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## **Pneumoconiosis in coalminers and exposure to dust of variable quartz content**

Miller BG, Kinnear AG



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PNEUMOCONIOSIS IN  
COALMINERS AND  
EXPOSURE TO DUST  
OF VARIABLE QUARTZ  
CONTENT

BG Miller  
AG Kinnear

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INSTITUTE OF OCCUPATIONAL MEDICINE

PNEUMOCONIOSIS IN COALMINERS AND EXPOSURE TO DUST  
OF VARIABLE QUARTZ CONTENT

by

BG Miller, AG Kinnear

FINAL REPORT ON CEC RESEARCH CONTRACT 7260-04/025/08

Duration of project: December 1985 - May 1988

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INSTITUTE OF OCCUPATIONAL MEDICINE

Final Report on CEC Contract 7260-04/025/08

PNEUMOCONIOSIS IN COALMINERS AND EXPOSURE TO DUST  
OF VARIABLE QUARTZ CONTENT

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SUMMARY

In the course of the British National Coal Board's Pneumoconiosis Field Research programme, medical officers examining chest radiographs taken in 1978 from workers at a colliery in Midlothian considered that a small number showed unusually rapid progression of pneumoconiotic abnormalities. A case-control study based on these radiographs suggested an association with workplace exposure to dusts containing higher proportions of quartz than had previously been seen in the research, and further investigations were initiated.

This report describes the design and execution of a study in which existing radiographs for men at this colliery were subjected to intensive re-examination, with the objective of relating any evidence of radiographic abnormalities to data already held on the individual men's exposures to respirable airborne dust in the coalmine, and on lung function and smoking habits.

All available radiographs from over 1400 men employed at that colliery who had attended any of the medical research surveys in 1970, 1974 and 1978 were collected; these were classified for pneumoconiotic abnormalities according to the ILO (1980) scheme, by an experienced panel of non-medical readers reading each radiograph independently and in randomised order, on two separate occasions. On the second occasion, the reading included radiographs which had been collected from the same men during a survey by the NCB's Medical Service in 1980. In an additional reading, two medically qualified readers experienced in the radiology of pneumoconiosis viewed series of radiographs from a sample of the men, and classified the films within those series for progression of disease over time.

Analyses of the data from these classifications, using the statistical techniques of logistic regression, confirmed that appearances of small pneumoconiotic shadows of profusion at least 1/0 on the ILO (1980) scale were associated most strongly with the

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estimates of individuals' exposures to respirable coalmine dusts from before the 1970 to after the 1974 surveys, and particularly with estimates of exposures to the quartz components of these dusts. This pattern of results was apparent in the differences between radiographs from different men taken at the same survey, and also in the changes within the lungs of individual men revealed by examination of individuals' radiographs in their temporal sequence. There was no evidence that the men's smoking habits were an important modifying factor in this association.

Lung function variables measured at the surveys were analysed using linear regression techniques to adjust for age and smoking habits as necessary. These analyses suggested that a slightly higher rate of loss of lung function between 1974 and 1978 was experienced by men with higher exposures to the non-quartz fraction of the dust. Changes in lung function observed between the 1970 and 1974 data did not, however, show such an association. Cross-sectional analyses comparing different men's lung function at the same survey suggested an association between higher exposures and higher lung function. This was interpreted as probably due to a selection effect in the population studied. There was no evidence of a relationship between apparently dust-related lung function effects and the radiographic abnormalities ascribed to quartz exposures in the same men.

The need is identified for a follow-up study to investigate progression and any new incidence of pneumoconiosis in these men since their last survey appearances, taking account of whether they continued in coalmining employment after this colliery closed in 1982.



## 1. INTRODUCTION

### 1.1 Background

The recognition of silicosis as a lung disease of workers exposed to dusts containing high proportions of quartz predated any recognition of coalworkers' pneumoconiosis as a separate disease entity, and indeed when symptoms similar to those of silicosis were first documented in coalworkers, it was presumed that these were due to quartz in the coalmining environment, an impression which appeared to be confirmed by the similarities displayed by radiography when this technique became available (Seaton, 1983).

The principal evidence for a distinction between the two diseases was obtained by a series of studies carried out by the Medical Research Council (MRC) in mining communities in South Wales, stimulated by concern over an apparent epidemic of lung disease in that region's coalminers. These studies demonstrated that the disease was found in men exposed to dust containing little or no quartz (Medical Research Council, 1942, 1943), and Gough (1940) described the disease in coal trimmers at docks in South Wales whose exposure was to virtually pure coal dust. Coalminers' pneumoconiosis was prescribed as an occupational disease eligible for compensation in 1943.

The MRC's surveys continued. Following nationalisation of the coal industry in 1947, the first British dust standards for coalmines were introduced by the National Coal Board (1949), but these were based on little hard quantitative evidence. To obtain such evidence, the NCB began the Pneumoconiosis Field Research (PFR), a longitudinal study involving five-yearly examinations of coalminers in collieries selected to cover the range of types of coal and mining conditions in the British coalfields. The stated aim (Fay, 1957) was "to establish what environmental conditions should be maintained if mineworkers are not to be disabled by the dust they breathe". Since 1969, this research has been organised and carried out by the Institute of Occupational Medicine.

Hurley *et al* (1982) reported on the principal findings on pneumoconiosis and dust exposure, from data from surveys up to the fifth round of PFR surveys. These confirmed unambiguously the correlation between quantitative estimates of coalmine dust exposure and simple pneumoconiosis which had been identified from earlier analyses, and refined the risk estimates. Important unexplained differences in risks remained between some of the collieries, and were not explicable in terms of differences between the collieries in the levels of quartz in the coalmine dusts; these levels were generally low (average 5%). However, a case-control study of men with unusually rapid progression of pneumoconiosis (Jacobsen and MacLaren, 1982) suggested that higher quartz exposures were associated with a more aggressive form of the disease, and perhaps influenced the risks of developing Progressive Massive Fibrosis (PMF). Further important quantification of pneumoconiotic risks, particularly for the development of PMF, was reported by MacLaren and Soutar (1985).

## 1.2 Quartz and Pneumoconiosis at one Scottish Colliery

Colliery P was the one Scottish colliery at which more than three PFR surveys took place. It received a total of six PFR surveys between 1954 and 1978. A sample of ex-miners from the cohort defined by attendance at the first survey received a follow-up examination at the same time as the PFR survey team were conducting the 5th routine survey, in 1974.

The prevalence of pneumoconiosis at colliery P since the research started was low, and this reflected the Scottish experience generally. However, the medical officer who read and classified the radiographs taken at the 6th PFR survey in 1978 considered that 21 radiographs from the 623 taken showed progression of simple pneumoconiosis when compared with radiographs taken four years previously from the same men at the 5th PFR survey.

This observation spurred a case-control study (Seaton *et al*, 1981), which took as cases the 21 men from whom these radiographs had been taken, and 21 age-matched controls selected from the men who attended the 5th and 6th surveys at the same colliery, and whose radiographs had been classified as showing no pneumoconiosis. A second reader examined the radiographs without knowledge of their status as cases or controls, and classified progression in 18 of the 21 cases and in none of the controls, confirming the pattern of the original readings. Comparison of the estimates of exposure for cases and controls in the period between the 5th and 6th surveys showed significantly higher values on average among the cases for the respirable mixed-dust exposure, quartz exposure, and highest for percentage quartz in dust, which averaged 13.0 for the controls. Similar patterns of difference were apparent in the estimates of the men's lifetime exposures to dust and quartz.

The authors reported that quartz levels in this period were higher than had previously been typical, because adverse geological conditions in one seam had led to excursions of the powerful coal-getting machinery into siliceous rock in the roof and floor of that seam, leading to the creation of free silica dust amongst the coal. They concluded that this unusually high release of quartz had been responsible for the unusually rapid pneumoconiotic response of miners exposed to dust levels which, in normal circumstances, would have been expected to carry a low risk for the development of pneumoconiosis.

It was considered desirable to investigate further, and accordingly a project was designed in which it was proposed to make an extensive study of all the radiographs taken from men working at this colliery in the 1970's, and to collate these classifications with the detailed data already available on the environmental conditions in which these men had worked, along with the questionnaire and measured data from the medical surveys. This report describes the planning, execution and analysis of that project, and the conclusions which were drawn.

## 2. OBJECTIVES OF THE PROJECT

The principal objectives to which the design and execution of this project were addressed were as follows:

1. *To make an intensive study of recent chest radiographs from men working at one coalmine in Scotland, classifying systematically any pneumoconiotic abnormalities observed;*
2. *To examine the relationships between estimates of exposures to respirable coalmine dust and its constituent components, particularly quartz, and the presence of radiographic abnormalities;*
3. *To examine relationships between estimated exposures and the progression of abnormalities over time;*
4. *To examine the relationships between estimates of exposures and measurements of lung function taken at the same surveys as the radiographs;*
5. *To examine relationships between the radiographic appearances and the measurements of lung function.*



### 3. METHODS

#### 3.1 Definition of Study Population by Availability of Radiographs

It was desired to include in the study men who had attended the 4th, 5th and 6th PFR surveys, which took place in 1970, 1974 and 1978 respectively. Interrogation of computer files and tabulation of the men surveyed by their patterns of attendance at combinations of the three surveys yielded the numbers in Table 3.1. A total of 1416 men were recorded as having attended at least one of the surveys; 401 men had attended all three, 392 had attended two, and 623 had appeared at only one of the three surveys. The target population for the present study was defined as consisting of these 1416 men, and the planning of the exercise to reread their radiographs was based on the total of 2610 radiographs.

The chest radiographs from the PFR are stored in envelopes each of which contains the whole series of radiographs from a man's survey attendances. On extraction of the envelopes required, two extra radiographs were discovered whose existence had not been apparent from the computer records, bringing the number designated for inclusion in the study to 2612, as shown in Table 3.1. The identities of 47 radiographs not found were noted, and the planning of the reading exercises proceeded, with provision for their inclusion should they be found before the completion of the exercise.

##### 3.1.1 Assessments of Radiographs by the IOM Panel of Readers

The 2612 radiographs for this study were allocated at random to 13 nearly equal-sized batches, subject to the constraint that all radiographs from the same man were allocated to the same batch. Men were stratified according to whether they had one, two or three radiographs for inclusion, and these strata were spread approximately equally across the batches. Men for whom some or all of the radiographs had not been found were placed in the last batch, to maximise the chance of their discovery before the reading was due to take place. Recording forms for the sessions were printed by computer from the batch lists.

