levels of PM10 from the scrap metal foundry, which closed in 2000, still has a higher than expected SMR. Nevertheless the number of deaths registered in the last two years suggests that the death rate is declining to the national average. It is also interesting that Kato Amiandos, which has the highest exposure to the asbestos mine, has the second highest SMR.

Nevertheless it is important to understand that these results are based on small numbers, and there is still plenty of scope for improving the completeness of death registration.

COMMENTS

1. We used three sources of ascertainment in an attempt to obtain an accurate count of the number of deaths that had occurred in the index villages. Our investigation showed the priest from Kyperounda kept meticulous records and we felt confident that he had a complete record of deaths. The picture in Kato Amiandos was

slightly different in as much that the village does not have its own priest and we had to rely on obtaining priest records as reported to the District office in Lemesos. Our evaluation of mortality data showed a fairly large discrepancy between priest records and registration data for the year 2000, with registration under recording the number of death. However, for the four-year period from 2001 to 2004 there was a large level of agreement between priest records and registration data. This confirms the fact that the completeness of death registration has improved considerably, and we felt confident in using the data from the national register of deaths. A census of cemeteries was also useful in that it helped us evaluate the accuracy of the data from the registration of deaths.

2. Following a careful assessment of the data we decided to aggregate data for the period 2001 to 2004 to calculate SMRs. It is common practise when making geographic comparisons in mortality rates between small areas to aggregate data in order to overcome the potentially large random variations in the number of deaths that occur from year to year. The aggregation of data reduces the problem of random variation and so produces more reliable results.

3. We used three years of national data and population data from the 2001 census to calculate national age specific rates.

4. While the calculation of SMRs for the index villages showed that there is no statistical difference at the 95% confidence level in the mortality experience of Kyperounda and Kato Amiandos and the other control villages, it should be noted that the SMR in Kato Amiandos was 46% higher than expected. It seems probable that the long-term exposure to asbestos has resulted in a small excess of deaths.

5. In order to do epidemiological studies it is essential to have accurate mortality. We strongly recommend that improvement in collection and recording of deaths should be maintained and further improved.

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Section 9

Social medical survey of Kyperounda and Kato Amiandos

A medical survey was undertaken to assess the respiratory health of the residents of Kyperounda and Kato Amiandos. A questionnaire was developed after holding a number of discussions with community leaders from the two villages. A major objective of the survey was to gather information on the views, opinions and perceptions of the villagers. Factors studied included smoking history, respiratory problems, previous medical problems, current symptoms and occupational details. Respiratory health was assessed using a modified version of the British Thoracic Society's questionnaire.

The sampling frame for the survey was residents of the two villages aged 50 years and over who had been invited to have their lung function tested by spirometry. Two Greek-speaking interviewers gathered data prior to the respondent undergoing spirometry testing.

1. Demographic characteristics of responders

Just less than three hundred questionnaires (293) were completed. The age sex breakdown of respondents is presented in Table 1. The age structure of responding men and women was similar. Over half respondents were in the 60-74 age group, and 15% were aged over 75.

Table 1 Age sex breakdown of respondents

	Males		Females		Persons	
Age group	n	(%)	n	(%)	n	(%)
30-59 years	37	(25.0)	46	(31,7)	83	(28.3)
60-74 years	82	(55.4)	84	(57.9)	166	(56.7)
75 and over	29	(19.6)	15	(10.3)	44	(15.0)
All ages	148	(100)	145	(100)	293	(100)

The age structure of male respondents from Kato Amiandos was slightly older than responding males in Kyperounda—19.4% of men in the smaller village were aged 75 and over compared to 7.9% of men in Kyperounda. The age structure of responding females was similar in the two villages.

The vast majority of respondents have lived in the villages for over 30 years, and only 2.1% for less than 20 years.

Among the male respondents 70% were retired and 28% were in full-time employment. Among females 58% were retired, 25% were housewives and 16% in full-time employment.

2. Occupational exposure

Occupational exposure was measured by the question: 'Have you ever worked in the asbestos mine?' The age-sex breakdown of the response to this question is shown in Table 2. As expected, men exhibited much higher rates of occupational exposure than women did. Three-quarters of male respondents (74.6%) had worked on the mine. There was a significant age differential, with all males aged over 75 having worked on the mine, compared to only half of those aged under 50. Among females respondents, 16.7% had worked on the mine, as had 26.7% of those aged over 75.

Table 2 Worked in the asbestos mine by sex and age group

Age group	Male Worked on mine Yes		No		Females Worked on mine Yes		No	
	n	%	N	%	n	%	n	%
30-59 years	19	17.4	17	47.2	4	16.7	41	34.5
60-74 years	62	56.9	19	52.8	16	66.7	67	56.3
75 and over	28	25.7	0	0	4	16.7	11	10.5
All ages	109	100	36	100	24	100	119	100

Analysis by village of residence showed much higher exposure rates in Kato Amiandos. Among men in Kato Amiandos, 86.4% had worked on the mine compared to 72.4% of men living in Kyperounda. Among the women living is Kato Amiandos 48.4% had worked on the mine compared to only 8% of Kyperounda women.

3. Household exposure

Household exposure was measured by the question: 'Have you ever lived in the same household as someone who worked on the mine?' Table 3 shows the age-sex breakdown of household exposure for female respondents. As with occupational exposure, there is an age gradient, with the older women having higher rates of household exposure. Of the woman aged 75 and over, 80% had a household exposure compared to just over half (53.3%) of the under 60s.

Table 3 Household exposure by age breakdown for females

Age group	Lived in same household as someone who worked in mine? Yes		No		All	
	n	(%)	n	(%)	n	(%)
30-59 years	24	(53.3)	21	(46.7)	45	(100)
60-74 years	57	(67.9)	27	(32.1)	84	(100)
75 and over	12	(80.0)	3	(20.0)	15	(100)
All ages	93	(64.6)	51	(35.4)	144	(100)

Women living in Kato Amiandos had higher rates of household exposure than women living in Kyperounda did. Of the 31 females from Kato Amiandos, 80.6% lived in the same household as someone who worked on the mine, compared to 60.2% of the of the 133 women respondents in Kyperounda. There was no evidence of any other significant exposure to asbestos besides the mine. Only 3 people had worked in another occupation associated with asbestos.

4. Smoking Behaviour

The smoking status of men is shown in Table 4.

Table 4 — Smoking status by age group of men

	Age group							
	30-59 years		60-74 years		75 and over		All ages	
Smoking status	n	(%)	n	(%)	n	(%)	n	(%)
Regular	12	(32.4)	13	(15.9)	1	(3.6)	26	(17.7)
Occasional	1	(2.7)	2	(2.4)	0	(0)	3	(2.0)
Gave up	9	(24.3)	43	(52.4)	16	(57.1)	68	(46.3)
Never	15	(40.5)	24	(29.3)	11	(39.3)	50	(34.0)
Total	37	(100)	82	(100)	28	(100)	147	(100)

Only 17.7% of male respondents were current regular smokers. It is interesting to note that the largest group are those who have given up smoking (46.3%). It is also significant that older men smoke less that their younger counterparts. This is because so many of them (57.1%) have given up smoking. It is disappointing to see that almost a third of men in the 30-59 age group (32.4%) are regular smokers. For some of the analysis on lung function tests the smoking variable has been divided into two groups—those who have never smoked and those with a smoking history. In other words, the large groups of older men who have given up have been combined with the current smokers. There was no difference between the smoking pattern of those who worked on the mine and the rest of the population.

As expected in rural Cyprus very few women smoke. This survey showed 98% of women had never smoked. Indeed, most of those who had smoked had given up. In the analysis, therefore, it is not necessary to control household exposure among women for smoking. Smoking habits among men were very different, although we very surprised to see that only 18% very still regular smokers.

5. Perceived Health Status

Table 5 shows self-perceived health status by age and sex.

