

Mortality study of workers at the Hillhouse PVC plant

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SUMMARY

Background

An epidemiological survey of workers exposed to polyvinyl chloride (PVC) had been carried out by the IOM in 1979. The study found (i) an association between breathlessness and exposure to PVC dust in cigarette smokers, (ii) lower FEV₁ in men who had higher PVC dust exposure and who were current smokers and (iii) lower FVC in men who had higher PVC dust exposure and who had been employed at the time of the survey. To assist in sample selection for the surveys, identification data had been received for 1700 men, including all 1501 current workers in 1979. These identification data, including work histories, were still available, together with data from medical surveys of 663 current workers examined in 1979, making possible a study of mortality of this group of workers.

Objectives

The aim of the current study was to carry out a follow-up mortality analysis of the men studied in the earlier IOM research to investigate (i) whether there was evidence that mortality from respiratory diseases is different among workers at the Hillhouse PVC plant from that in the general population in the same geographical area, (ii) to what extent any differences were specific to particular age groups, calendar periods or work area within the plant, (iii) to what extent did respiratory health in 1979 predict future mortality and (iv) what evidence there was regarding other differences in mortality possibly related to occupation within the PVC plant.

Men studied and methods

The total study population comprised 1700 individuals who had worked at the ICI Hillhouse site during or prior to 1979, a subgroup of whom had attended the medical survey carried out by the IOM in 1979. Of the 1700 individuals, 1501 were current workers when the earlier IOM research was carried out, 90 were leavers and 109 were pensioners. During data processing, two records were identified as duplicates and two as women; these records were omitted leaving a final study group of 1696 men.

Demographic data were available for all 1696 men and occupational histories, extracted from plant records, were available for the 1501 current workers. These histories gave occupations in broad categories only. The present study included new visits to the plant to help determine associated exposures. Detailed individual occupational histories, smoking and respiratory health data were also available for a subset of 661 current workers who had participated in the medical survey in 1979, and whose average length of employment at the plant at that time was 14 years. Indices of individuals' cumulative exposure to PVC dust up to 1979 had been derived for the earlier study, using detailed workplace measurements taken at that time, and were also still available for analysis.

The period of follow-up for the mortality analyses was from 1st January 1979 to 31st December 2003. Mortality details for the study group were obtained from the Office for National Statistics (ONS). Tracing was successful for all except 17 individuals and, in addition, 8 men were found to have died prior to the start of follow-up. The statistical analyses were therefore based on 1671 men, of whom 1484 were current workers at the time of cohort identification and 655 had attended medical survey.

Specific interest was in deaths from non-malignant respiratory disease (NMRD), ischaemic heart disease (IHD) and lung cancer. Death rates amongst men in the same local, geographical and national regions, of the same age and over the same time period, were compared with those observed in the study cohort. Further analyses examined possible relationships between exposure to PVC dust and mortality from the causes of interest, taking account of age and calendar year. For the subgroup of 661 who had attended the previous survey, some of these exposure-response analyses also included data on smoking habits and

respiratory health in 1979. The study did not include any updating of work histories or of smoking histories beyond 1979.

Results and Discussion

Tracing and cohort completeness: Cohort identification was complete for all current workers in the plant in 1979, and for a subset of more heavily exposed pensioners and leavers, with tracing of vital status and cause of death for the study group achieving a success rate of over 99%. The final results therefore are representative of current workers in 1979, though less representative of pensioners/leavers at that time. Partly for this reason, and partly because of unavailability of work history data, the main analyses of this study were carried out in current workers only – all current workers ('Population 2') and the subset who had attended medical survey in 1979 ('Population 3').

Reliability of exposure data: Exposure estimation was generally reliable for exposures up to 1979, but no information exists for exposures after that date. Exposures up to 1979 were based on estimates of dust concentrations in 1979, and time accumulated in exposed jobs up to that date. No data were available to allow adjustment for possibly higher dust concentrations prior to 1979. Estimates of individuals' exposures, especially those of younger men who are most likely to have accumulated further exposures after 1979, therefore become less valid as length of follow-up increases. This may be less of a problem for the analysis of lung cancer mortality where latency of disease development is typically 10 to 20 years following first exposure. Indicator variables for exposure are likely to be more robust over time but provide a relatively crude assessment of potential exposures.

Deaths from all causes: There was no evidence of an increase in all-cause mortality in the study cohort of 1671 men, or its subgroups, compared to national and local reference populations. Patterns of mortality over time were consistent with a reduction of the Healthy Worker Effect with increasing length of follow-up, as would be expected.

Non-malignant respiratory disease: Analyses of all current workers in 1979 (1484 men) showed no evidence that exposure to PVC dust was related to increased risk of death from NMRD. For example, compared with Lancashire, the SMR for NMRD was 67 (95% CI 49-93). Analyses of Population 3 (i.e. the 655 men who had attended medical survey in 1979) did not show a relationship with cumulative dust exposure. The earlier (1979) study showed some links between PVC exposure and early signs of lung disease, particularly among smokers. The present study showed some links between early signs of lung disease and later risks of death from NMRD. It doesn't necessarily follow that exposure to PVC dust affects the risk of mortality from NMRD, but there is a possibility that it does. Overall, however, the evidence was of generally low death rates from NMRD and no evidence of a direct link with exposure to PVC dust. This finding is reassuring in view of the results of the previous epidemiological study.

Lung cancer: A possible relationship between lung cancer mortality and exposure to PVC dust was examined in detail in this population, and in the subset of 655 men who had attended medical survey. Among current workers in 1979, a statistically significantly increased probability of death from lung cancer was found in those who had ever worked in a PVC exposed job compared to those who had never done so. However, this difference was explained largely by unusually low lung cancer mortality among the *unexposed* workers (e.g. SMR 35 for Population 2 compared with Lancashire rates, $p < 0.05$). We do not know why this was so. In particular, data for 1979 showed that the smoking habits (in terms of % current smokers) of unexposed workers, available for men in Population 3, were similar to those of men of the same age in the general population of England and Wales and, as far as we can establish, of North-West England also. However, because mortality in the non-exposed workers was unusually low, the contrast between exposed and non-exposed workers is not very informative.

External analyses nevertheless showed, for workers ever exposed to PVC dust, an increased SMR for lung cancer mortality (SMR = 130, Population 2) compared to regional rates from Lancashire; an excess that was close to statistical significance at the usual 5% level (95% CI 97-174). However, when the North-West Region rather than Lancashire was used as reference population, the SMR was lower, 119 (95% CI: 89,159) and not nearly significant at the usual 5% levels of statistical significance. In addition, it is notable that all except one of the lung cancer cases in this study group occurred in current or ex-smokers, so that any suggestion of an elevated risk in the exposed group is based on results from smokers and ex-smokers only, and the available 1979 data showed that 56% of exposed workers were current smokers, a higher proportion than for unexposed workers (44%) or the general population (45%). Finally, we analysed lung cancer mortality in relation to time spent (up to 1979) in a PVC job (Populations 2 and 3), and with cumulative dust index up to 1979 (Population 3 only) among the exposed group. Analysis of time spent in PVC jobs up to 1979 among those exposed showed no association with lung cancer mortality in Population 2 and an increased hazard ratio, but far from statistically significant, in those who attended medical survey. However, in Population 3 (i.e. those who attended survey in 1979) there was no association with cumulative dust index.

Some previous studies of workers exposed to PVC dust have indicated a possible relationship with lung cancer. However there are limitations in the methodology of all the studies particularly in relation to adjustment for smoking status. We do not know to what extent this may have affected estimates of the risks from exposure to PVC dust in these studies, although in the present study adjustment for smoking status had little effect on the estimated risks.

Ischaemic heart disease: There was no evidence of an overall excess of IHD mortality among workers exposed to PVC dust, compared to rates in the general population, and a statistically significant deficit of mortality from IHD among unexposed workers.

Analyses of the larger study population (Population 2) showed no association between mortality from IHD and time spent in a PVC job among those exposed. Analyses of the subset of men who attended medical survey (Population 3) showed a raised hazard ratio, though not statistically significant, for IHD mortality associated with time in a PVC exposed job and a statistically significant association, after adjustment for age and smoking habit, between cumulative dust index for PVC dust exposure and mortality from ischaemic heart disease. Among the 829 current workers who did not attend medical survey, there was no evidence of an association between IHD mortality and time spent in a PVC job.

These contradictory results are difficult to interpret. Literature on occupational exposure to dust does not show an association with IHD mortality, even in very dusty occupations such as coalmining. There is evidence that long-term exposure to particles in outdoor air increases the risk of mortality from cardiovascular diseases, but (i) the outdoor particles, being mostly from combustion sources, are very different from PVC dust and have surface properties that would not be expected to be found in PVC dust; and (ii) air pollution studies are based on the general population, which contains more vulnerable people (e.g. elderly and/or chronically ill) than a working cohort. Outdoor particles are smaller on average. The mortality risks from outdoor particles are associated especially with particles of aerodynamic diameter less than 2.5 µm. If PVC dust were adversely affecting IHD mortality, the effect would be seen more clearly in workers exposed to emulsion rather than suspension dust, and there was only weak evidence in this direction (far from statistically significant) in the current study.

Other workplace factors

There was no evidence of an association between mortality and exposure to asbestos, TFE or lead. There was weak evidence of an association, not statistically significant, between time

worked in a VCM job and mortality from IHD. This finding for VCM was confounded with emulsion PVC exposure (as all jobs with emulsion PVC exposure were also classified as exposed to VCM) and reflects the weak evidence of an association between emulsion PVC and IHD noted above. In general, results regarding risks of exposure to PVC dust were unaffected by adjustment for smoking habits.

Conclusions

Non-malignant respiratory disease: There was no evidence of any association between NMRD mortality and exposure to PVC dust, a finding that is reassuring in view of the results of the previous epidemiological study. The earlier (1979) study showed some links between PVC exposure and early signs of lung disease, particularly among smokers. The present study showed some links between early signs of lung disease and later risks of death from NMRD. It doesn't necessarily follow that exposure to PVC dust affects the risk of mortality from NMRD, but there is a possibility that it does. Overall, however, the evidence was of generally low death rates from NMRD and no evidence of a direct link with exposure to PVC dust.

Lung cancer: This study provides no direct evidence of an association between exposure to PVC and lung cancer. Within those exposed, there was no evidence of an exposure-response relationship with surrogates of exposure. The most suggestive finding, of an elevated SMR among those exposed to PVC, can be explained by increased smoking prevalence in this group, and/or by chance variations in a study of this size.

Ischaemic heart disease: We think that the present limited evidence does not justify a conclusion that exposure to PVC dust increases the risk of IHD, but that it is important to be aware of the possibility, and that it would be very helpful if the result could be checked in other data. The present study does not show a need for any strong new measures to reduce exposures. It is however prudent to maintain dust levels as low as practicable. Those who work in the industry are in the best position to know how to do this most effectively.

1 BACKGROUND

1.1 BACKGROUND INFORMATION ON PVC USE

Polyvinyl chloride (PVC) is manufactured as a fine white powder by the polymerisation of vinyl chloride monomer (VCM). Workers known as PVC baggers handle this powder. Like most plastics, PVC contains hydrogen and carbon, but unlike most plastics, PVC also contains chlorine. PVC is a hard plastic that can be made softer and more flexible by the addition of plasticisers, depending on the required application. Stabilisers are always added to PVC in order to prevent degradation during processing and afterwards. The addition of these stabilisers gives unique properties to PVC but some of these additives can also be hazardous to humans and the environment. Since PVC is a highly versatile polymer, it is one of the most widely used plastic materials. It has excellent electrical insulation properties, good impact strength and weatherproof attributes.

Common uses of PVC include use in building materials and construction (e.g. pipes, fittings, window frames, cables and flooring), the automotive industry (e.g. dashboards, sun visors and seat coverings), the healthcare field (e.g. catheters, blood bags and heart and lung bypass sets) and also for various household goods and packaging.

1.2 INFORMATION ON PRODUCTION OF PVC

Vinyl chloride (VCM), the monomer from which PVC is made, was first produced by the chemist Justus von Liebig in 1835. PVC was accidentally synthesised in 1872 by Eugen Baumann, when the polymer appeared as a white solid inside flasks of vinyl chloride that had been left exposed to sunlight.

It was not until the late 1920s that the first commercial production of PVC took place in the USA. However, production increased dramatically during the Second World War when PVC was used in place of rubber to insulate the wires in electrical cables. Currently there are more than 25 million tonnes of PVC produced annually worldwide. In the late 1970s when the IOM carried out the original survey at the Hillhouse site the total world production of PVC was less than half of the present figure.

In the late 1970s there were three main methods of producing PVC: suspension, emulsion and bulk or mass production, with the vast majority being produced by the suspension process (Burgess, 1982).

The initial commercial processes were based on the emulsion process where a latex was first produced and the PVC was then separated by spray drying. This was an expensive process and most manufacturers worked to develop practical suspension processes, which produce coarser PVC particles.

The suspension process involves a polymerisation process where water, VCM and an initiator are added to a reaction vessel (autoclave). The system is sealed and heated to about 60°C. This reacts exothermically to convert between 80 and 90% of the VCM to PVC in about 6 hours. The slurry is then passed to a stripping stage where most of the residual VCM is removed and sent to a recovery plant for reuse. The residual PVC/water slurry is dewatered in a centrifuge and then dried using hot air. The final product is then sent to storage. The emulsion process is similar in outline to the suspension process described above, with the exception that spray drying is used.

PVC is insoluble in VCM and so any PVC that deposits on the walls of the autoclave is unlikely to be removed thereafter. In the early process these residues were removed between each batch by manual scraping. However, from about 1968 when it was recognised that

exposure to relatively low levels of VCM presented a potential cancer risk for the workers the cleaning was carried out using water jets and solvents. From about the mid 1970s protective clothing and breathing apparatus were used by workers involved in cleaning autoclaves.

1.3 A BRIEF HISTORY OF PVC PRODUCTION IN ICI

In 1940 the ICI general Chemicals Group built its first PVC production plant at Runcorn in Cheshire. This plant operated using the emulsion process and produced a product known as Corvic, i.e. Runcorn polyvinyl chloride. In 1944 a second plant was opened on the Hillhouse site, operated by ICI on behalf of the UK Ministry for Supply. This plant, which used the same process as the Runcorn site, had a nominal capacity of 5,000 tonnes of PVC per year. There were initial production difficulties hence this output was not achieved until 1945. This plant was known as Corvic 1.

There was increasing demand for PVC with better electrical properties and in 1944 the Runcorn plant was converted to produce suspension grade PVC (also known as granular PVC), which was sold as Corvic DQ, i.e. dielectric quality. The product from the emulsion was renamed Corvic HO, "Hillhouse Ordinary".

In the period from 1946 to 1950 there were a number of technical innovations that increased the production of Corvic HO to 10,000 tonnes per year. However, because of increasing demand it was decided to build a second plant on the Hillhouse site and to close the Runcorn plant. The Corvic 2 plant was built in an old phosgene building (CG3) and started operation in 1951 with a capacity of 7,500 tonnes per year.

In 1951 two large ball mills were installed in the Corvic 1 plant to produce a fine grade known as Corvic PM, i.e. paste making, which was previously made in Welwyn Garden City in the "Welvic" paste plant.

In 1954 a new suspension plant was built alongside the Number 2 plant so that the two plants could share some facilities. The combined nominal capacity of the Corvic 2/3 plant was 15,000 tonnes per annum. In 1956 the Corvic 4 plant was opened and further expanded in 1957.

By 1960 the combined capacity of the four plants on the Hillhouse site was 69,000 tonnes per annum, but it was clear that this was insufficient to meet demand and Corvic 5 plant was constructed at the south end of the Hillhouse site with a target capacity of 45,000 tonnes per year. Corvic 6 was built adjacent to Corvic 5 and started production in 1966. The Corvic 7 and 8 plants, which started in 1970 and 1978, were built in Runcorn.

In 1980 the Corvic 9 plant opened producing both emulsion and suspension grades. Initial capacity of this plant was 54,000 tonnes per annum. Corvic 10 was built in Wilhelmshaven in northern Germany in 1981, with an initial capacity of 115,000 tonnes per annum. ICI also purchased a suspension PVC plant in Barry in Wales.

Part of the suspension grade PVC produced at Hillhouse was processed further in three separate plants: Darvic and Welvic 1 and 2. In the Darvic plant suspension grade PVC was mixed with various additives, fillers and pigments (including lead and cadmium compounds) to form sheets. The Welvic plants PVC chips were made from suspension grade product.

There were also a number of unrelated chemical plants that operated on the Hillhouse site, both before the beginning of PVC production and thereafter. Important plants were Fluon (polytetrafluoroethylene) manufacture, Victrex, Vielan and a VCM manufacturing plant (VC4). Some workers only worked on these other plants, but some, mostly maintenance workers, operated in a number of plants as required.

1.4 HEALTH RISKS OF PVC MANUFACTURE

Three workers in a PVC polymerisation section of a B.F. Goodrich plant near Louisville, Kentucky were diagnosed with liver angiosarcoma in the late 1960s (Creech and Johnson, 1974). The frequency of this rare liver tumour was reported to have increased in workers exposed to over 10000 ppm VCM in cleaning reactor vessels, which caused a major occupational health crisis in the VCM/PVC industry in the mid-1970s (Mastrangelo *et al*, 2003). Afterwards a number of cohort studies were carried out. Studies of PVC workers in Australia, Italy, Germany and the U.K. have shown increased risks for certain types of occupational cancer (e.g. brain tumours, lung cancer and tumours of the hemolymphatic systems) are associated with exposure to vinyl chloride. The link between angiosarcoma of the liver and long-term exposure to vinyl chloride is the only one which has been confirmed by the International Agency for Research on Cancer (IARC, 1974 *Summaries & Evaluation: Volume 7: Vinyl Chloride*).

Many of the studies carried out into workers involved in the PVC industry examine the effects of vinyl chloride monomer (VCM) rather than PVC dust. However, there have been a few investigations of an association between PVC dust exposure and an increase in lung cancer incidence, and their conclusions have been inconsistent. A study of 4806 males ever employed in a synthetic fibre plant between 1942 and 1973 found an association between exposure to PVC dust and excess mortality from lung cancer, and in particular for adenocarcinoma and large cell undifferentiated cancer (Waxweiler *et al*, 1981). The authors report that these types of lung cancer are only weakly related to cigarette smoking, and they conclude that, although no smoking data were available, cigarette smoking was probably not a major confounding variable. However, they note that the role of smoking as a promoter or cocarcinogen cannot be ruled out.

A nested case-control study was recently published that evaluated the potential relationship between PVC dust exposure and lung cancer (Mastrangelo *et al.*, 2003). In this study, 38 cases of lung cancer and 224 controls were selected from 543 claimants in a lawsuit against the plant. Statistically significant differences were noted between cases and controls with respect to cigarette smoking, age at hire, and years of PVC bagging ($p=0.001$). The risk of lung cancer was estimated by odds ratios (OR) with 95% confidence intervals (CI), calculated using logistic regression models. The authors reported that in PVC baggers exposed to high levels of respirable PVC particles in the workplace, the lung cancer OR increased by 20% for each extra year of work (OR = 1.20; 95% CI 1.08 to 1.35; $p = 0.0010$) after adjustment for age and smoking habit. No relationship was found between lung cancer and cumulative VCM exposure. The authors concluded that this study showed an increased risk of lung cancer associated with exposure to PVC dust, and that previous cohort studies failed to recognize such excess, probably because they used VCM exposure as the risk indicator.

These findings should be interpreted with caution, bearing in mind the small numbers of lung cancer cases, the potential for selection bias (by using cases and controls who were participants in a law suit) and the lack of adjustment for potential exposures to other chemicals. There are also some limitations in the adjustment for smoking data in the study, as this is carried out only for cases and controls combined when there were known differences in smoking habit between the two groups.

Two mortality studies of workers in the vinyl chloride industry were reported in the late 1980s (Jones *et al*, 1988; Wu *et al*, 1989). Both studies included both workers exposed to VCM and workers exposed to PVC dust. Neither study found any association between PVC dust exposure and mortality from any cause, although both reported an association between VCM exposure and angiosarcoma of the liver.

Jones *et al* had studied a total of 5498 male workers employed in the vinyl chloride industry in the U.K. for a minimum of one year during 1940 to 1974 with their mortality experience followed up through to 31st December 1984. A significant excess of non-secondary liver tumours were found, resulting in 11 deaths, of which seven were due to angiosarcomas. All angiosarcoma deaths occurred in autoclave workers. There was evidence of a strong healthy worker effect. The incidence of deaths from other cancers was not increased as a result of exposure to VCM nor was there any evidence of an increase in mortality from chronic liver disease. The incidence of death from respiratory disease was low and was unaffected by exposure to PVC dust.

Wu *et al* (1989) carried out a mortality study in a cohort of workers at a vinyl chloride polymerisation plant, with an extended period of observation from 1974 to 1986. Workers at this plant consisted of those who may have been exposed to VCM and/or PVC dust, those who had no exposure to either substance. Potential exposure to VCM was reported for 76% of jobs in the work force. Statistically significant excess risks among the total cohort were observed for liver, lung and brain cancer. The SMR for liver cancer for the subcohort of workers exposed to VCM was 333 (90% C.I. (202,521)). No significant excess risks for the subcohort were found for brain cancer (SMR = 145; 90% C.I. (78,249)) or lung cancer (SMR = 115; 90% C.I. (96,141)). To investigate dose response, nested case-control studies for liver, brain and lung cancer were conducted among the total cohort (including the non-exposed). For these studies there were two exposure variables, cumulative dose of vinyl chloride monomer and cumulative dose of polyvinyl chloride dust. Cumulative dose was defined as the product of level and duration of exposure. The only significant association between disease risk and cumulative dose was for liver cancer and cumulative dose of vinyl chloride monomer. Further division of the liver cancers into angiosarcoma (n =12) and other liver cancers (n = 7), based on review of death certificates and medical records, showed that the dose response existed only for angiosarcomas.

Further studies looked primarily at relationships between health and exposure to VCM. A study of 451 workers (Theriault *et al*, 1981) exposed to VCM for more than five years compared to 870 non-exposed workers from the same company showed an excess risk of digestive cancer in the exposed group (RR = 6.25; 95% C.I. (2.69, 14.52)). In addition the SMR for digestive cancer was higher than that in the general population (SMR 259, p-value < 0.01). No significant excesses were found with any other cancers.

During the period 1945 to 1980, a study of 2031 male workers (Hagmar *et al*, 1990) who had been employed for at least 3 months at a PVC processing plant found that all-cause mortality was increased and this increase was close to being significant statistically (SMR = 116; 95% C.I. (99,136)). Significant increases were observed in deaths from violence or intoxication (SMR = 153; 95% C.I. (109,213)), deaths from all cancers (SMR = 128; 95% C.I. (106,161)) and deaths from respiratory cancer (SMR = 213; 95% C.I. (127,346)). Six brain tumours were observed against an expected 2.6, however, this increase was not significant statistically (SMR = 229; 95% C.I. (84,498)). Deaths caused by ischaemic heart disease were not increased (SMR = 100; 95% C.I. (73,135)). There was no evidence of liver hemangiosarcoma. When a latency period of greater than or equal to ten years from the start of employment was applied, the risk patterns were unchanged. No significant exposure-response associations were observed between cancer morbidity and exposure estimates for VCM, asbestos, or plasticisers.

Mortality and cancer incidence were followed up from 1964 to 1984 in 717 men who were employed for at least three months in three Swedish PVC processing plants (Lungberg *et al*, 1993). Observed mortality and cancer incidence among Swedish citizens were close to expected for most diagnoses. There was a marked excess of deaths from circulatory diseases among immigrants, mostly from Finland. This may be the result of the higher coronary mortality in Finland compared to Sweden. Five cases of malignant melanoma in the whole

study cohort had occurred as compared to 1.5 expected (SMR = 3.4; 95% C.I. (1.1, 7.9)). It is possible that this result is due to chance but the authors felt that it merited further investigation since an increased incidence of malignant melanoma had previously been found among Norwegian PVC manufacturing workers.

A study of 1100 workers exposed to VCM matched for age (within 2 years), plant and physician to 1100 non-exposed controls followed up over seven years (Laplanche et al, 1992), showed that 40 deaths occurred in the exposed workers and 43 deaths occurred in the non-exposed workers (RR = 1.0; 95% C.I. (0.6, 1.5)). Amongst the exposed workers there were 48 cases of cancer compared to 32 cases in the non-exposed workers (RR = 1.3; 95% C.I. (0.8, 2.1)). There were three cases of angiosarcoma in the liver in the exposed group and eight cases of lung cancer in the exposed group compared to six cases in the non-exposed group. Deaths from cardiovascular disease (excluding those with Raynaud's disease) occurred in 123 exposed workers compared to 93 non-exposed workers (RR = 1.4; 95% C.I. (1.0, 1.8)), mainly due to hypertension.

1.5 PREVIOUS IOM WORK CARRIED OUT IN 1979

1.5.1 Background

In the late 1970s, an epidemiological study of polyvinyl chloride (PVC) workers at the ICI Plastics Division at the Hillhouse plant was carried out by the IOM (Soutar et al, 1979). The full working study population at ICI Hillhouse at this time was 2308 men, which consisted of 1501 current employees, 339 pensioners and 468 leavers. A sample of this population was selected for medical survey, the sample being chosen to include preferentially higher exposed workers, as estimated from histories of work at ICI up to 1979 supplied by the company from their records at that time. In total 841 workers were surveyed and, after exclusions due to missing or invalid survey data, 818 study participants were included in the statistical analysis. The 818 study participants comprised 663 current employees, 98 pensioners and 57 leavers (Soutar et al, 1979).