The 13 batches were read twice, in the same order, by a panel of five readers with paramedical backgrounds but without medical qualifications, who have been self-trained (Copland *et al*, 1981) to record their assessments of chest radiographs according to the conventions of the ILO (1980) Scheme for the systematic classification of pneumoconiotic appearances.

Only 18 radiographs remained missing by the first reading of batch 13. Between the first and second readings of the 13 batches, 69 of the radiographs were unavoidably removed for the purposes of an entirely different project, and they were not made available in time for the second reading. In total, over both readings, 72 radiographs were read only once, and 2525 were each read twice.

A routine Medical Service survey took place at Colliery P in 1980. Radiographs from this survey were obtained for 447 of the study members. These were mixed with radiographs which had been only read once in the panel's duplicate reading exercise, and organised into five batches of 590 radiographs in all. The panel read these batches once.

### 3.1.2 Assessments of Progression in Series of Radiographs

Three chest physicians with experience of the radiographic appearances of pneumoconiosis agreed to assess progression of pneumoconiosis over this period by viewing, side-by-side, the series of radiographs taken at different surveys from the same man. Series were collected for all men for whom more than one radiograph had been found, provided that at least one radiograph was from the 1978 or 1980 survey. Suitable series existed for 632 men, comprising in all 2035 radiographs, and their distributions by different combinations of surveys are shown in Table 3.2. The series were allocated randomly to 18 batches of about 113 radiographs, and recording forms were produced by computer from the batch lists.

A short form of the ILO (1980) Classification scheme was used. Only radiograph quality, small and large pneumoconiotic abnormalities, and optional comments were recorded, according to an explicit protocol supplied to the readers; the sections of the Classification dealing with pleural and other abnormalities were omitted.

It was intended that each of the three readers should make appointments, as convenient to them, to read batches of radiographs allocated by an adaptation of a balanced incomplete blocks design (Cochran and Cox, 1957). However, one of the three readers was prevented, by pressure of other work, from being able to read these radiographs. The intended allocation was abandoned; ten batches were read by the first reader alone, four by the second reader, and the remaining four were read by both to give a comparison of their reading levels.

### 3.1.3 Organising Radiological Data

Data from all four reading exercises described above were first punched directly into computer files. They were then loaded into a database designed specially for the needs of this project, using the facilities of the computer database management system SIR (Robinson *et al.*, 1980). All data were checked on entry for validity and consistency, and corrected as necessary.

## 3.2 Collation of Existing Data

While the reading exercises, and the reinterpretations of existing radiographs which were at their heart, generated new data for this study, the remainder of the required data already existed, in the computer records of the PFR. In the following sections, the key elements of these data, their extraction and reorganisation are described.

### 3.2.1 Personal Data

In the PFR, each participant coalworker was identified by a code which combined a letter identifying the colliery with a four-digit number allocated sequentially within each colliery, and all data on the men in this study were identified and indexed by their PFR code number as they were loaded into the project database.

Name, National Insurance number and date of birth were extracted from existing files for each man. Dates of birth recorded in different files were often recorded on different occasions, and multiple versions of these were cross-checked for consistency. In the few cases of discrepancy, the date which appeared on the majority of records was taken.

### 3.2.2 Data from Medical Surveys

At each PFR survey, a full-sized postero-anterior chest radiograph was taken. From the second survey onwards, additional data were also collected from the participants. Height and weight were measured, and a questionnaire on smoking habits and respiratory symptoms was administered by trained personnel (Rae *et al.*, 1971). Lung function measurements were taken using a modified Gaensler spirometer; forced expired volume in one second (FEV) and forced vital capacity (FVC) were recorded, the subject making three forced expirations after a practice blow (Rogan *et al.*, 1973). Questionnaire data on smoking habits, and data on lung function, were extracted for the men in the study from the records of the 4th, 5th and 6th PFR surveys, and incorporated into the project database.

There was one feature of the 5th survey lung function data already known to be unusual. Normally, all lung function measurements were carried out by one experienced technician, but at the 5th survey at this colliery a recently employed, inexperienced technician took most of the measurements, while an experienced technician took about 120 measurements to allow comparisons of performance in the field. Investigation of these data suggested strongly that the inexperienced technician was recording results at a slightly lower level than the experienced one. In order that this could be allowed for if desired, an indicator was placed on file with the 5th survey lung function data to show which technician had recorded them. No other survey was affected.

### 3.2.3 Data on Occupational Exposures

Throughout the PFR, differences in exposures experienced by the coalworkers studied have been characterised by cumulating the products of time worked in occupations and concentrations of respirable dust typical of those occupations over the periods of a man's employment in coalmining (Hurley *et al.*, 1979; 1982). By calculating concentrations of constituent fractions of the dust, notably ash and quartz (Dodgson and Whittaker, 1973), it has been possible similarly to calculate estimates of cumulative exposures to these constituents.

For this study, it was decided to retain separately the exposure data from inter-survey periods ISP 3 (between 3rd and 4th surveys), ISP 4 (between 4th and 5th), and ISP 5 (between 5th and 6th), and to form a cumulative total of any exposure from ISP 0, ISP 1 and ISP 2, that is up to the 3rd survey. All the relevant exposure data were extracted from computer files and loaded to the database. From ISP 3 onwards, a distinction was maintained between "measured" exposures, based on information on the men's activities obtained from the colliery payroll systems, and "unmeasured" exposures based on interview data on activities not captured by that system, and the measured and unmeasured components were stored separately. Exposure data were available for ISP 5 by individual quarter years, and this level of detail was retained in the database.

Addition of all the relevant exposure data to the project database marked the completion of data collation and reorganisation.

### 3.3 Statistical Methods

Tabulations and summaries of the data were carried out in many cases directly from the database, using the facilities provided within the database management system SIR (Robinson *et al*, 1980). Where this was not possible, the facilities of the statistical package GENSTAT (Alvey *et al*, 1977) were employed. This package was also used for the more complicated analyses involving the fitting of linear regression (Draper and Smith, 1981) and logistic regression models (Cox, 1970). Fitting of the logistic models was by the method of maximum likelihood, and tests of significance were based on deviances (Nelder and Wedderburn, 1972).

## 4. RESULTS

The presentation of results in this chapter begins with a description of the data which already existed in the computer records of the PFR, and which were brought together for the purposes of the current project. Subsequent sections describe the data generated by the exercises in which the chest radiographs were reread, and the results of statistical analyses involving these newly acquired data, and of lung function data from the same men. Much of the technical detail of the analyses, which underlies the inferences reported in this chapter, is presented in Appendices 1 to 3.

### 4.1 Distributions of Existing Data in Study Population

#### 4.1.1 Age and Smoking Habits

Table 4.1 summarises the distributions of age and smoking habits for the men attending each of the 4th, 5th and 6th PFR surveys at colliery P (including a few for whom radiographs were not found). Age was calculated arbitrarily as on the first day of the months in which most of each survey took place; these were December 1970, October 1974, and November 1978. The data on smoking habits utilised in this table are those collected at the survey in question; thus a man who appeared at different surveys and replied differently to the questions on smoking, for example if he had stopped smoking since the previous survey, will contribute to different smoking groups at the different surveys. Within each survey, however, the breakdown is exhaustive and mutually exclusive. From both the 4th and 5th surveys, there were a few men for whom data from questionnaire and other medical data were not found, but for the 6th survey there were 46 men with no such data. These corresponded to a batch of questionnaires which is believed to have been lost due to a clerical error before their data were entered to the computer.

Table 4.1 clearly shows the contraction of the workforce over the period; the number at the 6th survey is around half that at the 4th. In general, the reduction in numbers over the period was relatively greater in the older men, as would be expected in a time of contraction.

The data record that 14 men over 65 attended at the 5th survey; this survey combined routine PFR examinations of current employees with follow-up surveys of men who had left the industry, and we included data from follow-up examinations in this study, but only where the men concerned had previously attended routinely at the 4th survey. The oldest ex-worker attending the 5th survey was 68.

The current smokers constituted nearly 75% of those at the 4th survey. The corresponding figure at 6th survey was 64%; this change is consistent with the increased proportion of young non-smokers generally, but in this data set appears to be more clearly associated with a preferential loss, over the intervening years, amongst the oldest smokers. At all surveys, the proportion of non-smokers was considerably lower among the younger men than among the older.

#### 4.1.2 Distributions of Height and Weight

Data on the heights and weights of those attending the surveys are summarised in Table 4.2. These data are generally unremarkable, the only trend being towards a slight increase with time in average height. This is consistent with the lower proportions at the later survey of older workers.

#### 4.1.3 Distributions of Lung Function Variables

Data available on the lung function measurements taken at the surveys are summarised in Table 4.3. All men with at least one satisfactory measurement are included in the tabulation of each variable from each survey. The mean of between one and (usually) three values was calculated for each man, and the tabulated values are unweighted means of these means.

At each survey, the highest values for both FEV and FVC are amongst nonsmokers, with little difference between the ex- and current smokers. This observation is consistent both with the higher proportion of younger workers among the non-smokers, and with the known capacity of exposure to tobacco smoking to induce loss of lung function.

Table 4.3 shows an apparently transitory decline in the mean values at the 5th survey. This is most evident in the mean FVCs, and is believed to be an artefact of measurement due to the inexperience of the technician who performed most of the 5th survey lung function measurements; see 3.2.2 above. Such an artefact would have a potentially serious effect on any inferences from observed patterns of change in lung function between surveys.

#### 4.1.4 Distributions of Dust Exposure Variables

Table 4.4 summarises the data on the total working times recorded for each man in the periods up to the 3rd survey, and between the 3rd, 4th, 5th and 6th surveys thereafter; also summarised are the estimates derived from these times of individuals' exposures to respirable coalmine dust, and to the proportion of that dust measured as quartz.

By definition of the study population, most of the data on times worked from 1970 onwards were measured, that is taken from the payroll systems and supplemented by more detailed records of precisely where the men had worked, which were provided by full-time research staff stationed at the colliery. There were a few men who attended the 5th survey as ex-miners, and these would have had a work history questionnaire applied. There were larger numbers of men with some unmeasured time in ISP 3, between 1964 and 1970; during this period, transfers from the closures of other collieries were taking place, and these data are likely to concern time at other collieries, or time for which data had been lost and was later recovered by interview. During ISP 5, when the colliery population was declining, almost all the men's time was accounted for direct from the payroll, and the number of men with any computer record of unmeasured time relating to dusty work was negligible; these data were omitted from consideration.