Table 5 — Self-perceived health status by age and sex

Age group	30-59 years		60-74 years		75 and over		All years	
	Men	Women	Men	Women	Men	Women	Men	Women
	n = 37	n = 45	n = 82	n= 83	n = 28	n = 15	n = 147	n = 143
	Percentage							
Good health	70.3	33.3	24.4	20.5	39.3	6.7	38.8	23.1
Fair health	27.0	64.4	65.9	75.9	46.4	80.0	52.4	72.7
Poor heath	2.7	2.2	9.8	3.6	14.3	13.3	8.8	4.2
All	100	100	100	100	100	100	100	100

The question 'How would you describe your general health?' was used to assess the state of the general health of respondents.

What is noticeable is that women, as a rule, perceive their health to be less good than men do, despite the fact it is the men who have the highest rates of cigarette smoking and occupational exposure to asbestos. Among the youngest age group (30-59 years), for example, only a third on women (33.3%) perceived their health to be good compared to 70.3% of men. There is a similar sex differentiation in the oldest age group, with almost 40% of old men perceiving their health to be good compared to just 6.7% of older women. Most women perceive their health to be fair. It is interesting that in the middle age group (60-74) more men (9.8%) than women (3.6%) perceive their health to be poor.

Table 6 shows self-perceived health status by occupational exposure. In this analysis we have controlled for age, as the non-exposed population is younger than the exposed population, and because health status is strongly age related, to make a meaningful comparison between the groups it is necessary to compared populations of similar age structure. We have therefore excluded the over 70s, most of whom are in the exposed group. Among both men and women who have been occupationally exposed, more perceive their health status to be poor, as can be seen in Table 6.

Table 6 — Perceived health status by occupation exposure among those aged 30 to 69 years

	Worked on mine			
	Men		Women	
	Yes: n = 50	No: n = 34	Yes: n = 14	No: n = 93
	Percentage who perceive health good, fair, poor			
Good	38.0	52.9	21.4	28.0
Fair	54.0	44.2	71.4	68.8
Poor	8.0	2.9	7.2	3.2
All	100	100	100	100

Pearson's Chi-squared, p=0.318 Pearson's Chi-squared, p=0.707

Although a greater proportion of occupational exposed men perceive their health to be poor compared to the non-exposed group, a Chi-squared test shows that there is no statistical difference in the perception of health status between exposed and non-exposed groups. Similarly, among women there is no significant difference between the occupationally exposed and non-exposed groups.

Table 7 shows the perception of health status by smoking history. Note that the smoking history group includes both current and past smokers who have given up the habit. Once again there is no statistical difference in the perception of health status between the groups

Table 7	Perceived health status by smoking history among males	
	History of smoking (n = 97)	Never smoked (n = 50)
	Percentage who perceive health good, fair, poor	
Good	35.1	46.0
Fair	56.7	44.0
Poor	8.2	10.0
All	100	100

Pearson's Chi square = 2.151, P=0.341

Table 8 shows the perception of health status by household exposure among women. Once again, there is no statistical difference in the perception of health status between exposed and non-exposed women.

Table 8	Perceived health status by household exposure: Females			
	Lived in same household as someone who worked in mine			
	Yes		No	
	n	(%)	n	(%)
Good	21	(22.6)	12	(24.0)
Fair	68	(73.1)	36	(72.0)
Poor	4	(4.3)	2	(4.0)
Total	93	(100)	50	(100)

Pearson's Chi square = 0.041, P=0.98

6. Respiratory symptoms

Questions from the modified British Thoracic Society's were used to ascertain the prevalence of respiratory symptoms. Table 9 shows the proportion of men in the 30-69 age group that suffered with each symptom by exposure group.

Table 9	Respiratory symptoms for men aged 30-69 by occupational exposure				
	Exposed n = 50		Non-exposed n = 34		
	n	(%)	n	(%)	P value
Cough in morning in winter months	24	(48.0)	13	(38.2)	0.255
In winter usually cough during day or night	14	(28.0)	7	(20.6)	0.306
Cough for 3 months in last 12 months	6	(12.0)	4	(11.8)	0.537
Bring up phlegm in the morning in winter	27	(54.0)	14	(41.2)	0.176
Cough up phlegm during day or night	17	(34.0)	8	(23.5)	0.251
Cough phlegm for 3 months in a year	5	(10.0)	6	(17.6)	0.157
During last 3 years cough and phlegm for 3 months	8	(16.0)	4	(11.8)	0.430
Dyspnoea when walking on small uphill	18	(36.0)	12	(35.3)	0.564
Dyspnoea when walking with others of own age	16	(32.0)	11	(32.4)	0.285
Wheezing from your chest	14	(28.0)	6	(17.6)	0.204

A chi-squared statistical test was performed for each symptom, and the p values are reported. The exposed group reported higher rates of winter cough, higher rates of winter phlegm in the morning, and higher rates of wheezing. An examination of the table shows that for none of the symptoms was there a statistical difference between the exposed and non-exposed. The reason for the failure to demonstrate statistical differences is due to the relatively small numbers involved in the study.

Table 10 shows a similar analysis for household exposure. Again the household group has a higher rate of respiratory symptoms than the non-exposed group. Yet the difference in the prevalence of symptoms between the exposed and non-exposed groups did not reach statistical significance (see p values).

Table 10 — Respiratory symptoms for women aged 30-69 by household exposure

	Exposed n = 66		Non-exposed n = 43		
	n	(%)	n	(%)	P value
Cough in morning in winter months	29	(43.9)	20	(46.5)	0.791
In winter usually cough during day or night	22	(33.3)	8	(18.6)	0.091
Cough for 3 months in last 12 months	8	(12.1)	0	(0)	0.016
Bring up phlegm in the morning in winter	29	(43.9)	13	(30.2)	0.151
Cough up phlegm during day or night	18	(27.2)	7	(16.2)	0.182
Cough phlegm for 3 months in a year	7	(10.6)	1	(2.3)	0.105
During last 3 years cough and phlegm for 3 months	6	(9.1)	0	(0)	0.105
Dyspnoea when walking on small uphill	32	(48.5)	15	(34.9)	0.161
Dyspnoea when walking with other of own age	27	(40.1)	12	(27.9)	0.166
Wheezing from your chest	9	(13.6)	3	(7.0)	0.277

7. Medical condition by exposure

Respondents were asked to list the illnesses from which they have personally suffered. The most common diseases recorded were heart disease, bronchitis and depression. Five respondents reported that they had cancer, four of whom were aged over 60, and three were among the group who had never smoked. Table 11 shows the prevalence of cancer by exposure group.

Table 11 — Self report prevalence of cancer by occupational exposure

	Occupationally exposed		Not exposed		All	
	n	(%)	n	(%)	n	(%)
Diagnosis of cancer	4	(3%)	1	(0.6%)	5	(1.7%)
No cancer	128	(97%)	154	(99.4%)	282	(98.3%)
Total	132	(100%)	155	(100%)	287	(100%)

The difference in self-report cancers between the groups just failed to reach statistically significant level. (Fisher's exact test p=0.139). This means that the difference between the groups may be a chance finding.

Our analysis of self-reported diseases by occupational exposure is shown in table 12. Note that the occupationally exposed men had higher rates of heart disease and bronchitis. Of men who worked on the mine 28.4% reported that they had heart disease and 19.3% bronchitis, compared to 16.7% and 8.3% in the non-exposed controls. Four exposed men reported a history of depression compared to none in the non-exposed group. Pearson's chi-squared test showed that none of these differences reached statistical significance. However, if we aggregate the self-reported morbidity by the exposed group (60 morbid conditions), it is significantly much higher than that of the non-exposed group (9 morbid conditions). Chi-squared p=0.0017

Table 12 Self reported diseases by exposure: Males

	Occupationally exposed = 109		Non-exposed = 36		All = 145	
	n	(%	n	%	n	%
Heart disease	31	(28.4)	6	(16.7)	37	(25.5)
Bronchitis	21	(19.3)	3	(8.3)	24	(16.5)
Depression	4	(3.7)	0	(0)	4	(2.8)
Cancer	4	(3.7)	0	(0)	4	(2.8)
Mesothelioma	0	(0)	0	(0)	0	(0)

Turning to household exposure among females there is no difference in the rate of heart disease or bronchitis between exposed and non-exposed women. That is, 27.2% of exposed women reported that they suffered with heart disease compared to 30.0% of non-exposed women. For bronchitis, 10.9% of exposed had suffered with the condition compared to 9.8% of non-exposed women. Depression was twice as common (17.6%) among exposed women compared to the non-exposed (9.8%). One exposed woman reported mesothelioma and one non-exposed woman reported cancer. The total morbid conditions reported by those with a household exposure were 52 (56%), is not statistically different from the 25 (50%) reported by the non-exposed group.