The prevalence of respiratory symptoms and chest radiographic and lung function abnormalities were assessed in the epidemiological study. These health endpoints were related to estimates of exposure to respirable PVC dust, based on measurements of dust levels at the time of the survey and detailed occupational histories collected from the men themselves by interview with a trained member of the survey team; i.e. the company work histories were used to help select the sample for survey, and not for exposure estimation within the study proper. Chest radiographs were read by three epidemiological readers. Small rounded opacities of category 0/1 or greater were classified on 1% of the radiographs by two of the three readers and on 6% of radiographs by the third reader. For this reader, an association was found between increasing dust exposure and presence of small opacities. Exposure to respirable PVC dust was also associated with a decline in mean ventilatory capacity, suggesting that PVC dust causes a small but detectable effect on the respiratory health of the exposed workforce.

A follow-up medical survey which took place in 1980 included an additional 229 men from the Hillhouse plant, selected from the same study population. Men who had worked at any time in the plants where higher PVC dust levels had been found during the environmental survey, but who had not been included in the study in 1979, were invited to attend the follow-up study. Soutar et al (1981) concluded that exposure to PVC dust caused a detectable reduction in lung function and an increase in prevalence of slight abnormalities of the chest radiograph.

The rather short average exposure time of the population was one of the limitations of the studies. Current men had been employed at the Hillhouse plant for 14 years on average, pensioners had been employed for 17 years and leavers for 5 years.

1.5.2 Results from previous IOM work

Environmental Survey

Within the PVC plants, an environmental survey of dust concentrations in the plants manufacturing or further processing PVC had been carried out. This involved personal sampling of respirable dust in 130 men who worked in these plants (see Appendix 1 for details). During a preliminary visit to the plant subjective estimates of dustiness had been made. Selection of men to wear the dust samplers had been based on these assessments and on measurements of particle sizes of typical PVC dusts.

Respirable dust levels were found to be highest for the drying and packing operations in an older plant where PVC had been made by the emulsion method and in the mixing process in a PVC processing plant. Over a shift, the highest mean average respirable dust exposure for any occupation was 2.88 mg/m³ (standard deviation 1.84). Further details on these exposure estimates are given in Appendix 1.

Respiratory Symptoms

There was no association between chronic bronchitis, acute chest illnesses, acute bronchitis, pneumonia, pleurisy or asthma with exposure to PVC dust.

Breathlessness when hurrying on level ground or walking up a slight hill was associated with exposure to PVC dust. However, this relationship was found only in cigarette smokers and was not found in non-smokers or ex-smokers.

Lung function

Lung function was measured by forced expiratory volume in one second (FEV₁), which measures the rate at which air can be blown out of the lungs through the air passages, and forced vital capacity (FVC), which measures the volume of air expired in a full breath.

Forced expiratory volume in one second (FEV₁) was lower among men who had higher PVC dust exposure. This result was significant statistically. Principally this result was seen in current cigarette smokers but when non-smokers were considered separately, this result was confirmed, implying that there were differences in the response to PVC dust according to smoking habit. The estimated reduction in FEV₁ in all men in relation to exposure to the mean PVC dust exposure for one year was approximately one seventh of that caused by ageing by one year, and of a similar magnitude to the annual loss caused by smoking 20 cigarettes per day.

FVC was significantly reduced at higher exposures to PVC dust in men who were employed at the time of the study. The magnitude of this reduction was less than that of FEV₁.

Chest radiographs

The chest radiographs were read by three independent expert readers. Small rounded opacities in the radiographs were detected by one of these readers more commonly in men with higher exposures to PVC dust than in men with lower or no exposure to PVC dust. An effect of PVC dust was not detected by the other two readers, although they detected small

rounded opacities in a few cases. However, lung function was reduced in men with small rounded opacities compared to those without.

Autoclave Workers

In autoclave workers, the observed effects of PVC dust that were seen for lung function and in the chest radiographs were not related to residual vinyl chloride monomer in PVC dust. It was noted in the study carried out in 1979 that in the past, men working on the autoclaves may have been exposed to significant amounts of VCM. It is unlikely that the observed effects of PVC dust were due to exposure to VCM as these could not be explained by an effect of working on the autoclaves.

Factors Other than PVC Dust Effects

The associations with exposure to PVC dust were detected against a background of other non-occupationally-induced effects. There was a strong relationship between cough, sputum, and other respiratory symptoms and smoking habit. In addition, deterioration in lung function and small opacities in the chest radiograph were strongly associated with age.

1.6 THE CURRENT STUDY

A unique opportunity to study the subsequent mortality of approximately 1500 current workers and 200 ex-workers from the ICI Hillhouse site (where the remaining PVC plant is now owned by EVC) in 1979 was available from the data obtained in the course of setting up and conducting the epidemiological survey (1979) and the medical survey (1980) of the respiratory health of workers. With the active support of ICI experts and EVC management and workers, the current study was commissioned to do this. Although a cohort of 1700 people is not large, the potential follow-up period was about 25 years, implying that there would be a lot of information about mortality. Also, for the subset who had attended medical surveys, data were available on respiratory health and smoking habits in 1979, as well as detailed work histories up to that time. These additional data enriched the possibilities of a mortality study now.

2 OBJECTIVES

The aim of the present study was to use the existing records of a PVC-exposed workforce employed for at least part of the time period 1967-1979 to investigate more about the effects of long-term exposure to respirable PVC. This was achieved by initiating a mortality follow-up of this workforce and examining the cause-specific mortality of those who died.

The specific objectives of this study were to investigate:

1. Is there evidence that mortality from respiratory diseases (specifically non-malignant respiratory disease and lung cancer) is different among workers at the Hillhouse plant from that in the general population in the same geographical area?
2. To what extent are any differences in mortality patterns specific to particular age groups, calendar periods or work areas within Hillhouse?
3. To what extent did respiratory health in 1979 (lung function, symptoms, radiology) predict future mortality?
4. What evidence, if any, is there regarding other differences in mortality (from other causes including all cause mortality, ischaemic heart disease, all cancer mortality and cancer at a range of other sites) possibly related to occupation or exposure within the Hillhouse plant?

3 STUDY METHODS

3.1 IDENTIFICATION OF STUDY COHORT

Identification data were available for a total of 1700 individuals at the ICI Plastics Division at the Hillhouse plant. These included all 1501 individuals who had been identified as current workers at Hillhouse at the time of cohort identification in 1979 (see Section 1.5.1, earlier). Included among them were 892 men who had attended epidemiological medical surveys carried out by IOM (663 current workers from the first survey carried out in 1979 and 229 additional current workers from the further medical survey in 1980).

The data available for the 1501 current workers included surname, date of birth, NI number and initials rather than full forenames. No address information was available. Work histories at ICI were available up to 1979 for all workers. These had been supplied by ICI at the time of data collection, to help in the selection of the sample to be invited to medical survey. (That sample was designed to include a disproportionately high number of higher-exposed workers.) Included in these histories were each individual's start and end dates in jobs classified into around 100 broad work categories. These work categories were recorded as three or four alpha/numeric characters each representing a different job or work area. Code lists were available to interpret approximately 83% of all alpha/numeric codes listed.

Ninety leavers and 109 pensioners for whom there were data on surname and initials, date of birth and address at time of data collection were also included in the cohort. These were but a small proportion of all those who, in 1979, were former workers at ICI Hillhouse. Examining mortality in relation to occupation within Hillhouse among this subgroup was not possible since no occupational histories were identified for these men. Nevertheless, they were included in the mortality tracing.

Information from medical survey was available for the 663 men who had attended during the 1979 IOM study. These data included smoking habit, estimated cumulative dust exposure to 1979, lung function measurements, respiratory symptoms and chest radiograph readings. Survey information for the 229 men attending the additional survey in 1980 had not been retained in an accessible form and so is no longer available.

3.2 ESTABLISHING VITAL STATUS

3.2.1 Tracing strategy

The identification data held by the IOM for the 1700 individuals were sent to the ICI Epidemiological Unit where information was held on all deaths among ICI employees from 1972 onwards, including date of death. The identification details for these individuals were augmented where possible from the ICI pension or personnel records. Additional details that were given, where available, included full forenames and address details.

The main way of establishing vital status of the study cohort was with the assistance of the Office for National Statistics (ONS) in England. Subject to safeguards on confidentiality and other ethical considerations, the ONS assists mortality tracing for *bona fide* research studies by means of its access to the National Health Service Central Register (NHSCR). Written confirmation that the present study had the approval of workforce representatives as well as of management was required by ONS and this was supplied following consultations with representatives of the current workforce at the Hillhouse plant, when the objectives of the present study were explained.

The desired time-period for tracing in the present study coincided with a time when ONS was revising its procedures for supporting studies in the light of various changes, including

devolved administrations in Scotland and Wales. The present study was the first since devolution where an application for mortality tracing in England had been made by a research organisation based in Scotland. This implied setting up of new procedures and a delay in getting tracing started. Once these difficulties were resolved, data on the 1700 individuals were sent to the Office for National Statistics (ONS) for tracing and flagging by name and date of birth. Notification of the details of any deaths that had occurred was received by the IOM. In addition, the IOM received notification of those who remained untraced.

3.2.2 Processing of mortality data; definition of follow-up

As described in Section 3.2.1, notifications of deaths in the study cohort and notifications of those remaining untraced were received by the IOM. Where deaths had occurred, the IOM received a copy of the details from the death certificate. In some cases only text descriptions of these deaths were given and in other cases the deaths had been coded according to the International Classification of Diseases and Causes of Death (ICD) published by the World Health Organisation (WHO). Where death notifications from ONS were uncoded (a total of 259 deaths), ICD codes were added to the records by a member of the study team. Where only one cause of death was noted (59 deaths), or where there were multiple causes all from the same cause group (46 deaths), this cause was taken to be the underlying cause of death. In the remaining 154 deaths, the multiple causes recorded on the death certificate were reviewed by a consultant physician who applied the standard rules for identification of underlying cause of death.

Two ICD revisions were covered by the period of study follow-up (1979-2003). These two revisions were the 9th (World Health Organisation, 1977) and the 10th (World Health Organisation, 1992) revisions, which were used from the periods 1979 to 2000, and from 2001 to date, respectively.

Those men who were traced and who were not deceased were flagged on the ONS systems so that their vital status could be updated, if required, at a future date. The mortality follow-up of the study cohort remains ongoing now that the flagging system has been set up.

3.2.3 Definition of study follow-up period

There is, inevitably, a time-lag between date of death, and notification of those deaths to the IOM. The 31 December 2003 was taken as the end of the follow-up period for the present study because, although mortality information was available for some individuals through 2004 and into early 2005, we were not sure that notification of deaths after end of 2003 was complete.

3.2.4 External reference mortality rates

Comparisons were made between cause-specific mortality of the cohort and death rates experienced in a reference population. Data on numbers of deaths and mid-year populations were available for specific causes for males and by age and calendar year, local, geographical and national regions. The corresponding information on population size in the same local, geographical and national regions was also available. This information was used to form the denominators for the calculation of rates. The required data on population size and numbers of deaths was supplied by ONS.

Data files were held containing populations sizes and numbers of deaths covering the following:

| | |
|--------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Calendar years: | 1979 – 2003 |
| Age groups (population data): | 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90+ |
| Age groups (death data): | 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84, 85-89, 90-94, 95+ |
| Regions: | <ul style="list-style-type: none"> • England, Wales and elsewhere; • North West Standard Region (1979-1996); • North West GOR (1997-2003); • Lancashire County. |

In the data on population sizes, from 2001 onwards the population data were recorded separately for those aged 85-89 and for those aged 90+. Prior to this (from 1979 to 2000), the population data for those aged 85-89 and for those aged 90+ was combined.

Table 3.1 lists the causes of death for which SMR analyses were calculated and the corresponding ICD codes for the different revisions.

Table 3.1: Causes of death for which SMR analyses (comparisons with reference rates) were carried out, and corresponding ICD codes for relevant revisions.

| Cause of death | ICD code revision | |
|------------------------------------------|-------------------|------------------|
| | 9 th | 10 th |
| All-causes | 001-E999 | A00-Z99 |
| All internal causes (Natural causes) | 001-799 | A00-R99 |
| External causes – accidents and suicides | E800-E999 | S00-Z99 |
| Ischaemic heart disease | 410-414 | I20-I25 |
| Non-malignant respiratory disease | 460-519 | J00-J99 |
| Chronic bronchitis | 491 | J42 |
| Emphysema | 492 | J43 |
| All cancers | 140-239 | C00-D48 |
| Lip, oral and pharyngeal cancers | 140-149 | C00-C14 |
| Digestive & peritoneal cancer | 150-159 | C15-C26 |
| Oesophageal cancers | 150 | C15 |
| Stomach cancer | 151 | C16 |
| Liver cancer | 155 | C22 |
| Laryngeal cancer | 161 | C32 |
| Lung cancer | 162 | C34 |
| Malignant melanoma | 172 | C43 |
| Peptic ulcer | 533 | K27 |

3.3 USE OF WORK HISTORY DATA

Work histories covering employment at ICI were available for the 1501 current employees having been obtained in 1978-79 from ICI personnel records. Approximately 100 broad job categories had been used in total, though some had been used only very occasionally.

The ICI Hillhouse plant, which is now owned by EVC, was visited on the 10th and 11th February 2005. Seven long-service employees were interviewed about their experience while working on the site, with particular emphasis on the PVC plants. This information was used by the occupational hygienist to assist in classification of potential exposures to PVC and other substances in each of the job categories.

After reviewing the work history information available for the subjects it was decided that it was practicable to assess exposure only as a dichotomous variable, e.g. either exposed or not exposed to PVC dust. The main reason for this relatively crude categorisation of the exposure was because of the general nature of the job titles available. Many of these referred only to the plant they worked in, e.g. Corvic 6, rather than the exact job title, e.g. packer.

Assessment of exposure to PVC dust was based on the expert opinion of the assessor in the light of the information available from the interviews and other sources. For each job title identified in the work history exposure to PVC dust was assessed as either yes (Y), no (N), possible (P) or unknown (U). Identified exposure to PVC dust corresponds to an average respirable dust concentration greater than about 0.2mg/m³ (and perhaps ranging up to more than 10mg/m³). Other jobs on the Hillhouse site may have had exposure to other particulates, e.g. carbon black, but no exposure assessment has been made for aerosol exposures other than PVC.

Where there was some uncertainty about the exact meaning of the job code in the work history file a "U" code was used. It is believed that most of the U coded jobs would not have PVC exposure. In addition, we indicated whether exposure to PVC dust would have been to emulsion (E), suspension (S) or possible mixed/unknown (M) grades. Further subdivision of PVC exposure into compound and resin exposure was not possible in the current study.

The following plants were categorised as:

| | |
|------------|--------------------------------------------------------------------------------------------|
| Emulsion | Corvic 1, 4, 9 (although plant 9 was not operating at the time of the original IOM survey) |
| Suspension | Corvic 2, 3, 5, 6, Welvic 1 & 2, Darvic (C 7 and 8 at Runcorn) |

Finally an assessment of whether the job could have entailed important exposure to vinyl chloride monomer (VCM), tetrafluoethylene (TFE), asbestos (A) or lead or other metal pigments (Pb) was provided. Lead exposure in the plant was primarily to lead pigment. In each case these assessments were based on the job that the individual carried out or the plant where they worked. For example, it was assumed that all workers on a PVC production plant could have been exposed to VCM.

In addition exposure indices based on detailed work histories linked with occupational hygiene monitoring were available for a subset of the cohort comprising 663 current workers from the medical survey in 1980. During the medical survey current personal exposures to respirable PVC dust had been measured by occupation in each plant in which PVC was manufactured or processed. One hundred and thirty reliable personal samples had been obtained. Sixty-six job/dust categories had been derived from these 130 measurements and from knowledge of the factory conditions. For each individual, a 'dust index' had been derived from these dust measurements and the occupational history such that the dust levels in

each of a man's occupations had been multiplied by the years that he had spent in that occupation; the exposures from each occupation had been summed to provide a total 'dust index'. These estimates did not represent actual dust exposure, since only current (1980) dust levels were known, but represented an index of relative dust exposure for comparison with medical responses.

3.4 DATA ON RESPIRATORY HEALTH

As described in section 1.5, in the late 1970s, 818 men were surveyed at Hillhouse, of which 663 were current workers. Health data including information on chronic bronchitis, breathlessness and lung function were available for the 663 men. In addition data were also available on smoking, height and weight, and x-rays were taken and read epidemiologically. During the study, identification data (name, date of birth, NI number) for these men were stored in an electronic data file and these men were allocated an identification number. However, to preserve confidentiality of individuals, the x-rays and health data for these men were stored in a separate electronic data file with different identification numbers (ID numbers).

Hence, before the health data could be analysed, the ID numbers contained in the data file with the health data for the 663 men had to be matched up with the ID numbers contained in the data file with the identification data for the 663 men. Matches were made for 661 of the 663 men.

Those attending survey had been seen by appointment when a medical survey team visited the factory in 1980. Details of respiratory symptoms had been obtained by administration of the Medical Research Council Questionnaire of Respiratory Symptoms (MRC, 1976). The symptoms of interest in this study were as follows:

Chronic bronchitis: Men had been classified as having chronic cough if they responded positively to **either** usually coughing first thing in the morning in the winter **or** usually coughing during the day or at night in the winter and coughing like this on most days for as much as three months each year. Likewise, men had been classified as having chronic phlegm if they responded positively to **either** usually bringing up phlegm from their chest first thing in the morning in winter **or** bringing up phlegm from their chest during the day or at night in the winter **and** bringing up phlegm from their chest like this on most days for as much as three months each year. Hence the presence of chronic bronchitis had been defined as the presence of chronic cough on most days for as much as three months each year **and** chronic phlegm on most days for as much as three months each year.

Breathlessness: The presence of breathlessness had been defined as being short of breath when hurrying on level ground or walking up a slight hill.

Forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) had been measured using a modified Gaensler spirometer (Gaensler, 1951; McKerrow, 1960). The men had been given a practice expiration, after which, three technically satisfactory forced expirations were recorded. The analysis had been based on the largest values of FEV₁ and FVC, but these had not necessarily been recorded from the same breath.

Predicted FEV₁ and predicted FVC were calculated in the current study using the standard prediction equations (Quanjer, 1983):

$$\text{Predicted FEV}_1 = (4.301 \times \text{height}) - (0.029 \times \text{age}) - 2.492$$

$$\text{Predicted FVC} = (5.757 \times \text{height}) - (0.026 \times \text{age}) - 4.345$$

Predicted values of FEV₁ and FVC were then compared with the observed values of FEV₁ and FVC using the ratio of (observed FEV₁/expected FEV₁) and similarly for observed and expected FVC. These standardised FEV₁ and FVC variables were used in the subsequent statistical analysis.

The men's standing height had been measured and they had been weighed fully clothed.

A standard technique (95 – 120 kV) had been used to take full-size posterior-anterior chest radiographs. These had been read independently by three medically qualified epidemiological film readers using the ILO (International Labour Office, 1972) classification scheme for the identification of rounded and irregular opacities.

3.5 STATISTICAL ANALYSIS

3.5.1 Descriptive summaries

The numbers of men entering the final cohort were tabulated by their age distribution at entry to the study, exposures and mortality experience.

In addition, for those who had attended medical survey and for whom data were available on lung function, symptoms and radiology, tabular summaries were produced for symptoms of chronic bronchitis and breathlessness and for lung function. Age group was cross-tabulated against smoking status, the results of the radiographs were summarised, and predicted lung function measurements were compared with observed lung function measurements.

3.5.2 Comparison of mortality with national and regional reference populations

The statistical package GENSTAT (Genstat 6 Committee, 2002) was used to analyse the mortality data. Standardised Mortality Ratios (SMRs) were used to compare death rates between the reference population and the study cohort. Differences were described between subgroups classified by age and calendar period.

Particular interest was in deaths from respiratory causes - Non-Malignant Respiratory Disease (NMRD, which includes chronic bronchitis and emphysema); and lung cancer. Other causes of interest included all-cause mortality and ischaemic heart disease, partly because this is such a widespread cause of death in the general population.

A table of person-years at risk for the study cohort classified by calendar year and age groups was constructed. For each year between a man's entry into follow-up (start of 1979) and either his death or the end of follow-up (end of 2003), his mid-year age was calculated and allocated to the appropriate age group. If the individual survived that year, the appropriate cell of the table was augmented by one year's risk time, or a fraction of a year if he died part way through that year.

To obtain cause-specific death rates by calendar year, age group and region, the numbers of deaths from each cause of interest in the reference population were divided by the reference population size. These death rates were then multiplied by the cohort person-years at risk to give an estimate of the average numbers of deaths to be expected in the study cohort if the reference population rates were applied. From these estimates, marginal totals of observed and expected deaths were calculated, and the SMR was calculated as the ratio of the total number of observed deaths to the total number of expected deaths expressed as a percentage. Assuming that counts of the numbers of observed deaths in the cohort were likely to follow a Poisson distribution, and assuming that sampling variation in the reference rates was

negligible, standard errors of the calculated SMRs were derived. Where the SMR was greater than 100, this indicated that the mortality rates were higher in the study cohort than in the reference population, and where the associated 95% confidence intervals (C.I.s) were wholly above 100, this indicated that the result was significant statistically.

Observed deaths in the study cohort were compared with numbers of deaths expected from national (England and Wales) and regional (North West Region; Lancashire) mortality rates. Standardised mortality ratios were calculated for the whole study group, and for current workers at time of cohort identification. SMRs were also calculated separately for workers ever exposed to PVC and those who were unexposed.

3.5.3 Analysis of exposure response relationship

The method of Cox Proportional Hazards is a regression model for survival data. The format of the model assumes that the age specific risk of mortality can be described as a hazard function, with covariates modifying the hazard by multiplicative relative hazard coefficients. The risk is parameterised as the product of a time dependent baseline hazard function $h_0(t)$ and a regression expression involving terms for explanatory variables such as age and exposure. A typical example of how to express a hazard function is

$$h_i(t) = \exp \left(\sum_j \beta_j x_{ij} \right) h_0(t)$$

where $h_i(t)$ is the hazard function for the i th individual; x_{ij} ($j = 1, \dots, p$) are the covariates; β_j are regression coefficients representing logarithms of relative hazard; and $h_0(t)$ is a baseline hazard function shared by any individuals for whom all covariates are zero. Estimation of the unknown coefficients (β) and their variance-covariance matrix is done by an iterative method that maximises the partial likelihood function involving the regression terms but eliminating the baseline hazard. The effects of the relevant covariate on mortality are quantified by each β_j , on the log scale, so that the exponential is interpreted as a ratio between mortality rates.

The Cox Proportional Hazards regression model was used to examine the relationship between mortality and exposure. This model examines the relationship between risk of death from a specific cause and characteristics of the individuals, including their exposures. Discrete indicator variables (e.g. ever/never worked in a specific workplace) or continuous covariates (e.g. time in broad occupational groups, cumulative dust index) can be analysed.

Length of time included in the follow-up was used as the basic time axis for the present study. This was calculated from the start of follow-up (1st January 1979) to date of death or emigration or end of follow-up period (31st December 2003).

Analysis for both the workers current at the time of cohort identification and for the subset who attended medical survey was carried out for all-cause mortality and the three key causes of death: non-malignant respiratory disease, ischaemic heart disease and lung cancer. For non-malignant respiratory disease, ischaemic heart disease and lung cancer, deaths from other causes were treated as censored events (i.e. information on the individual was included in the analysis up to the date on which death occurred, at which time the individual was deemed to have left the cohort). The statistical package S-Plus (1988, 2002 Insightful Corporation) was used to perform the analyses. Interest was in the relationship between mortality and PVC dust for the current employees and the survey attendees and was also in whether the relationship between PVC dust and mortality varied according to health status for those who had attended medical survey.

Age was modelled as a continuous variable in the baseline model for the 1501 current workers. The exposure measurements for PVC were then added to the baseline model.

Comparisons were made between subjects exposed to each type of PVC (all PVC, emulsion, suspension) and those with no PVC exposure. Thus, for example, subjects with emulsion PVC exposure were compared to subjects with no exposure to PVC, with subjects with exposure to suspension or mixed PVC excluded from the analyses. Other alternative models were also examined, including those adjusting simultaneously for the effects of different types of PVC in those with any PVC exposure. Use of other formulations led to small changes in the numerical results but the general patterns of the results and the conclusions from the analyses were unchanged.

For the survey attendees, possible effects of age and smoking habit were adjusted for by using these terms as the basic model for analysis. Age was modelled as a continuous variable. Smoking habit was treated as a factor with three categories, non-smokers, current smokers and ex-smokers, and as a continuous variable for packyears (cumulative amount smoked up to 1979) for current and ex-smokers. The dust exposure measurement was added to the basic model. Lung function and respiratory symptoms variables were then added separately, one at a time, to a model that was adjusted for the possible effects of age, smoking habit and also included a term for dust exposure.

4 POPULATION CHARACTERISTICS AND EXPOSURE

4.1 RESULTS OF TRACING EXERCISE

As described in section 3.1, identification data were available for 1700 individuals at Hillhouse. Of these 1501 were current workers, 90 were leavers and 109 were pensioners. The data for these 1700 workers were sent to the ICI Epidemiological Unit and were returned to the IOM with additional information on dates of death for those known to have died. At this stage, it was noted that two individuals in the data set had duplicate records with the same surname, initials and date of birth information. The duplicate information was deleted for both individuals concerned, one a leaver and one a pensioner.

Unique identification data for the remaining 1698 individuals were sent to ONS for tracing. During the tracing process, two of the 90 leavers were found to be females. They were excluded from any further analysis leaving a total of 1696 males in the analysis cohort.