The last column displays the number of men for whom a non-zero time was recorded in the measured and unmeasured categories in the different periods. The great majority of men had recorded exposures in ISPs 3 and 4, and fewer had

times in ISP 5, as expected from knowledge of the workforce contractions. Consideration of the numbers of non-zero values for the measured, unmeasured and total times shows that while 1220 men had non-zero measured times in ISP 3, inclusion of unmeasured times produced non-zero values for only another 36 men. In ISP 4 only 9 more men had non-zero values on inclusion of the unmeasured time. In general, then, the unmeasured times for ISPs 3 and 4 served to fill in sporadic periods of unrecorded times for a small proportion of the men.

The second and third sections of Table 4.4 contain similar summaries of the estimated exposures to the quartz and non-quartz fractions of the respirable dust. Since these exposures are calculated from the times recorded in the various occupational groups, they show the same numbers of non-zero values, with the exception of ISP 4 measured (and total) quartz exposures which are one less; here, one man had time allotted to an occupational group with a low dust concentration and a zero recorded proportion of quartz.

The footnote to Table 4.4 shows that the values for ISP 3 are based on only 1415 men. Initial data summaries showed that the whole (quartz + non-quartz) dust exposure for one man was around  $110 \text{ g.hr.m}^{-3}$ , more than twice the next highest value. Investigation of the individual recorded times from which this value had been cumulated revealed an impossibly large total number of recorded shifts over all the occupational groups. It was concluded that the ISP 3 figures were unreliable for this man, and they were excluded from analyses using the ISP 3 exposures.

It is not possible to discern from Table 4.4 whether those who had the highest exposures to dust also had the highest quartz exposures. In fact, the compositional data showed a considerable degree of variation in the proportions of quartz in the dust exposures of different men at different periods. These are summarised in Table 4.5. For each man in each period, and retaining the distinction between measured and unmeasured time in ISPs 3 and 4, the cumulated quartz exposure was expressed as a percentage of the cumulated whole dust exposure; and the table shows the minimum, arithmetic mean, and maximum of these percentages. (Since the concept of a percentage is only defined for a positive denominator, values corresponding to zero exposures are undefined, and the means in Table 4.5 were calculated only over the defined values, whose numbers are shown in the table. This contrasts with the tabulations in Table 4.4, where zero exposures were included in the calculation of means.)

Taken together, the data in Tables 4.4 and 4.5 clearly show the reduction of both mean and maximum dust exposures over ISPs 3, 4 and 5, coinciding with the dramatic increase in the proportion of quartz in the dust, reaching a maximum of around 30% in ISPs 4 and 5.

#### 4.2 Summary of Data from the IOM Panel's Assessment of Radiographs

In this section are summarised the assessments made by the IOM reading panel. All the readings were of individual radiographs assessed independently in random order, and classified according to the ILO (1980) classification scheme. The five readers of the panel are identified throughout by the code numbers 101, 104, 105, 106, 112, by which their identities are routinely coded and distinguished on the IOM computer.

Data presented in this section are from the three independent randomised radiograph reading exercises described in 3.1. These were the large readings of all available radiographs from surveys 4, 5 and 6, (coded XRLV and XRVL) and the third, smaller, exercise to include radiographs missed from either of these, plus the radiographs from the 1980 PXR survey of the NCB Medical Service (coded XREX).

#### 4.2.1 Radiograph Quality

In their assessments of the technical quality of the radiographs they examined, readers 101 and 106 classified none as less than acceptable. Readers 105 and 112 scored the radiograph as "poor" on 97 (1.7%) and 31 (0.6%) occasions respectively. None of the readers considered any radiographs "unreadable", except for 104 on 8 occasions; this reader only classified one radiograph "poor". Comparing readers pairwise, exact agreement on quality score was reached on around 80% of occasions.

#### 4.2.2 Profusion of Small Opacities

Table 4.6 shows the frequencies with which each of the readers assigned the 12 levels of profusion of small opacities to the radiographs they considered readable. The three reading exercises are shown separately, so that each radiograph makes at most a single contribution to each reader's assessments for each exercise, though the exercises had many radiographs in common.

The overall distributions of profusion are typical of those seen throughout the PFR and much other research in cross-sectional studies of employed populations. The majority of radiographs show little or no signs of abnormality, and the numbers showing progressively higher profusion categories decrease progressively; the distributions are heavily skewed, with long right tails. The distributions show another feature, often called the "middling tendency"; that is, the tendency for assessments of profusion with the same category on the 4-point scale to concentrate in the corresponding central category on the 12- (or 11-)point scale. For example, in exercise XRLV, the five readers made a total of 3556 allocations of radiographs to category 1, but these were not split even approximately equally to the three categories 1/0, 1/1, 1/2. Category 1/1 accounted for 1921 of these, well over a half. The same phenomenon can be observed elsewhere in the tables, nor is it concentrated in the assessments of any one reader. This tendency is interpreted as a consequence of the definition of the 12 categories as an elaboration of the older 4-point scale. Both personality and experience may be important in determining the relative frequencies of any reader's usage of the central and side categories of the elaborated scale.

The Table shows obvious differences between the readers in the relative frequencies with which they assign radiographs to the categories representing higher degrees of abnormalities. For example, in exercise XRLV, reader 106 made 2594 assessments, and 2478 of these, that is over 95%, were in categories 0/0 and 0/1; of the same number, reader 105 allocated 1389, or 54%, to these lowest categories, and reader 101 allocated 1453 or 56%. Similar differences in reading patterns are seen in the other two exercises.

More detailed comparisons, of different readers' opinions of the same radiographs, and of the same reader's classifications of the same radiographs on two separate occasions, may be found in Appendix 1. The conclusions drawn from them were

that within-reader agreement was much better than between-reader; but that readers had a strong tendency to agree on the presence of advanced simple pneumoconiosis, even although they did not agree on the exact category of profusion.

#### 4.2.3 Shape and Size of Small Opacities

Table 4.7 summarises, for the radiographs in reading exercise XRLV, how each of the five readers used the codes in the ILO (1980) classification scheme for the types of small opacities seen, described as p,q,r (representing increasing sizes of rounded opacities), s,t,u (representing increasing sizes of irregular opacities). Under the ILO (1980) scheme, whenever small opacities are recorded, one of these alphabetic codes is used to describe the shape and size of the type of opacities observed to be most abundant; a second different letter is added to represent the next most common type (or, if there is only one type, the same letter is repeated). The 36 possible combinations have been condensed in this table by grouping together those letters describing the same general shape of opacities, regardless of their size, so that the opacities described are classified variously as all rounded, rounded with some irregular, irregular with some rounded, and all irregular.

It is clear from the Table that, even allowing for the differences across readers observed above in the proportions of radiographs classified as showing small opacities, the proportional allocations of the radiographs to the four shape categories differed enormously. Of 1920 radiographs classified by reader 101 as showing small opacities, 1620 (84%) were classified as being all round; whereas of 1510 radiographs classified by reader 112 as showing small opacities, only 9 (0.6%) were classified as all round.

#### 4.2.4 Category of Large Opacities

Table 4.8 shows the distribution of the assessments made by each reader of the presence and category of large opacities on each radiograph during reading exercise XRLV. Each reader except 101 made a few classifications of opacities of category A (approximate (sum of) maximum diameter(s) between 10 mm and 50 mm), and each reader except 105 made a very few classifications of category B (...between 50 mm and the area of the right upper zone of the lung). There were no classifications of category C.

While the fraction of radiographs on which large opacities were recorded as present was small overall, these could still be significant if a majority of the readers were agreeing on their presence in a small number of cases. Of the 58 cases in which the presence of large opacities (A or B) was recorded on a radiograph 33 were from radiographs for which only one reader made such a recording, and five radiographs were classified as showing large opacities by two readers. Classifications of large opacities were made by three, four and all five readers on 2, 1 and 1 radiographs respectively. Consensus on large opacities in this exercise is thus seen to have been low.

Similarly poor consensus on the presence of large opacities was apparent in these readers' results from the duplicate and supplementary reading exercises XRVL and XREX.

### 4.3 Logistic Regression Analyses of Small Opacities Profusion

Regression analyses were used to investigate the relationships between the panel's assessments of the small opacities profusions and the data on individuals' exposures to respirable coalmine dust and quartz, with due allowance for other factors such as age and possibly smoking habits. This section describes how the analyses were performed and presents the results.

Because of the poor consensus between readers on assessments of shape and size of small opacities and presence of large opacities, it was judged that regression analyses of these variables would not be informative, and they are not considered further here.

#### 4.3.1 Definition of Response Variable for Analysis

Most of the radiographs from the 4th, 5th and 6th surveys had been read twice by five readers; in addition, these readers had all read the available 1980 radiographs once. The profusions from these assessments were summarised for analysis by the calculation, from the available assessments for each radiograph, of a median profusion on the 12-point scale. The median was considered undefined, and not analysed, for any radiograph for which fewer than five readings were available. Medians for the 1980 radiographs were therefore based on five readings, while the rest were based on ten, except in the rare cases where a radiograph was judged unreadable.

Because the medians for the 1980 radiographs were based only on the five assessments from the last reading exercise, there was thus a systematic difference in the way that these radiographs were treated. Changes over time in readers' habits, for example in the levels at which they recorded profusions, could obviously have had a systematic effect on the assessments of radiographs which would reduce the comparability of data across surveys. The data demonstrated clearly that any such systematic shift was small in comparison to the substantial differences between the readers; see, for example, Table 4.6. Any possible influence of such a shift was minimised by performing separate analyses for radiographs from different surveys.

Table 4.9 describes the distribution of the calculated median categories of profusion for the radiographs from each survey. This table shows that no radiograph had a median profusion greater than 2/3; also that the "middling tendency" shown in Table 4.6 and discussed in 4.2.3 was much less evident in the summarised data.