In response to the question 'Has anybody in your family died from lung cancer or mesothelioma?' the following response was elicited: Fifteen respondents identified a family member who had died from lung cancer all of which were from Kyperounda. With regard to mesothelioma, seven respondents said that a family member had died from the condition, of which six were from Kyperounda. However this does not necessarily mean that there were seven different cases of mesothelioma. This information can be used to inform a study into the incidence of mesothelioma

Table 13 Self reported diseases by household exposure: Females

	Exposed = 92		Non-exposed = 50		All = 142	
	n	%	n	%	N	%
Heart disease	25	(27.2)	15	(30.0)	40	(28.2)
Bronchitis	10	(10.9)	5	(9.8)	15	(10.5)
Depression	16	(17.6)	4	(8.2)	20	(14.3)
Cancer	0	(0)	1	(2.0)	1	(0.7)
Mesothelioma	1	(1.1)	0	(0)	1	(0.7)

8. OPINIONS ON HOW MINE AFFECTED HEALTH

Three questions were asked about perceptions of how the mine had affected health and the environment. Predictably, 90% of respondents believe that the quality of life in the village has changed since the closure of the mine, and 88% believe that the mine has adversely affected the quality of the environment.

Opinions on the way that the mine has affected health are shown in Table 14. There is a large difference in the perception between exposed and non-exposed groups on the way in which the mine has affected their personal health. Among the men, half of the exposed group (52.8%) believes that their health has been adversely affected by the mine and just over a third of the non-exposed group (38.9%). Interestingly, over a quarter of the men (26.9%) who worked on the mine say that it has had no adverse affect on their health. Among the women, less than a third (30.4%) believe that the mine has had a great affect on their health.

Table 14	In your opinion, how much has the asbestos mine affected your personal health?			
Affect on personal health?	Males = 144		Females = 141	
	Occupationally Exposed n=108	Occupationally Non-exposed n=36	Occupationally Exposed n=23	Occupationally Non-exposed n=118
	Percentage			
Not affect	26.9	55.5	52.2	46.2
Moderate affect	20.4	5.6	17.4	11.9
Great affect	52.8	38.9	30.4	41.5
	100	100	100	100

9. SURVEY OF TROODOS VILLAGES

In 2000 the Ministry of Health undertook a survey of villagers who were concerned about the health impact of being exposed to asbestos dust. Residents who were concerned about their health were invited to complete a health questionnaire, which gathered data on exposure history and respiratory problems. We have entered the data from the questionnaire into an Access database and undertaken a preliminary examination of the data as it pertains to the villages of Kato Amiandos and Kyperounda. Table 15 shows the age sex breakdown of the surveyed population.

Table 15	Age sex breakdown of survey respondents					
Age group	Male		Female		Persons	
	n	(%	n	%	N	%
30-59 years	37	(25.9)	78	(20.9)	115	(22.3)
60-74 years	89	(62.2)	201	(53.9)	290	(52.6)
75 and over	17	(11.9)	94	(25.2)	111	(21.5)
All	143	(100)	373	(100)	516	(100)

Among the surveyed population there were 86 residents of Kyperounda and 56 residents of Kato Amiandos. Among the Kyperounda respondents, 17% of the females were aged 75 and over; among the males none were aged over 75. Among Kato Amiandos respondents, 15% of both males and females were aged over 75.

Table 16 shows self-reported symptoms by the respondents from the two villages, for men and women.

Table 16 Self-reported respiratory symptoms for respondents from the village populations of Kato Amiandos and Kyperounda

	Kato Amiandos				Kyperounda			
	Males n=36		Female n=33		Males n=86		Females n=15	
	n	(%)	n	(%)	n	(%)	n	%
Cough in winter	13	(36.1)	9	(27.3)	28	(32.6)	6	(40.0)
Phlegm in winter	14	(38.9)	6	(18.2)	39	(45.3)	4	(26.7)
Dyspnoea	16	(44.4)	19	(57.6)	43	(50.0)	10	(66.7)

The rate of winter cough is slightly more common among females; despite the fact men have higher rates of smoking and occupational exposure to asbestos. The men, however, have higher rates of phlegm in winter than the women. The symptom distribution is similar between the villages. Moreover, the rate of symptoms is similar to that reported by occupationally exposed men and women with a household exposure in our study.

Table 17 Self-reported diseases and medical conditions by the village populations of Kato Amiandos and Kyperounda: Percentage of respondents with disease

	Kato Amiandos		Kyperounta	
	Males n=36	Female n=33	Males n=86	Females n=15
Heart disease	50.0 %	54.5 %	30.2 %	20.0 %
Bronchitis	25.0 %	42.4 %	33.7 %	33.3 %
Asthma	5.6 %	15.2 %	9.3 %	26.7 %
Allergic rhinitis	22.2 %	36.4 %	26.7 %	53.3 %
Lung cancer	0 %	3.0 %	0 %	0 %
Mesothelioma	5.6 %	0 %	0 %	0 %

Table 17 shows self-reported diseases among responding villagers. As with symptoms, so the prevalence rate of self-reported disease is similar to that reported in our survey.

COMMENTS

1. Occupational exposure was largely age dependent, with older people more likely to have worked on the mine. Three-quarters of men in the survey had worked on the mine and one quarter of females. The residents of Kato

Amiandos had higher levels of occupational exposure than residents of Kyperounda.

2. Household exposure was largely a factor among women. Two-thirds of the women in the survey lived in a household with someone who worked on the mine. As with occupational exposure, household exposure was strongly age dependent. There was no evidence of any other significant source of asbestos exposure among the village populations.
3. There is evidence that the health of those who have worked on the mine has been adversely affected. A higher proportion of men who have been occupational exposed perceive their health to be poor compared to their non-exposed counterparts. Those who have occupationally exposed have higher rates of heart disease and bronchitis. The occupationally exposed are more likely to cough in morning in winter months and more likely to bring up phlegm in the morning in winter than their non-exposed counterparts. However, because of the relatively small numbers involved in our analysis none of these differences achieved statistical significance at the 95% confidence level. This does not mean that these are not real differences, but that the differences cannot be established by statistical tests that demand confidence at the 95% level. It seems highly likely that if more residents were examined that the reported difference would reach statistical difference. Moreover, it must be remembered that the failure to demonstrate a statistical difference does not necessarily mean that there is not a real difference.
4. There is some evidence that household exposure has adverse affects on respiratory symptoms. However, those with household exposure had similar rates of heart disease and bronchitis as their non-exposed counterparts. Rates of self-reported depression were twice as high among exposed women.
5. The level of smoking among older men appears to have declined as many have given up the smoking habit. However, it seems probable that many of the older men had smoked for many years before giving up, and therefore we included them in the group with a history of smoking for the purposes of analysis. We would recommend a health promotion campaign among the villages to encourage men to give up the habit.
6. Although the rate of self-reported cancers in the occupationally exposed group was not statistical different, it is of concern that those with an occupational exposure probably have a higher risk of developing cancer.
7. We have identified one self-reported case of mesothelioma from our own survey, while the survey conducted in 2000 by the Ministry of Health identified two such cases. Respondents reported a number of family members who had died with lung cancer and mesothelioma. These findings suggest the importance of conducting a study of the incidence of lung cancer and mesothelioma in the exposed population.