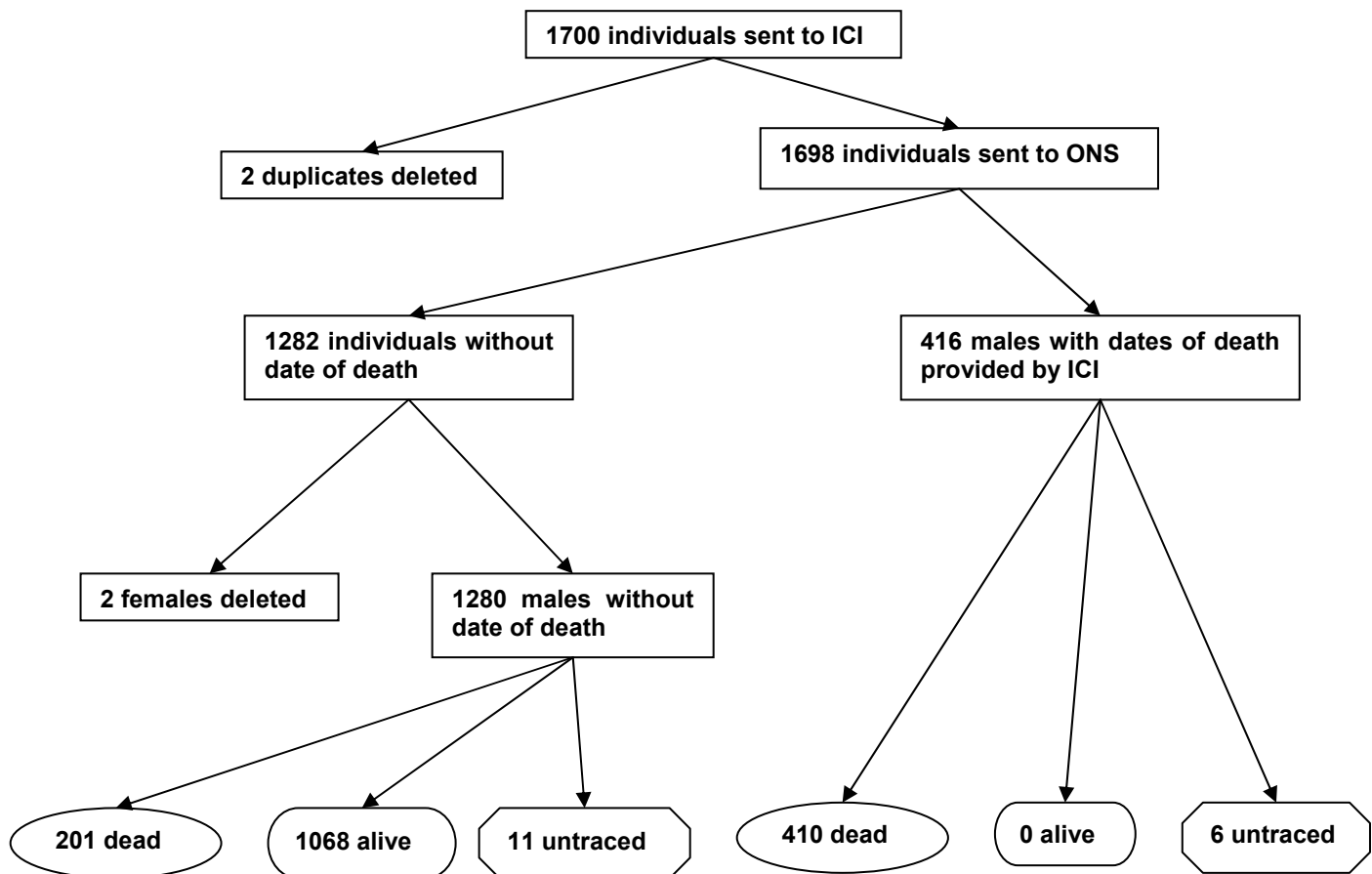


Figure 4.1: Flowchart with results of tracing exercise

The results of the tracing process are shown in Figure 4.1. At the end of the tracing process in February 2005, 611 deaths had been reported and only seventeen men had not been traced, with the remaining 1068 men alive. Fourteen of those identified as alive had been lost to follow-up before the end of the follow-up period, due to emigration from the UK. Their vital status is therefore known only for part of the follow-up period. For one of the seventeen untraced men, insufficient information was available for tracing and for the remaining sixteen men there were no records traced in the ONS system. Eight of the 1679 individuals who had been traced were in Scotland and information on these was sent to the General Registrar's Office (Scotland) for tracing. Two of these eight men were dead and six were still alive.

4.2 TIME PERIOD OF FOLLOW-UP

The start of follow-up for the SMR analysis comparing observed mortality with mortality in the reference population was 1st January 1979 (date of cohort identification) and follow-up ended on 31st December 2003 (the last full year before tracing commenced), giving 25 full years of follow-up.

Of the 611 deaths identified in the full study cohort, one man was reported as having died in 1972, another man as having died in 1973 and six other men as having died in 1978. Those who had died in 1978 had all died in the last 6 weeks of the year (i.e. close to the time of cohort identification). The man who died in 1972 was a leaver, the man who died in 1973 was a pensioner, and four of the six men who died in 1978 were current workers and the other two were pensioners. These eight deaths were removed from the analysis, on the grounds that either they did not fulfil the criterion of being alive on 1 January 1979 and so had been wrongly included in the original cohort, or else their vital status as notified to us by ONS was wrong. (We think the former reason is the most likely.)

A further 42 men died during 2004 and early February 2005, and so for the mortality analyses were treated as alive for the full period of follow-up. Hence the SMR analysis applied to 561 deaths between 1979 and 2003.

4.3 STUDY POPULATION

For the analyses described in this report three nested subgroups were used. These will now be referred to as population 1, population 2 and population 3, respectively. Population 1 consists of the full study cohort of 1696 men (1501 current workers, 87 leavers and 108 pensioners), of whom 17 were untraced, and eight died prior to the start of follow-up, leaving an analysis group of 1671. Population 2 consists of a reduced subgroup of the 1501 men identified by the plant as current workers at the time of cohort identification, of whom 13 were untraced and four died prior to start of follow-up, resulting in an analysis subgroup of 1484. Population 3 consists of a further reduced subgroup of 661 current workers who attended the medical survey during 1980, of whom six were untraced leaving an analysis group of 655 men.

4.4 COHORT FOR MORTALITY ANALYSIS

4.4.1 Age at start of follow-up in 1979

The distribution of the men's ages at 1st January 1979 is shown in Table 4.1. The majority of the study cohort was aged between 30 and 59 years old, with relatively few aged under 30 or aged 60 and over.

Table 4.1: Distribution of men included in population 1 by age at start of follow-up, with percentages in italics.

| Age Group (start of follow-up) | N | % |
|---------------------------------------|-------------|-----------|
| 15-19 | 59 | <i>4</i> |
| 20-24 | 91 | <i>5</i> |
| 25-29 | 100 | <i>6</i> |
| 30-34 | 202 | <i>12</i> |
| 35-39 | 176 | <i>11</i> |
| 40-44 | 200 | <i>12</i> |
| 45-49 | 224 | <i>13</i> |
| 50-54 | 240 | <i>14</i> |
| 55-59 | 230 | <i>14</i> |
| 60-64 | 95 | <i>6</i> |
| 65-69 | 34 | <i>2</i> |
| 70-75+ | 20 | <i>1</i> |
| Total | 1671 | |

4.4.2 Time at risk

The number of deaths and the total person-years at risk for the analysis cohort over the follow-up period are shown in Table 4.2.

Table 4.2: Number of deaths and total person-years at risk in population 1 by year of follow-up

| Year of follow-up | Number of deaths | Person-years at risk |
|--------------------------|-------------------------|-----------------------------|
| 1979 | 9 | 1665 |
| 1980 | 11 | 1659 |
| 1981 | 15 | 1642 |
| 1982 | 12 | 1626 |
| 1983 | 16 | 1614 |
| 1984 | 13 | 1600 |
| 1985 | 17 | 1581 |
| 1986 | 20 | 1565 |
| 1987 | 20 | 1546 |
| 1988 | 31 | 1520 |
| 1989 | 15 | 1498 |
| 1990 | 25 | 1477 |
| 1991 | 24 | 1346 |
| 1992 | 23 | 1328 |
| 1993 | 29 | 1295 |
| 1994 | 25 | 1271 |
| 1995 | 28 | 1245 |
| 1996 | 30 | 1217 |
| 1997 | 33 | 1180 |
| 1998 | 34 | 1148 |
| 1999 | 17 | 1122 |
| 2000 | 21 | 1109 |
| 2001 | 32 | 1075 |
| 2002 | 27 | 1046 |
| 2003 | 34 | 1015 |
| Total | 561 | 34393 |

From Table 4.2, it can be seen that there was a large increase in the number of deaths in the study cohort in 1988 when there were 31 deaths, and a decrease in 1989 when there were only 15 deaths. The average of 23 deaths per year in 1988-89 fits the general pattern. There was also a large decrease in the number of deaths between 1998 when there were 34 deaths, 1999 when there were only 17 deaths and 2000 when there were 21 deaths. This large decrease levelled off again in 2001 when there were 32 deaths. There were no compensating high numbers of deaths in adjacent years. The Office of National Statistics was informed about these patterns in the deaths and the details from the death certificates were double checked. Reassurance was given by ONS that these patterns are due to random fluctuations in the deaths during the follow-up period.

4.4.3 Causes of death

The numbers of deaths that occurred between 1st January 1979 and 31st December 2003 coded by principal underlying cause are summarised in Table 4.3. The 9th and 10th revisions of the ICD coding system were used to define the groups and subgroups. Every individual has a unique underlying cause of death, but there is some overlap in the table due to some causes being included more than once. “Non-malignant respiratory disease” is made up of all deaths from chronic bronchitis, all deaths from emphysema and all deaths from any other type of non-malignant respiratory disease. “Digestive & peritoneal cancer” is made up of oesophageal cancers, stomach cancer, liver cancer and all other digestive and peritoneal cancers. “All cancers” is made up of lip, oral cavity and pharyngeal cancers, digestive and peritoneal cancers, laryngeal cancers, lung cancer, malignant melanoma of skin and all other cancers. “All internal causes (Natural causes)” are made up of ischaemic heart disease, non-malignant respiratory disease, all cancers, peptic ulcers and other internal causes. “All-causes” are made up of all internal causes and external causes – accidents and suicides.

Table 4.3 shows that deaths in the analysis cohort were predominantly from cancers (179 men) and ischaemic heart disease (183 men). The majority of cancer deaths were from lung cancer (56 men) followed by digestive and peritoneal cancer (51 men).

Table 4.3: Summary of numbers of deaths in selected cause groups for populations 1, 2 and 3, respectively

| Cause of death | ICD code revision | | | No. of deaths | | |
|------------------------------------------|-------------------|------------------|------------------|--------------------------|--------------------------|-------------------------|
| | 9 th | 10 th | 10 th | Population 1 1671 men | Population 2 1484 men | Population 3 655 men |
| | | | | | | |
| All-causes | 001-E999 | A00-Z99 | | 561 | 442 | 207 |
| All internal causes (Natural causes) | 001-799 | A00-R99 | | 548 | 433 | 205 |
| External causes – accidents and suicides | E800-E999 | S00-Z99 | | 13 | 9 | 2 |
| Ischaemic heart disease | 410-414 | I20-I25 | | 183 | 143 | 70 |
| Non-malignant respiratory disease | 460-519 | J00-J99 | | 50 | 37 | 17 |
| Chronic bronchitis | 491 | J42 | | 3 | 2 | 1 |
| Emphysema | 492 | J43 | | 0 | 0 | 0 |
| All cancers | 140-239 | C00-D48 | | 179 | 147 | 73 |
| Lip, oral and pharyngeal cancers | 140-149 | C00-C14 | | 2 | 2 | 1 |
| Digestive & peritoneal cancer | 150-159 | C15-C26 | | 51 | 39 | 21 |
| Oesophageal cancers | 150 | C15 | | 10 | 9 | 7 |
| Stomach cancer | 151 | C16 | | 8 | 4 | 4 |
| Liver cancer | 155 | C22 | | 6 | 6 | 3 |
| Laryngeal cancer | 161 | C32 | | 1 | 1 | 0 |
| Lung cancer | 162 | C34 | | 56 | 50 | 27 |
| Malignant melanoma | 172 | C43 | | 0 | 0 | 0 |
| Peptic ulcer | 533 | K27 | | 1 | 0 | 0 |

4.5 EXPOSURE ESTIMATION FOR POPULATION 2

4.5.1 Visit to Hillhouse plant

A visit took place at the Hillhouse plant in early 2005. This visit was carried out by two members of the study team, including a senior occupational hygienist. The purpose of the visit was to obtain historical information about the plant from discussions with current workers, and a tour of the current facilities on site. A summary of the findings of this visit is given here.

In the earlier plants most operations were reportedly done manually and it was not really until the 1980s that there was any widespread introduction of automation. There was reportedly no local ventilation on dusty operations until the introduction on the Corvic 9 plant. A number of interviewees reported that there was settled dust on most inaccessible horizontal surfaces in the PVC plants. Most PVC plants were reportedly quite noisy.

The Welvic plants were reportedly older than many others on site and the premix area where pigments were weighed was said to be “very dusty”, although the remainder of the plant was less dusty. When IOM monitored in the late 1970s the average respirable dust levels in the mixing areas of the Welvic plants were about 1 – 2 mg/m³ compared with levels in other areas of the plant were generally less than 0.5 mg/m³. Lead based pigments were used in the flexible sheet made in the Welvic plants. Workers in these plants were under health surveillance. These plants operated 24 hours per day on a shift system.

The Darvic plant shared the pigment area with the Welvic plants, but they had their own weighing section close to the Welvic 1 plant. The Darvic plant operations were said to be less dusty than the Welvic plant. However, during the IOM survey the measured respirable dust levels were comparable, i.e. <0.5 mg/m³ in both types of plant.

Exposure to PVC dust has probably decreased with time because of improvements in technology, although emulsion grades were reputedly always dustier than suspension grades. At the time of the original IOM survey the average respirable dust exposure level in Corvic 4 dryers and packers (Emulsion) was approximately 2.8 mg/m³ while the corresponding level for workers on Corvic 2 (Suspension) was about 0.6 mg/m³. It seems reasonable to assume that within either emulsion or suspension plants that exposure was higher prior to about 1965 when compared to exposure from 1966 onwards.

Most workers reportedly did not wear respirators prior to the mid 1980s. Some workers said that even after this time usage of respirators was not widespread.

The majority of fitters were assigned to specific plants, although some worked in a central team. They reported being exposed to PVC dust when undertaking maintenance on equipment. During the IOM survey in the late 1970s the exposure of maintenance staff to respirable dust was comparable to other staff on the less dusty plant jobs, e.g. on Corvic 4 the average respirable dust level for maintenance staff was 0.8 mg/m³ and the other staff not involved with packing or drying were exposed to between about 0.5 and 1 mg/m³.

Interviews with maintenance staff identified that asbestos was present on heater banks, steam pipes and some other hot plant. From the description of the material used on heater banks it was probably chrysotile (white) asbestos string or rope. It was reported that prior to about 1980 there was little concern about the usage of asbestos in such situations and maintenance fitters may have worked with asbestos at most once or twice each week, although some fitters did not recall any work with asbestos. More extensive work with asbestos insulation was done by specialist ladders rather than the fitters. About the mid 1980s asbestos lagging was

reportedly removed from the site. For most of the maintenance staff exposure to asbestos prior to 1980 is not considered to be an important risk, after that date exposure was probably negligible.

4.5.2 Estimation of exposures

The methods used to estimate exposures for population 2 are described in section 3.3. The output of the estimation procedures was, for each potential exposure, an indicator representing whether or not each subject had been potentially exposed and the number of years exposed up to the time of cohort identification in 1979. Exposures were estimated for four main PVC exposures:

- Total PVC (exposure to any type of PVC)
- Emulsion PVC
- Suspension PVC
- Mixed PVC (both emulsion and suspension in the same job)

Exposures were also estimated for four other potential exposures within the plant:

- VCM
- Asbestos
- TFE
- Lead (primarily lead pigment)

Table 4.4 shows the number of individuals with exposure to each of these substances, and for those who have exposure, shows the mean, minimum and maximum number of years exposed.

Table 4.4: Number of subjects in population 2 exposed to PVC and other chemicals with average, minimum and maximum time exposed.

| Exposure | No. of subjects with non-zero exposure | Average years exposure (for exposure > 0) | Minimum years exposure (for exposure > 0) | Maximum years exposure (for exposure >0) |
|----------------|----------------------------------------|-------------------------------------------|-------------------------------------------|------------------------------------------|
| Total PVC | 996 | 12.1 | 0.1 | 32.4 |
| Emulsion PVC | 274 | 8.9 | 0.1 | 31.0 |
| Suspension PVC | 758 | 11.1 | 0.1 | 32.4 |
| Mixed PVC | 133 | 9.3 | 0.3 | 32.4 |
| VCM | 552 | 10.4 | 0.1 | 32.4 |
| Asbestos | 372 | 9.5 | 0.1 | 32.2 |
| TFE | 195 | 7.7 | 0.1 | 27.4 |
| Lead | 446 | 10.4 | 0.1 | 32.4 |

Two-thirds of the study group had been exposed to PVC dust, with length of exposure ranging from around one month to over 32 years (i.e. since the start of PVC production at Hillhouse). Most of these individuals had been exposed to suspension PVC (76% of those exposed), with fewer exposed to emulsion PVC (27%) or mixed PVC (13%). There was some overlap between these three groups with 8 subjects who, during their time at Hillhouse, had worked in jobs with emulsion PVC exposure only, jobs with suspension PVC exposure only and jobs with mixed exposure to suspension and emulsion PVC. In addition, 153 subjects had worked in different jobs from two of the three subgroups. Average times exposed to emulsion and mixed PVC were lower than for total and suspension PVC.

Over one third of the study group were exposed to VCM, and 30% were exposed to lead. All of these subjects were also exposed to PVC dust. Fewer subjects were exposed to asbestos or

to TFE, and these subgroups included individuals with and without PVC dust exposure. Only six subjects were exposed to both asbestos and TFE. There was some overlap between exposures to the other substances.

4.6 CHARACTERISTICS OF POPULATION 3

For population 3, additional information was available on smoking status and health data, which was not available for population 2. This additional information was used in the analysis of population 3.

Table 4.5 shows the distribution of age group at the start of the study against smoking status at the start of the study for the 655 men. As noted earlier for the full study group, the majority of men were aged between 30 and 59 years of age. Current cigarette smokers at the time of data collection in 1979 were the most numerous group, comprising nearly half (47%) of the total. Most of the current cigarette smokers, current cigar/pipe smokers, and ex-smokers were aged between 40 and 59 years old. The age distributions of current cigarette smokers and of ex-smokers were similar. Lifelong non-smokers were on average younger, and current cigar or pipe smokers older.

Table 4.5: Distribution of age and smoking for population 3. Each cell contains number and *percentage of column total*

| Age group | Smoking status | | | | | | | | |
|-----------|----------------|----|--------------------------|----|---------------------------|----|-----------|----|-----|
| | Non-smoker | | Current cigarette smoker | | Current cigar/pipe smoker | | Ex-smoker | | All |
| | N | % | N | % | N | % | N | % | N |
| 15-24 | 17 | 14 | 14 | 5 | 0 | 0 | 3 | 2 | 34 |
| 25-29 | 11 | 9 | 10 | 3 | 0 | 0 | 8 | 4 | 29 |
| 30-34 | 19 | 16 | 35 | 11 | 2 | 5 | 21 | 11 | 77 |
| 35-39 | 18 | 15 | 35 | 11 | 2 | 5 | 17 | 9 | 72 |
| 40-44 | 17 | 14 | 53 | 17 | 8 | 18 | 24 | 13 | 102 |
| 45-49 | 11 | 9 | 53 | 17 | 12 | 27 | 34 | 18 | 110 |
| 50-54 | 14 | 12 | 55 | 18 | 7 | 16 | 37 | 20 | 113 |
| 55-59 | 5 | 4 | 42 | 14 | 10 | 23 | 25 | 14 | 82 |
| 60-64+ | 6 | 5 | 12 | 4 | 3 | 7 | 15 | 8 | 36 |
| All | 118 | | 309 | | 44 | | 184 | | 655 |

4.6.1 Exposure patterns

Figure 4.2 shows the distribution of cumulative dust index for the 655 men. As can be seen, this distribution is very skewed with very few of the men having exposures of more than 40 mg.m⁻³.years.

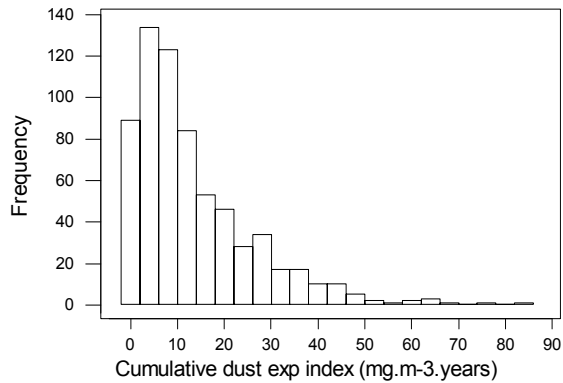


Figure 4.2: Histogram of cumulative dust index ($\text{mg.m}^{-3}.\text{years}$) for population 3

Figure 4.3 is a scatterplot of the cumulative dust index ($\text{mg.m}^{-3}.\text{year}$) against age (years). From this plot we can see that cumulative dust exposures were low for younger men, who would have worked for a relatively short time in the industry, whereas the greater spread of exposures for older workers reflects differences in exposure intensity among workers with longer times spent in the industry in a variety of jobs, as well as differences in years worked at the plant.

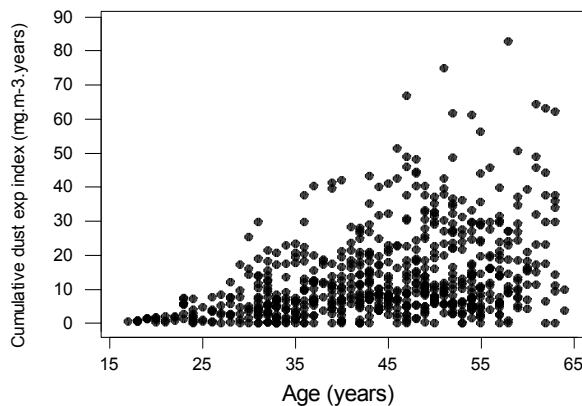


Figure 4.3: Scatterplot of cumulative dust index ($\text{mg.m}^{-3}.\text{year}$) vs age (years) for population 3

Although estimated dust index data is available only for population 3, it is possible to make some comparisons of exposure between this group and population 2 using the information from the work histories provided by ICI at the time of cohort identification. Table 4.6 summarises this information for population 3, and can be compared to the information for population 2 summarised previously in Table 4.4.

Table 4.6: No of subjects exposed to PVC and other chemicals with average, minimum and maximum time exposed (population 3).

| Exposure | No of subjects with non-zero exposure | Average years exposure (for exposure > 0) | Minimum years exposure (for exposure > 0) | Maximum years exposure (for exposure >0) |
|----------------|---------------------------------------|-------------------------------------------|-------------------------------------------|------------------------------------------|
| Total PVC | 545 | 13.8 | 0.1 | 32.4 |
| Emulsion PVC | 206 | 10.3 | 0.1 | 31.0 |
| Suspension PVC | 402 | 12.7 | 0.1 | 32.4 |
| Mixed PVC | 38 | 8.0 | 0.5 | 32.4 |
| VCM | 327 | 11.6 | 0.1 | 32.4 |
| Asbestos | 107 | 8.6 | 0.1 | 32.2 |
| TFE | 60 | 5.6 | 0.1 | 18.2 |
| Lead | 272 | 12.0 | 0.1 | 32.4 |

As expected, a higher proportion of subjects in population 3 were exposed to PVC dust (83%) than in population 2 (67%). This is because exposed subjects were preferentially selected to attend medical survey. Among those exposed, 74% were exposed to suspension PVC, 38% to emulsion PVC and 7% to mixed PVC. This represents a higher proportion exposed to emulsion PVC and a lower proportion to mixed PVC than in population 2. Length of time exposed to PVC is similar in the two groups, with employment times being, on average, about one year longer in population 3.

Exposure patterns for other substances are similar in the two groups, with higher proportions of subjects in population 3 exposed to VCM and lead reflecting the higher proportion with PVC exposure. Exposure to asbestos and to TFE occurred among fewer subjects and for shorter times on average, as in population 2.

4.6.2 Health status

Of the 655 men for whom health data were available 64 (10%) reported symptoms of chronic bronchitis and 149 (23%) reported symptoms of breathlessness. There were very few signs of radiological abnormalities. Of the 655 men, 647 men (99%) had no rounded opacities, one man's radiograph could not be classified, four men had rounded opacities of median profusion 0/1 and three men had rounded opacities of median profusion 1/0. Similarly, for irregular opacities, 645 (98%) had no irregular opacities, five men had irregular opacities of median profusion 0/1 and two men had irregular opacities of median profusion of 1/0. For the remaining three men with irregular opacities, one film reader had classified the irregular opacities as having median profusion 0/1, a second reader had classified the irregular opacities as having median profusion 1/0 and a third reader had not given a classification for these irregular opacities. Low profusions, particularly of irregular opacities, can be associated with heavy cigarette smoking. None of the profusions recorded from these men had clinical significance.

A ratio of observed FEV₁ to expected FEV₁ of less than 80% was reported in 90 men (14%) when the health data were collected in 1979 and a ratio of observed FVC to expected FVC of less than 80% was reported in 33 men (5%).

5 RESULTS OF STATISTICAL ANALYSES

5.1 COMPARISONS OF MORTALITY WITH REFERENCE POPULATIONS

During the course of examining the reference rates, it was noticed that in 1999 the mid-year population size for the North West region rapidly accelerated and the number of deaths decreased rapidly in 1997 and then subsequently increased after 1997 to levels that were higher than prior to this sudden fall. In addition in Lancashire there was a steep and sustained decrease in the number of deaths from 1998 onwards. These patterns were referred back to ONS for investigation. After further correspondence with ONS, corrected data were received and used in the final analyses reported here.

As described in section 3.5.2, the observed death rates for a number of causes, were compared to national (England and Wales) age and year specific death rates obtained from ONS. The results of this analysis were expressed as Standardised Mortality Ratios (SMR) with 95% confidence intervals (C.I.s). Comparisons were carried out for the three study populations – the full study group comprising all current workers in the late 1970s and a small selection of leavers and pensioners (population 1); all current workers in the late 1970s (population 2) and current workers who attended medical survey in 1979 (population 3). Results reported here are for population 2. Results of comparisons with England and Wales are shown in Table 5.1 and of comparisons with local rates in Tables 5.2 and 5.3. Results for populations 1 and 3 are given in Appendix 2, Tables A2.1 to A2.6.