Comparisons between the columns of Table 4.9 are not easy to make, because the values differ greatly between rows and because the column totals are different. In Table 4.10 the numbers are re-expressed as percentages of the column totals. This Table presents the impression of the amount of pneumoconiotic abnormalities in the population decreasing over the first three surveys, which runs against intuition. However, this comparison is between different sub-populations which are not necessary directly comparable in structure. The patterns in Table 4.10 are consistent with preferential loss of older workers, which is in turn consistent with the descriptions of the age distributions observed at the three PFR surveys, as shown in Table 4.1.

Because the ILO (1980) profusion scale is ordered but not fully quantified, the principal analyses were performed on a binary variable formed by dichotomising the median variable between two major categories of profusion. Separate analyses were

performed, by logistic regression methods, on binary variables split between categories 0 and 1, and between categories 1 and 2, although the low numbers showing disease sufficiently extreme to attract a median classification of 2/1 or greater meant that the latter analyses had low statistical power.

#### 4.3.2 Summary of Results of Logistic Regression Analyses

In this section is presented a summary and overview of the results of analysing the panel's assessments of the radiographs from the four surveys. In the course of the investigations, a great many regression models were fitted, and the results from these necessarily underlie and inform the interpretations presented here. Detailed tabulations of these results, with commentary, form the bulk of Appendix 1.

Separate analyses were performed of the assessments of radiographs taken at different surveys. All analyses showed a highly significant relationship between the frequency of recordings of opacities at least 1/0 on the ILO (1980) 12-point scale, and the age of the individuals at survey. Taken over all the surveys, the increase in the log-odds per year of age was relatively constant at around 0.06 to 0.09. Age was included in all the regression models, before any of the exposure variables was added.

The exposure variables considered as potential predictors of the probability of a radiograph being classified as abnormal had been calculated to represent time-weighted total concentrations of respirable quartz, and of the respirable non-quartz fraction of the dusts, for each man in each inter-survey period. Exposures up to the 3rd PFR survey were totalled, while those for ISPs 3, 4 and 5 were retained separately.

After allowance for age, the frequency at 4th survey of opacities of categories 1/0+ was found to increase significantly with increasing estimates of non-quartz dust exposure prior to 3rd survey. Association with quartz exposure over the same period was also significant, but less strongly. Frequency of opacities 2/1+ was much lower, and did not show any significant relationship with exposures either prior to 3rd survey or in ISP 3.

At 5th survey, frequency of small opacities 1/0+ showed significant associations with ISP 3 and ISP 4 exposures to both dust and quartz, but not with the previous exposures. The effect was considerably stronger with the ISP 4 exposures than with the ISP 3, and was a little stronger with quartz than with dust from both periods. Fitting combinations of variables suggested that once ISP 4 quartz was allowed for, no other exposure variable showed an association. Similar results were obtained from the analyses of opacities 2/1+, although the significance levels were rather lower in these analyses.

Frequency of small opacities at the 6th survey showed no associations with previous exposures, but significant relationships with ISP 3, 4 and 5 dust and quartz. Once again, ISP 4 exposures were most strongly associated, followed by ISP 3 and then ISP 5. At each survey, the association was stronger with the quartz than with the dust exposure. After allowance for ISP 4 quartz, no other variable appeared to be significantly associated. Here, analyses of opacities 2/1+ showed similar results.

With the radiographs taken at the 1980 Medical Service survey, the frequency of small opacities 1/0+ showed similar associations, but in this case the strongest was with ISP 3 quartz; again, the association in any ISP was stronger with quartz than

with dust. Opacities 2/1+ showed similar results, although here the ISP 4 exposures showed stronger associations than ISP 3, and dust in ISP 5 showed a stronger association than the quartz.

Additional analyses including variables to distinguish smokers and ex-smokers from lifelong non-smokers showed evidence of an effect of smoking on small opacities 1/0+ at 5th survey, but not at the other surveys. However, none of the conclusions regarding associations with dust and quartz exposures was altered by the inclusion of smoking habits, which had negligible effect on the magnitudes of the estimated coefficients. The estimates were likewise little affected by the inclusion of non-linear terms in age.

The conclusion that the frequencies with which the five readers recorded small opacities 1/0+ were associated more strongly with exposure to quartz than to dust was consistent over all the surveys, and was strengthened by the observation that, when both dust and quartz from the same ISP were in the model, the quartz exposure made a significant contribution after adjustment for the dust, but the reverse was not the case.

Consistency was also observed in the magnitudes of the coefficients of the exposures both between and within surveys; from the analyses at 6th survey, the coefficients for the increase in log-odds per  $\text{g.hr.m}^{-3}$  of dust exposure in ISPs 3, 4 and 5 were 0.363, 0.431 and 0.425; while for the 1980 survey the corresponding estimates were 0.384, 0.375 and 0.360. At each of these surveys, however, inclusion of more than one quartz variable did not improve model fit over inclusion of the most strongly associated single variable.

The possibility was considered that these variables all represented the same information about individuals' exposures, a situation which could arise if the same men worked in the same conditions in each inter-survey period. Examination of the correlations between exposures, and of graphical displays, suggested that this was at most only partially true. Some further analyses were performed to aid interpretation. If, for example, two variables contained the same information about the association with small opacities, then inclusion of both of them, with their coefficients constrained to be equal, would be equivalent to forcing the same information into the regression twice, which in turn should produce a coefficient half that of either entered separately. In practice, regression with equality constraints on coefficients is straightforward to achieve, by adding together the explanatory variables concerned.

Regression of 6th survey opacities 1/0+ on combined ISP 4 and 5 quartz exposure yielded a coefficient of 0.280, which was less than either of the individual coefficients, but greater than a half of each. This combined exposure variable gave a slight improvement in model fit over either ISP 4 or ISP 5 quartz separately, as did combined ISP 3 and ISP 4 quartz. Of all the combinations tried, the lowest residual deviance was 511.0, with 614 degrees of freedom, with combined ISP 3, 4 and 5 quartz, for which the estimated regression coefficient was 0.192.

Analyses of opacities 1/0+ from the 1980 survey showed very similar results. In this case the smallest residual was given by the variable combining all of the previous, ISP 3, ISP 4 and ISP 5 quartz exposures, with a residual deviance of 435.1 on 441 degrees of freedom, and a regression coefficient of 0.167. A deviance of 435.6 was obtained from the combination of previous, ISP 3 and ISP 4 quartz exposures, for which the coefficient was 0.207.

These results from the 6th and 1980 surveys suggested that there was considerable overlap in the exposure information from different ISPs, and that the possibility of distinguishing separate effects from the different periods was very limited. Similar analyses for the 5th survey data yielded rather different results. Here, no combined exposure variable yielded a smaller residual deviance than had been obtained in the earlier analyses by adding ISP 4 quartz alone, although again the combined variables had considerably smaller coefficients than for ISP 4 quartz.

#### 4.4 Data from Serial Readings by Medical Readers

In this section are summarised the assessments made by the two medical readers, in the reading exercise which was specifically designed to examine progression of opacities between surveys. The readings differed from those described in 4.2 in that the assessments were made with all the radiographs from the same man visible at once. The protocol used was a shortened form of the ILO (1980) scheme, which provided only for the recording of radiograph quality, of parenchymal abnormalities appearing as small or large opacities, and of any comments which the reader wished to make. Pleural abnormalities, and other abnormalities normally recorded by alphabetic codes, were excluded from the protocol for this exercise, and were not assessed. Throughout this section, the readers are identified by the code numbers 010 and 011 by which their identities are routinely coded and distinguished on the IOM computer.

##### 4.4.1 Radiograph Quality

Reader 010 was the more critical of radiograph quality, and classified only 64% of the radiographs he saw as of "good" quality, compared with 91% for reader 011. Most of the rest, however, were classified as "acceptable" for classification purposes, even if their quality was not of the highest standard. Both readers judged around 1% of the radiographs as being of "poor" quality, but only for one radiograph did reader 011 consider a radiograph's quality so bad as to be unreadable.

Despite the overall differences in how critical they were of radiograph quality, both readers recorded much lower proportions of "good" radiographs from the 1980 PXR survey than in the 5th and 6th PFR surveys. There was a curious discrepancy in the radiographs from the 4th survey, in which reader 010 recorded a relatively low proportion of "good" radiographs compared with reader 011's recordings. However, it may be unwise to make too much of comparisons between the readers' results, since they were classifying different radiographs, in the main; and the distinction between "good" and "acceptable" quality was considered unlikely to hold serious importance for comparisons of small opacities.

##### 4.4.2 Progression of Small Opacities

Table 4.11 displays, for each medical reader separately, comparisons between the profusions of small opacities recorded for radiograph pairs from consecutive surveys. Since these radiographs were read side-by-side, this was considered likely to provide a measure of the progression of disease within an individual which would be least susceptible to the random effects of within-reader variation. While the breakdowns within each section of the table are mutually exclusive and exhaustive, the different sections are not independent breakdowns; a man's 4th and 5th

survey radiographs can contribute to the comparisons of the first section, while the same 5th survey radiograph can be compared in the second section to the 6th survey radiograph, and so on, for men whose radiographs covered more than two consecutive surveys. The totals highlight the difference between the numbers of radiographs seen by the two readers, with reader 010 assessing 14 batches and reader 011 assessing 8.

Pairs of radiographs where the classification of profusion at the two surveys differed lie off the diagonal, and, since the row classification is in each case from the later survey, radiograph pairs in which the profusion of opacities was assessed to have increased are enumerated below the diagonal. Numbers above the diagonal represent radiograph pairs where the later radiograph was given a lower category of profusion than the earlier radiograph. Reader 010 recorded such apparent regression in 12 assessments of radiograph pairs, and reader 011 in only 3 pairs. Apart from one pair where reader 011 recorded regression of two categories, these regressions were all of a single category on the ILO 12-point scale.

Reader 010 saw 962 radiograph pairs where the first and second radiographs were judged to lie in the same category of profusion, and 50 in which the profusion was judged to have increased. The highest increase was a jump of five categories (from 0/1 to 2/2). Reader 011 classified 497 radiograph pairs with the radiographs in the same category, and 75 with increases in profusion, and a maximum increase of six categories (from 0/0 to 2/2). Both readers recorded fewer and smaller increases in profusion in the roughly two years between the 6th and 1980 surveys, and more frequent and larger increases in the roughly four years between 5th and 6th surveys.