Section 10

Rapid Appraisal

1. INTRODUCTION

Rapid appraisal is a useful technique to supplement the findings of the medico-social survey. The idea is to ascertain the views and opinions of local people who have first hand knowledge of the social and health affects of the asbestos mine on life in the village communities.

While the interviews were based on a semi-structured questionnaire, residents of the two villages were encouraged to freely express their views of the situation. Views and opinions were ascertained from a wide range of people who live in the villages and had worked in the mine.

2. METHODOLOGY

We collected information using a semi-structured interview technique. This ensured that residents in the villages were asked about specific issues but also had the freedom to address a range of other issues that had not necessarily been raised by the interviewer.

People were selected for interview mainly at random with the research investigators visiting the coffee shops and talking to people who had a story to relate. We interviewed some people on their own and also had group discussions in the coffee shops. These proved very lively, sometime amusing, and always interesting. In addition we had in depth discussions with the local council leaders in both villages and obtained their views of collective community feelings in the area.

3. COLLECTIVE VIEWS AND OPINIONS FROM THE VILLAGES

We heard stories from many men from both villages who had worked in the mine for almost their whole working life. Their stories were full of human interest. They described scenes where thousands of men were digging the mine with pickaxes, while others were sifting the asbestos fibres manually, and yet others were loading asbestos into lorries. In the early days the workers were given no uniforms to wear and no masks to protect their lungs from inhaling the massive amount of dust that was generated. According to the men they only offered masks from 1980 onwards. People travelled by bus to the mine from all over the island and many slept on the mine during the week.

The management of the company frequently used dynamite to open up the rocks for mining. They were provided with shower facilities once a week. The authorities had built a local hospital to look after the workers and deal with any accidents. People in the village recalled a few fatal accidents from the mine. In the early years people used to work from dawn to dusk before the second world war they were earning around six shillings a day. They were allowed 15 minutes break in the morning to have their breakfast and half an hour to eat their lunch.

Despite the difficult working conditions and very hard way of life men described a fantastic community spirit. The mine brought the people together as a community and most formed life long friendships. Men working in the mine often brought their wives to stay with them and many babies were born in the local hospital.

For entertainment in the evenings they were able to attend a local cinema which the authorities had built especially for them. They described conditions whereby they did not have a change of clothes for a whole week and even then it was a case of having the same clothes washed at home during the weekend. Men were going home at weekend with clothes full of white (asbestos type) dust and therefore exposing their households to asbestos fibres.

4. SOME INDIVIDUAL STORIES OF SPECIAL INTEREST

This is the story of an 84-year-old man from Kato Amiandos who worked in the asbestos mine for over 50 years.

The gentleman was born in 1921 and worked in the mine for over 50 years. He started working in the asbestos mine when he was fifteen years old. He described the working conditions at the beginning as very hard work from dawn to dusk, working six days a week. They were allowed fifteen-minute break in the morning to have their breakfast, which normally consisted of bread some green olives, or halloumi cheese and a tomato, plus half an hour for their lunch. The miners dug out asbestos with pickaxes. The soil was sifted with a shovel to separate the asbestos fibres from the rubbish. When he went home in the evening his clothes were full of white dust and his wife had to shake the dust out and hang them on the clothesline so that they were ready for him to wear the next morning. The house was often full of dust, and he described the whole village of Kato Amiandos as being covered with white dust from the mine like a sheet of snow. He described the condition of fruit trees dying when they had too much dust on them over a long period of time and the stream of water running down the mountain being white from the dust.

Most people from other villages who worked in the mine used to sleep there during the week and go home only for Sunday. He recalls the introduction of an 8-hour working week in 1944, following a strike by all the workers demanding improvements in working conditions.

This elderly gentleman could also recall the introduction of machinery in the mine in 1956. One of the most unwanted effects of this machinery was an increase in the dust which used to be spread all over the village of Kato Amiandos and was blown by the wind all the way to the sea at Limassol. Workers had dust all over their clothes and at the end of the day when they finished work they used to queue up to have the dust cleaned off their clothes with air pressure. He remembers the introduction of shift work around 1960 and the supply of protective masks for the workers to wear in 1980.

With the introduction of the machinery in 1956 the workforce of around 13,000 was gradually reduced to around 500 people and when the mine closed down in 1988 they only had 250 employees.

This man has been a smoker for over 50 years and although he has had a few breathing problems, including hospital treatment, he felt that his general health was good. A lot of his friends who worked with him on the mine have had severe respiratory problems and he recalls colleagues who have died from chest problems. However he is not going to give up smoking now and thinks he is lucky to be alive and says that he will enjoy smoking to the end of his days.

Another man in the village of Kato Amiandos, aged 72, also started work in the mine at the age of 15 and worked for 30 years. He had several types of jobs in the mine from digging to loading sacks of asbestos fibres onto lorries to be transported to the port in the Lemesos. He also described working conditions as very poor and he remembers clearly how he looked like a snowman going home in the evening with his clothes completely covered in white dust. He now suffers from emphysema and has had a few admissions to hospital because of his lung problems.

The story of another man from Kyperounda, aged 64, who worked in the mine for 13 years until it closed in 1988, described many of the same issues. He described a strong community spirit and was sorry that the mine has closed down as the feeling of togetherness had diminished. It was not only the work that brought people together, they also shared a social life with many political and other discussions took place in the coffee shops. While the mine was open there was a local cinema and they had good shopping facilities. The community was more vibrant as many young married couples were bringing up their families. Most of the young people now leave the villages for a life in towns with the result that the population of the villages are shrinking with some of the smaller villages like Kato Amiandos facing extinction.

The council leader of Kato Amiandos corroborated this view of the danger facing the smaller villages. He holds the view that unless the government takes some action the current generation living in Kato Amiandos would be the last as there are no young people with families living in the village anymore.

5. Summary of Views and Opinions

Over the course of the interviews a number of common themes emerged.

Most of the people that we interviewed were of the opinion that the asbestos mine has had a considerable impact on the health of the workers. Many suffered from respiratory conditions, which led to repeated admissions to hospital, particularly in the winter months. People described colleagues who died from cancer and mesothelioma although the majority of villagers did not really understand the term mesothelioma. Most people thought that the health of the local population had improved following the closure of the mine.

With regard to the social issues we heard descriptions of the poor working conditions and very hard way of life mixed with good community spirit and togetherness that were lost with the closure of the mines. However most people are happy that the mine has closed down and the environment has improved considerably, even though more needs to be done by the government to cover with plants and trees the grey areas left from the open cast mining.

Section 11

Lung Sample Analysis for Asbestos Fibres

1. Introduction

To assess the environmental exposure to asbestos in ambient air we undertook to examine the asbestos fibre count in goats from the area. The idea behind this part of the study was to ascertain whether goats' lungs would provide a reliable method for ascertaining the extent of environmental exposure. If this proved to be the case then it could be used in the next phases of the study.

From the start we encountered difficulties in finding goats in the villages of Kyperounda and Kato Amiandos. The Council leaders in both villages informed us that most people in the villages had stopped breeding goats and that this was part of a government strategy to clean up the environment. Although we included a question in our census questionnaire we managed to find only two households in Kyperounda that had goats, both of which agreed to sell us one goat for the purposes of our research study. One of the goats was from the east part of the Kyperounda village and the other from the west.

In Kato Amiandos there was only one household that bred goats, which they mainly for milk production. Despite several requests directly by members of the research team, from representatives of the Ministry of Health and also by their Council leader the family refused to part with any of their goats.

The two goats that were given to us from Kyperounda had the following identification numbers. The goat from the west (nearest to the asbestos mine) of the village had the identification number (ID) 207559342 and the goat from the east of the village (furthest away from the asbestos mines) ID 206590254. Both goats were approximately 12 years old.