For England and Wales, there were very few expected deaths from emphysema, lip, oral and pharyngeal cancer, liver cancer, laryngeal cancer, malignant melanoma of the skin and peptic ulcer. Observed and expected deaths are given for these causes but no SMRs or 95% C.I.s were calculated.

For none of the causes of death examined was there a statistically significantly increased SMR compared to the mortality experience in England and Wales. For population 2, the SMRs for oesophageal cancer and lung cancer were slightly raised compared to expected levels in England and Wales, although the increases were not significant statistically. When comparisons were made with the more local reference rates for the North West region and Lancashire the increases were no longer apparent, suggesting that they are likely to be due to regional factors more generally rather than to occupation in the Hillhouse plant.

Analyses of population 1 and population 3 (Appendix 2) also showed no statistically significantly raised SMRs compared to any of the reference populations. For population 1 there were a few causes (all internal causes, ischaemic heart disease, all cancers and oesophageal cancer) with small increases in SMRs compared to the rates in England and Wales but, as for population 2, these increases were no longer apparent in comparisons with more local reference rates suggesting a regional, not occupational, effect.

Table 5.1: SMRs and 95% C.I.s for causes of interest for population 2. Results are standardised by age and year of death for England and Wales

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 442 | 459.7 | 96.2 | 87.6 | 105.5 |
| All internal causes (Natural causes) | 433 | 440.9 | 98.2 | 89.4 | 107.9 |
| External causes – accidents and suicides | 9 | 16.0 | 56.4 | 29.3 | 108.3 |
| Ischaemic heart disease | 143 | 142.9 | 100.1 | 84.9 | 117.9 |
| Non-malignant respiratory disease | 37 | 46.1 | 80.2 | 58.1 | 110.8 |
| Chronic bronchitis | 2 | 4.0 | * | * | * |
| Emphysema | 0 | 2.8 | * | * | * |
| All cancers | 147 | 146.5 | 100.3 | 85.4 | 117.9 |
| Lip, oral and pharyngeal cancers | 2 | 2.6 | * | * | * |
| Digestive & peritoneal cancer | 39 | 43.0 | 90.8 | 66.3 | 124.3 |
| Oesophageal cancers | 9 | 7.3 | 123.4 | 64.2 | 237.1 |
| Stomach cancer | 4 | 9.2 | 43.5 | 16.3 | 115.9 |
| Liver cancer | 6 | 2.2 | * | * | * |
| Laryngeal cancer | 1 | 1.5 | * | * | * |
| Lung cancer | 50 | 46.6 | 107.3 | 81.3 | 141.6 |
| Malignant melanoma | 0 | 2.7 | * | * | * |
| Peptic ulcer | 0 | 0.3 | * | * | * |

Table 5.2: SMRs and 95% C.I.s for causes of interest for population 2. Results are standardised by age and year of death for North West Region

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 442 | 498.9 | 88.6 | 80.7 | 97.3 |
| All internal causes (Natural causes) | 433 | 483.8 | 89.5 | 81.5 | 98.3 |
| External causes – accidents and suicides | 9 | 15.1 | 59.5 | 30.9 | 114.3 |
| Ischaemic heart disease | 143 | 159.1 | 89.9 | 76.3 | 105.9 |
| Non-malignant respiratory disease | 37 | 55.1 | 67.2 | 48.7 | 92.7 |
| Chronic bronchitis | 2 | 4.8 | * | * | * |
| Emphysema | 0 | 2.3 | * | * | * |
| All cancers | 147 | 156.4 | 94.0 | 80.0 | 110.5 |
| Lip, oral and pharyngeal cancers | 2 | 3.1 | * | * | * |
| Digestive & peritoneal cancer | 39 | 46.1 | 84.7 | 61.9 | 115.9 |
| Oesophageal cancers | 9 | 8.5 | 106.4 | 55.4 | 204.6 |
| Stomach cancer | 4 | 9.9 | 40.5 | 15.2 | 108.0 |
| Liver cancer | 6 | 2.2 | * | * | * |
| Laryngeal cancer | 1 | 1.8 | * | * | * |
| Lung cancer | 50 | 53.6 | 93.3 | 70.7 | 123.1 |
| Malignant melanoma | 0 | 0.6 | * | * | * |
| Peptic ulcer | 0 | 0.4 | * | * | * |

Table 5.3: SMRs and 95% C.I.s for causes of interest for population 2. Results are standardised by age and year of death for Lancashire

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 442 | 504.6 | 87.6 | 79.8 | 96.1 |
| All internal causes (Natural causes) | 433 | 487.8 | 88.8 | 80.8 | 97.5 |
| External causes – accidents and suicides | 9 | 16.8 | 53.5 | 27.8 | 102.7 |
| Ischaemic heart disease | 143 | 164.7 | 86.8 | 73.7 | 102.3 |
| Non-malignant respiratory disease | 37 | 55.1 | 67.2 | 48.7 | 92.7 |
| Chronic bronchitis | 2 | 6.1 | 32.9 | 8.2 | 131.7 |
| Emphysema | 0 | 2.4 | * | * | * |
| All cancers | 147 | 150.9 | 97.4 | 82.9 | 114.5 |
| Lip, oral and pharyngeal cancers | 2 | 3.1 | * | * | * |
| Digestive & peritoneal cancer | 39 | 45.4 | 86.0 | 62.8 | 117.7 |
| Oesophageal cancers | 9 | 8.8 | 102.6 | 53.4 | 197.3 |
| Stomach cancer | 4 | 9.3 | 42.9 | 16.1 | 114.2 |
| Liver cancer | 6 | 2.1 | * | * | * |
| Laryngeal cancer | 1 | 1.7 | * | * | * |
| Lung cancer | 50 | 49.0 | 102.0 | 77.3 | 134.6 |
| Malignant melanoma | 0 | 0.7 | * | * | * |
| Peptic ulcer | 0 | 0.3 | * | * | * |

The SMRs for all-cause mortality, non-malignant respiratory disease, ischaemic heart disease and lung cancer by calendar period of follow-up for England and Wales are shown in Table 5.4. Results for the North West region and for Lancashire are given in Appendix 2 in Tables A2.7 and A2.8.

For all-cause mortality the SMRs show some evidence of a general increase over calendar time. This is a pattern typically observed among working populations, and is likely to represent a decrease in the ‘Healthy Worker Effect’ (whereby mortality in a working population is generally lower than in the general population which includes individuals who are not fit enough to work) as the length of follow-up increases. For non-malignant respiratory disease, the SMR was much higher in the calendar period 1991 to 1996 than in the other calendar periods. Similar patterns were observed in the results for the North West region and for Lancashire.

Table 5.4: SMRs and 95% C.I.s for all-cause mortality and key causes for population 2. Results by calendar period for England and Wales

| Calendar period | | All-cause mortality | Non-malignant respiratory disease | Ischaemic heart disease | Lung cancer |
|-----------------|----------|---------------------|-----------------------------------|-------------------------|--------------|
| 1979-1984 | Observed | 48 | 3 | 20 | 7 |
| | Expected | 64.8 | 4.5 | 24.3 | 7.4 |
| | SMR | 74.1 | 66.7 | 82.2 | 94.2 |
| | 95% C.I. | (55.8,98.3) | (21.5,206.8) | (53.0,127.4) | (44.9,197.5) |
| 1985-1990 | Observed | 90 | 3 | 34 | 9 |
| | Expected | 94.5 | 6.9 | 33.8 | 10.9 |
| | SMR | 95.3 | 43.5 | 100.6 | 82.2 |
| | 95% C.I. | (77.5,117.2) | (14.0,135.0) | (71.9,140.7) | (42.8,158.0) |
| 1991-1996 | Observed | 127 | 18 | 36 | 15 |
| | Expected | 124.2 | 12.5 | 39.2 | 13.0 |
| | SMR | 102.3 | 144.3 | 91.9 | 115.4 |
| | 95% C.I. | (86.0,121.7) | (90.9,229.0) | (66.3,127.4) | (69.5,191.3) |
| 1997-2003 | Observed | 177 | 13 | 53 | 19 |
| | Expected | 176.3 | 22.2 | 45.6 | 15.2 |
| | SMR | 100.4 | 58.4 | 116.2 | 124.9 |
| | 95% C.I. | (86.6,116.3) | (33.9,100.7) | (88.8,152.2) | (79.7,195.8) |
| Total | Observed | 442 | 37 | 143 | 50 |
| | Expected | 459.7 | 46.1 | 142.9 | 46.6 |
| | SMR | 96.2 | 80.2 | 100.1 | 107.3 |
| | 95% C.I. | (87.6,105.5) | (58.1,110.8) | (84.9,117.9) | (81.3,141.6) |

5.2 EXTERNAL ANALYSES IN RELATION TO EXPOSURE

Each of the individuals in populations 2 and 3 was classified according to whether they had ever worked in a PVC dust exposed job. Of the 1484 men in population 2, 996 (67%) were exposed and 488 (33%) were not exposed; in population 3, 545 (83%) of the 655 men were exposed and 110 (17%) not exposed. The differences in proportions exposed reflect the sampling strategy to preferentially include more highly exposed workers in the medical survey attended by workers in population 3.

Comparisons with external mortality rates were carried out separately for exposed and unexposed workers in populations 2 and 3. Results for key causes of death are shown in Tables 5.5 and 5.6 for populations 2 and 3 respectively. Because of the regional effect identified in the external mortality analyses of the study group as a whole, results are here compared to regional rates. The tables here show the results of comparisons for Lancashire, as an illustration of the patterns found. Results for the North-West are detailed in Appendix 2, Tables A2.9 and A2.10.

Table 5.5: SMRs and 95% C.I.s for causes of interest for population 2 subdivided by exposure group. Results are standardised for age and year of death for Lancashire

| Cause of death | Exposure | Observed | Expected | SMR | 95% C.I. | |
|--------------------------------------|-----------|----------|----------|-------|----------|-------|
| All causes | Exposed | 336 | 353.9 | 94.9 | 85.3 | 105.7 |
| | Unexposed | 106 | 150.8 | 70.3 | 58.1 | 85.1 |
| All internal causes (Natural causes) | Exposed | 330 | 342.8 | 96.3 | 86.4 | 107.2 |
| | Unexposed | 103 | 145.0 | 71.0 | 58.6 | 86.2 |
| Ischaemic heart disease | Exposed | 111 | 116.2 | 95.5 | 79.3 | 115.1 |
| | Unexposed | 32 | 48.5 | 66.0 | 46.7 | 93.4 |
| Non-malignant respiratory disease | Exposed | 25 | 38.6 | 64.8 | 43.8 | 95.9 |
| | Unexposed | 12 | 16.5 | 72.7 | 41.3 | 128.1 |
| All cancers | Exposed | 120 | 106.3 | 112.9 | 94.4 | 135.0 |
| | Unexposed | 27 | 44.6 | 60.5 | 41.5 | 88.2 |
| Digestive & peritoneal cancer | Exposed | 33 | 32.0 | 103.1 | 73.3 | 145.1 |
| | Unexposed | 6 | 13.4 | 44.9 | 20.2 | 99.9 |
| Lung cancer | Exposed | 45 | 34.6 | 130.0 | 97.0 | 174.1 |
| | Unexposed | 5 | 14.4 | 34.8 | 14.5 | 83.6 |

Table 5.6: SMRs and 95% C.I.s for causes of interest for population 3 subdivided by exposure group. Results are standardised for age and year of death for Lancashire

| Cause of death | Exposure | Observed | Expected | SMR | 95% C.I. | |
|--------------------------------------|-----------|----------|----------|-------|----------|-------|
| All causes | Exposed | 182 | 205.5 | 88.6 | 76.6 | 102.4 |
| | Unexposed | 25 | 37.5 | 66.6 | 45.0 | 98.6 |
| All internal causes (Natural causes) | Exposed | 180 | 199.4 | 90.3 | 78.0 | 104.4 |
| | Unexposed | 25 | 36.2 | 69.0 | 46.6 | 102.1 |
| Ischaemic heart disease | Exposed | 62 | 67.5 | 91.9 | 71.6 | 117.8 |
| | Unexposed | 8 | 12.1 | 65.9 | 33.0 | 131.9 |
| Non-malignant respiratory disease | Exposed | 17 | 22.5 | 75.5 | 46.9 | 121.4 |
| | Unexposed | 0 | 4.1 | * | * | * |
| All cancers | Exposed | 67 | 61.9 | 108.2 | 85.2 | 137.5 |
| | Unexposed | 6 | 11.3 | 53.2 | 23.9 | 118.5 |
| Digestive & peritoneal cancer | Exposed | 20 | 18.6 | 107.3 | 69.2 | 166.3 |
| | Unexposed | 1 | 3.4 | * | * | * |
| Lung cancer | Exposed | 26 | 20.1 | 129.1 | 87.9 | 189.6 |
| | Unexposed | 1 | 3.7 | * | * | * |

Among those exposed to PVC dust, there are no statistically significantly raised SMRs compared to Lancashire rates. However, in both populations there is an elevated SMR for

lung cancer of around 130, which is close to statistical significance in population 2. SMRs for the unexposed group are generally low, especially for deaths from cancer.

Results for comparisons with the North-West region showed similar patterns, but the SMRs for lung cancer among the exposed workers were lower than for the comparisons with Lancashire (SMR=119 for population 2 and SMR=118 for population 3).

5.3 INTERNAL ANALYSES OF MORTALITY DATA

5.3.1 Exposure response for current employees using work history data

Cox Proportional Hazards modelling was used to analyse the exposure response relationship for the 1484 current workers (population 2) from the study cohort. The period of follow-up that was used in the analysis was from the start of follow-up (1st January 1979) until death, loss to follow-up, or end of follow-up (31st December 2003).

Analyses were carried out for all-cause mortality, NMRD, ischaemic heart disease and lung cancer. A term adjusting for the effect of age was included in all models, followed by exposure variables including indicators for ever/never worked in a PVC exposed job, total time in a PVC job (among those with any exposure), and exposures (ever/never, total time) to other substances including VCM and lead. Differences in exposures to different types of PVC, namely emulsion, suspension and mixed, were also examined, as described in section 3.5.3.

Results are expressed as hazard ratios and their associated 95% confidence intervals. A hazard ratio of greater than one indicates an increase in risk. If the confidence interval excludes the value one, then the result is significant statistically.

The hazard ratios and 95% C.I.s from the Cox Proportional Hazards modelling for age and ever/never worked in a PVC job are shown in Table 5.7 for population 2 and Table 5.8 for population 3, along with the ever/never worked with the various types of PVC exposure. Similar information, but for time worked in PVC jobs is summarised in Tables 5.9 and 5.10. In each analysis, the total PVC variable is fitted in model 2 (after adjustment for age) and in models 3 to 5 variables representing exposure to emulsion process, suspension process or mixed process are fitted.

For all causes of death except NMRD, the odds ratios for ever working in a PVC job are greater than one, reflecting the differences in mortality rate in the two groups shown in the SMR tables 5.5 and 5.6. The difference between the exposed and unexposed groups was statistically significant for all cause mortality and mortality from lung cancer in population 2, and was most pronounced for lung cancer. Similar patterns were seen for population 3, but in this smaller group none of the increases were significant statistically. For none of the causes of death was there a statistically significant association between mortality and time spent in a PVC exposed job. The odds ratios for 10 years spent in a PVC job were slightly elevated for ischaemic heart disease and lung cancer in population 3 only, but the increases were not significant statistically.

Within each cause, there is little difference in the hazard ratios for having ever/never worked in jobs with exposure to PVC of different types (i.e. the hazard ratios are similar for having ever worked in a job exposed to emulsion PVC and for having worked in a job exposed to suspension PVC). For all cause mortality and for IHD, there is some evidence of a stronger association with time worked in an emulsion PVC job, but the associations are not significant significantly.

Table 5.7: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 2. Model 1: Age; Model 2: ever worked in PVC exposed job and Model 3: Ever worked in job using emulsion process, suspension process or mixed process

| | All-cause mortality | | NMRD | | Ischaemic heart disease | | Lung cancer | |
|--------------------------------------------------|---------------------|-------------|-----------|-------------|-------------------------|-------------|-------------|-------------|
| | 442 deaths | | 37 Deaths | | 143 deaths | | 50 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Age (10 years) | 2.77 | (2.48,3.10) | 5.37 | (3.20,8.98) | 2.94 | (2.40,3.61) | 2.19 | (1.62,2.96) |
| Model 2 | | | | | | | | |
| Ever worked in PVC exposed job | 1.16 | (1.04,1.30) | 0.93 | (0.66,1.32) | 1.21 | (0.99,1.47) | 1.97 | (1.24,3.12) |
| Model 3 | | | | | | | | |
| Ever worked in job using emulsion process only | 1.14 | (0.96,1.36) | 0.89 | (0.48,1.68) | 1.27 | (0.94,1.70) | 1.88 | (1.04,3.40) |
| Model 4 | | | | | | | | |
| Ever worked in job using suspension process only | 1.18 | (1.05,1.32) | 1.03 | (0.72,1.48) | 1.22 | (0.99,1.50) | 1.93 | (1.20,3.11) |
| Model 5 | | | | | | | | |
| Ever worked in job using mixed process | 1.14 | (0.98,1.32) | 0.66 | (0.35,1.23) | 1.16 | (0.89,1.51) | 2.07 | (1.23,3.49) |

Table 5.8: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 3. Model 1: Age; Model 2: ever worked PVC exposed job and Model 3: ever worked in job using emulsion process, suspension process or mixed process

| | All-cause mortality | | NMRD | | Ischaemic heart disease | | Lung cancer | |
|--------------------------------------------------|---------------------|-------------|-----------|-------------|-------------------------|-------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Age (10 years) | 2.64 | (2.23,3.14) | 3.97 | (1.99,7.94) | 3.42 | (2.48,4.73) | 1.49 | (1.00,2.20) |
| Model 2 | | | | | | | | |
| Ever worked in PVC exposed job* | 1.15 | (0.93,1.42) | NC | NC | 1.18 | (0.82,1.71) | 2.26 | (0.83,6.14) |
| Model 3 | | | | | | | | |
| Ever worked in job using emulsion process only | 1.16 | (0.90,1.49) | NC | NC | 1.16 | (0.74,1.81) | 2.40 | (0.82,7.01) |
| Model 4 | | | | | | | | |
| Ever worked in job using suspension process only | 1.14 | (0.92,1.42) | NC | NC | 1.19 | (0.81,1.74) | 2.15 | (0.78,5.94) |
| Model 5 | | | | | | | | |
| Ever worked in job using mixed process | 1.17 | (0.91,1.51) | NC | NC | 1.19 | (0.77,1.85) | 2.34 | (0.81,6.74) |

*NC indicates that the model did not converge due to lack of data.

Table 5.9: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 2 adjusted for age. Model 1: total time in PVC exposed job (among those exposed) and Model 2: time in job involving emulsion process, suspension process or mixed process

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 442 deaths | | 37 deaths | | 143 deaths | | 50 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 2 | | | | | | | | |
| Total time in PVC exposed job (10 years) | 1.02 | (0.88,1.17) | 1.00 | (0.60,1.66) | 1.08 | (0.84,1.38) | 1.00 | (0.67,1.50) |
| Model 3 | | | | | | | | |
| Time in PVC job: emulsion process (10 years) | 1.41 | (0.96,2.08) | 0.87 | (0.23,3.31) | 1.41 | (0.75,2.65) | 0.65 | (0.20,2.06) |
| Model 4 | | | | | | | | |
| Time in PVC job: suspension process (10 years) | 0.94 | (0.78,1.13) | 1.10 | (0.61,2.01) | 0.96 | (0.70,1.32) | 0.76 | (0.46,1.27) |
| Model 5 | | | | | | | | |
| Time in PVC job: mixed process (10 years) | 0.82 | (0.62,1.07) | 0.46 | (0.07,2.89) | 0.94 | (0.60,1.46) | 0.76 | (0.37,1.59) |

Table 5.10: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 3 adjusted for age. Model 1: total time in PVC exposed job and Model 2: time in job involving emulsion process, suspension process or mixed process

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 2 | | | | | | | | |
| Total time in PVC exposed job (10 years) | 1.15 | (0.92,1.43) | 0.77 | (0.39,1.50) | 1.36 | (0.93,2.00) | 1.47 | (0.76,2.84) |
| Model 3 | | | | | | | | |
| Time in PVC job: emulsion process (10 years) | 1.58 | (0.99,2.52) | 0.71 | (0.16,3.21) | 1.50 | (0.66,3.40) | 0.71 | (0.18,2.85) |
| Model 4 | | | | | | | | |
| Time in PVC job: suspension process (10 years) | 0.90 | (0.67,1.21) | 0.80 | (0.34,1.85) | 1.15 | (0.70,1.91) | 0.91 | (0.39,2.15) |
| Model 5 | | | | | | | | |
| Time in PVC job: mixed process (10 years) | 1.09 | (0.70,1.72) | 1.25 | (0.23,6.80) | 1.24 | (0.62,2.46) | 1.01 | (0.30,3.41) |

Exposures to other substances might confound the effects of PVC dust. In the present study, it was possible, as described in section 3.3 to assess whether jobs at the Hillhouse plant had involved exposure to VCM, asbestos, TFE and lead. Cox Proportional Hazards modelling was used to analyse the effects of these possible confounding exposures separately, adjusting for the effect of age. Table 5.11 shows the hazard ratios and 95% C.I.s from the Cox Proportional Hazards modelling adjusted for age and each of ever/never exposed to VCM, ever/never exposed to asbestos, ever/never exposed to TFE and ever/never exposed to lead for population 2, and Table 5.12 shows the same information for population 3. Similar information is shown in Tables 5.13 and 5.14 where total time in job involving exposure to each of VCM, asbestos, TFE and lead was used in place of ever/never exposed to these substances.

None of these variables was significantly related to mortality from the four causes examined, when expressed as ever/never indicators. Hazard ratios for exposure to VCM and to lead were slightly raised for mortality from lung cancer in population 2 and for exposure to VCM in population 3. Notably, the jobs which were classified as potential VCM or lead exposure were also classified as having potential exposure to PVC dust. When included simultaneously in a model which included a term for PVC dust exposure, the associations with VCM and lead were much reduced.

Analyses of time worked in jobs exposed to VCM, asbestos, TFE and lead showed no statistically significant associations with mortality from NMRD or lung cancer. Where the hazard ratios in these analyses were greater than one, the confidence intervals were wide and far from significant at conventional levels. For all-cause mortality in population 2, the hazard ratio for time in a job exposed to VCM was raised and close to significance at the 5% level, and also raised, though less significant statistically for IHD. These increases were also apparent in population 3, where the hazard ratios were higher, and statistically significant for all-cause mortality but not IHD.

As noted above, jobs with exposure to VCM were also classified as exposed to PVC dust. In particular, all the jobs classified as exposed to emulsion PVC dust were also classified as VCM exposed, although the exposures to VCM and emulsion PVC dust were likely to have occurred in different tasks within the broad job categories. Further analyses of the study group were therefore carried out which separated VCM exposure into (i) exposure to VCM in jobs also classified as exposed to emulsion PVC, and (ii) exposure to VCM in jobs with no emulsion PVC exposure. These analyses showed clearly that in population 2, the non-significantly raised hazard ratios for VCM reflected those for emulsion PVC (shown in Table 5.9) and there was no evidence of an additional effect of VCM exposure on mortality in jobs with no exposure to emulsion PVC. This pattern was not evident in population 3, where the hazard ratios for VCM exposure were only slightly reduced for exposure to VCM in jobs with no exposure to emulsion PVC compared to jobs where both substances were present.

Table 5.11: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 2 adjusted for age. Model 1: ever worked in job involving exposure to VCM; Model 2: ever worked in job involving exposure to asbestos.; Model 3: ever worked in job involving exposure to TFE; Model 4: ever worked in job involving exposure to lead exposure; Model 5: ever worked in a job involving exposure to lead after adjustment for PVC exposure (Lung cancer only)and Model 6: ever worked in a job involving exposure to VCM after adjustment for PVC exposure (Lung cancer only)

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 442 deaths | | 37 deaths | | 143 deaths | | 50 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Ever worked in job involving VCM exposure | 1.01 | (0.91,1.11) | 0.80 | (0.55,1.16) | 1.00 | (0.84,1.18) | 1.25 | (0.95,1.66) |
| Model 2 | | | | | | | | |
| Ever worked in job involving asbestos exposure | 1.06 | (0.96,1.18) | 0.75 | (0.48,1.16) | 1.00 | (0.83,1.22) | 0.97 | (0.70,1.36) |
| Model 3 | | | | | | | | |
| Ever worked in job involving TFE exposure | 0.91 | (0.78,1.06) | 0.66 | (0.32,1.35) | 0.86 | (0.66,1.14) | 0.37 | (0.14,0.99) |
| Model 4 | | | | | | | | |
| Ever worked in job involving lead exposure | 1.07 | (0.98,1.18) | 1.10 | (0.79,1.53) | 1.17 | (0.99,1.39) | 1.26 | (0.95,1.67) |
| Model 6 | | | | | | | | |
| Ever worked in a PVC exposed job | | | | | | | 1.97 | (1.21,3.20) |
| Ever worked in a job involving VCM exposure | | | | | | | 1.00 | (0.74,1.35) |

Table 5.12: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 3 adjusted for age. Model 1: ever worked in job involving exposure to VCM; Model 2: ever worked in job involving exposure to asbestos.; Model 3: ever worked in job involving exposure to TFE, Model 4: ever worked in job involving exposure to lead and Model 5: ever worked in a job involving exposure to VCM, after adjustment for PVC exposure (lung cancer only)

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|-------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Ever worked in job involving VCM exposure | 1.02 | (0.89,1.17) | 0.81 | (0.49,1.34) | 0.93 | (0.73,1.18) | 1.32 | (0.89,1.94) |
| Model 2 | | | | | | | | |
| Ever worked in job involving asbestos exposure* | 1.11 | (0.94,1.32) | 0.52 | (0.19,1.42) | 1.15 | (0.87,1.53) | 0.97 | (0.57,1.65) |
| Model 3 | | | | | | | | |
| Ever worked in job involving TFE exposure | 0.91 | (0.71,1.18) | NC | NC | 0.39 | (0.14,1.04) | 0.60 | (0.22,1.63) |
| Model 4 | | | | | | | | |
| Ever worked in job involving lead exposure | 1.01 | (0.88,1.15) | 1.28 | (0.79,2.08) | 1.15 | (0.90,1.45) | 1.04 | (0.71,1.52) |
| Model 5 | | | | | | | | |
| Ever worked in job involving PVC exposure | | | | | | | 2.08 | (0.74,5.86) |
| Ever worked in job involving VCM exposure | | | | | | | 1.14 | (0.76,1.71) |

*NC indicates that the model did not converge due to lack of data.