Detailed comparisons between the assessments of small opacities profusion made by the two medical readers, based on the pairs of radiographs in the four batches which both readers saw, are given in Appendix 2. The limited data suggest that reader 011 read at a higher level of profusion, on average. Differences between the readers' assessments of the degree of progression represented by pairs of radiographs were based on even more limited data; these suggested that reader 011 also recorded progression more frequently than reader 010, but that the differences were less marked than were observed in the profusions assigned to the individual radiographs.

#### 4.4.3 Progression of Large Opacities

There were hardly any recordings of the presence of large opacities, and none at all were recorded by either reader for films from the 4th or 5th surveys. Reader 010 recorded two films with category A and one with category B appearing from 5th to 6th survey, while reader 011 recorded only one instance of the appearance of category A over the same period. In the period between 6th survey and the 1980 PXR survey, reader 011 recorded one change of category from B to C and no other large opacities, and reader 010 recorded a change from B to C, one from 0 to A and one apparent regression from category A to 0 over the same period.

The number of cases where large opacities were recorded was insufficient for analysis by regression modelling techniques, and no further analyses of the assessments of this variable were carried out.

## 4.5 Logistic Regression Analyses of Serial Readings

### 4.5.1 Choice of Variable for Analysis

The independent randomised readings made by the five members of the panel were summarised by the calculation of a median before analysis, but this approach could not be adopted for the serial readings, because a large proportion of the films were seen by only one of the two readers, while the remainder were seen by both. It was decided, therefore, to analyse all the data from the conjunction of the readers' individual assessments. For this approach, it was necessary to take into account reader differences, which were estimated from the four batches on which the readers overlapped.

Because the focus of interest was in progression of disease, the analyses were of the progression between consecutive surveys. This was calculated as the number of steps of difference on the ILO (1980) 12-point scale of profusion of small opacities between the earlier and later surveys. Two variables were analysed, being those produced by dichotomising the data according to whether they showed or did not show one step or more, or two steps or more, of progression.

Table 4.12 summarises the numbers of film pairs which the medical readers assessed as showing various numbers of steps of progression on the 12-point scale in the relevant inter-survey periods. The logistic regression analyses reported in the following sections were based on these data.

### 4.5.2 Summary of Results of Logistic Regression Analyses of Progression

This section summarises the results of analysing the medical readers' assessments of radiographic progression between adjacent surveys within the series of radiographs which each reader examined. Detailed tabulations of these results, with commentary, may be found in Appendix 2.

Reader differences were significant, and were retained in the models, for all the analyses. Age was significant in the majority of the models, and was retained in all models for comparability. Frequency of observing one or more steps of progression over ISP 4 was not associated with exposures previous to 3rd survey, but was associated significantly with dust and quartz exposures in ISPs 3 and 4. The strongest associations were with ISP 3 quartz followed by ISP 4 quartz, but in models with more than one exposure variable only ISP 3 quartz remained significant in the presence of the other variables. Frequency of two or more steps was low, and showed no significant associations with any of the exposure variables.

Progression of at least one step over ISP 5 showed significant associations with all of the ISP 3, 4 and 5 dust and quartz exposure variables, the strongest being with ISP 4 quartz, followed by ISP 3 quartz, ISP 4 dust and ISP 3 dust. This was the only analysis of radiographic abnormalities in which, when more than one exposure variable was included in the model, more than one was significant. The strongest association was demonstrated by the model including both ISP 3 quartz and ISP 4 quartz, and the coefficients of these were similar, but somewhat greater than half the corresponding individual coefficients. Analyses of two or more steps of progression showed similar results, with reduced significance.

There was, as expected, a lower rate of change in the relatively short two-year period between the 6th and the 1980 survey (ISP 6). However, occurrences of progression again showed strongest association with ISP 4 quartz exposure, followed by ISP 4 dust, and ISP 5 dust and quartz in that order. With more than one variable included, only ISP 4 quartz was significant in the presence of other exposures. Analysis of two or more steps was based on only six positive results, all by one of the readers. It was unclear, on the evidence of such small numbers, whether or not these associations had occurred by chance.

The inclusion of terms for the smoking habits of the individuals had little effect on the conclusions. Smoking terms exceeded the 5% significance level only for progression in ISP 5; and allowance for smoking habits had only the smallest effect on either the estimated magnitudes or the statistical significance of the age and exposure coefficients. It was concluded that models ignoring smoking effects were adequate for reliable inferences about the effects of exposures. The analyses of progression in ISPs 4 and 6 gave results similar to those from the analyses of profusion, in that although the response was significantly associated with each of the dust and quartz exposures after 3rd survey, addition of more than one variable to the model at a time did not improve the model fit. In the same way as reported in 7.5.1 above, these analyses were supplemented by extra runs including variables with combined exposures obtained by adding together the individual exposure variables from different inter-survey periods. Analysis of progression 1+ in ISP 4 gave the lowest residual deviance with ISP 3 and 4 quartz combined, at 219.8 with 501 degrees of freedom, only just less than with ISP 3 quartz alone. The estimated coefficient of the combined exposure was 0.263, compared with 0.450 for ISP 3 quartz. In the analysis of progression 1+ in ISP 6, no combined exposure variable improved the model over that containing just ISP 4 dust or ISP 4 quartz.

The results of analysing progression in ISP 5 were unique in that they showed evidence of independent effects of the quartz exposures in ISP 3 and ISP 4, but here the combined ISP 3, 4 and 5 quartz exposure gave the same residual deviance for one degree of freedom less, and an estimated coefficient of 0.356, where those for ISP 3 and 4 had been estimated at 0.434 and 0.484 respectively.

As with the results from the analyses of profusion, the inference that progression was associated with quartz, rather than with non-quartz exposure, was strengthened by regression models for progression in ISPs 4 and 5 with both quartz and dust from the same period, in which it was observed that the quartz remained significant in the presence of the dust, but that the reverse was not true.

#### 4.6 Lung Function Data from Medical Surveys

This section summarises the findings from the cross-sectional analyses of differences between individuals' lung function variables at each survey, and from the analyses of change in individuals' lung function between adjacent surveys. These analyses were performed by the application of standard linear regression models, and the technical details of the models fitted, with commentary, may be found in Appendix 3.

#### 4.6.1 Summary of Findings from Cross-sectional Analyses

Lung function at each survey was typified by the mean values of forced expiratory volume (FEV) in one second, and forced vital capacity (FVC), both in litres, from usually three (and only occasionally fewer) forced expirations, taken from data already held on computer for the men studied in this project.

FEV and FVC at each survey were analysed separately, using techniques of multiple regression. Both variables showed at each survey, as expected, strong associations with age and with height, which appeared the most successful indicator of differences in individuals' body sizes. FEV was significantly lower in smokers than in non-smokers, but FVC showed no significant differences between groups according to their smoking habits. Measurements at the 5th survey were taken by two different technicians, and there was significant evidence of a difference, on average, between the values they recorded; this was allowed for in the analyses.

Inclusion of the dust and quartz exposure variables in the regressions produced unexpected results. After allowing for age, height, smoking habits and technician effects as appropriate, both FEV and FVC at 4th survey showed significant positive associations with ISP 3 dust and, less strongly, ISP 3 quartz. FEV at 5th survey showed similar positive associations with ISP 4 dust, and, less strongly, ISP 4 quartz, while 5th survey FVC showed much stronger associations with ISP 4 dust and quartz, and less strongly with ISP 3 dust and quartz. Lung function variables at 6th survey did not show significant associations with exposure variables.

All of the significant associations with the 4th and 5th survey FEV and FVC were in the direction of better lung function with increased exposures, an effect which was considered biologically implausible. The effect may have been an artefact of the population structure of the study group, perhaps as a result of some selection process connected with fitness for work.

Additional analyses to test the adequacy of the regression models suggested that models with non-linear terms up to the cubic in age provided an improved fit. These reduced somewhat, but did not remove, the apparent positive associations mentioned above, and thus did not alter the conclusions regarding exposures.

#### 4.6.2 Summary of Findings from Analyses of Change in Lung Function

Lung function data from men attending more than one survey were used to observe directly changes in lung function over inter-survey periods. By subtracting the later value from the earlier value, the amounts by which both FEV and FVC had dropped (or gained, if negative) in the ISP were calculated. This was done for those pairs of measurements which spanned ISP 4, and independently for ISP 5, and the changes were analysed by linear regression methods.

Regression models for the changes in both FEV and FVC in ISP 4 included significant terms for age, height, smoking habits and an effect due to which technician took the 5th survey measurements. Allowing for these factors, the strongest association of FEV with an exposure variable was with ISP 3 dust exposure, but this failed to reach even the 10% significance level. For FVC, previous quartz and previous dust exposures almost reached significance at 10%, but none of the other exposure variables reached this significance level.

Evidence of associations in the data from ISP 5 was more convincing. Highly significant associations were found with all the ISP 3, 4 and 5 exposure variables, the strongest being with ISP 4 and 5 dust exposures. Models including more than one exposure variable did not improve the fit, however, and no exposure variable was significant in the presence of one of the others.

As with the cross-sectional analyses of FEV and FVC, additional modelling suggested that the dependence on age was non-linear, and better modelled by the inclusion of quadratic and cubic terms. With the baseline models altered in this way, reanalysis of the ISP 4 lung function variables showed no evidence of associations with any of the exposure variables. For ISP 5, the inclusion of a cubic relationship with age reduced the significance of the exposure variables, but the associations with ISP 4 and ISP 5 dust were still the most strongly significant. The direction of these associations was of increasing rate of loss of lung function with increasing dust exposure in ISPs 4 and 5, which contrasted with the cross-sectional results but was consistent with published work, and biologically plausible.

Analyses which distinguished the individuals according to whether their radiographs had been assessed as showing small opacities of profusion at least 1/0+ failed to suggest that small opacities caused by exposure were a precursor of loss of lung function. Again, this was consistent with other published work.

## 5. DISCUSSION

To recap, the objectives of this project, stated in Chapter 2, were: to make an intensive study of chest radiographs taken from men working in Colliery P between 1970 and 1980; to relate any abnormalities on those radiographs to the men's histories of exposure to respirable dust and its components, particularly quartz; and to examine the relationships between those exposures, the progression of radiographic abnormalities, and measurements of lung function.