The two goats were slaughtered under supervision at the abattoir, their lungs were removed and put into separate bags provided with the ID numbers and taken to the Cyprus government veterinary laboratory. The Veterinary Pathologist of the Public Veterinary Services Mr Tomazos agreed to prepare the samples, in line with the protocol that was prepared by Dr Dave Furness from the University of Keele. The samples were preserved in 4% formaldehyde and transported to the Laboratory of the University of Keele in the United Kingdom within 24 hours.

2. Objective for goat lung tissue analysis

The first objective was to ascertain whether there was evidence of an exposure to environmental asbestos. A secondary objective was to investigate whether it would be appropriate to use goat lung tissues for the assessment of environmental exposure to asbestos during the three remaining stages of this four-year medical research project.

3. Preparation

Lung samples from two goats, 207559342 and 206590254, in 4% formaldehyde were received at the laboratory. Four replicates of approximately 1g pieces of fixed tissue from each were dried overnight at 60°C, weighed and digested with 30 mL 5% potassium hydroxide overnight at 70°C.

After centrifugation and washing 3X, the samples were re-suspended in 10 mL distilled water and 5X0.25 μL volumes were taken out per sample and placed on glass slides. Although air-drying was used for the first samples, the artefacts produced made clear analysis difficult.

Therefore, a second set of 0.25 μL samples were placed under a cover slip and analysed by light and subsequently by transmission electron microscopy TEM. Asbestos-like fibres were counted through the whole volume and the counts extrapolated back to the amount per dry weight.

4. RESULTS FROM PHASE OPTICAL MICROSCOPY (PCOM)

A total of 25 samples were analysed with phase optical microscopy. Thirteen samples were taken from the goat that lived in the west part of Kyperounda village and twelve from the one that lived in the east.

The data shown in table 1 below are the raw data from the 13 samples showing the actual number of fibres counted from the lung tissue samples of the goat from the west of Kyperounda village.

Table 1

Optical microscopy analysis of specimens from the east of Kyperounda
Goat ID Number 207559342 (west of the village)

Specimen	Numbers of elongate fibres/0.25					Dry weight
207559342-A-1	5	4	0	4	1	0.2394 g
207559342-A-2	8	2	6	6	8	0.2193 g
207559342-A-3	205	148	183	197	170	0.3143 g
207559342-A-4	5	2	5	6	4	0.4165 g
207559342-A-5	15	5	3	6	6	0.2048 g
207559342-A-6	4	4	1	3	2	0.1965 g
207559342-A-7	2	3	13	0	0	0.1314 g
207559342-A-8	5	1	5	0	0	0.2602 g
207559342-A-9	5	7	5	0	0	0.3814 g
207559342-A-10	76	8	1	0	0	0.1605 g
207559342-A-11	3	2	2	0	0	0.1666g
207559342-A-12	1	4	4	0	0	0.2027 g
207559342-A-13	2	3	1	0	0	0.1936

Notes:

1. **It should be noted that the specimen 207559342-A-3 shows a much higher number of asbestos fibres than all the other specimens from the same lung**
2. **The specimens were analysed in three different series and it has not been possible to reproduce the findings of Specimen A3.**
3. **The interpretation the readings for specimen A-3 should be treated with caution**.

The data shown in table 2 below are the raw data from the 12 samples of the goat that lived in the east part of Kyperounda.

Table 2

Optical microscopy analysis of specimens from the east of Kyperounda
Goat ID Number 206590254 (east of the village)

Specimen	Numbers of elongate fibres/0.25					Dry weight
206590254-B-1	6	5	3	3	2	0.2225 g
206590254-B-2	6	2	0	2	2	0.1571 g
206590254-B-3	3	4	2	0	2	0.2208
206590254-B-4	1	1	0	1	4	0.2472 g
206590254-B-5	11	11	14	0	0	0.1892 g
206590254-B-6	7	9	4	0	0	0.1338 g
206590254-B-7	3	6	1	0	0	0.1926 g
206590254-B-8	0	3	5	0	0	0.1143 G
206590254-B-9	5	0	2	0	0	0.1508 G
206590254-B-10	2	6	2	0	0	0.1212 g
206590254-B-11	2	4	3	0	0	0.1536 g
206590254-B-12	1	2	3	0	0	0.1719 g

A comparison of the results from the two goats using the number of fibres as function of dry weight is shown in table 3 below:

Table 3

Comparison of fibres as a function of dry weight of goat lung tissue specimens between the goat in the west and the goat in the east of Kyperounda village

Goat ID Number 207559342 (West of the village)		Goat ID Number 206590254 (East of the village)	
Specimen	Numbers of elongate fibres/g	Specimen	Numbers of elongate fibres/g
207559342-A-1	2339181	206590254-B-1	3174603
207559342-A-2	5012531	206590254-B-2	2005013
207559342-A-3	1.51×10^8	206590254-B-3	1837928
207559342-A-4	3675856	206590254-B-4	1169591
207559342-A-5	13671.88	206590254-B-5	25370
207559342-A-6	5450	206590254-B-6	19930
207559342-A-7	18265	206590254-B-7	6923
207559342-A-8	5637	206590254-B-8	9332
207559342-A-9	5943	206590254-B-9	6189
207559342-A10	6978	206590254-B-10	9901
207559342-A-11	4802	206590254-B-11	7813
207559342-A-12	5920	206590254-B-12	4654
207559342-A-13	4132	-----------------	---------------
Mean	**29,163/g***	**Mean**	**9,171/g**

Note * The mean for Goat ID Number 207559342 excluding specimen A-3 is 12,439/g

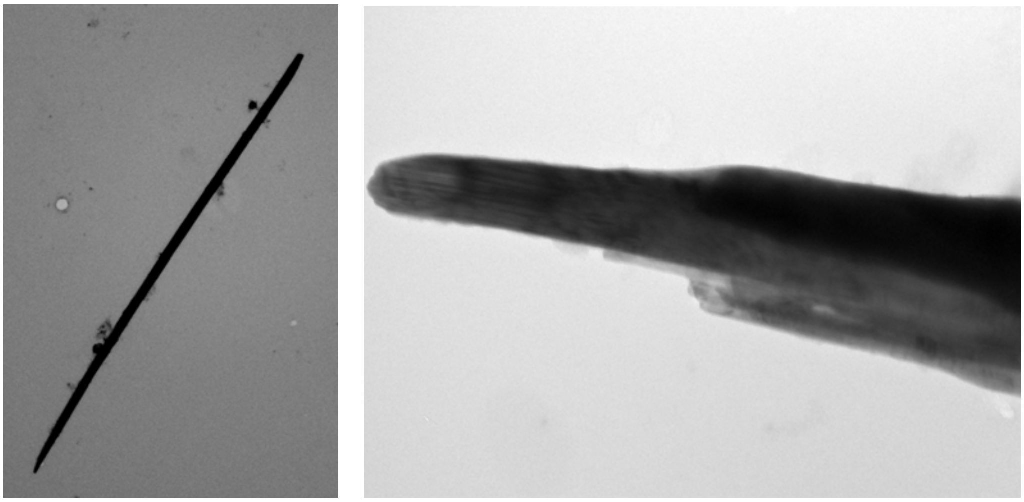
5. TRANSMISSION ELECTRON MICROSCOPY (TEM) ANALYSIS OF MINERAL FIBRES IN LUNG TISSUE

5.1 Preparation

A total of 25 samples were used for the transmission electron microscopy analysis. The samples used for transmission electron microscopic (TEM) analysis were the same extracted samples used for the light microscopic analysis. The fluid was centrifuged to concentrate the fibres and small volumes allowed to dry onto pioloform coated 2X1 mm slot grids. After drying they were examined by bright field TEM and a subset were analysed by X-ray microanalysis without further cleaning.