Table 5.13: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 2 adjusted for age. Model 1: total time spent in job involving exposure to VCM; Model 2: total time spent in job involving exposure to asbestos; Model 3: total time spent in job involving exposure to TFE and Model 4: total time spent in job involving exposure to lead exposure

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|---------------------------------------------------------------|---------------------|-------------|-----------------------------------|--------------|-------------------------|-------------|-------------|-------------|
| | 442 deaths | | 37 deaths | | 143 deaths | | 50 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Total time in job involving VCM exposure Per 10 years | 1.19 | (0.97,1.45) | 0.69 | (0.30,1.58) | 1.29 | (0.91,1.84) | 1.30 | (0.76,2.21) |
| Model 2 | | | | | | | | |
| Total time in job involving asbestos exposure Per 10 years | 0.93 | (0.76,1.14) | 2.04 | (0.81,5.10) | 0.97 | (0.68,1.39) | 0.78 | (0.39,1.55) |
| Model 3 | | | | | | | | |
| Total time in job involving TFE exposure Per 10 years | 1.00 | (0.66,1.52) | 2.07 | (0.27,15.56) | 1.41 | (0.66,3.01) | NC | NC |
| Model 4 | | | | | | | | |
| Total time in job involving lead exposure Per 10 years | 0.95 | (0.79,1.14) | 1.26 | (0.69,2.31) | 0.91 | (0.68,1.23) | 0.80 | (0.48,1.32) |

*NC indicates that the model did not converge due to lack of data.

Table 5.14: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 3 adjusted for age. Model 1: total time spent in job involving exposure to VCM; Model 2: total time spent in job involving exposure to asbestos; Model 3: total time spent in job involving exposure to TFE and Model 4: total time spent in job involving exposure to lead exposure

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|------------------------------------------------|---------------------|-------------|-----------------------------------|--------------|-------------------------|--------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Total time in job involving VCM exposure | 1.52 | (1.16,1.98) | 0.69 | (0.25,1.91) | 1.44 | (0.90,2.33) | 1.61 | (0.80,3.22) |
| Model 2 | | | | | | | | |
| Total time in job involving asbestos exposure* | 0.97 | (0.69,1.36) | 1.99 | (0.27,14.56) | 1.24 | (0.74,2.07) | 1.10 | (0.35,3.50) |
| Model 3 | | | | | | | | |
| Total time in job involving TFE exposure* | 1.17 | (0.52,2.66) | NC | NC | 0.96 | (0.03,27.84) | NC | NC |
| Model 4 | | | | | | | | |
| Total time in job involving lead exposure | 0.94 | (0.74,1.20) | 1.06 | (0.50,2.24) | 1.20 | (0.80,1.79) | 0.84 | (0.41,1.72) |

*NC indicates that the model did not converge due to lack of data.

To allow direct comparisons with population 2, for whom no data on smoking were available, all the analyses reported in Tables 5.7 to 5.14 adjust for age only. However, as noted previously, smoking information was available for population 3, and so further analyses, including adjustment for smoking habit, were carried out to investigate any potential effect of smoking on the relationship between mortality and PVC dust exposure. Table 5.15 shows the association with ever/never worked in a PVC exposed job, and jobs with exposure to emulsion and suspension PVC, for population 3 after adjustment for smoking status. Table 5.16 shows similar information for time worked in PVC exposed jobs.

It can be seen from these tables that the probability of death from NMRD and lung cancer were higher (but not statistically significantly most probably due to the small numbers of deaths) among current smokers compared to non smokers (HR: 1.7 for NMRD and 2.6 for lung cancer). Only one of the subjects who died from lung cancer and one of those who died from NMRD were non-smokers in 1979. There was some evidence of an increase in lung cancer risk with increasing amount smoked (“packyears”) among ex-smokers but not current smokers. After adjustment for smoking status and amount smoked, the coefficients for the dust effects were effectively unchanged, with only small differences in magnitude. No evidence of an increased dust effect among current or ex-smokers was found (results not shown here).

For population 3, it was also possible to examine the effect of physique on mortality, a factor which may be important for ischaemic heart disease. Analyses of IHD mortality in relation to physique, expressed as body mass index (BMI = weight divided by the square of height), showed a significant association with higher BMI associated with a higher risk of dying from IHD. After adjustment for BMI, the hazard ratios associated with PVC exposure were unchanged.

Table 5.15: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 3 adjusting for age and smoking. Model 1: ever worked PVC exposed job and Model 2: ever worked in job using emulsion process, suspension process or mixed process

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|--------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Age (10 years) | 2.62 | (2.19,3.12) | 4.14 | (2.00,8.54) | 3.48 | (2.49,4.86) | 1.30 | (0.83,2.05) |
| Smoking: Current smokers vs Non-smokers | 1.21 | (0.93,1.58) | 1.57 | (0.53,4.65) | 0.99 | (0.66,1.50) | 2.52 | (0.89,7.15) |
| Ex-smokers vs Non-smokers | 0.87 | (0.73,1.03) | 0.83 | (0.40,1.69) | 0.73 | (0.54,0.99) | 0.59 | (0.29,1.20) |
| Packyears: Current smokers | 1.04 | (0.93,1.17) | 1.08 | (0.76,1.52) | 1.05 | (0.87,1.28) | 1.05 | (0.77,1.45) |
| Ex-smokers | 1.15 | (0.98,1.34) | 1.04 | (0.50,2.16) | 1.29 | (0.99,1.67) | 1.89 | (1.26,2.84) |
| Model 2 | | | | | | | | |
| Ever worked in PVC exposed job | 1.12 | (0.91,1.38) | NC | NC | 1.14 | (0.79,1.65) | 2.02 | (0.74,5.50) |
| Model 3 | | | | | | | | |
| Ever worked in job using emulsion process only | 1.13 | (0.87,1.45) | NC | NC | 1.10 | (0.70,1.73) | 2.21 | (0.73,6.63) |
| Model 4 | | | | | | | | |
| Ever worked in job using suspension process only | 1.12 | (0.90,1.40) | NC | NC | 1.16 | (0.79,1.70) | 1.98 | (0.71,5.47) |
| Model 5 | | | | | | | | |
| Ever worked in job using mixed process | 1.12 | (0.87,1.45) | NC | NC | 1.18 | (0.75,1.85) | 2.03 | (0.69,5.99) |

Table 5.16: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling for population 3 adjusted for age and smoking. Model 1: total time in PVC exposed job and Model 2: time in job involving emulsion process, suspension process or mixed process

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Age (10 years) | 2.62 | (2.19,3.12) | 4.14 | (2.00,8.54) | 3.48 | (2.49,4.86) | 1.30 | (0.83,2.05) |
| Smoking: Current smokers vs Non-smokers | 1.21 | (0.93,1.58) | 1.57 | (0.53,4.65) | 0.99 | (0.66,1.50) | 2.52 | (0.89,7.15) |
| Ex-smokers vs Non-smokers | 0.87 | (0.73,1.03) | 0.83 | (0.40,1.69) | 0.73 | (0.54,0.99) | 0.59 | (0.29,1.20) |
| Packyears: Current smokers | 1.04 | (0.93,1.17) | 1.08 | (0.76,1.52) | 1.05 | (0.87,1.28) | 1.05 | (0.77,1.45) |
| Ex-smokers | 1.15 | (0.98,1.34) | 1.04 | (0.50,2.16) | 1.29 | (0.99,1.67) | 1.89 | (1.26,2.84) |
| Model 2 | | | | | | | | |
| Total time in PVC exposed job (10 years) | 1.18 | (0.94,1.46) | 0.81 | (0.42,1.55) | 1.39 | (0.96,2.03) | 1.48 | (0.79,2.80) |
| Model 3 | | | | | | | | |
| Time in PVC job: emulsion process (10 years) | 1.74 | (1.08,2.79) | 0.80 | (0.16,4.08) | 1.65 | (0.68,3.97) | 0.80 | (0.20,3.28) |
| Model 4 | | | | | | | | |
| Time in PVC job: suspension process (10 years) | 0.93 | (0.69,1.25) | 0.88 | (0.37,2.10) | 1.16 | (0.70,1.91) | 0.87 | (0.37,2.06) |
| Model 5 | | | | | | | | |
| Time in PVC job: mixed process (10 years) | 1.17 | (0.75,1.81) | 1.18 | (0.24,5.74) | 1.28 | (0.65,2.54) | 1.30 | (0.44,3.87) |

5.3.2 Exposure response for current workers using cumulative dust data

Estimates of cumulative dust exposure were available only for the 655 men who attended medical survey (population 3). The exposure response relationship for these men was analysed using Cox Proportional Hazards modelling. The follow-up period used in this analysis was from the start of follow-up (1st January 1979) until death, loss to follow-up, or end of follow-up (31st December 2003).

Analyses were carried out for all-cause mortality, non-malignant respiratory disease, ischaemic heart disease and lung cancer. Explanatory variables that were analysed in the Cox Proportional Hazards models were age, smoking and cumulative dust index.

Table 5.17 shows the hazard ratios and 95% C.I.s from the Cox Proportional Hazards modelling including smoking and cumulative dust index for each of all-cause mortality, non-malignant respiratory disease, ischaemic heart disease and lung cancer. For all these causes of death, as age increases, the probability of death increases, as would be expected. This result is significant statistically for all-cause mortality, non-malignant respiratory disease and ischaemic heart disease but not for lung cancer, perhaps because of the relatively small number of deaths.

For example, for a ten year increase in age, the probability of dying from ischaemic heart disease during the follow-up period was increased by 3.2 times (95% C.I: 2.24,4.45). The probability of death from respiratory causes (NMRD, lung cancer) was greater for current smokers compared with non-smokers, although this association was not significant statistically for either of the causes of death.

There was a statistically significant association between cumulative dust index and mortality from ischaemic heart disease with the probability of mortality from ischaemic heart disease increasing by 17% for a 10 mg.m⁻³year increase in cumulative dust index. None of the other causes were associated with this exposure index.

Table 5.17: Hazard ratios and 95% C.I.s from Cox Proportional Hazards for age, smoking and cumulative dust index (among those exposed) for population 3

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|----------------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Age (10 years) | 2.59 | (2.15,3.11) | 4.18 | (1.94,8.99) | 3.16 | (2.24,4.45) | 1.36 | (0.84,2.19) |
| Smoking: Current smokers vs Non-smokers | 1.21 | (0.93,1.57) | 1.58 | (0.53,4.70) | 0.95 | (0.62,1.43) | 2.56 | (0.90,7.29) |
| Ex-smokers vs Non-smokers | 0.87 | (0.73,1.03) | 0.83 | (0.41,1.70) | 0.74 | (0.55,1.01) | 0.59 | (0.29,1.20) |
| Packyears: Current smokers | 1.05 | (0.93,1.17) | 1.07 | (0.75,1.52) | 1.08 | (0.89,1.31) | 1.04 | (0.75,1.44) |
| Ex-smokers | 1.15 | (0.98,1.34) | 1.02 | (0.49,2.13) | 1.27 | (0.98,1.65) | 1.88 | (1.25,2.83) |
| Ever exposed to PVC dust | 0.86 | (0.62,1.21) | NC | NC | 0.98 | (0.48,2.02) | NC | NC |
| Cumulative dust index (10 mg.m⁻³.year) | 1.01 | (0.92,1.12) | 0.99 | (0.70,1.39) | 1.17 | (1.01,1.36) | 0.90 | (0.64,1.25) |

*NC indicates that the model did not converge

5.3.3 Mortality in relation to health status at medical survey

Further analyses examined the associations between health indices from medical survey - the lung function variables FEV₁, FVC, chronic bronchitis and breathlessness – and mortality. Both FEV₁ and FVC were expressed as a percentage predicted value.

All models included terms for the effects of age, smoking and cumulative dust index, then terms for each lung function variable were added separately. Interactions between age and smoking, smoking and FEV₁, and smoking and FVC were fitted. None of these interactions were significant statistically and so these were not included in the final models. Age, cumulative dust index, FEV₁ and FVC were tested for non-linearity using the pspline (polynomial smoothing spline) function to fit spline terms within the Cox models. None of the non-linearity terms were significant statistically, hence the final models fitted were all linear models.

Table 5.18 shows the hazard ratios and 95% C.I.s for the Cox Proportional Hazards modelling when each of FEV₁, FVC, chronic bronchitis and breathlessness are added separately to the model that has been adjusted for age, smoking and cumulative dust index. Probability of death was slightly increased in men who had a lower values of observed FEV₁/expected FEV₁. For all-cause mortality and non-malignant respiratory disease, this result was significant statistically. Similarly for observed FVC/expected FVC, there was a slight increase in the probability of death for lower lung function values, significant statistically for all-cause mortality and non-malignant respiratory disease.

The probability of death from non-malignant respiratory disease was statistically significantly increased in those who had reported chronic bronchitis. Those reporting of symptoms of chronic bronchitis were approximately twice as likely to die from non-malignant respiratory disease than those without. These results had a very wide 95% C.I. due to the small numbers of deaths but the increase was significant statistically. For all causes of death of interest except lung cancer, the risk of death was increased in men who had reported breathlessness when hurrying on level ground or walking up a slight hill and these increased risks were significant statistically. For example, the risk of death from all-cause mortality increased by 18% (95% C.I. 2% to 36%) in men who had reported breathlessness compared to men who had not reported breathlessness.

Table 5.18: Hazard ratios and 95% C.I.s from Cox Proportional Hazards modelling. Analysis of the effects of lung function data adjusted for age, smoking and cumulative dust index for population 3

| | All-cause mortality | | Non-malignant respiratory disease | | Ischaemic heart disease | | Lung cancer | |
|----------------------------------------------------------------------|---------------------|-------------|-----------------------------------|-------------|-------------------------|-------------|-------------|-------------|
| | 207 deaths | | 17 deaths | | 70 deaths | | 27 deaths | |
| | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. | HR | 95% C.I. |
| Model 1 | | | | | | | | |
| Observed FEV ₁ /Expected FEV ₁ (10% reduction) | 1.18 | (1.09,1.28) | 2.73 | (2.04,3.65) | 1.09 | (0.94,1.25) | 1.12 | (0.88,1.43) |
| Model 2 | | | | | | | | |
| Observed FVC/Expected FVC (10% reduction) | 1.20 | (1.09,1.32) | 2.62 | (1.90,3.60) | 1.15 | (0.98,1.36) | 1.05 | (0.80,1.38) |
| Model 3 | | | | | | | | |
| Chronic Bronchitis | 1.03 | (0.83,1.26) | 1.81 | (1.07,3.06) | 0.93 | (0.63,1.36) | 0.73 | (0.35,1.52) |
| Model 4 | | | | | | | | |
| Breathlessness | 1.17 | (1.01,1.35) | 1.83 | (1.12,2.99) | 1.34 | (1.05,1.70) | 0.90 | (0.57,1.43) |

6 DISCUSSION

6.1 REPRESENTATIVENESS OF COHORT

The study cohort included all 1501 workers currently working at the Hillhouse plant in 1979, when cohort identification was carried out for the subsequent IOM medical survey. In addition it included 199 (25%) of the 807 pensioners and leavers who had left the plant between 1st January 1967 and 1979. This subgroup of ex-workers comprised only those individuals who had been invited to attend medical survey, and was not a representative subset of all ex-workers, partly because the survey selection was designed to preferentially include more workers from dusty jobs and partly because the group will have been subject to the kinds of study participation effects (e.g. availability, willingness to attend) which are unavoidable in a study of this kind.

Tracing of vital status information at ONS resulted in successful traces for over 99% of the study cohort. Clearly, this is a very high success rate. Four records were excluded from the study cohort as they were either found to be duplicates or referred to women, who were not included in the study cohort. The full study cohort ('Population 1') therefore consists of all current workers at the plant in 1979 together with a subset of the more heavily exposed leavers and pensioners.

Occupational data were available only for the workers who were currently employed in 1979. For this reason, and because the subgroup of ex-workers was not representative of ex-workers more generally, the main analyses for the present study are based on the population of all current workers in 1979 ('Population 2'). This was a group of men who, as far as we can determine, comprise the entire current working population in 1979, with the exception of 17 men who were untraceable at ONS, and so are almost fully representative of the workforce at that time.

For some variables (smoking status, cumulative dust exposure) information was available only for the subset of current workers who attended medical survey ('Population 3') and so these results are based on the smaller group. For all other variables we base our main inferences on the larger, and more fully representative, group of all current workers.

6.2 RELIABILITY OF EXPOSURE ESTIMATION

The extent and quality of the available exposure estimates varied in different subgroups of the study population. No information was available for the ex-workers included in the study cohort and so these individuals were excluded from analyses internal to the study group which investigated the effects of PVC and other exposures on mortality.

For all of the current workers in 1979, broadly categorised work histories were extracted from plant records at the time of cohort identification, in 1979. In general these work histories included only crude classifications of job and place of work. For example, often they included information identifying only the plant (e.g. Corvic, Welvic) in which the individual worked, and not the job within that plant. Historical information on the plant processes, augmented by discussion with long-serving employees at Hillhouse, was used during the present study to classify each of the work descriptions from these histories according to whether or not it was likely to involve exposure to PVC dust, VCM, asbestos, TFE and/or lead. Where possible, PVC exposure was sub-classified according to whether it involved emulsion PVC, suspension PVC or both. Start and end dates of each work history record allowed the calculation of total numbers of years spent by each individual in jobs with these potential exposures.

The primary attribution of PVC exposure in relation to these work histories was based on the plant identifiers, and included as exposed all occupations at those plants (and only those plants) that produced PVC. It is likely that the dust was dispersed widely throughout the plant, and so the classification into ever/never exposed to PVC is broadly accurate. However, there was a great deal of variation in the concentrations of PVC and other substances experienced by workers within each plant, for example between someone bagging PVC, where levels of PVC would have been relatively high, and someone working an autoclave where PVC dust levels would have been lower (the incrustation of PVC on the walls of the autoclaves were too wet for inhalation). The highest average measured PVC exposures during the survey in 1979 had been about 3 mg/m³. Exposure for other PVC exposed workers had been between 0.2 to 1 mg/m³. Historic exposures would have been higher, although these probably never exceeded more than about 10 mg/m³.

VCM classification was based on work in the PVC manufacturing plants, although the majority of exposure would have occurred in the autoclave section. It is thought to be an accurate reflection of potential exposures, although as for PVC dust there will have been a great deal of variation in the level of exposure between subjects because of differences in jobs. There is considerable overlap between the classification of exposure to VCM and to PVC dust. The categorisations for asbestos are less reliable since these are based on job title (e.g. maintenance) and only a small proportion of these men actually worked with asbestos. Asbestos exposure appeared to be relatively short-term and to fairly low concentrations, amongst a small number of people, implying that asbestos exposure was not an important contributor to any observed lung cancer risk in the study population.

Because the classification of exposure as “ever” or “never” exposed to PVC dust and VCM is based on work in specific plants there may be other exposures that are also exposed with these work locations that could confound these assessments. However, we believe that it is unlikely that we have missed any important exposures to any known or suspected human carcinogens.

For the subset of the current men who attended medical survey, further exposure information was available in the form of an estimated cumulative dust index. This index was calculated during the previous IOM study, using individual detailed work histories combined with estimated dust concentrations from occupational hygiene surveys of the plant. As for ex-workers, those current workers who attended the medical survey were on average more highly exposed than other current workers due to the preferential sampling of workers in more dusty occupations.

For the estimation of *exposures up to 1979*, therefore, the most accurate and reliable index is the cumulative dust index calculated for the 655 medical survey attendees, followed by the index of time worked in exposed jobs which was calculated for the 1484 workers of population 2 in the present study, using the broad work history records. However, there is a major limitation of both these indices. The available occupational and work histories cover employment up to 1979 only, while the follow-up period for this study continues to the end of 2003, some 24 years later. It is clear that the validity of these indices, as measures of individuals' cumulative lifetime exposures up to a given period of the follow-up, will decrease over time, and that the extent to which they accurately represent individuals' true exposure experience will vary both by calendar time of follow-up and age of the individual in 1979. In particular, exposure indices for younger members of the study cohort are likely to be, possibly greatly, underestimated as it is probable that these men continued working in the PVC industry subsequent to 1979, thereby incurring possibly substantially more exposure during the follow-up period. In contrast, for older members of the study cohort who were near the end of their working experience at Hillhouse in 1979, the available exposure indices are likely to be more representative of their actual lifetime exposures, right throughout the 25-year follow-up period. For the analysis of lung cancer, it should be noted that latency of disease development is typically 10 to 20 years following first exposure, so that the

limitations of the exposure time variables for analysis of this cause are likely to be less than for diseases which would be expected more immediately following exposure.

Consequently, although the indicator exposure variable which for each individual provides a classification of never/ever exposed to PVC is a crude dichotomisation, it is likely to be the most robust over the period of follow-up. Typically in industrial populations, workers are more likely to start work in exposed jobs, and subsequently move or be promoted to non-dusty jobs than vice versa. Therefore, for all workers who had worked in a PVC exposed job prior to 1979, the indicator variable will be accurate and we believe that few of those who had not been exposed to PVC in the earlier part of their career at Hillhouse would have subsequently moved into a PVC exposed job. Any small misclassification of exposure from such changes in job over time will be in the direction of including individuals with some (later) PVC exposure in the unexposed group, thus underestimating any differences between the groups. Its consequence would therefore be likely to lessen any apparent association of PVC with mortality.

6.3 AVAILABILITY OF SMOKING DATA

Information on smoking habits (as current smoker of cigarettes, or of 'pipe or cigars', as ex-smoker, or as lifelong non-smoker) was available only for the 655 men who attended medical survey and not for the wider population. Cumulative amount smoked up to 1979 was available for current and ex-smokers.

Among the subgroup attending medical survey, non-smokers were on average younger, and cumulative dust exposure index was, on average, higher among current and ex-smokers than among lifelong non-smokers. In addition, the proportion of current and ex-smokers who had ever worked in a PVC exposed job, as classified using the work history data, was higher than among non-smokers.

Analyses of the 655 men were therefore carried out with and without adjustment for smoking habit, and with some investigation of any interactions between dust and smoking effects. The results of these analyses showed that the inclusion of the smoking variable (smoking status and/or packyears) had very little effect on the magnitude of the coefficients of the dust variables in the regression models.

This provides reassurance, in the absence of any information on smoking habit in the wider study group, that the dust effects are robust to the inclusion or not of smoking habit in the regression analyses. This is particularly important in the present context because in the 1979 study some of the key results indicating an effect of PVC dust on respiratory disease were found among current smokers only.

6.4 STUDY FINDINGS – COMPARISON WITH THE GENERAL POPULATION

All cause mortality

As expected with studies of working populations, the all-cause mortality experience of the study cohort was somewhat better than that in the national and regional reference populations; i.e. the observed number of deaths was lower than the number expected based on the external reference populations, giving an SMR of less than 100. Population 2 consists of men, all of whom were employed at the plant at the start of mortality follow-up in 1979, and the lower SMRs compared with the general population reflect the various influences, known as healthy worker effects (HWE), whereby people in employment are healthier, and so have lower risks of death, than people in the general population of the same age and gender. The HWE

operates differentially by cause of death; for example, the effect is more marked for chronic diseases such as IHD or for NMRD than for cancer.

There are well-known regional variations in death rates within England and Wales, with relatively favourable death rates in the South-East. It is not surprising therefore that the deficit is most marked for comparisons with both regional reference populations, where the SMR for all-cause mortality – at 89 and 88 for North-West England and for Lancashire respectively – is statistically significantly lower than 100.

Cause-specific mortality

Compared with the external reference populations, the SMRs from almost all causes studied were very close to or less than 100. In particular, there was no evidence of excess NMRD, where regional comparisons gave an SMR of 67.

The highest recorded SMR was for oesophageal cancer (SMR 123 compared with England and Wales) though, being based on only 7.3 expected deaths, the associated C.I. was very wide (64-137) and the excess was not statistically significant. There was little evidence of a higher SMR in comparisons with more local reference rates from North-West region and from Lancashire. This suggests strongly that the effect was regional rather than specifically associated with occupation at the Hillhouse site.

The SMR for lung cancer also varied somewhat according to the reference population, with values of 107, 93 and 102 for England and Wales, North-West Region and Lancashire, respectively. The associated C.I.s, being based on 50 observed deaths, were much shorter than for oesophageal cancer, but nevertheless were not at all significant statistically.

6.5 STUDY FINDINGS – ASSOCIATIONS WITH EXPOSURE

For Populations 2 and 3, it was possible to examine relationships between mortality and occupational history of exposure to PVC dust for current workers in 1979. Two indices of PVC exposure were used, as discussed above – ever/never worked in a PVC job prior to 1979 and time worked in a PVC job up to 1979. These indices were based on work histories obtained from factory personnel records in 1979. For the subset of men who had attended medical survey (Population 3), additional analyses were carried out in relation to the more detailed cumulative dust index for exposure to 1979. This dust index was based on work histories obtained from the subjects themselves at interview, and occupation-specific dust concentrations as measured in 1979.