In analyses which examined the lung function variables FEV and FVC from each survey separately, as cross-sectional views of the study group at distinct points in time, the results showed the expected average increase in men of greater height, decrease in older men, and lower FEV in smokers. Lung function variables at 6th survey showed no evidence of a relationship with exposures, but the data from the 4th and 5th surveys showed evidence of associations with exposures in the inter-survey periods preceding these surveys; the direction of these associations, however, was of higher lung function values in men with higher exposures. It seemed biologically implausible that the inhalation of coalmine dust could cause an increase in lung function, or even a decrease in the natural rate of age-related loss. Modelling of the age dependence by a cubic rather than a linear relationship diminished this relationship somewhat, but did not eradicate it.

A longitudinal view of these data produced a quite different inference. The losses experienced in FEV and FVC in inter-survey periods 4 and 5, by each individual man who attended consecutive surveys, were calculated by simple subtraction. These losses (or gains, where the values were negative) were analysed as responses, and initial analyses showed weak evidence of increased loss in ISP 4 of FVC in men with higher exposures to dust in ISP 3, and also some suggestion of decreased loss of FEV and FVC with higher exposures prior to 3rd survey. Allowing a cubic rather than linear adjustment for age had the effect of removing all suggestion of association with exposure. In contrast, the changes in lung function over ISP 5 showed rather stronger evidence of greater rates of loss in men with higher dust exposures in ISPs 4 and 5, and slightly less strong with ISP 3 exposures, but no relationship with previous exposures, even with linear adjustment for age. Allowing a cubic adjustment for age altered the regression estimates for the dependence on ISP 3, 4 and 5 exposures and reduced somewhat the apparent strength of the evidence, which however remained statistically significant.

One interpretation of these apparently contradictory findings is that the longitudinal analyses, depending on direct observations of change, are intrinsically more reliable as indicators of the effects of exposure; and that the results therefore point to a real effect of the exposures to dust between 3rd and 6th survey on the rates of loss of FEV and FVC in ISP 5, after allowance for other factors. There is biological plausibility in an assumption that some sort of damage has, in some men at least, occurred as a consequence of the exposure of the lungs to the insult of inhaled coalmine dust. It is also consistent with the observation of greater loss of FEV in men with higher exposures to dust which emerged from the analysis of change in FEV between 2nd and 4th surveys in five PFR collieries not including colliery P (Love and Miller, 1982). That finding was the first published demonstration of an effect of coalmine dust on rates of change of FEV, and was seen as confirmation of earlier work on cross-sectional comparisons by Rogan *et al* (1973), who showed lower FEV values in men with higher cumulative exposures to respirable dust and inferred that the differences were dust-related.

The reanalysis reported by Love and Miller (1982) was motivated by the recognition that differences between FEV values from individuals examined cross-sectionally were less secure evidence of exposure-related changes than might be provided by examination of differences in longitudinally observed rates of change, but in that case the two analyses pointed to the same conclusion. In the present work, the cross-sectional analyses showing higher FEV in men with higher exposures appear implausible and contradictory as evidence of an effect of dust, but may simply be an aspect of differences within the population studied. In particular, they may point to selection effects within the population.

No population in any epidemiological study is entirely free from selection effects of one sort or another. In occupational epidemiology, apart from those explicitly introduced by the chosen study design, the selection effects may include the initial selection at recruitment of men fit enough to work in an industry, which may be physically demanding, as was traditionally the case in coalmining. Those who prove unequal to their tasks may be selected out of that industry, or to other less demanding tasks within it. In the coalmines, an additional factor was that, at least before the widespread introduction of mechanised coal-getting, the hardest physical tasks were those at the coal face, which were also associated with the highest concentrations of airborne respirable dust. It is thus easy to envisage situations where research could discern an association between high lung function and conditions of high exposure to dust. Situations may also be envisaged where these selection effects are extended over time by the transfer of men who show (possibly) exposure-related health effects to jobs where dust concentrations are lower, which would tend to reinforce such an association. A further factor in this particular colliery during the 1970s was the contraction in the workforce which preceded the closure in 1982, and again it is quite conceivable that the selection of men who would take redundancy or early retirement settlements would not have been random, and that the choices of individuals or of supervisors, or both, might have been influenced by the presence of respiratory problems.

Our ability to envisage such plausible mechanisms does not prove that they, or similar, were responsible for the findings from this study, nor that some quite different and hitherto unsuspected effect was not the cause. We believe, however, that the evidence of the longitudinal analyses points to a deleterious effect of dust exposure on lung function, and we note that the associations were stronger with the non-quartz fraction of the dust than with the quartz. We believe that these analyses have provided an interesting example of the possibility of drawing erroneous inferences about change from differences observed cross-sectionally.

Results from cross-sectional analyses of profusions of small opacities on the men's chest radiographs were more consistent with assessments of radiological changes between radiographs taken at consecutive surveys, and viewed side-by-side. The IOM panel of readers are without medical qualifications, but have many years experience in the classification of abnormalities according to the ILO (1980) classification and its immediate predecessors. They classified the available radiographs independently and in random order, and, with the exception of the radiographs from the 1980 survey, on two separate occasions. Their assessments of profusion for each radiograph were summarised by medians, which were analysed by converting them to binary variables and using logistic regression methods.

Exposures recorded for these men prior to the 3rd survey showed associations only with small opacities on the 4th survey radiographs, and not at any of the later surveys. Profusions of small opacities at 4th and 5th surveys showed little evidence of association with the early exposures, but strong evidence of associations with

exposures in ISP 3 and particularly in ISP 4; the association was stronger with the variables estimating exposures to quartz than with those for the non-quartz fraction of the dust. The radiographs taken in 1980 showed a similar pattern, although in this case the association was stronger with ISP 3 quartz than with ISP 4 quartz.

Similar results were obtained from the analysis of the side-by-side readings of series of radiographs performed by two medical readers. The probability that the profusion of small opacities should have progressed by at least one step on the ILO (1980) 12-point scale between 4th and 5th surveys was strongly associated with the ISP 3 and 4 exposures, the strongest association being with ISP 3 quartz. Changes in ISP 5 were rather more strongly associated with exposures in ISPs 3, 4 and 5, the strongest being with ISP 4 quartz; ISP 5 was the only period over which changes of two or more steps could be shown to be associated with exposure variables. ISP 6 was employed as a label for the period between the 6th PFR and the 1980 Medical Service surveys, a period of about two years. Even over this short period, progression of one or more steps was shown to be associated with exposure variables, and most strongly with those in ISP 4.

These findings are, firstly, self-consistent. Despite the fact that the two reading exercises used different readers and entirely different protocols, they both pointed to an association between abnormalities observed on the radiographs taken at 5th, 6th and 1980 surveys, and exposures to coalmine dust in the period between the 4th and 1980 surveys. Further, almost all of the strongest associations were with those variables representing exposure to the quartz fraction of the dust, rather than the non-quartz fraction. In addition, the assessments recorded independently by both medical readers, of change over ISP 5, that is between 5th and 6th surveys, included significant numbers of radiograph series where the change was assessed at several, rather than one or two, steps on the ILO (1980) 12-point scale (see Table 4.28). In this assessment of unusual radiological changes in that particular period, and in the association of those changes with the quartz fraction of the men's exposures, these analyses are consistent with and reinforce the findings of the relatively small case control study from this colliery reported by Seaton *et al* (1981).

The present study has extended these findings; Seaton *et al* (1981) considered for their cases and controls only the radiograph pairs spanning ISP 5. While our analyses have confirmed the element of unusual progression over that period, and the association with quartz, they have also shown similar associations for progression on a more limited scale observed over ISP 4 and ISP 6. While this may be seen as confirmation that the initial finding was not an artefact, it also suggests that the problem was not isolated in ISP 5, but was present if less obvious in the preceding and following periods. Again, this was consistent with the findings of a case-control study of radiological changes in less than 100 men between the 3rd and 5th PFR surveys (ISPs 3 and 4) at 10 collieries (of which colliery P was one) reported by Jacobsen and Maclaren (1982).

Reliable estimation of the quantitative aspects of these relationships may present more problems than simply demonstrating that they exist. In the first place, the cross-sectional analyses have depended upon converting the median profusion, by which the several assessments were summarised, into a simple binary variable, by dichotomising at a chosen point on the ILO (1980) scale. This common practice seems intuitively likely to sacrifice information. In addition, it is necessary to consider how realistic were the measures of exposure as indicators of the effective dose to the individual, how biologically significant was the chosen response variable,

and what was the temporal relationship between the accumulation of dose and the development of response. Data from radiological surveys carried out four years apart can show only the extent to which abnormalities have developed or progressed in an inter-survey period, but by their nature contain no information on short-term differences in rates of change in the periods before or between surveys. Even the most detailed measurements of respirable dust concentrations within working environments, coupled with the most painstaking recording of individual men's occupational activities, can stand only as a surrogate measure of the biological dose; differences in individuals' work patterns may be taken into account by adopting personal rather than static sampling strategies, but would not eliminate a number of imponderables, such as how much of the dust breathed is deposited in the lung, how much eliminated by mucociliary clearance, how much removed or deactivated by the lung's cellular defences, and other questions such as how long any noxious fraction remains active in the lung and how long a response takes to become manifest and visible on a radiograph.

There is, as always in epidemiology, the additional likelihood that any quantitative answers to these questions would hold only in the average, and that differences between individuals would be an important factor. Little direct evidence can ever be available on such questions, but animal experiments can yield some insights, even if inferences about the human context by extrapolation from animal experimentation must be treated with extreme caution.

Robertson *et al* (1984) reported on a series of experiments in which laboratory rats breathed airborne dusts sampled from two faces in a colliery adjacent to and working the same coal seam as in colliery P; the dusts had quartz contents 7% and 25% quartz, and separate groups of rats were exposed for 12 months to these dusts and to a third dust of quartz content 13% prepared by mixing the low quartz and high quartz dusts, all at the same airborne concentration. After dusting, or after a follow-up period, randomly chosen animals were sacrificed and their lung and associated lymph tissues were examined for pathological changes. Those exposed to the high quartz dust showed considerably higher profusions in the lungs of discrete cellular pigmented nodules, and produced nodules earlier. The low quartz group produced few pulmonary nodules. All exposed animals exhibited an extensive general reactive tissue response, as indicated by elevated lung tissue weights in comparison with those of control animals. All treatment groups displayed massive hypertrophy of the lymph nodes, but this was greatest in the animals exposed to the dust with high quartz. Analyses of weights and compositions of the dusts contained in the excised lungs and lymph nodes indicated that quartz was cleared from the lung after dusting ceased, and deposited in the lymph nodes, faster than the other components of the dust. However, the dusts retrieved from both lungs and lymph nodes contained higher proportions of quartz than had been measured in the dusts before the experiment started.