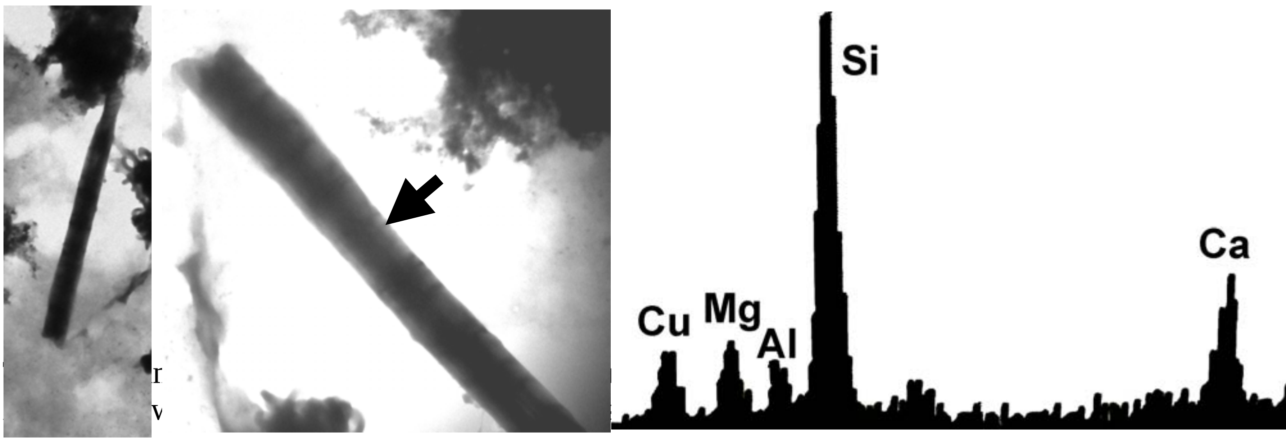
5.2 Results

The imaging revealed a number of rod like structures, which were reminiscent of images, and descriptions of asbestos fibres in the literature:



Low power and high power TEM images of the fibres.

X-ray microanalysis was performed on the samples, but only one yielded a viable spectrum, which is illustrated below, right. The left and central images are low and high power TEMs of the fibre analysed.



(Al), magnesium (Mg), calcium, (Si) silicon, (Ca) and iron (not shown on this part of the spectrum) detected. Copper (Cu) is artifactual because it is the material of the slot grid used to suspend the sample, and can be disregarded. This spectrum should be interpreted with caution and not quantitatively because the sample preparation is crude and there has been no calibration. Nevertheless, the spectrum is consistent with an asbestos fibre (high in silicon).

The elements found are most consistent with **chrysotile** asbestos. The magnesium peak is rather low compared with the silicon peak for **chrysotile**, but higher than would be expected for most other asbestos types. Detectability of magnesium can be poor because it has low molecular mass and lies to the edge of our detection range. **Anthophyllite** is also a possibility because of the presence of significant magnesium but calcium should not be present, as far as our information suggests. **Crocidilite** and **amosite** have little magnesium and may show some evidence of potassium, which we have not detected.

6. NUMBERS AND LENGTH OF CHRYSOTILE ASBESTOS FIBRES IDENTIFIED

The numbers and length of fibres identified as Chrysotile are shown in table 4 below:

Table 4
Number and length of asbestos fibres identified as Chrysotile with Transmission electron microscopy (TEM)

Goat ID Number 207559342 (West of the village)			Goat ID Number 206590254 (East of the village)		
Specimen	No	Length µm	Specimen	No	Length µm
207559342-A-1	0	--	206590254-B-1	0	--
207559342-A-2	0	--	206590254-B-2	0	--
207559342-A-3	0	--	206590254-B-3	0	--
207559342-A-4	0	--	206590254-B-4	0	--
207559342-A-5	0	--	206590254-B-5	0	--
207559342-A-6	1*	13.3	206590254-B-6	0	--
207559342-A-7	0	--	206590254-B-7	0	--
207559342-A-8	0	--	206590254-B-8	0	--
207559342-A-9	1	24.8	206590254-B-9	1	25.2
207559342-A10	0	--	206590254-B-10	1	4.5
207559342-A-11	0	--	206590254-B-11	0	--
207559342-A-12	0	--	206590254-B-12	0	--
207559342-A-13	0	--			

Note* There was one additional Chrysotile fibre found in 207559342-A-6. It was photographed but the laboratory was unable to measure its length.

7. ANALYSIS OF RESULTS FROM OPTICAL AND ELECTRON MICROSCOPY

The data from the optical microscopy indicate that there was one specimen in one goat where the count of fibres was significantly higher than all the other samples in the same goat. The specimens were analysed in a series on three different occasions and the high count of fibres did not prove reproducible.

The mean number of fibres for the goat from the west part of Kyperounda village was 29,163/g, including the specimen with the high count (specimen 207559342-A-3 as shown in tables 1 and 3). However, if the one specimen with the high count of fibres is excluded from the calculation the mean is 12,439/g. The mean number of fibres from the goat from the east part of Kyperounda is 9,171/g. If we exclude the specimen with the high count there is no statistically significant difference in the number of fibres between the two goats.

The finding of only 5 chrysotile asbestos fibres from the transmission electron microscopy does not lend itself to a valid conclusion of heavy environmental asbestos exposure. The presence and length of chrysotile may indicate that the goats breathed in these fibres, either recently or in the past. An interesting point is that chrysotile was found in both goats and no gradient of proximity to the asbestos mines could be established.

8. COMPARISON WITH HUMAN FIBRE LOADS AND OTHER STUDIES

One study using Corsican goats examined chrysotile and tremolite asbestos fibres in the lungs and parietal pleura. The results showed both chrysotile and tremolite fibres were detected. In the exposed goats, the geometric mean concentrations of asbestos fibres longer than 1 μm were 0.27×10^6 fibres/g dry lung tissue and 1.8×10^6 fibres/g dry pleural tissue.

The concentrations in the Corsican goats study did not differ significantly between the upper, middle, and lower lung samples. The highest concentration was 1.8×10^6 f/g dry lung. Mean lung tissue concentrations were below one million f/g dry lung in all exposed goats (GM (GSD) 0.27×10^6 f/g (2.8), range $0.055–0.84 \times 10^6$f/g).

The ratio of tremolite and chrysotile concentrations was higher in patients (7.4) than in the goats (1.2). This may be related either to differences in duration of exposure or to the faster clearance of chrysotile from the lungs. Human and animal lung fibre burden studies have consistently showed that amphiboles accumulate in the lungs to a much greater extent than chrysotile

On the whole data on fibre loads in the literature tend to vary considerably. This partly reflects differences in laboratory methodology (Gysleth et al., 1985) but presumably also reflects substantial variations in the type and duration of exposure and the health of the subject, human or animal.

In one American study of shipyard workers, values range from$1.3 X10^6$ to $2.7 X10^6$ fibres per g (dry weight) (Warnock, 1989). In a Finnish study of a sample from the whole population including unexposed and exposed subjects, values ranged from $0.3 X10^6$ to $163.1 X10^6$ (Karjalainen et al., 1994). The lower values were from subjects not exposed directly to asbestos through work. The authors found that concentrations exceeding a threshold of 1.1 $X10^6$ were present in 33% of subjects known to have received asbestos exposure.

In a second study, the Finnish group noted that there was a higher natural incidence of fibres in unexposed Finnish subjects than in other countries (Karjalainen et al., 1996). Thus we should bear in mind that there might be geographical differences related to mineralogical and geological features at a given location, which may naturally produce exposure, in addition to the possibility of specific activity (such as a mine) causing exposure to asbestos.

9. ASSOCIATION BETWEEN FIBRE LENGTH AND FIBRE-TYPE TOXICITY:

There are numerous animal studies that demonstrate the influence of fibre length and pathogenicity/carcinogenicity. The early studies using intrapleural implantation/instillation and intraperitoneal injection in rats clearly show a direct relationship between fibre size and carcinogenic activity. The longer the fibre, the more carcinogenic it was in these studies. These same studies provided the basis for the hypothesis that short fibres, i.e. shorter than 8 um in length may not represent a significant carcinogenic risk.