Lung cancer

Analyses of lung cancer mortality showed one finding which, initially, seemed to suggest a possible risk: results from the internal analysis of current workers in 1979 showed a statistically significantly increased probability of death from lung cancer in those who had ever worked in a PVC exposed job compared to those who had never done so, with a doubling of the probability of lung cancer (RR 1.97; 95% CI: 1.24, 3.12) in exposed men compared to those not exposed.

However, more detailed analyses did not provide evidence of a work-related excess.

- i. External analyses of lung cancer mortality in relation to the general population showed that levels of lung cancer mortality among the unexposed workers were significantly lower than expected (e.g. SMR 35 for Population 2 compared with Lancashire rates). Thus, the difference between exposed and unexposed workers is

explained in part by the fact that lung cancer death rates in the unexposed group were untypically low. We do not know why this was so.

- ii. Data on smoking habits in 1979, available for Population 3 only, showed differences in smoking habits in 1979 between the exposed and unexposed groups. Among the subgroup for whom smoking data were available (in Population 3), 56% of exposed workers were current smokers and 29% ex-smokers in 1979 compared to 44% and 25% of unexposed men. Given the strong and well-established relationship between smoking and lung cancer, then these differences in smoking habits explain at least part of the difference in lung cancer mortality between exposed and non-exposed workers.
- iii. External analyses nevertheless showed an increased SMR for lung cancer mortality (SMR = 130, Population 2) compared to regional rates from Lancashire. The difference was not statistically significant, but was nearly so, with the 95% CI (97-174) only just including the expected value of 100. When the North-West Region rather than Lancashire was used as reference population, the SMR was lower, though still higher than 100, and not nearly significant at the usual 5% levels of statistical significance. It is notable that all except one of the lung cancer cases in this study group occurred in current or ex-smokers, so that any suggestion of an elevated risk in the exposed group is based on results from smokers and ex-smokers only.
- iv. The smoking habits of exposed workers may also substantially explain the excess lung cancer in exposed workers because, in 1979, average prevalence of current smokers in England was 45% among men aged 16 or over, and more recent statistics suggest that smoking habits in the North-West region are similar to those in England as a whole. These smoking data do not, however, explain the very low lung cancer death rates in unexposed workers.
- v. Finally, we analysed lung cancer mortality in relation to time spent (up to 1979) in a PVC job (Populations 2 and 3), and with cumulative dust index up to 1979 (Population 3 only) among the exposed group. Analysis of time spent in PVC jobs up to 1979 among those exposed showed no association with lung cancer mortality in population 2 and an increased hazard ratio, but far from statistically significant, in those who attended medical survey. However, among the survey attenders there was no association with cumulative dust index.

Non-malignant respiratory disease (NMRD)

Analyses of all current workers in 1979 (1484 men) showed no evidence that exposure to PVC dust was related to increased risk of death from NMRD. For example, compared with Lancashire, the SMR for NMRD was 67 (95% CI 49-93). Analyses of Population 3 (i.e. the 655 men who had attended medical survey in 1979) did not show a relationship with cumulative dust exposure. The earlier (1979) study showed some links between PVC exposure and early signs of lung disease, particularly among smokers. The present study showed some links between early signs of lung disease and later risks of death from NMRD. It doesn't necessarily follow that exposure to PVC dust affects the risk of mortality from NMRD, but there is a possibility that it does. Overall, however, the evidence was of generally low death rates from NMRD and no evidence of a direct link with exposure to PVC dust. This finding is reassuring in view of the results of the previous epidemiological study.

Ischaemic Heart Disease (IHD)

External analyses of the study group showed no evidence of an overall excess of IHD mortality among workers exposed to PVC dust, compared to rates in the general population, and a statistically significant deficit of mortality from IHD among unexposed workers. This deficit among unexposed workers was reflected in a raised hazard ratio (of borderline statistical significance) for ischaemic heart disease in relation to ever/never worked in a PVC exposed job.

Analyses of the larger study population (Population 2) and of the subset who did not attend medical survey showed no association between mortality from IHD and time spent in a PVC job among those exposed. Analyses of the subset of men who attended medical survey showed a raised hazard ratio, though not statistically significant, for IHD mortality associated with time in a PVC exposed job and a statistically significant association, after adjustment for age and smoking habit, between cumulative dust index for PVC dust exposure and mortality from ischaemic heart disease. As noted in section 6.3, there were limitations in the smoking data available, in particular in that amount smoked was available up to 1979 only, and it is possible that the models fitted do not adjust fully for the effects of smoking on IHD. However, we think that residual smoking effects, if any, are likely to be confounded with age and hence with time worked in a PVC job rather than with cumulative dust exposure.

These contradictory results are difficult to interpret. Literature on occupational exposure to dust does not suggest an association with IHD mortality. A mortality study of 16,000 workers who were employed in the steel industry in the early 1970s showed no excess of IHD mortality (Hutchison *et al*, 1996). Analyses of the same cohort over a shorter follow-up (reported in Hurley *et al*, 1990) had suggested excess mortality from IHD in younger steel workers, though the overall SMR for IHD had been unremarkable, but this was no longer apparent in the later study. A mortality study of over 30,000 coalworkers (Miller *et al*, 1981) showed no clear evidence of an association between cumulative exposure to coalmine dust and mortality from IHD.

Comparison with results from outdoor air pollution are complicated by (i) differences in the source (small particles in outdoor air are primarily from combustion sources) and surface properties that would not be expected to be found in PVC dust; and (ii) the fact that air pollution studies are based on the general population, which contains more vulnerable people (the elderly, the very young) than a working cohort. Nonetheless, there is strong evidence that, in the general population, long-term exposure to ambient particles is associated with and most probably causes an increase in mortality risks from cardiovascular causes (e.g. Pope *et al.*, 2002). The relationships with particles outdoors are linked especially with particles of aerodynamic diameter less than 2.5 µm, suggesting that if PVC dust were adversely affecting IHD mortality, the effect would be seen more clearly with emulsion rather than suspension dust and there was only weak evidence of this, far from statistically significant, in the current study. We discuss this further below.

Emulsion and suspension PVC, and other workplace factors

There was some evidence of a stronger association with time spent in a job exposed to emulsion PVC rather than suspension PVC for all-cause mortality and, as noted above, weak evidence of a difference between PVC types for IHD mortality. There was also evidence of a significant increase in all-cause mortality associated with time spent in a job exposed to VCM, while for IHD the hazard ratio was greater than one, but not at all significant statistically.

These results are not independent. All jobs classified as exposed to emulsion PVC were also classified as exposed to VCM, although the exposures were likely to have occurred in

different tasks within the broad job classifications (i.e. workers were not likely to have been exposed to both substances simultaneously). In the larger Population 2, there was no evidence of an association of either all-cause or IHD mortality with VCM in jobs which were not also classified as exposed to emulsion PVC, suggesting that the results most likely reflect the effects of emulsion PVC rather than VCM. The pattern was less clear in Population 3, where the hazard ratios were only slightly lower for jobs with exposure to VCM but not emulsion PVC than for jobs classified as exposed to both substances. As noted earlier (Section 6.1), in analyses of characteristics that are common to Populations 2 and 3, we give priority in interpretation to results from Population 2 because it is larger and is fully representative of current workers in 1979.

For IHD the hazard ratios for time in jobs with exposure to emulsion PVC were not statistically significantly greater than one, with 95% confidence intervals typically ranging from around 0.75 to 3.0, providing only weak evidence of any association as noted above.

For all-cause mortality, the association with time spent in emulsion PVC jobs was close to statistical significance in Population 2 and statistically significant in Population 3, after adjustment for smoking status. This seems to be an isolated result, not consistent with other evidence from the study. Compared to external reference populations there was no overall excess mortality in the subgroup exposed to emulsion PVC (SMR, compared to Lancashire rates, of 93, which is very similar to the SMR of 95 for all PVC exposed workers), nor was there significantly increased mortality in the emulsion PVC exposed group compared to unexposed workers at the Hillhouse site. There was no evidence of an association between time worked in emulsion PVC jobs and causes of death (e.g. respiratory, IHD), identified *a priori* as biologically plausibly associated with dust exposure. Furthermore, examination of the 22 deaths from causes other than those studied as part of the current study, showed a wide range of causes with no apparent patterns or groupings –half of the deaths were from cancers of various sites (including bladder, brain, pancreas, lymphoma and myeloma) and half were from other internal causes (including alcoholic liver damage, cerebro-vascular disease, diabetes, renal failure, perforated bowel, atherosclerosis). It is implausible that exposure to emulsion PVC dust could have affected such a wide range of causes, but not those identified *a priori* as biologically relevant. Taken together, these findings do not support a causal role of occupational exposure to emulsion PVC in relation to all-cause mortality.

Other diseases

An excess of deaths from liver cancer, based on only six deaths, occurred mainly in workers who had been classified in the current study as exposed to VCM throughout their working time at the Hillhouse works. This finding is consistent with previous findings of excess liver cancer among VCM workers. Results for other causes of deaths studied i.e. other cancers, and deaths from accidents or suicide, showed no evidence of increased risks.

6.6 STUDY FINDINGS – ASSOCIATIONS WITH HEALTH IN 1979

For the 655 men who attended medical survey in 1979, mortality was examined in relation to health status at survey. After adjustment for age, smoking and dust exposure, reduced levels of lung function variables FEV₁ and FVC were positively associated with mortality from all causes, and more strongly to mortality from NMRD. Mortality from NMRD was also strongly associated with the presence of chronic bronchitis and breathlessness at the 1979 medical survey. It is perhaps unsurprising that individuals already showing signs of respiratory disease during 1979 were more likely to die from respiratory causes subsequently. Consequently, because the earlier study showed associations between PVC dust and respiratory symptoms and function, we do not rule out some effect of PVC dust exposure on NMRD mortality also, despite the negative results on associations between PVC exposure and

NMRD. If any risk had been strong, however, we think it would have shown through as a clear or suggested relationship with exposure, and there was no evidence of that.

Presence of breathlessness in 1979 was also positively associated with subsequent mortality from ischaemic heart disease, perhaps reflecting that breathlessness can be a symptom of heart disease. Inclusion of the term for breathlessness in the regression model did not materially affect the strength of the association between ischaemic heart disease and cumulative dust index.

6.7 CONCLUSIONS

Cohort completeness: Cohort identification was complete for all current workers in the plant in 1979, and for a subset of, on average, more heavily exposed pensioners and leavers, with tracing of vital status and cause of death for the study group achieving a success rate of over 99%. The final results therefore are representative of current workers in 1979, though less representative of pensioners/leavers at that time. Indeed, analyses in relation to various indices of PVC exposures up to 1979 were carried out on current workers only.

Exposure reliability: Exposure estimation was generally reliable for exposures up to 1979, but no information exists for exposures after that date. Estimates of individuals' exposures, especially those of younger men who are most likely to have accumulated further exposures after 1979, therefore become less valid as length of follow-up increases. This may be less of a problem for the analysis of lung cancer mortality where latency of disease development is typically 10 to 20 years following first exposure. Indicator variables for exposure are likely to be more robust over time but provide a relatively crude assessment of potential exposures.

External mortality comparisons: For none of the causes of death examined was there a statistically significantly increased SMR compared to the mortality experience in England and Wales. The SMR for oesophageal cancer was slightly raised compared to expected levels in England and Wales, although the increase was not significant statistically. When comparisons were made with the more local reference rates for the North West region and Lancashire the increase was no longer apparent, suggesting that it was likely to be due to regional factors more generally rather than to occupation in the Hillhouse plant.

Non-malignant respiratory disease: There was no evidence of any association between NMRD mortality and exposure to PVC dust, a finding that is reassuring in view of the results of the previous epidemiological study. The earlier (1979) study showed some links between PVC exposure and early signs of lung disease, particularly among smokers. The present study showed some links between early signs of lung disease and later risks of death from NMRD. It doesn't necessarily follow that exposure to PVC dust affects the risk of mortality from NMRD, but there is a possibility that it does. Overall, however, the evidence was of generally low death rates from NMRD and no evidence of a direct link with exposure to PVC dust.

Lung cancer: This study provides no direct evidence of an association between exposure to PVC and lung cancer. Within those exposed, there was no evidence of an exposure-response relationship with surrogates of exposure. The most suggestive finding, of an elevated SMR among those exposed to PVC, can be explained by increased smoking prevalence in this group, and/or by chance variations in a study of this size.

Ischaemic heart disease: We think that the present limited evidence does not justify a conclusion that exposure to PVC dust increases the risk of IHD, but that it is important to be aware of the possibility, and that it would be very helpful if the result could be checked in other data. The present study does not show a need for any additional new measures to reduce exposures. It is however prudent to maintain dust levels as low as practicable. Those who work in the industry are in the best position to know how to do this most effectively.

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APPENDIX 1 – ENVIRONMENTAL SURVEY DETAILS

Extracted from Soutar *et al* (1979)

From: Section 3.3: Environmental Survey

Current personal exposures to respirable PVC dust were measured by occupation in each plant in which PVC was manufactured or processed. The sampling device used samples a 'respirable' fraction of total airborne dust in accordance with the Johannesburg Convention including 50% of all particles with an aerodynamic diameter of $5\mu\text{m}$ and a density of 1.0 gm/cm^3 , and excluding 100% of the particles above $7.1\mu\text{m}$.

Personal dust sampling was planned to include 180 men, with emphasis on those in the dustier occupations. Preliminary estimates of dustiness were based on subjective observation during a previous visit to the works and on particle size measurements of typical suspension and emulsion PVC dusts. Thus the major sampling effort was directed towards occupations in the drying and packing areas in plants C2 to C6 and mixing areas in W1 and W2 (plant C1 is now closed). Plants making emulsion and paste polymer received more study than those making suspension polymer.

In the event only 130 reliable personal samples were obtained; the dust tended to cause failure of the sampling pumps, which required frequent servicing. The numbers of men sampled in each occupation and plant are set out in Tables 3 to 12 in the results section (reproduced below, table numbers taken from the original report). Numbers of men in each shift and numbers of samples are also indicated. Office staff were not included in the survey. Plant A, which processed polyethylene, was the only non-PVC plant included in the survey.

Three shifts are worked daily at each plant, one six-hour shift and two nine-hour shifts. Samples were taken on the afternoon shift (1 pm to 10 pm) except for one occasion when a morning shift (7 am to 1 pm) was monitored. Plants C2 to C6 and W1 and W2 were monitored on more than one day to reduce errors due to daily variations in dust concentrations.

From: Results: section 4.1:

The mean airborne respirable dust samples to which 130 workers in various occupational groups were exposed during the survey are shown, by plant, in Tables 3 to 12.

Respirable dust levels were generally low except for the C4 drying and packing operations and mixing process in plant W1. The highest mean average dust exposure over any occupation over a shift was 2.88 mg/m^3 .

The concentrations measured by the static samplers were low compared to those from the personal samplers and were not used in the analysis.

Table 3: Dust concentrations in occupational groups in Plant C4

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|--------|
| | | | Mean | s.d. |
| Autoclaves | 13 | 4 | 0.46 | (0.18) |
| Driers | 6 | 7 | 2.59 | (1.56) |
| Packers | 9 | 14 | 2.88 | (1.84) |
| Recovery operator | 1 | 1 | 0.65 | - |
| Fork truck driver | 2 | 2 | 0.89 | - |
| Drier foreman | 1 | 1 | 0.94 | - |
| Cleaner | 1 | 1 | 1.19 | - |
| Maintenance | 9 | 3 | 0.84 | (0.48) |

Table 4: Dust concentrations in occupational groups in Plant C2 and C3

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|--------|
| | | | Mean | s.d. |
| Autoclaves | 8 | 2 | 0.17 | - |
| Driers | 3 | 5 | 0.54 | (0.31) |
| Packers | 5 | 7 | 0.60 | (0.33) |
| Fork truck driver | 1 | 1 | 0.70 | - |
| Maintenance | 10 | 3 | 0.21 | (0.13) |

Table 5: Dust concentrations in occupational groups in Plant C5 and C6

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|--------|
| | | | Mean | s.d. |
| Autoclaves | 19 | 0 | - | - |
| Driers | 6 | 4 | 0.50 | (0.28) |
| Packers* | 9 | 7 | 0.38 | (0.12) |
| Fork truck driver | 1 | 1 | 0.29 | - |
| Foreman | 1 | 1 | 0.35 | - |

*including polymer recovery

Table 6: Dust concentrations in occupational groups in Plant W1

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|-----------------------|-------------------------|-----------------------|-----------------------------------------------------|--------|
| | | | Mean | s.d. |
| Premix team | 7 | 4 | 1.41 | (0.74) |
| Mixing unit operators | 9 | 17 | 1.86 | (1.27) |
| Foreman | 1 | 1 | 0.49 | - |
| Fork truck driver | 2 | 1 | 0.86 | - |
| Cleaner | 1 | 1 | 0.72 | - |

Table 7: Dust concentrations in occupational groups in Plant W2

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|--------|
| | | | Mean | s.d. |
| Premix team | 6 | 4 | 1.04 | (0.48) |
| Dry blend units | 6 | 5 | 0.86 | (0.84) |
| Unit controller | 2 | 2 | 0.57 | - |
| Ground floor team | 4 | 6 | 0.37 | (0.20) |
| Fork truck driver | 1 | 0 | - | - |
| Cleaners | 2 | 2 | 0.23 | - |
| Supervisor | 1 | 1 | 0.61 | - |

Table 8: Dust concentrations in occupational groups in Plant D

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|------|
| | | | Mean | s.d. |
| Assembly | 4 | 1 | 0.13 | - |
| Press operator | 2 | 1 | 0.38 | - |
| Polishing | 1 | 1 | 0.49 | - |
| Fork truck driver | 1 | 1 | 0.22 | - |
| Trimmer | 1 | 1 | 0.14 | - |
| Mill cutter | 1 | 1 | 0.37 | - |
| Premix operator | 1 | 1 | 0.10 | - |

Table 9: Dust concentrations in occupational groups in laboratory (Plant W1)

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|--------|
| | | | Mean | s.d. |
| Testers | 6 | 3 | 0.34 | (0.11) |

Table 10: Dust concentrations in occupational groups in laboratories (Plants C2/C3, C5/C6)

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|--------|
| | | | Mean | s.d. |
| Chemists | 3 | 2 | 0.19 | - |
| Testers | 3 | 3 | 0.23 | (0.17) |

Table 11: Dust concentrations in occupational groups at the central workshops

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|------------------------------------|-------------------------|-----------------------|-----------------------------------------------------|-------------|
| | | | Mean | <i>s.d.</i> |
| Fitters and instrument technicians | 12 | 3 | 0.52 | (0.30) |

Table 12: Dust concentrations in occupational groups in Plant A (not PVC)

| Occupational Group | Number of men per shift | Number of men sampled | Respirable dust concentration (mg.m ⁻³) | |
|--------------------|-------------------------|-----------------------|-----------------------------------------------------|-------------|
| | | | Mean | <i>s.d.</i> |
| Mixer operators | 3 | 3 | 0.35 | (0.05) |
| Packers | 2 | 1 | 0.47 | - |

APPENDIX 2 – ADDITIONAL SMR RESULTS

Additional external mortality analyses are contained in this Appendix. These include results for population 2 and comparisons with regional reference rates.

List of tables included:

| | |
|--------------|---------------------------------------------------------------|
| Table A2.1: | Population 1: England and Wales |
| Table A2.2: | Population 1: North-West Region |
| Table A2.3: | Population 1: Lancashire |
| Table A2.4: | Population 3: England and Wales |
| Table A2.5: | Population 3: North-West Region |
| Table A2.6: | Population 3: Lancashire |
| Table A2.7: | Population 2: Rates by calendar period. North-West Region |
| Table A2.8: | Population 2: Rates by calendar period. Lancashire |
| Table A2.9: | Population 2: Subdivided by exposure group. North-West Region |
| Table A2.10: | Population 3: Subdivided by exposure group. North-West Region |

Table A2.1: SMRs and 95% C.I.s for causes of interest for population 1. Results are standardised by age and year of death for England and Wales.

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 561 | 546.1 | 102.7 | 94.6 | 111.6 |
| All internal causes (Natural causes) | 548 | 519.3 | 105.5 | 97.1 | 114.8 |
| External causes – accidents and suicides | 13 | 19.1 | 68.1 | 39.6 | 117.4 |
| Ischaemic heart disease | 183 | 169.6 | 107.9 | 93.3 | 124.7 |
| Non-malignant respiratory disease | 50 | 55.8 | 89.6 | 67.9 | 118.2 |
| Chronic bronchitis | 3 | 5.7 | 52.8 | 17.0 | 163.8 |
| Emphysema | 0 | 4.4 | * | * | * |
| All cancers | 179 | 169.6 | 105.6 | 91.2 | 122.2 |
| Lip, oral and pharyngeal cancers | 2 | 3.2 | * | * | * |
| Digestive & peritoneal cancer | 51 | 49.7 | 102.7 | 78.0 | 135.1 |
| Oesophageal cancers | 10 | 8.3 | 120.3 | 64.7 | 223.6 |
| Stomach cancer | 8 | 10.9 | 73.3 | 36.7 | 146.6 |
| Liver cancer | 6 | 2.4 | * | * | * |
| Laryngeal cancer | 1 | 1.9 | * | * | * |
| Lung cancer | 56 | 54.4 | 102.9 | 79.2 | 133.8 |
| Malignant melanoma | 0 | 9.0 | * | * | * |
| Peptic ulcer | 1 | 0.4 | * | * | * |

Table A2.2: SMRs and 95% C.I.s for causes of interest for population 1. Results are standardised by age and year of death for North West Region

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 561 | 589.1 | 95.2 | 87.7 | 103.4 |
| All internal causes (Natural causes) | 548 | 572.2 | 95.8 | 88.1 | 104.1 |
| External causes – accidents and suicides | 13 | 16.9 | 77.0 | 44.7 | 132.6 |
| Ischaemic heart disease | 183 | 187.5 | 97.6 | 84.4 | 112.8 |
| Non-malignant respiratory disease | 50 | 67.7 | 73.9 | 56.0 | 97.5 |
| Chronic bronchitis | 3 | 6.7 | 44.9 | 14.5 | 139.2 |
| Emphysema | 0 | 2.7 | * | * | * |
| All cancers | 179 | 180.9 | 98.9 | 85.4 | 114.5 |
| Lip, oral and pharyngeal cancers | 2 | 3.5 | * | * | * |
| Digestive & peritoneal cancer | 51 | 53.3 | 95.7 | 72.7 | 125.9 |
| Oesophageal cancers | 10 | 9.6 | 104.5 | 56.2 | 194.1 |
| Stomach cancer | 8 | 11.7 | 68.2 | 34.1 | 136.5 |
| Liver cancer | 6 | 2.5 | * | * | * |
| Laryngeal cancer | 1 | 2.0 | * | * | * |
| Lung cancer | 56 | 62.2 | 90.0 | 69.3 | 117.0 |
| Malignant melanoma | 0 | 0.7 | * | * | * |
| Peptic ulcer | 1 | 0.4 | * | * | * |

Table A2.3: SMRs and 95% C.I.s for causes of interest for population 1. Results are standardised by age and year of death for Lancashire

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 561 | 598.6 | 93.7 | 86.3 | 101.8 |
| All internal causes (Natural causes) | 548 | 579.7 | 94.5 | 86.9 | 102.8 |
| External causes – accidents and suicides | 13 | 18.9 | 68.9 | 40.0 | 118.6 |
| Ischaemic heart disease | 183 | 195.2 | 93.8 | 81.1 | 108.4 |
| Non-malignant respiratory disease | 50 | 67.9 | 73.6 | 55.8 | 97.1 |
| Chronic bronchitis | 3 | 8.4 | 35.8 | 11.6 | 111.1 |
| Emphysema | 0 | 2.9 | * | * | * |
| All cancers | 179 | 175.1 | 102.2 | 88.3 | 118.4 |
| Lip, oral and pharyngeal cancers | 2 | 3.4 | * | * | * |
| Digestive & peritoneal cancer | 51 | 52.7 | 96.8 | 73.6 | 127.4 |
| Oesophageal cancers | 10 | 9.9 | 100.7 | 54.2 | 187.2 |
| Stomach cancer | 8 | 11.2 | 71.5 | 35.7 | 142.9 |
| Liver cancer | 6 | 2.3 | * | * | * |
| Laryngeal cancer | 1 | 1.9 | * | * | * |
| Lung cancer | 56 | 57.0 | 98.2 | 75.6 | 127.6 |
| Malignant melanoma | 0 | 0.7 | * | * | * |
| Peptic ulcer | 1 | 0.3 | * | * | * |

Table A2.4: SMRs and 95% C.I.s for causes of interest for population 3. Results are standardised by age and year of death for England and Wales

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 207 | 221.4 | 93.5 | 81.6 | 107.2 |
| All internal causes (Natural causes) | 205 | 212.8 | 96.3 | 84.0 | 110.5 |
| External causes – accidents and suicides | 2 | 7.1 | 28.2 | 7.1 | 112.9 |
| Ischaemic heart disease | 70 | 69.2 | 101.2 | 80.0 | 127.9 |
| Non-malignant respiratory disease | 17 | 22.2 | 76.5 | 47.5 | 123.0 |
| Chronic bronchitis | 1 | 1.9 | * | * | * |
| Emphysema | 0 | 1.4 | * | * | * |
| All cancers | 73 | 70.9 | 102.9 | 81.8 | 129.5 |
| Lip, oral and pharyngeal cancers | 1 | 1.2 | * | * | * |
| Digestive & peritoneal cancer | 21 | 20.8 | 100.8 | 65.7 | 154.6 |
| Oesophageal cancers | 7 | 3.5 | * | * | * |
| Stomach cancer | 4 | 4.5 | * | * | * |
| Liver cancer | 3 | 1.0 | * | * | * |
| Laryngeal cancer | 0 | 0.7 | * | * | * |
| Lung cancer | 27 | 22.6 | 119.5 | 82.0 | 174.3 |
| Malignant melanoma | 0 | 1.2 | * | * | * |
| Peptic ulcer | 0 | 0.1 | * | * | * |