These findings were entirely consistent with the radiological observations which had been made at colliery P (Seaton *et al*, 1981), of greater profusions of radio-opaque pulmonary nodules in men with higher exposures to quartz in coalmine dust. The rat lung has been found to be a useful experimental model for dust-induced lung damage, but does not necessarily correspond exactly to the situation in the human lung; if the findings of Robertson *et al* (1984) are relevant to human subjects, they give some insight into the complexity of the mechanisms by which the lung tissues and their defence systems interreact with dusts of varying quartz contents, but they also confirm, by the considerable differences in responses exhibited by animals of the same strain exposed to the same conditions, that differences in human responses to the same environmental conditions are likely to be sizeable. Again,

this is consistent with epidemiological evidence from men working side-by-side in coalmines, whose radiographs can show no evidence of abnormality in one man and progressive massive fibrosis in his neighbour.

Such individual differences in responses may have played a part in producing the observed relationships in time of the radiological abnormalities to the exposure histories, given that most of the analyses were based on relatively small numbers of positive responses. Selection effects such as those already mentioned in the context of lung function may also have had some influence, although the pathological changes detected as small opacities on radiographs may be less apparent to the individual concerned than might be the case with a loss of lung function. Nevertheless, coalminers are informed if their radiographs show signs of progression, and the effects of such information on decisions regarding, say, voluntary redundancy or early retirement in a colliery threatened by closure are open to speculation.

Population selection effects and individual differences in susceptibility may be part of the explanation for our inability to discern unambiguous patterns in the temporal relationships between the exposures and the radiological responses from surveys four years apart. Another factor likely to have had an effect is the well-recognised tendency of men in industries such as coalmining to retain similar jobs over periods of time, which induces at least some element of correlation between the exposures to which men are subject in different periods. This seems the likeliest explanation for the considerable reductions in the estimated regression coefficients of relationships with dust and quartz which were obtained from analyses in which the exposures from adjacent periods were added together. This phenomenon can be imagined at its most extreme in the hypothetical situation where each exposed man spends all his working life in the same exposure conditions, and where the risk of a particular response occurring is related to the total cumulative exposure up to the point when the response is measured. Then an estimate of the relationship of the response to precise measurements of the total exposure should give a representative picture of the underlying relationship; but a measurement of the exposure over a shorter period would be governed by the same information about the exposure conditions, and analysis with respect to such a measurement would produce a regression coefficient inflated by a factor which corresponded inversely to the ratio of the length of that period to the length of the man's working life. The situation here, as in most real data sets, was nowhere near as simple as in this hypothetical case; exposure conditions changed over time, individuals joined and left employment, and there was a spread of ages and of lengths of exposures. Further, although examination of the exposure data showed a definite tendency for men with low exposures in one ISP to have low exposures in the next ISP also, the individual exposure estimates at adjacent ISPs were far from identical. For example, amongst the data used for the analyses of profusion at 5th survey, the raw linear correlation between ISP 3 and ISP 4 quartz exposure estimates was 0.63, and that between the corresponding dust exposures 0.68. These values are considerably less than the correlations between dust and quartz exposures in the same ISP, which were typically about 0.9, but they are certainly not negligible; similar values were obtained from the data analysed for other surveys.

However, with the exception of the analyses of progression in ISP 5, the analyses of data from both the panel's readings of profusion and the serial readings of progression showed associations individually with all the exposures after the 3rd PFR survey, but inclusion of more than one exposure variable in any model did not in general improve the fit. The introduction of variables which combined

exposures over more than one ISP produced slight improvements in some analyses, but uniformly smaller coefficients for the exposure effects than were estimated for the single ISPs. It was therefore not possible from these analyses to draw unambiguous inferences about the relative importance of exposures in the different ISPs.

Radiological progression of one or more step in ISP 5 was exceptional in that it showed significant associations jointly and simultaneously with quartz exposures in ISP 3 and ISP 4, and the equivalent analysis of two or more steps had ISP 3 quartz significant and ISP 4 quartz just short of the 5% significance level when both were in the model. The data tabulations showed clearly that more progression was assessed by both medical readers for ISP 5 than for the other ISPs, and it is likely that the inability to show similarly detailed associations in the other ISPs is due to a combination of the lower numbers of men progressing and the element of correlation between the exposures at adjacent ISPs. Thus the analyses of progression at ISP 5 provide the strongest information regarding the magnitudes of the risks to which the men were exposed, while the results from the other ISPs can be taken as qualitative, if not quantitative, confirmation of the existence of a relationship between the development of radiological abnormalities and the dust, and in particular quartz, to which the men were exposed in the late 1960s and early 1970s. This conclusion was strengthened by the observation, in the analyses of profusion at 5th, 6th and 1980 survey, and of progression over ISP 4 and ISP 5, that when quartz and dust variables, from the ISP for which the association with exposure was strongest, were both in the regression model simultaneously, then the quartz made a significant contribution in the presence of dust, but dust made no significant contribution after adjustment for quartz.

Examination of the consistency of the magnitudes of estimates from these regression models with those from other PFR analyses is also not straightforward, because although the broad methodology was similar to that used in other studies, published work (e.g. Hurley *et al.*, 1982) has often chosen a different point on the 12-point scale at which to dichotomise the response, different sets of readers, and on occasions exposure variables on a logarithmic scale (which for the present data fitted less well than on the linear scale).

The cross-sectional analyses of lung function showed results which were ascribed to strong selection effects, but those which examined change were more easily related to published work. Love and Miller (1982) (L&M) reported on regression analyses of changes standardised to an 11-year period in the five PFR collieries C, F, K, W and X. The smokers in L&M were losing FEV about 49ml in 11 years faster than the non-smokers, an excess in the rate of loss of about 4.5ml per year. In this study, the rates of loss for smokers were estimated as about 82ml in four years faster than the non-smokers, that is an excess of about 21ml per year, in ISP 4; for ISP 5, the excess was estimated at 28ml in four years, that is 7ml per year. These values were larger than, but of the same order of magnitude as, those in L&M. Estimates of coefficients of rate of loss on age and height from the present study were also about three to four times the size of those in L&M. Comparison of the age coefficients may not be entirely appropriate, since a linear model for age effects was replaced by a cubic. L&M's estimate of the effect of lifetime cumulative dust exposure on rate of loss was  $0.033\text{ml per g.hr.m}^{-3}$ , whereas the estimate for ISP 4 or ISP 5 dust on loss of FEV in ISP 5, after adjustment for a cubic age effect, was about  $1.7\text{ml per g.hr.m}^{-3}$ . This large discrepancy is probably partly due to the fact that L&M used lifetime cumulative exposures, while the present analyses were in terms of specific ISPs; the correlation between exposures in different ISPs would have a similar effect on the

analysis of lung function as was observed in the analyses of radiological abnormalities.

Other factors may have contributed to these differences; none of the other collieries was Scottish, and regional differences in climate, environment and social habits may have played a part in addition to differences in working practices or composition of the coalmine dusts. An additional factor may have been differences in the extent of estimation error in the exposure estimates. One of the assumptions made in regression analysis is that the explanatory variables are known, that is measured without error, and it has long been known that if this requirement is not met the estimate produced is biased, towards zero if the variable involved is the only one in the regression model. Correlation between explanatory variables in models with more than one variable complicates matters considerably (Cochran, 1968).

Work by Heederik and Miller (1988) on a subset of the data from this project has demonstrated how making adjustments for estimation error of different sizes could lead to the estimation of adjusted coefficients which were much larger than the unadjusted ones, and that such adjustments also had effects on the age estimates in the same model, even although age is known without estimation error. Further investigations would be required to assess the reliabilities of the components of our estimates of individuals' exposures, in order to fix a suitable level at which adjusted estimates could be produced. It may be noted, however, that the data studied by Love and Miller (1982) were from the 2nd to the 4th PFR surveys, and that a sizeable part of the estimation of exposures prior to this period depended on the men's recall, and on assumptions about airborne concentrations for periods before the programme of detailed measurements began. The present data were from a later period, and most of the data contributing to the exposures of interest were derived from contemporary records of men's activities and occupational conditions. It is therefore reasonable to expect that the level of estimation error in the present data will have been less than in those used by Love and Miller (1982), with presumably a smaller effect on the coefficients. Much less is known about the effect of estimation errors in variables in non-linear regression models such as the logistic; statistical techniques to adjust for error do not seem to be readily available in this case.

Despite these difficulties in establishing the magnitudes of the effects involved, there seems little doubt of the main findings. The analyses both of profusion and progression of small opacities from the 5th PFR survey onwards showed associations with the dust to which men were exposed in a period which began after the 3rd PFR survey, and the associations appeared consistently stronger with estimates of the exposures expressed as quartz rather than as whole dust. Differences in lung function variables FEV and FVC did not appear to show plausible effects of dust, but selection effects were proposed as an explanation for the effects which were observed. Changes between surveys in these lung function variables did show an association between exposure to dust, rather than to quartz, and increased rate of loss of function. There was little evidence of a direct relationship between the quartz effect on small opacities and the dust effect on lung function.

Some suggestions for further work have arisen. Further work on the influence of estimation error in the exposure variables on the estimated strength of the observed relationships could be informative, if based on realistic data-based assessments of the reliabilities of those estimates.

One important area in which further work is needed is in the re-examination of the men involved; these men, or at least some of them, were exposed to levels of quartz untypical of those covered by the rest of the PFR investigations. Although the evidence of an acute reaction to that exposure in some of the men is strong, little is known about whether the resulting radiological abnormalities might continue to develop, and whether their progress might depend on whether or not a man continued to work in conditions of dust exposure. Further exposure might add to the risks, but the mechanisms involved may be more complex. Robertson *et al* (1984) discuss suggestions from Le Bouffant *et al* (1983), that other minerals such as illite may have a short-term protective effect against quartz-induced damage, which may vanish after exposure to these minerals ceases; the animal inhalation work of Robertson *et al* (1984) produced a small amount of data consistent with this hypothesis.