However, the same investigations, particularly the intraperitoneal studies also demonstrated that if the dose was high enough even so-called "innocuous" particulates, e.g. titanium dioxide, caused the induction of peritoneal mesotheliomas, albeit at a lower incidence than long fibres. Additionally, the latter studies also demonstrated that if even long fibres, e.g. wollastonite and some SVFs, were not carcinogenic if they were not biopersistent in the peritoneal cavity. While few inhalation studies have been conducted to study the influence of the fibre length on the pathology of asbestos, there is one persuasive study of crocidolite asbestos in rats. In that study, short crocidolite (<2.0 um length) did not cause either pulmonary cancer or mesotheliomas in rats, even at relatively high exposure levels, while longer crocidolite was highly carcinogenic.

Other circumstantial evidence for considering fibre length as being critical to the carcinogenic potential of fibres is provided by the observation that amorphous silica has been shown to be noncarcinogenic in several inhalation studies in rats, while some types of glass fibres of similar chemistry have shown to have carcinogenic activity. In fact, amorphous silica has been used as a "negative control" in rodent inhalation studies.

A final piece of evidence for the importance of fibre length for the carcinogenic of asbestos and SVFs is found in the hilar lymph nodes that drain the lungs of animals exposed via inhalation to both asbestos and SVFs. These lymph nodes are literally filled with macrophages containing short fibres and fibre fragments with no evidence of pathology or neoplastic change in either the lymph nodes or adjacent tissues.

To summarize studies in animals of short fibres and nonfibrous particulates have shown that both are potentially carcinogenic if they are introduced into a confined cavity, e.g. pleural or peritoneal, at sufficiently high doses. But the same studies clearly show that the carcinogenic potential is definitely less than fibres of the same type that are longer.

However, inhalation studies (although limited in number) suggest that short fibres have not caused cancer in animals. The other part of the equation that needs to be considered is the influence of pulmonary clearance and biopersistence on the carcinogenic potential of particulates. As noted above, even long fibres are not carcinogenic in animals unless they are biopersistent in the animal.

10. CLEARANCE/BIOPERSISTENCE OF SHORT FIBRES:

Biopersistence is the sum of physiological clearance processes and physicochemical processes which together account for the retention halftime of the fibrous or non-fibrous material in the lung. Physicochemical processes include dissolution, leaching, breaking and splitting, depending on the fibrous material, that can occur intra- as well as extra-cellularly, and differences in pH in both locations are of importance here. Clearance rates of fibres of different length categories have been determined from short and long term inhalation studies. Generally, short fibres are cleared rapidly if biosoluble (pH differs intracellularly vs extracellularly), or at rates similar to non-fibrous particles. Breakage of long fibres will give input into short fibre category.

Most important physiological clearance mechanism in alveolar region is clearance by alveolar macrophages (AM). Of importance is fibre length with respect to phagocytosis and removal by alveolar macrophages. Short fibres are easily phagocytised; fibres longer than 20 µm are not. Species differences in AM size. Thus, clearance for long fibres is prolonged, as is that for short fibres when high lung burdens are reached (particle overload). Also, intrinsic toxicity of short fibres has to be considered which influences clearance. Inflammatory conditions in the lung (for example, smokers) also contribute to impairment of alveolar macrophage-mediated mechanical clearance and need to be considered.

11. COMMENT

The data from the analysis of 25 samples using the optical microscopy indicate that the fibre densities are low, in fact below the unexposed values of the Finnish study by Karjalainen et al. (1994) which were themselves described as higher than the norm. This suggests these data represent purely incidental minor exposure to mineralogical fibres from the natural environment. Consistent with the findings of our spirometry study, there is no evidence of an environmental exposure to asbestos in ambient air.

The results from the transmission electron microscopy (TEM) (25 samples) indicate that at least a very small proportion of the fibres we have identified have a composition similar to asbestos, and the spectrum is most consistent with chrysotile asbestos. However the number of chrysotile fibres found was so small that it makes it impossible to draw conclusions of environmental exposure. It is possible that from the mining operations of the past the land has been contaminated with asbestos and movement of the goats hooves may cause some asbestos fibres to be transolated onto fodder foliage.

The Corsican study has found evidence of increased concentrations of asbestos fibres in lung and pleural tissue samples of goats from areas with asbestos contaminated soils in northeast Corsica. These results indicate that tissue samples from local animals may be useful indicators of environmental background exposure when human samples are unavailable or scarce.

During our search for animals in the villages of Kyperounda and Kato Amiandos it became impossible to find a representative number of goats to cover all the geographical area to the degree that enable valid conclusions to be drawn. As a minimum there would be a requirement to use at least 10 goats from all the villages around the asbestos mines, and this could be considered in the three remaining stages of the research study.

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Section 12

Conclusions and recommendations

Our study has focused on the effect of asbestos exposure on the health of the resident population of Kypertounda and Kato Amiandos. We basically addressed three questions. First, what was the health impact of occupational exposure on those men who worked on the asbestos mine? Second, we examined the impact of household exposure on those women who had members of their household working on the mine. Third, we assessed the health effects of those who have not been exposed to the asbestos mine.

We concluded the following:

1. There was a significant health effect from both occupational and household exposure. In this study we found clear evidence of significant restrictive lung disease patterns among those who were exposed to asbestos. Indeed there appeared to be gradient according to the level of exposure. Highest rates of restrictive lung disorder were found among the occupationally exposed men in Kato Amiandos (41.7%), followed by occupationally exposed men in Kyperounda (28.3%). Women with a household exposure had higher rates (19.0%) than non-exposed women (4.0%). This finding shows that the spirometry was successful in measuring exposure to asbestos. We found that the greatest impact was on men who worked on the mine and who were or had been smokers. The level of restrictive lung disease showed a gradient according to the type of exposure, with smoking having almost as great an impact as asbestos exposure. We believe that there is a clear message. While nothing can be done to reduce the impact of past asbestos exposure, the level of smoking among men remains a significant and important health hazard. The fact that it is as harmful to lung function as exposure to years of asbestos dust illustrates the real health effect. We recommend that the Cyprus Government should develop policies to reduce cigarette smoking.

2. The spirometry tests showed that the force vital capacity (FVC) for non-exposed, non-smoking males (see table 9) and females (see table 12) were slightly higher than predicted values (100). We therefore concluded that this group had normal respiratory function, and that there is no evidence of an environmental exposure to asbestos in ambient air.

3. While there were more cancers among the exposed population, the difference did not reach statistical significance at the 95% confidence level. Moreover, a number of residents were aware of family members who had died from lung cancer and mesothelioma. It is important to ascertain the true incident of lung cancer and mesothelioma. We recommend that a subsequent stage of this study concentrate on accurately describing the incidence of lung cancer and mesothelioma.

4. We evaluated the completeness of the mortality data as recorded by the national registration system. We found that the number of deaths provided by the registration system was virtually the same as that provided by priest records. We

concluded that registration data was now sufficiently accurate to be used to calculate SMRs in the index villages.

5. The calculation of standardised mortality ratios (SMR) were based on 67 observed deaths in Kyperounda and 14 observed deaths in Kato Amiandos over the period 2001-2004. The SMR for Kyperounda was 99 (CI 78-129) and for Kato Amiandos 146 (CI 72-232). While the calculation of SMRs for the index villages showed that there is no statistical difference at the 95% confidence level in the mortality experience of Kyperounda and Kato Amiandos and the other control villages, it should be noted that the SMR in Kato Amiandos was 46% higher than expected. It seems probable that the long-term exposure to asbestos has resulted in a small excess of deaths. It is important that the mortality rates of the exposed villages should be monitored over the next decade.

6. We believe that there is a problem in the measurement of the body mass index (BMI). The BMI showed very high rates of obesity among the village populations. It seems likely that the current method of calculating BMI is flawed in that it does not take account of a person's body shape. It seems highly likely that the current measure is over diagnosing obesity in the Cyprus population. Nevertheless this is an extremely important issue, and the true extent of the overweight/obesity prevalence should be measured by a properly designed study.