Table A2.5: SMRs and 95% C.I.s for causes of interest for population 3. Results are standardised by age and year of death for North West Region

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 207 | 240.4 | 86.1 | 75.1 | 98.7 |
| All internal causes (Natural causes) | 205 | 233.8 | 87.7 | 76.5 | 100.6 |
| External causes – accidents and suicides | 2 | 6.7 | 30.0 | 7.5 | 120.1 |
| Ischaemic heart disease | 70 | 77.0 | 90.9 | 71.9 | 114.9 |
| Non-malignant respiratory disease | 17 | 26.6 | 63.8 | 39.7 | 102.7 |
| Chronic bronchitis | 1 | 2.3 | * | * | * |
| Emphysema | 0 | 1.1 | * | * | * |
| All cancers | 73 | 75.8 | 96.3 | 76.5 | 121.1 |
| Lip, oral and pharyngeal cancers | 1 | 1.5 | * | * | * |
| Digestive & peritoneal cancer | 21 | 22.4 | 93.9 | 61.2 | 144.0 |
| Oesophageal cancers | 7 | 4.1 | * | * | * |
| Stomach cancer | 4 | 4.8 | * | * | * |
| Liver cancer | 3 | 1.1 | * | * | * |
| Laryngeal cancer | 0 | 0.9 | * | * | * |
| Lung cancer | 27 | 26.0 | 103.7 | 71.1 | 151.3 |
| Malignant melanoma | 0 | 0.3 | * | * | * |
| Peptic ulcer | 0 | 0.2 | * | * | * |

Table A2.6: SMRs and 95% C.I.s for causes of interest for population 3. Results are standardised by age and year of death for Lancashire

| Cause of death | Observed | Expected | SMR | 95% C.I. | |
|------------------------------------------|-----------------|-----------------|------------|-----------------|-------|
| All-causes | 207 | 243.0 | 85.2 | 74.3 | 97.6 |
| All internal causes (Natural causes) | 205 | 235.7 | 87.0 | 75.9 | 99.7 |
| External causes – accidents and suicides | 2 | 7.3 | 27.2 | 6.8 | 108.8 |
| Ischaemic heart disease | 70 | 79.6 | 87.9 | 69.6 | 111.1 |
| Non-malignant respiratory disease | 17 | 26.6 | 63.8 | 39.7 | 102.7 |
| Chronic bronchitis | 1 | 2.9 | * | * | * |
| Emphysema | 0 | 1.2 | * | * | * |
| All cancers | 73 | 73.2 | 99.7 | 79.3 | 125.5 |
| Lip, oral and pharyngeal cancers | 1 | 1.5 | * | * | * |
| Digestive & peritoneal cancer | 21 | 22.0 | 95.4 | 62.2 | 146.3 |
| Oesophageal cancers | 7 | 4.3 | * | * | * |
| Stomach cancer | 4 | 4.5 | * | * | * |
| Liver cancer | 3 | 1.0 | * | * | * |
| Laryngeal cancer | 0 | 0.8 | * | * | * |
| Lung cancer | 27 | 23.8 | 113.5 | 77.8 | 165.4 |
| Malignant melanoma | 0 | 0.3 | * | * | * |
| Peptic ulcer | 0 | 0.1 | * | * | * |

Table A2.7: SMRs and 95% C.I.s for all-cause mortality and key causes for population 2. Results by calendar period for North West Region

| Calendar period | | All-cause mortality | Non-malignant respiratory disease | Ischaemic heart disease | Lung cancer |
|------------------------|----------|----------------------------|------------------------------------------|--------------------------------|--------------------|
| 1979-1984 | Observed | 48 | 3 | 20 | 7 |
| | Expected | 69.7 | 5.3 | 27.0 | 8.3 |
| | SMR | 68.8 | 56.8 | 74.1 | 84.4 |
| | 95% C.I. | (51.9,91.3) | (18.3,176.1) | (47.8,114.9) | (40.2,177.1) |
| 1985-1990 | Observed | 90 | 3 | 34 | 9 |
| | Expected | 100.5 | 8.1 | 37.6 | 12.3 |
| | SMR | 89.5 | 37.0 | 90.5 | 73.1 |
| | 95% C.I. | (72.8,110.1) | (11.9,114.7) | (64.7,126.7) | (38.1,140.6) |
| 1991-1996 | Observed | 127 | 18 | 36 | 15 |
| | Expected | 131.1 | 14.9 | 42.2 | 14.7 |
| | SMR | 96.9 | 122.0 | 85.3 | 102.0 |
| | 95% C.I. | (81.4,115.3) | (76.8,193.6) | (61.5,118.2) | (61.5,169.2) |
| 1997-2003 | Observed | 177 | 13 | 53 | 19 |
| | Expected | 197.5 | 26.9 | 52.4 | 18.3 |
| | SMR | 89.6 | 48.3 | 101.2 | 103.9 |
| | 95% C.I. | (77.3,103.8) | (28.0,83.1) | (77.3,132.5) | (66.3,162.9) |
| Total | Observed | 442 | 37 | 143 | 50 |
| | Expected | 498.9 | 55.1 | 159.1 | 53.6 |
| | SMR | 88.6 | 67.2 | 89.9 | 93.3 |
| | 95% C.I. | (80.7,97.3) | (48.7,92.7) | (76.3,105.9) | (70.7,123.1) |

Table A2.8: SMRs and 95% C.I.s for all-cause mortality and key causes for population 2. Results by calendar period for Lancashire

| Calendar period | | All-cause mortality | Non-malignant respiratory disease | Ischaemic heart disease | Lung cancer |
|-----------------|----------|---------------------|-----------------------------------|-------------------------|--------------|
| 1979-1984 | Observed | 48 | 3 | 20 | 7 |
| | Expected | 71.8 | 5.4 | 28.0 | 7.7 |
| | SMR | 66.9 | 55.9 | 71.5 | 90.9 |
| | 95% C.I. | (50.4,88.7) | (18.0,173.2) | (46.1,110.8) | (43.3,190.6) |
| 1985-1990 | Observed | 90 | 3 | 34 | 9 |
| | Expected | 105.3 | 8.7 | 40.4 | 11.3 |
| | SMR | 85.5 | 34.3 | 84.1 | 79.5 |
| | 95% C.I. | (69.5,105.1) | (11.1,106.4) | (60.1,117.6) | (41.4,152.9) |
| 1991-1996 | Observed | 127 | 18 | 36 | 15 |
| | Expected | 136.0 | 14.7 | 45.4 | 13.6 |
| | SMR | 93.4 | 122.1 | 79.3 | 110.1 |
| | 95% C.I. | (78.5,111.1) | (76.9,193.8) | (57.2,109.9) | (66.4,182.6) |
| 1997-2003 | Observed | 177 | 13 | 53 | 19 |
| | Expected | 191.5 | 26.2 | 50.8 | 16.4 |
| | SMR | 92.4 | 49.5 | 104.3 | 116.2 |
| | 95% C.I. | (79.7,107.1) | (28.8,85.3) | (79.7,136.5) | (74.1,182.1) |
| Total | Observed | 442 | 37 | 143 | 50 |
| | Expected | 504.6 | 55.1 | 164.7 | 49.0 |
| | SMR | 87.6 | 67.2 | 86.8 | 102.0 |
| | 95% C.I. | (79.8,96.1) | (48.7,92.7) | (73.7,102.3) | (77.3,134.6) |

Table A2.9: SMRs and 95% C.I.s for causes of interest for population 2 subdivided by exposure group. Results are standardised for age and year of death for North-West Region

| Cause of death | Exposure | Observed | Expected | SMR | 95% C.I. | |
|--------------------------------------|-----------|----------|----------|-------|----------|-------|
| All causes | Exposed | 336 | 349.9 | 96.0 | 86.3 | 106.9 |
| | Unexposed | 106 | 149.0 | 71.1 | 58.8 | 86.0 |
| All internal causes (Natural causes) | Exposed | 330 | 339.9 | 97.1 | 87.2 | 108.2 |
| | Unexposed | 103 | 143.9 | 71.6 | 59.0 | 86.8 |
| Ischaemic heart disease | Exposed | 111 | 112.3 | 98.9 | 82.1 | 119.1 |
| | Unexposed | 32 | 46.8 | 68.3 | 48.3 | 96.6 |
| Non-malignant respiratory disease | Exposed | 25 | 38.6 | 64.8 | 43.8 | 95.9 |
| | Unexposed | 12 | 16.5 | 72.7 | 41.3 | 128.1 |
| All cancers | Exposed | 120 | 110.1 | 109.0 | 91.2 | 130.4 |
| | Unexposed | 27 | 46.3 | 58.3 | 40.0 | 85.0 |
| Digestive & peritoneal cancer | Exposed | 33 | 32.5 | 101.6 | 72.3 | 143.0 |
| | Unexposed | 6 | 13.6 | 44.1 | 19.8 | 98.2 |
| Lung cancer | Exposed | 45 | 37.8 | 118.9 | 88.8 | 159.2 |
| | Unexposed | 5 | 15.7 | 31.8 | 13.2 | 76.3 |

Table A2.10: SMRs and 95% C.I.s for causes of interest for population 3 subdivided by exposure group. Results are standardised for age and year of death for North-West Region

| Cause of death | Exposure | Observed | Expected | SMR | 95% C.I. | |
|--------------------------------------|-----------|----------|----------|-------|----------|-------|
| All causes | Exposed | 182 | 203.3 | 89.5 | 77.4 | 103.5 |
| | Unexposed | 25 | 37.2 | 67.3 | 45.5 | 99.6 |
| All internal causes (Natural causes) | Exposed | 180 | 197.8 | 91.0 | 78.6 | 105.3 |
| | Unexposed | 25 | 36.0 | 69.5 | 46.9 | 102.8 |
| Ischaemic heart disease | Exposed | 62 | 65.3 | 94.9 | 74.0 | 121.8 |
| | Unexposed | 8 | 11.7 | 68.2 | 34.1 | 136.5 |
| Non-malignant respiratory disease | Exposed | 17 | 22.5 | 75.5 | 46.9 | 121.4 |
| | Unexposed | 0 | 4.1 | * | * | * |
| All cancers | Exposed | 67 | 64.1 | 104.5 | 82.2 | 132.7 |
| | Unexposed | 6 | 11.7 | 51.3 | 23.1 | 114.2 |
| Digestive & peritoneal cancer | Exposed | 20 | 18.9 | 105.7 | 68.2 | 163.8 |
| | Unexposed | 1 | 3.4 | * | * | * |
| Lung cancer | Exposed | 26 | 22.0 | 118.0 | 80.3 | 173.3 |
| | Unexposed | 1 | 4.0 | * | * | * |

APPENDIX 3 – STATISTICAL TABLES, POPULATION 2

Further detailed results from the Cox Proportional Hazards analysis of mortality for population 2 are contained in this appendix.

Results are presented for each model as the regression coefficient and its standard error. Ratios of coefficient to standard error of around 2.0 represent statistical significance at the 5% level.

Table A3.1: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1020 | 0.006 | 0.1010 | 0.006 | 0.1040 | 0.009 | 0.1070 | 0.007 | 0.0993 | 0.009 |
| Ever worked in PVC exposed job | | | 0.1500 | 0.056 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.1310 | 0.088 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.1620 | 0.059 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1296 | 0.075 |

Table A3.2: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1680 | 0.026 | 0.1680 | 0.026 | 0.1750 | 0.042 | 0.1742 | 0.030 | 0.1670 | 0.042 |
| Ever worked in PVC exposed job | | | | | | | | | | |
| Ever worked in job using emulsion process only | | | -0.0692 | 0.176 | | | | | | |
| Ever worked in job using suspension process only | | | | | -0.1120 | 0.323 | | | | |
| Ever worked in job using mixed process | | | | | | | 0.0306 | 0.185 | -0.4230 | 0.323 |

Table A3.3: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1080 | 0.010 | 0.1080 | 0.010 | 0.1220 | 0.018 | 0.1040 | 0.012 | 0.1050 | 0.016 |
| Ever worked in PVC exposed job | | | 0.1910 | 0.100 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.2360 | 0.150 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.1970 | 0.107 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1450 | 0.135 |

Table A3.4: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0783 | 0.015 | 0.0763 | 0.016 | 0.0478 | 0.029 | 0.1080 | 0.023 | 0.0839 | 0.027 |
| Ever worked in PVC exposed job | | | 0.6771 | 0.235 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.6293 | 0.303 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.6560 | 0.244 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.7276 | 0.266 |

Table A3.5: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1020 | 0.006 | 0.1009 | 0.006 | 0.1004 | 0.010 | 0.1079 | 0.007 | 0.1012 | 0.009 |
| Ever worked in PVC exposed job | | | 0.1389 | 0.077 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0016 | 0.007 | | | | | | |
| Ever worked in job using emulsion process only | | | | | -0.1119 | 0.172 | | | | |
| Time in PVC job: emulsion process (years) | | | | | 0.0345 | 0.020 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.2073 | 0.089 | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0063 | 0.009 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1961 | 0.085 |
| Time in PVC job: mixed process (years) | | | | | | | | | -0.0203 | 0.014 |

Table A3.6: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1680 | 0.026 | 0.1680 | 0.027 | 0.1767 | 0.043 | 0.1722 | 0.030 | 0.1702 | 0.042 |
| Ever worked in PVC exposed job | | | 0.0692 | 0.268 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0000 | 0.026 | | | | | | |
| Ever worked in job using emulsion process only | | | | | -0.0120 | 0.560 | | | | |
| Time in PVC job: emulsion process (years) | | | | | -0.0144 | 0.068 | | | | |
| Ever worked in job using suspension process only | | | | | | | -0.0485 | 0.309 | | |
| Time in PVC job: suspension process (years) | | | | | | | 0.0099 | 0.031 | | |
| Ever worked in job using mixed process | | | | | | | | | -0.2085 | 0.361 |
| Time in PVC job: mixed process (years) | | | | | | | | | -0.0773 | 0.093 |

Table A3.7: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1080 | 0.010 | 0.1064 | 0.011 | 0.1176 | 0.019 | 0.1048 | 0.013 | 0.1062 | 0.016 |
| Ever worked in PVC exposed job | | | 0.1362 | 0.140 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0073 | 0.013 | | | | | | |
| Ever worked in job using emulsion process only | | | | | -0.0180 | 0.295 | | | | |
| Time in PVC job: emulsion process (years) | | | | | 0.0344 | 0.032 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.2248 | 0.159 | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0038 | 0.016 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1687 | 0.156 |
| Time in PVC job: mixed process (years) | | | | | | | | | -0.0067 | 0.023 |

Table A3.8: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0783 | 0.015 | 0.0763 | 0.017 | 0.0531 | 0.030 | 0.1139 | 0.023 | 0.0879 | 0.027 |
| Ever worked in PVC exposed job | | | 0.6775 | 0.276 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0001 | 0.021 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.8585 | 0.413 | | | | |
| Time in PVC job: emulsion process (years) | | | | | -0.0436 | 0.059 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.8462 | 0.299 | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0272 | 0.026 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.8082 | 0.283 |
| Time in PVC job: mixed process (years) | | | | | | | | | -0.0269 | 0.037 |

Table A3.9: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1020 | 0.006 | 0.1016 | 0.006 | 0.1011 | 0.006 | 0.1011 | 0.006 | 0.1007 | 0.006 |
| Ever worked in job involving VCM exposure | | | 0.0072 | 0.050 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | 0.0613 | 0.055 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.0962 | 0.077 | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.0717 | 0.049 |

Table A3.10: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1680 | 0.026 | 0.1630 | 0.026 | 0.1730 | 0.027 | 0.1650 | 0.026 | 0.1666 | 0.026 |
| Ever worked in job involving VCM exposure | | | -0.2270 | 0.193 | -0.2910 | 0.225 | | | | |
| Ever worked in job involving asbestos exposure | | | | | | | -0.4150 | 0.364 | | |
| Ever worked in job involving TFE exposure | | | | | | | | | 0.0959 | 0.168 |
| Ever worked in job involving lead exposure | | | | | | | | | | |

Table A3.11: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1080 | 0.010 | 0.1083 | 0.011 | 0.1083 | 0.010 | 0.1080 | 0.010 | 0.1070 | 0.010 |
| Ever worked in job involving VCM exposure | | | -0.0042 | 0.088 | 0.0030 | 0.099 | | | | |
| Ever worked in job involving asbestos exposure | | | | | | | -0.1460 | 0.141 | | |
| Ever worked in job involving TFE exposure | | | | | | | | | 0.1590 | 0.085 |
| Ever worked in job involving lead exposure | | | | | | | | | | |

Table A3.12: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0783 | 0.015 | 0.0802 | 0.016 | 0.0783 | 0.015 | 0.0768 | 0.015 | 0.0758 | 0.016 |
| Ever worked in job involving VCM exposure | | | 0.2256 | 0.142 | -0.0262 | 0.171 | | | | |
| Ever worked in job involving asbestos exposure | | | | | | | -1.0030 | 0.505 | | |
| Ever worked in job involving TFE exposure | | | | | | | | | 0.2306 | 0.143 |
| Ever worked in job involving lead exposure | | | | | | | | | | |

Table A3.13: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1020 | 0.006 | 0.1000 | 0.006 | 0.1015 | 0.006 | 0.1011 | 0.006 | 0.1011 | 0.006 |
| Ever worked in job involving VCM exposure | | | -0.1046 | 0.084 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | 0.0173 | 0.010 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | 0.1048 | 0.081 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | -0.0073 | 0.010 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.0977 | 0.126 | | |
| Time worked in job involving TFE exposure (years) | | | | | | | 0.0003 | 0.021 | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.1024 | 0.075 |
| Time worked in job involving lead exposure (years) | | | | | | | | | -0.0050 | 0.009 |

Table A3.14: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1680 | 0.026 | 0.1654 | 0.026 | 0.1706 | 0.027 | 0.1645 | 0.026 | 0.1642 | 0.026 |
| Ever worked in job involving VCM exposure | | | -0.0048 | 0.299 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | -0.0372 | 0.042 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | -0.8660 | 0.503 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | 0.0711 | 0.047 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.8332 | 0.772 | | |
| Time worked in job involving TFE exposure (years) | | | | | | | 0.0726 | 0.103 | | |
| Ever worked in job involving lead exposure | | | | | | | | | -0.0694 | 0.285 |
| Time worked in job involving lead exposure (years) | | | | | | | | | 0.0234 | 0.031 |

Table A3.15: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1080 | 0.010 | 0.1058 | 0.011 | 0.1084 | 0.010 | 0.1072 | 0.010 | 0.1073 | 0.011 |
| Ever worked in job involving VCM exposure | | | -0.1764 | 0.154 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | 0.0258 | 0.018 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | 0.0210 | 0.149 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | -0.0029 | 0.018 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.3234 | 0.256 | | |
| Time worked in job involving TFE exposure (years) | | | | | | | 0.0346 | 0.038 | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.2153 | 0.125 |
| Time worked in job involving lead exposure (years) | | | | | | | | | -0.0091 | 0.015 |

Table A3.16: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 2. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0783 | 0.015 | 0.0770 | 0.016 | 0.0795 | 0.015 | 0.0776 | 0.015 | 0.0779 | 0.016 |
| Ever worked in job involving VCM exposure | | | 0.0587 | 0.231 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | 0.0262 | 0.027 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | 0.1101 | 0.245 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | -0.0249 | 0.035 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | 0.0429 | 0.704 | | |
| Time worked in job involving TFE exposure (years) | | | | | | | NC | NC | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.3605 | 0.198 |
| Time worked in job involving lead exposure (years) | | | | | | | | | -0.0229 | 0.026 |

APPENDIX 4 – STATISTICAL TABLES, POPULATION 3

This appendix contains some further detailed tables of results from the Cox Proportional Hazards analysis of mortality for population 3.

For each model, results are presented as the regression coefficient and its standard error. Ratios of coefficient to standard error of around 2.0 represent statistical significance at the 5% level.

Table A4.1: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0972 | 0.009 | 0.0969 | 0.009 | 0.1020 | 0.015 | 0.1010 | 0.011 | 0.0954 | 0.016 |
| Ever worked in PVC exposed job | | | 0.1422 | 0.107 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.1480 | 0.128 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.1350 | 0.111 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1570 | 0.129 |

Table A4.2: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1380 | 0.035 | 0.1360 | 0.035 | 0.1530 | 0.079 | 0.1330 | 0.041 | 0.1120 | 0.102 |
| Ever worked in PVC exposed job | | | NC | NC | | | | | | |
| Ever worked in job using emulsion process only | | | | | NC | NC | | | | |
| Ever worked in job using suspension process only | | | | | | | NC | NC | | |
| Ever worked in job using mixed process | | | | | | | | | NC | NC |

Table A4.3: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1230 | 0.016 | 0.1230 | 0.016 | 0.1690 | 0.035 | 0.1190 | 0.020 | 0.1320 | 0.032 |
| Ever worked in PVC exposed job | | | 0.1650 | 0.188 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.1450 | 0.228 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.1700 | 0.195 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1770 | 0.225 |

Table A4.4: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0396 | 0.020 | 0.0369 | 0.021 | -0.0140 | 0.040 | 0.0547 | 0.029 | 0.0901 | 0.048 |
| Ever worked in PVC exposed job | | | 0.8147 | 0.510 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.8760 | 0.547 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.7669 | 0.518 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.8488 | 0.541 |

Table A4.5: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0972 | 0.009 | 0.0927 | 0.009 | 0.0912 | 0.016 | 0.1034 | 0.012 | 0.0947 | 0.016 |
| Ever worked in PVC exposed job | | | 0.0309 | 0.141 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0138 | 0.011 | | | | | | |
| Ever worked in job using emulsion process only | | | | | -0.1943 | 0.229 | | | | |
| Time in PVC job: emulsion process (years) | | | | | 0.0456 | 0.024 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.2189 | 0.166 | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0101 | 0.015 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1412 | 0.136 |
| Time in PVC job: mixed process (years) | | | | | | | | | 0.0089 | 0.023 |

Table A4.6: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1380 | 0.035 | 0.1447 | 0.037 | 0.1641 | 0.084 | 0.1407 | 0.044 | 0.1085 | 0.104 |
| Ever worked in PVC exposed job | | | NC | NC | | | | | | |
| Total time in PVC exposed job (years) | | | -0.0265 | 0.034 | | | | | | |
| Ever worked in job using emulsion process only | | | | | NC | NC | | | | |
| Time in PVC job: emulsion process (years) | | | | | -0.0348 | 0.077 | | | | |
| Ever worked in job using suspension process only | | | | | | | NC | NC | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0226 | 0.043 | | |
| Ever worked in job using mixed process | | | | | | | | | NC | NC |
| Time in PVC job: mixed process (years) | | | | | | | | | 0.0222 | 0.086 |

Table A4.7: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1230 | 0.016 | 0.1131 | 0.018 | 0.1575 | 0.037 | 0.1144 | 0.022 | 0.1301 | 0.033 |
| Ever worked in PVC exposed job | | | -0.0994 | 0.255 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0311 | 0.020 | | | | | | |
| Ever worked in job using emulsion process only | | | | | -0.1887 | 0.427 | | | | |
| Time in PVC job: emulsion process (years) | | | | | 0.0407 | 0.042 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.0475 | 0.299 | | |
| Time in PVC job: suspension process (years) | | | | | | | 0.0142 | 0.026 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1332 | 0.240 |
| Time in PVC job: mixed process (years) | | | | | | | | | 0.0213 | 0.035 |

Table A4.8: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0396 | 0.020 | 0.0222 | 0.025 | -0.0046 | 0.043 | 0.0580 | 0.032 | 0.0900 | 0.048 |
| Ever worked in PVC exposed job | | | 0.5414 | 0.561 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0385 | 0.034 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 1.0332 | 0.626 | | | | |
| Time in PVC job: emulsion process (years) | | | | | -0.0347 | 0.071 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.8415 | 0.613 | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0099 | 0.044 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.8471 | 0.551 |
| Time in PVC job: mixed process (years) | | | | | | | | | 0.0010 | 0.062 |

Table A4.9: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0962 | 0.009 | 0.0961 | 0.009 | 0.1019 | 0.016 | 0.0996 | 0.012 | 0.0895 | 0.017 |
| Smoking: Current smokers vs Non-smokers | 0.1940 | 0.134 | 0.1910 | 0.134 | 0.0429 | 0.230 | 0.2490 | 0.168 | 0.4120 | 0.289 |
| Ex-smokers vs Non-smokers | -0.1430 | 0.086 | -0.1390 | 0.086 | -0.2635 | 0.164 | -0.0880 | 0.108 | -0.0559 | 0.157 |
| Packyears (per 5000): Current smokers | 0.0422 | 0.058 | 0.0403 | 0.059 | 0.0595 | 0.095 | 0.0384 | 0.078 | 0.0298 | 0.104 |
| Ex-smokers | 0.1355 | 0.080 | 0.1315 | 0.080 | 0.2045 | 0.164 | 0.0985 | 0.104 | 0.0880 | 0.147 |
| Ever worked in PVC exposed job | | | 0.1150 | 0.107 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.1191 | 0.129 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.1160 | 0.112 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1170 | 0.131 |

Table A4.10: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1420 | 0.037 | 0.1420 | 0.037 | 0.1503 | 0.088 | 0.1348 | 0.043 | 0.1260 | 0.119 |
| Smoking: Current smokers vs Non-smokers | 0.4510 | 0.554 | 0.4710 | 0.557 | NC | NC | 0.3295 | 0.590 | NC | NC |
| Ex-smokers vs Non-smokers | -0.1910 | 0.364 | -0.1630 | 0.360 | NC | NC | -0.0065 | 0.420 | NC | NC |
| Packyears (per 5000): Current smokers | 0.0765 | 0.176 | 0.0655 | 0.182 | NC | NC | 0.1445 | 0.226 | NC | NC |
| Ex-smokers | 0.0353 | 0.374 | 0.0168 | 0.365 | NC | NC | -0.2600 | 0.584 | NC | NC |
| Ever worked in PVC exposed job | | | NC | NC | NC | NC | | | | |
| Ever worked in job using emulsion process only | | | | | NC | NC | | | | |
| Ever worked in job using suspension process only | | | | | | | NC | NC | | |
| Ever worked in job using mixed process | | | | | | | | | NC | NC |

Table A4.11: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1247 | 0.017 | 0.1244 | 0.017 | 0.1769 | 0.039 | 0.1190 | 0.021 | 0.1280 | 0.034 |
| Smoking: Current smokers vs Non-smokers | -0.0075 | 0.211 | -0.0050 | 0.212 | -0.6093 | 0.391 | 0.1550 | 0.278 | 0.4190 | 0.564 |
| Ex-smokers vs Non-smokers | -0.3163 | 0.155 | -0.3097 | 0.155 | -0.3162 | 0.287 | -0.1860 | 0.182 | 0.0195 | 0.270 |
| Packyears (per 5000): Current smokers | 0.0530 | 0.099 | 0.0505 | 0.100 | 0.2830 | 0.151 | 0.0302 | 0.134 | -0.0152 | 0.181 |
| Ex-smokers | 0.2535 | 0.132 | 0.2475 | 0.132 | 0.3425 | 0.245 | 0.2410 | 0.152 | -0.0057 | 0.247 |
| Ever worked in PVC exposed job | | | 0.1314 | 0.188 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.0924 | 0.232 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.1470 | 0.196 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1640 | 0.230 |

Table A4.12: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0266 | 0.023 | 0.0252 | 0.023 | -0.0243 | 0.044 | 0.0530 | 0.031 | 0.0796 | 0.052 |
| Smoking: Current smokers vs Non-smokers | 0.9244 | 0.532 | 0.8740 | 0.533 | NC | NC | 0.6853 | 0.558 | NC | NC |
| Ex-smokers vs Non-smokers | -0.5245 | 0.360 | -0.5150 | 0.356 | NC | NC | -0.5626 | 0.433 | NC | NC |
| Packyears (per 5000): Current smokers | 0.0520 | 0.162 | 0.0427 | 0.165 | NC | NC | -0.0760 | 0.240 | NC | NC |
| Ex-smokers | 0.6360 | 0.208 | 0.6100 | 0.206 | NC | NC | 0.5340 | 0.268 | NC | NC |
| Ever worked in PVC exposed job | | | 0.7030 | 0.511 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.7914 | 0.562 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.6807 | 0.519 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.7090 | 0.552 |

Table A4.13: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0962 | 0.009 | 0.0912 | 0.010 | 0.0889 | 0.017 | 0.1020 | 0.012 | 0.0882 | 0.017 |
| Smoking: Current smokers vs Non-smokers | 0.1940 | 0.134 | 0.1914 | 0.134 | 0.1062 | 0.231 | 0.2520 | 0.168 | 0.4140 | 0.288 |
| Ex-smokers vs Non-smokers | -0.1430 | 0.086 | -0.1438 | 0.086 | -0.2720 | 0.163 | -0.0879 | 0.108 | -0.0064 | 0.158 |
| Packyears (per 5000): Current smokers | 0.0422 | 0.058 | 0.0425 | 0.059 | 0.0760 | 0.097 | 0.0344 | 0.078 | 0.0345 | 0.104 |
| Ex-smokers | 0.1355 | 0.080 | 0.1355 | 0.080 | 0.2240 | 0.163 | 0.1000 | 0.104 | 0.1050 | 0.148 |
| Ever worked in PVC exposed job | | | -0.0160 | 0.141 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0162 | 0.011 | | | | | | |
| Ever worked in job using emulsion process only | | | | | -0.2957 | 0.233 | | | | |
| Time in PVC job: emulsion process (years) | | | | | 0.0553 | 0.024 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.1780 | 0.168 | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0076 | 0.015 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.0089 | 0.139 |
| Time in PVC job: mixed process (years) | | | | | | | | | 0.0154 | 0.022 |

Table A4.14: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1420 | 0.037 | 0.1490 | 0.038 | 0.1556 | 0.097 | 0.1389 | 0.046 | 0.1065 | 0.107 |
| Smoking: Current smokers vs Non-smokers | 0.4510 | 0.554 | 0.4670 | 0.556 | NC | NC | 0.3380 | 0.590 | NC | NC |
| Ex-smokers vs Non-smokers | -0.1910 | 0.364 | -0.1520 | 0.359 | NC | NC | -0.0098 | 0.417 | NC | NC |
| Paackyears (per 5000): Current smokers | 0.0765 | 0.176 | 0.0630 | 0.180 | NC | NC | 0.1350 | 0.228 | NC | NC |
| Ex-smokers | 0.0353 | 0.374 | 0.0080 | 0.362 | NC | NC | -0.2500 | 0.576 | NC | NC |
| Ever worked in PVC exposed job | | | NC | NC | | | | | | |
| Total time in PVC exposed job (years) | | | -0.0215 | 0.033 | NC | NC | | | | |
| Ever worked in job using emulsion process only | | | | | -0.0220 | 0.083 | | | | |
| Time in PVC job: emulsion process (years) | | | | | | | NC | NC | | |
| Ever worked in job using suspension process only | | | | | | | -0.0122 | 0.044 | | |
| Time in PVC job: suspension process (years) | | | | | | | | | NC | NC |
| Ever worked in job using mixed process | | | | | | | | | 0.0166 | 0.081 |
| Time in PVC job: mixed process (years) | | | | | | | | | | |

Table A4.15: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1247 | 0.017 | 0.1140 | 0.018 | 0.1621 | 0.040 | 0.1150 | 0.023 | 0.1250 | 0.034 |
| Smoking: Current smokers vs Non-smokers | -0.0075 | 0.211 | 0.0008 | 0.212 | -0.5355 | 0.397 | 0.1520 | 0.278 | 0.4280 | 0.564 |
| Ex-smokers vs Non-smokers | -0.3163 | 0.155 | -0.3183 | 0.155 | -0.3203 | 0.287 | -0.1860 | 0.182 | 0.0045 | 0.271 |
| Packyears (per 5000): Current smokers | 0.0530 | 0.099 | 0.0520 | 0.100 | 0.3055 | 0.160 | 0.0361 | 0.134 | -0.0041 | 0.181 |
| Ex-smokers | 0.2535 | 0.132 | 0.2550 | 0.131 | 0.3740 | 0.244 | 0.2365 | 0.152 | 0.0321 | 0.251 |
| Ever worked in PVC exposed job | | | -0.1506 | 0.253 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0332 | 0.019 | | | | | | |
| Ever worked in job using emulsion process only | | | | | -0.3093 | 0.447 | | | | |
| Time in PVC job: emulsion process (years) | | | | | 0.0500 | 0.045 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.0213 | 0.299 | | |
| Time in PVC job: suspension process (years) | | | | | | | 0.0145 | 0.026 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.1100 | 0.245 |
| Time in PVC job: mixed process (years) | | | | | | | | | 0.0247 | 0.035 |

Table A4.16: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0266 | 0.023 | 0.0100 | 0.027 | -0.0195 | 0.046 | 0.0574 | 0.034 | 0.0784 | 0.053 |
| Smoking: Current smokers vs Non-smokers | 0.9244 | 0.532 | 0.8603 | 0.533 | NC | NC | 0.6967 | 0.559 | NC | NC |
| Ex-smokers vs Non-smokers | -0.5245 | 0.360 | -0.5107 | 0.351 | NC | NC | -0.5698 | 0.437 | NC | NC |
| Packyears (per 5000): Current smokers | 0.0520 | 0.162 | 0.0555 | 0.161 | NC | NC | -0.0865 | 0.242 | NC | NC |
| Ex-smokers | 0.6360 | 0.208 | 0.6005 | 0.201 | NC | NC | 0.5440 | 0.274 | NC | NC |
| Ever worked in PVC exposed job | | | 0.4325 | 0.560 | | | | | | |
| Total time in PVC exposed job (years) | | | 0.0393 | 0.032 | | | | | | |
| Ever worked in job using emulsion process only | | | | | 0.8847 | 0.632 | | | | |
| Time in PVC job: emulsion process (years) | | | | | -0.0220 | 0.072 | | | | |
| Ever worked in job using suspension process only | | | | | | | 0.7831 | 0.614 | | |
| Time in PVC job: suspension process (years) | | | | | | | -0.0135 | 0.044 | | |
| Ever worked in job using mixed process | | | | | | | | | 0.6650 | 0.562 |
| Time in PVC job: mixed process (years) | | | | | | | | | 0.0262 | 0.056 |

Table A4.17: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0972 | 0.009 | 0.0974 | 0.009 | 0.0960 | 0.009 | 0.0970 | 0.009 | 0.0971 | 0.009 |
| Ever worked in job involving VCM exposure | | | 0.0168 | 0.070 | 0.1050 | 0.087 | | | | |
| Ever worked in job involving asbestos exposure | | | | | | | -0.0934 | 0.130 | | |
| Ever worked in job involving TFE exposure | | | | | | | | | 0.0065 | 0.070 |
| Ever worked in job involving lead exposure | | | | | | | | | | |

Table A4.18: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1380 | 0.035 | 0.1340 | 0.035 | 0.1450 | 0.036 | 0.1350 | 0.035 | 0.1340 | 0.035 |
| Ever worked in job involving VCM exposure | | | -0.2120 | 0.256 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | -0.6610 | 0.518 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | NC | NC | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.2450 | 0.248 |

Table A4.19: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1230 | 0.017 | 0.1222 | 0.017 | 0.1210 | 0.016 | 0.1220 | 0.016 | 0.1210 | 0.016 |
| Ever worked in job involving VCM exposure | | | -0.0697 | 0.122 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | 0.1420 | 0.144 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.9520 | 0.503 | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.1360 | 0.120 |

Table A4.20: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0396 | 0.020 | 0.0410 | 0.020 | 0.0396 | 0.020 | 0.0393 | 0.020 | 0.0392 | 0.020 |
| Ever worked in job involving VCM exposure | | | 0.2740 | 0.200 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | -0.0294 | 0.271 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.5082 | 0.509 | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.0384 | 0.195 |

Table A4.21: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0972 | 0.009 | 0.0921 | 0.009 | 0.0961 | 0.009 | 0.0968 | 0.009 | 0.0978 | 0.009 |
| Ever worked in job involving VCM exposure | | | -0.2793 | 0.126 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | 0.0416 | 0.014 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | 0.1221 | 0.123 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | -0.0033 | 0.017 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.1516 | 0.204 | | |
| Time worked in job involving TFE exposure (years) | | | | | | | 0.0161 | 0.042 | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.0476 | 0.109 |
| Time worked in job involving lead exposure (years) | | | | | | | | | -0.0060 | 0.012 |

Table A4.22: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1380 | 0.035 | 0.1362 | 0.035 | 0.1403 | 0.036 | 0.1355 | 0.035 | 0.1330 | 0.036 |
| Ever worked in job involving VCM exposure | | | 0.0146 | 0.387 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | -0.0366 | 0.052 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | -1.1360 | 1.013 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | 0.0689 | 0.102 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | NC | NC | | |
| Time worked in job involving TFE exposure (years) | | | | | | | NC | NC | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.2059 | 0.377 |
| Time worked in job involving lead exposure (years) | | | | | | | | | 0.0054 | 0.038 |

Table A4.23: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1230 | 0.016 | 0.1181 | 0.017 | 0.1207 | 0.017 | 0.1219 | 0.016 | 0.1187 | 0.017 |
| Ever worked in job involving VCM exposure | | | -0.3381 | 0.225 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | 0.0368 | 0.024 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | 0.0211 | 0.215 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | 0.0215 | 0.026 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | -0.9367 | 0.791 | | |
| Time worked in job involving TFE exposure (years) | | | | | | | -0.0041 | 0.172 | | |
| Ever worked in job involving lead exposure | | | | | | | | | 0.0033 | 0.199 |
| Time worked in job involving lead exposure (years) | | | | | | | | | 0.0179 | 0.021 |

Table A4.24: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|--------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0396 | 0.020 | 0.0322 | 0.022 | 0.0392 | 0.020 | 0.0408 | 0.020 | 0.0413 | 0.021 |
| Ever worked in job involving VCM exposure | | | -0.0330 | 0.318 | | | | | | |
| Time worked in job involving VCM exposure (years) | | | 0.0474 | 0.035 | | | | | | |
| Ever worked in job involving asbestos exposure | | | | | -0.0766 | 0.403 | | | | |
| Time worked in job involving asbestos exposure (years) | | | | | 0.0097 | 0.059 | | | | |
| Ever worked in job involving TFE exposure | | | | | | | | | NC | NC |
| Time worked in job involving TFE exposure (years) | | | | | | | | | NC | NC |
| Ever worked in job involving lead exposure | | | | | | | | | 0.1443 | 0.287 |
| Time worked in job involving lead exposure (years) | | | | | | | | | -0.0176 | 0.037 |

Table A4.25: Results of regression analysis by Cox Proportional Hazards modelling for all-cause mortality for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | | Model 6 | |
|----------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.0962 | 0.009 | 0.0956 | 0.009 | 0.0910 | 0.009 | 0.0910 | 0.009 | 0.0954 | 0.009 | 0.0933 | 0.009 |
| Smoking: Current smokers vs Non-smokers | 0.1940 | 0.134 | 0.1910 | 0.135 | 0.1430 | 0.136 | 0.1840 | 0.135 | 0.1870 | 0.136 | 0.1820 | 0.135 |
| Ex-smokers vs Non-smokers | -0.1430 | 0.086 | -0.1420 | 0.086 | -0.1110 | 0.086 | -0.1230 | 0.086 | -0.1400 | 0.086 | -0.1400 | 0.086 |
| Packyears (per 5000): Current smokers | 0.0422 | 0.058 | 0.0432 | 0.059 | 0.0254 | 0.058 | 0.0253 | 0.058 | 0.0429 | 0.058 | 0.0347 | 0.059 |
| Ex-smokers | 0.1355 | 0.080 | 0.1350 | 0.080 | 0.0890 | 0.080 | 0.1055 | 0.080 | 0.1355 | 0.080 | 0.1310 | 0.080 |
| Cumulative dust index (per 10 mg·m ⁻³ ·years) | | | 0.0115 | 0.050 | -0.0012 | 0.050 | 0.0004 | 0.051 | 0.0112 | 0.050 | 0.0094 | 0.050 |
| Observed FEV ₁ /Expected FEV ₁ | | | | | -0.0165 | 0.004 | | | | | | |
| Observed FVC/Expected FVC | | | | | | | | | | | | |
| Chronic Bronchitis | | | | | | | -0.0180 | 0.005 | 0.0261 | 0.106 | | |
| Breathlessness | | | | | | | | | | | 0.1560 | 0.075 |

Table A4.26: Results of regression analysis by Cox Proportional Hazards modelling for non-malignant respiratory disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | | Model 6 | |
|----------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1420 | 0.037 | 0.1405 | 0.038 | 0.1000 | 0.036 | 0.0962 | 0.034 | 0.1332 | 0.038 | 0.1310 | 0.038 |
| Smoking: Current smokers vs Non-smokers | 0.4510 | 0.554 | 0.4462 | 0.556 | -0.1145 | 0.572 | 0.1373 | 0.568 | 0.2714 | 0.566 | 0.4100 | 0.558 |
| Ex-smokers vs Non-smokers | -0.1910 | 0.364 | -0.1884 | 0.364 | -0.2987 | 0.399 | -0.0165 | 0.358 | -0.1720 | 0.364 | -0.1690 | 0.364 |
| Packyears (per 5000): Current smokers | 0.0765 | 0.176 | 0.0785 | 0.177 | 0.1065 | 0.168 | 0.1265 | 0.148 | 0.0830 | 0.169 | 0.0550 | 0.179 |
| Ex-smokers | 0.0353 | 0.374 | 0.0335 | 0.374 | -0.0685 | 0.410 | -0.1265 | 0.362 | 0.0580 | 0.372 | 0.0084 | 0.375 |
| Cumulative dust index (per 10 mg·m ⁻³ ·years) | | | 0.0212 | 0.165 | -0.0661 | 0.191 | -0.0339 | 0.180 | 0.0144 | 0.158 | 0.0078 | 0.166 |
| Observed FEV ₁ /Expected FEV ₁ | | | | | -0.1004 | 0.015 | | | | | | |
| Observed FVC/Expected FVC | | | | | | | | | | | | |
| Chronic Bronchitis | | | | | | | -0.0962 | 0.016 | 0.5945 | 0.267 | | |
| Breathlessness | | | | | | | | | | | 0.6050 | 0.251 |

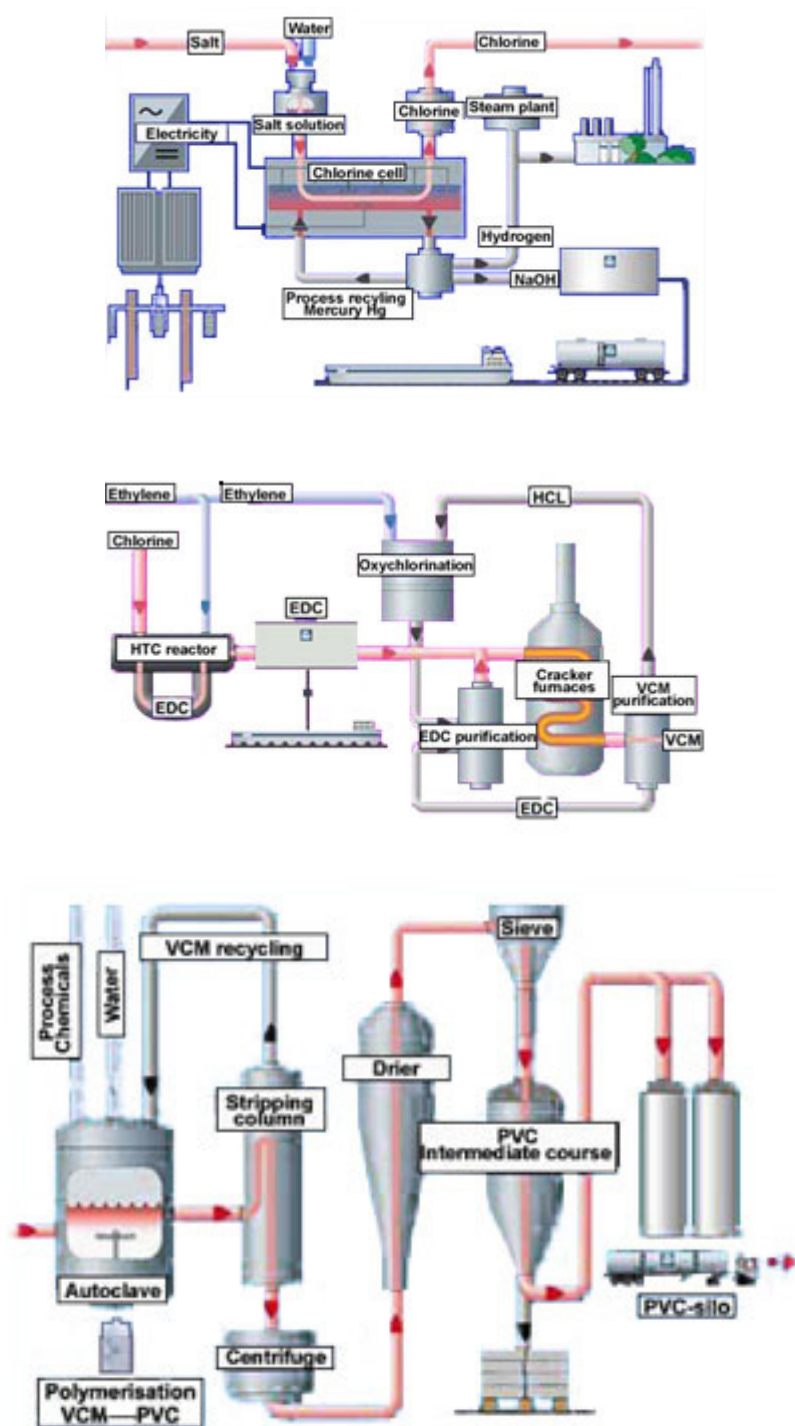
Table A4.27: Results of regression analysis by Cox Proportional Hazards modelling for ischaemic heart disease for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | | Model 6 | |
|----------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age (years) | 0.1247 | 0.017 | 0.1150 | 0.017 | 0.1126 | 0.017 | 0.1107 | 0.017 | 0.1154 | 0.017 | 0.1108 | 0.017 |
| Smoking: Current smokers vs Non-smokers | -0.0075 | 0.211 | -0.0568 | 0.213 | -0.0894 | 0.215 | -0.0746 | 0.213 | -0.0436 | 0.216 | -0.0803 | 0.215 |
| Ex-smokers vs Non-smokers | -0.3163 | 0.155 | -0.2966 | 0.155 | -0.2788 | 0.156 | -0.2783 | 0.156 | -0.2984 | 0.156 | -0.2942 | 0.155 |
| Packyears (per 5000): Current smokers | 0.0530 | 0.099 | 0.0730 | 0.099 | 0.0670 | 0.098 | 0.0635 | 0.098 | 0.0720 | 0.099 | 0.0575 | 0.100 |
| Ex-smokers | 0.2535 | 0.132 | 0.2425 | 0.132 | 0.2195 | 0.134 | 0.2200 | 0.134 | 0.2405 | 0.133 | 0.2405 | 0.132 |
| Cumulative dust index (per 10 mg.m ⁻³ .years) | | | 0.1573 | 0.075 | 0.1538 | 0.075 | 0.1540 | 0.075 | 0.1592 | 0.075 | 0.1589 | 0.074 |
| Observed FEV ₁ /Expected FEV ₁ | | | -0.0087 | 0.007 | | | | | | | | |
| Observed FVC/Expected FVC | | | | | | | -0.0144 | 0.008 | | | | |
| Chronic Bronchitis | | | | | | | | | -0.0735 | 0.194 | | |
| Breathlessness | | | | | | | | | | | 0.2895 | 0.124 |

Table A4.28: Results of regression analysis by Cox Proportional Hazards modelling for lung cancer for population 3. Table contains estimates of regression coefficients

| Terms in Cox model | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | | Model 6 | |
|----------------------------------------------------------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|---------|-------|
| | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE | Coeff | SE |
| Age | 0.0266 | 0.023 | 0.0302 | 0.024 | 0.0277 | 0.024 | 0.0294 | 0.024 | 0.0315 | 0.024 | 0.0310 | 0.024 |
| Smoking: Current smokers vs Non-smokers | 0.9244 | 0.532 | 0.9400 | 0.533 | 0.9310 | 0.534 | 0.9450 | 0.534 | 0.9607 | 0.534 | 0.9440 | 0.533 |
| Ex-smokers vs Non-smokers | -0.5245 | 0.360 | -0.5260 | 0.361 | -0.5020 | 0.363 | -0.5240 | 0.362 | -0.5310 | 0.362 | -0.5290 | 0.361 |
| Packyears (per 5000): Current smokers | 0.0520 | 0.162 | 0.0477 | 0.163 | 0.0263 | 0.164 | 0.0385 | 0.164 | 0.0590 | 0.165 | 0.0555 | 0.164 |
| Ex-smokers | 0.6360 | 0.208 | 0.6400 | 0.208 | 0.6050 | 0.212 | 0.6300 | 0.210 | 0.6365 | 0.209 | 0.6445 | 0.209 |
| Cumulative dust index (per 10 mg.m ⁻³ .years) | | | -0.0697 | 0.161 | -0.0797 | 0.162 | -0.0730 | 0.162 | -0.0699 | 0.162 | -0.0688 | 0.162 |
| Observed FEV ₁ /Expected FEV ₁ | | | | | -0.0113 | 0.012 | | | | | | |
| Observed FVC/Expected FVC | | | | | | | | | | | | |
| Chronic Bronchitis | | | | | | | -0.0053 | 0.014 | | | | |
| Breathlessness | | | | | | | | | -0.3130 | 0.372 | | |
| | | | | | | | | | | | -0.1030 | 0.236 |

APPENDIX 5 – DIAGRAM OF PVC PRODUCTION PROCESS TODAY



Applying science for a better working environment

The Institute of Occupational Medicine

The IOM is a major independent centre of scientific excellence in the fields of occupational and environmental health, hygiene and safety. We aim to provide quality research, consultancy and training to help to ensure that people's health is not damaged by conditions at work or in the environment. Our principal research disciplines are exposure assessment, epidemiology, toxicology, ergonomics and behavioural and social sciences, with a strong focus on multi-disciplinary approaches to problem solving.

Our beginnings

Our first major research programme began in the 1950s, on respiratory health problems in the coal mining industry. Major themes were quantification of airborne dust concentrations in different jobs, characterisation of types and constituents of the dusts, measurement of health effects, relationships between exposure and disease, and proposals for prevention. This research became an international benchmark for epidemiological studies of occupational health, and was the primary influence on dust standards in mines in the UK, US and other countries.

Current themes

Our current work spans many other industries including asbestos, MMMF, pesticides, chemicals, energy, telecoms, metals, textiles, construction, agriculture as well as the environment. While diseases of the respiratory tract remain a major interest, our scope now extends to many other health outcomes such as mortality, cardiovascular effects, cancer, back pain, upper-limb disorders, hearing loss, skin diseases, thermal stress and psychological stress. Related work includes the development and application of measurement and control systems, mathematical models and survey methods.

Who we work for

Our work in these areas is conducted for a wide range of organisations in the UK, the EU, and the US, including Government departments, international agencies, industry associations, local authorities, charitable organisations, and industrial and commercial companies. The IOM is a World Health Organisation (WHO) collaborating centre and is an approved institute of the Universities of Edinburgh and Aberdeen, enjoying collaborative research links with NIOSH, IARC, and many other institutes throughout the world.

Publication

We believe that our research findings should be publicly available and subject to the scrutiny of the international scientific community. We publish our findings in the peer reviewed scientific literature and through our own series of Research Reports.

Contact

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