7. It is most gratifying to see that the quality of hospital data is of good quality that epidemiological investigations can be undertaken. The diagnostic coding was 100% complete and this is a reflection of the quality of data. There was a small problem with 6.8% of hospital records from Paralimni Hospital missing coding on age, sex and area but this could be easily rectified.

8. The villages of Kyperounda and Kato Amiandos have an admission rate for chronic obstructive pulmonary disease, which is thirteen times higher than the national admissions rate. This is a highly statistically significant difference that cannot be explained by easy access to the hospital. Moreover proportion of hospital admissions for this diagnosis is seven times higher than that occurring elsewhere on the island

9. The admissions to hospital ratio for the whole of the Lemesos district, excluding the villages of Kyperounda and Kato Amiandos is significantly higher than elsewhere in Cyprus. It is therefore important that the scope of the investigation is expanded to include other villages in the Lemesos district that have experienced significant levels of exposure to asbestos

10. We found that over the whole of Cyprus there have been 48 hospital admissions for mesothelioma recorded over a five-year period from 1998 to 2002 although only 17 cases of mesothelioma have been reported in the Cyprus Cancer Registry. However the true incidence of mesothelioma can only be measured by a carefully designed study and this is included in the plans of the Ministry of Health for the final of a four-part study. We believe that the hospital admissions records we examined and those that would be available in subsequent years should make a real to contribution to a study of the prevalence of mesothelioma.

11. The medical and social questionnaire showed clear evidence that the health of those who have worked on the mine has been adversely affected. A higher proportion of men who have been occupational exposed perceive their health to be poor compared to their non-exposed counterparts. Those who have occupational exposed have higher rates of heart disease and bronchitis. The occupationally exposed are more likely to cough in morning in winter months and more likely to bring up phlegm in the morning in winter than their non-exposed counterparts.

12. We also found evidence from the medico-social questionnaires that household exposure has adverse affects on respiratory symptoms. However, those with household exposure had similar rates of heart disease and bronchitis as their non-exposed counterparts. Rates of self-reported depression were twice as high among exposed women

RECOMMENDATIONS

1. We recommend that mortality rates in exposed villages should be monitored over the next decade.
2. We recommend that the scope of the investigation should be expanded to include other villages in the Lemesos district that have experienced significant levels of exposure to asbestos. The mortality rates of all the villages exposed to the asbestos mines should be assessed, and a study of morbidity should also be included in any subsequent study as there are good data that could be used for analysis.
3. We recommend that the respiratory health of residents living in other villages that have been exposed to the asbestos mines should be included in any subsequent study
4. We recommend that a subsequent stage of this study should concentrate on accurately describing the incidence of lung cancer and mesothelioma.
5. We recommend that the Ministry of Health should immediately run anti smoking campaigns as a priority in the villages around the asbestos mines.
6. We recommend that the true extent of the overweight/obesity prevalence should be measured by a properly designed study.
7. We recommend that the list of people provided to the Ministry of Health by the researchers should have their health monitored regularly (on an annual basis) over the five to ten years.

APPENDIX

TERMS OF REFERENCE

3.1 The medical research study must commence within 10 (ten) days (the latest) from the date of signing the contracts and must be completed within 10 (ten) months (the latest) from the date of signing the contracts.

3.2 The Consultants must prepare, within 20 (twenty) days from the date of signing the contracts, a detailed research protocol in which must be shown through (amongst others) the ability of flexibility and overcoming of possible obstacles of the research, the originality and the way the re5earch data will be collected and evaluated. Also, it must be shown through the ability of the team of persons, described in Table A of subparagraph 2.12.3 (ε) (of the tender documents) to be coordinated and respond to the requirements of the terms of reference of the Medical Research.

3.3 The team of Consultants must have the possibility of cooperation with recognised scientific institutions abroad, which have indirect or direct relationship with the research project.

3.4 The team of Consultants will indispensably cooperate (during the course of the medical research) with the representative of the Ministry of Health on the following:

3.4.1 The investigation and review of data of the existing literature for the effects of asbestos fibres on the health of residents of the communities of Kato Amiandos and Kyperounda. For this purpose, the consultants must refer back and evaluate (amongst others) the data, which exist in hospital, clinics, outpatient departments and other places.

3.4.2 Preparation of a document based on the attached specimen of Annex 6, which must be completed by the consultants for the residents of communities of Kato Amiandos and Kyperounda based on a random stratified sample. It is hereby clarified that the full completion of the Medical Research for possible effects on the health of residents of the neighbouring communities of Kato Amiandos and Kyperounda. The next remaining parts will be conducted at a later stage when the findings of this part of the study have been evaluated.

3.4.3 According to the demographic report of 2001 Census, the total population of Kyperounda was 1495 persons and of Kato Amiandos was 219. Receiving a stratified random sampling from the population of K. Amiandos and Kyperounda will be examined according to the protocol, which will be agreed with the consultants. Also, at least two communities must be selected (which do not present potential exposure to asbestos) which will be used as control groups.

3.4.4 For the completion of the questionnaire of the medical research, the conduct of clinical and para-clinical examinations, spirometry testing etc the Ministry of Health will provide conveniences to the consultants to the Kyperounda Hospital and the Health Centre of K. Amiandos. The referral of cases for X-Ray, CAT Scanning or MRI, as well as other sub-clinical or laboratory examinations will be carried out after consultation with the representative of the Ministry of Health.

3.4.5 The expenses for the completion of Annex 6, namely the questionnaire of the medical research (part A and part B), the clinical medical examinations, spirometry tests and body measurements will be borne by the tenderer. The Ministry of Health will undertake the expenses for the X-Ray examinations, CAT-Scanning or MRI as well as other sub-clinical or laboratory examinations, which will be conducted after consultation with the consultants.

3.4.6 Calculation of Standardised Mortality Ratios and Age Specific Rates. For this purpose, data must be collected from hospitals, rural health centres, from records which are kept by priest concerning the burial in cemeteries in Kyperounda and K. Amiandos, collection of information from Community leaders and other persons from aforementioned communities as well as from the relatives of persons who may have died from diseases which are related with exposure to asbestos fibres. Similar data must be collected from the communities, which will be used as control groups. The Standardised Mortality Ratios and Age Specific Rates must be calculated both for the communities of K. Amiandos, Kyperounda and the control communities.

3.5 The tenderer must submit detailed statement of the laboratories he intends to cooperate for the analysis of the samples of paragraph 3.4.7 as well as his demands for temporary safe conservation and storage of samples until they will be despatched to their final destination

3.6 The Ministry of Health will provide the consultants with an office of 10 square metres space in Apartment 103, 20 Markou Drakou Str. for the safe storage and evaluation of findings of the medical research, for facilitating the meetings, between the consultants and the representative of the Ministry of Health aiming at the evaluation of data and the continuous monitoring of the course of the research. This office space will be used for safe keeping of all documents questionnaires, x-rays, maps, results of medical examinations, spirometry testing results, para-clinical and laboratory examinations, analysis of specimens and any other relevant documents which shall be the property of the Republic of Cyprus.

3.7 The team of Consultants, for the medical research study, will cooperate with Dr Andreas Georgiou, Chief Medical Officer, with specialties in Community Medicine (Social Medicine) and Hygiene, Occupational Medicine and General Medicine, who will be the representative of the Ministry of Health. It is hereby clarified that in case of conflicting opinions among the consultants and the representative of the Ministry of Health, the opinion of the representative of the Ministry of Health will prevail as regards the level, extent and quality of the services provided by the consultants (as these are defined in paragraphs 3.4.1, 3.4.2, 3.4.3, 3.4.4, 3.4.4, 3.4.5, 3,4,6, 3,4,7).

3.8 It is hereby clarified that the written consent of the representative of the Ministry of Health will be required for the payment of any instalment to the tenderer and/or the consultants (as defined in paragraph 2.8.1, in Annex 4 and the Sub-Annexes 4.1 and 4.2)

3.9 The tenderer must submit his final report (with an executive summary) to the Minister of Health and the Permanent Secretary of the Ministry of Health, which must be accepted.