The data we have examined here were almost all from men who were still in employment in the coalmine, but only some of those transferred to other collieries when colliery P closed. It is hoped that, within the next few years, it will be possible to carry out a follow-up survey amongst the survivors from the population, which would allow examination of any progression of abnormalities which may have taken place since exposure ceased, in comparison with men who remained employed in coalmining. Such a follow-up could provide a perspective on the long-term risks of exposure to coalmine dust containing sizeable proportions of quartz which would complement well the information on short-term risk from this study and its immediate predecessors.

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**Table 3.1** Distributions of numbers of radiographs available from three surveys, for 1416 men, by combinations of surveys attended, according to existing computer records. (In brackets are shown two radiographs not recorded on computer but found in envelopes.)

No of radiographs per man	Survey			
	4th	5th	6th	Total
One	433	(1)		433 (1)
		102		102
			88	88
Two	259	259		518
	18	(1)	18	36 (1)
		115	115	230
Three	401	401	401	1203
Total	1111	877 (2)	622	2610 (2)

**Table 3.2** Distributions, by combinations of survey attendances, of series of at least two radiographs selected for assessment of radiological progression.

No of radiographs per man	Survey				
	4th	5th	6th	1980	Total
Two	8		8		16
	6			6	12
		51	51		102
		23		23	46
			50	50	100
Three	119	119	119		357
	21	21		21	63
	11		11	11	33
		66	66	66	198
Four	277	277	277	277	1108
Total used	442	557	582	454	2035

**Table 4.1** Breakdown of numbers of men attending each PFR survey by smoking habits and by age (at start of month of survey) in 10-year groups.

Survey	Smoking habit	Age at survey						Total
		15-24	25-34	35-44	45-54	55-64	65-	
4th	Nonsmoker	36	34	22	31	27	0	150
	Exsmoker	5	15	24	49	41	0	134
	Smoker	77	105	161	272	211	0	826
	Unknown	1	0	0	0	0	0	1
	Combined	119	154	207	352	279	0	1111
5th	Nonsmoker	33	33	36	21	18	4	145
	Exsmoker	10	17	21	48	43	1	140
	Smoker	64	58	110	248	101	9	590
	Unknown	0	0	2	2	0	0	4
	Combined	107	108	169	319	162	14	879
6th	Nonsmoker	28	19	20	20	18	0	105
	Exsmoker	8	12	13	38	32	0	103
	Smoker	54	35	80	123	76	0	368
	Unknown	0	1	14	20	11	0	46
	Combined	90	67	127	201	137	0	622

**Table 4.2** Summary of data from each survey on height and weight for men completing tests.

Variable	Survey	No. of Men	Mean	Standard deviation
Height (cm)	4th	1110	170.2	6.4
	5th	876	170.4	6.8
	6th	578	171.1	6.7
Weight (kg)	4th	1110	73.2	11.5
	5th	876	73.6	11.7
	6th	578	75.1	11.6

Table 4.3 Summary of data from each survey on lung function measurements (mean of up to three satisfactory blows) for men completing tests, by smoking habits.

Variable	Survey	Smoking habit	No. of Men	Mean	Standard deviation
FEV (1)	4th	Nonsmoker	150	3.70	0.83
		Exsmoker	131	3.30	0.84
		Smoker	824	3.24	0.81
		Combined	1105	3.31	0.83
	5th	Nonsmoker	144	3.70	0.84
		Exsmoker	139	3.20	0.82
		Smoker	588	3.17	0.81
		Combined	871	3.27	0.84
	6th	Nonsmoker	105	3.71	0.82
		Exsmoker	102	3.24	0.80
		Smoker	366	3.23	0.82
		Combined	573	3.32	0.84
FVC (1)	4th	Nonsmoker	147	4.66	0.86
		Exsmoker	129	4.37	0.85
		Smoker	815	4.33	0.84
		Combined	1091	4.38	0.85
	5th	Nonsmoker	138	4.36	0.88
		Exsmoker	138	4.03	0.85
		Smoker	580	4.01	0.83
		Combined	856	4.07	0.85
	6th	Nonsmoker	105	4.68	0.90
		Exsmoker	102	4.27	0.86
		Smoker	364	4.27	0.86
		Combined	571	4.34	0.88

Table 4.4 Summary of data on exposure to the non-quartz and quartz fractions of respirable dust for all 1416 men in study population. Tabulated are the mean and maximum values, and the number of non-zero values, for each variable. Data derived from questionnaire on working history (unmeasured) are separated from routine monitoring data (measured) after 3rd survey.

Variable	Period	Mean	Max	No >0.0
	Up to 3rd survey	26.62	80.65	1118
	ISP 3* measured	7.10	34.83	1220
	ISP 3* unmeasured	1.38	11.66	294
	ISP 3* total	8.48	34.83	1256
Time (1000 hrs)	ISP 4 measured	3.86	10.46	1318
	ISP 4 unmeasured	0.11	6.96	47
	ISP 4 total	3.98	10.46	1327
	ISP 5 measured	3.49	11.23	940
	Up to 3rd survey	34.48	144.41	1118
	ISP 3* measured	10.22	48.01	1220
	ISP 3* unmeasured	1.74	33.89	294
	ISP 3* total	11.96	48.01	1256
Respirable non-quartz dust exposures (g.hr.m <sup>-3</sup> )	ISP 4 measured	5.17	27.80	1318
	ISP 4 unmeasured	0.16	21.33	47
	ISP 4 total	5.32	27.80	1327
	ISP 5 measured	3.66	21.74	940
	Up to 3rd survey	1.756	7.560	1118
	ISP 3* measured	1.040	5.835	1220
	ISP 3* unmeasured	0.123	3.022	294
	ISP 3* total	1.163	5.835	1256
Respirable quartz exposures (g.hr.m <sup>-3</sup> )	ISP 4 measured	0.656	7.893	1317
	ISP 4 unmeasured	0.021	3.829	47
	ISP 4 total	0.678	7.893	1326
	ISP 5 measured	0.505	5.100	940

\* ISP 3 values include only 1415 men

Table 4.5 Summary of data on proportion of quartz in non-zero exposures to respirable dust. Tabulated are the minimum, mean and maximum values of that proportion, expressed as a percentage, and the number of values over which they were calculated.

Variable	Period	No of Values	Min	Mean	Max
	Up to 3rd survey	1118	0.36	4.78	7.58
Fraction of quartz in respirable dust (%)	ISP 3 measured	1220	2.80	7.46	17.54
	ISP 3 unmeasured	294	1.82	5.13	9.12
	ISP 3 total	1256	1.82	7.23	17.54
	ISP 4 measured	1318	0.00	7.78	29.36
	ISP 4 unmeasured	47	2.40	7.60	15.22
	ISP 4 total	1327	0.00	7.77	29.36
	ISP 5 measured	940	1.44	8.75	31.79

Table 4.6 Numbers of assessments by five readers of the profusions of small opacities on radiographs read in the three independent randomised reading exercises.

Exercise : XRLV

Reader	Profusion of small opacities											Total	
	0/-	0/0	0/1	1/0	1/1	1/2	2/1	2/2	2/3	3/2	3/3		3/+
101	0	674	779	0	758	170	0	213	0	0	0	0	2594
104	0	1379	427	277	329	115	1	57	4	0	5	0	2594
105	0	1204	185	484	512	81	41	84	2	1	0	0	2594
106	0	2461	17	20	28	19	11	15	9	7	6	1	2594
112	0	1084	612	299	294	170	63	37	25	9	1	0	2594
<b>Total</b>	<b>0</b>	<b>6802</b>	<b>2020</b>	<b>1080</b>	<b>1921</b>	<b>555</b>	<b>116</b>	<b>406</b>	<b>40</b>	<b>17</b>	<b>12</b>	<b>1</b>	<b>12970</b>

Exercise : XRVL

Reader	Profusion of small opacities											Total	
	0/-	0/0	0/1	1/0	1/1	1/2	2/1	2/2	2/3	3/2	3/3		3/+
101	0	333	931	1	977	133	2	148	2	0	0	0	2527
104	0	1391	386	279	301	114	0	45	5	0	3	0	2524
105	0	1117	147	616	411	109	4	115	8	0	0	0	2527
106	0	2369	6	18	13	34	19	28	19	10	6	4	2526
112	0	1063	369	193	353	280	104	110	44	8	4	0	2528
<b>Total</b>	<b>0</b>	<b>6273</b>	<b>1839</b>	<b>1107</b>	<b>2055</b>	<b>670</b>	<b>129</b>	<b>446</b>	<b>78</b>	<b>18</b>	<b>13</b>	<b>4</b>	<b>12632</b>

Exercise : XREX

Reader	Profusion of small opacities											Total	
	0/-	0/0	0/1	1/0	1/1	1/2	2/1	2/2	2/3	3/2	3/3		3/+
101	0	49	136	11	211	83	24	52	6	0	0	0	572
104	0	314	107	45	65	22	2	12	0	0	0	0	567
105	0	243	96	91	79	41	2	16	4	0	0	0	572
106	0	472	9	15	18	19	9	15	4	7	3	1	572
112	0	235	113	49	83	58	16	15	3	0	0	0	572
<b>Total</b>	<b>0</b>	<b>1313</b>	<b>461</b>	<b>211</b>	<b>456</b>	<b>223</b>	<b>53</b>	<b>110</b>	<b>17</b>	<b>7</b>	<b>3</b>	<b>1</b>	<b>2855</b>

**Table 4.7** Distribution of radiographs from reading exercise XRLV by predominant and secondary classification of shape (rounded = p,q,r; irregular = s,t,u) of all opacities classified as  $\geq 0/1$  in profusion, by each reader.

Shape of Opacities	Reader				
	101	104	105	106	112
Round	1620	598	171	72	9
Round/Irreg	0	106	387	30	250
Irreg/Round	0	0	0	7	138
Irregular	300	511	832	24	1113
Any opacities	1920	1215	1390	133	1510
None (0/0)	674	1379	1204	2461	1084
<b>Total</b>	<b>2594</b>	<b>2594</b>	<b>2594</b>	<b>2594</b>	<b>2594</b>

**Table 4.8** Distribution of readers' assessments of profusions of large opacities on the radiographs seen in the first reading exercise XRLV.

Reader	Large opacities				Total
	None	A	B	C	
101	2593	0	1	0	2594
104	2574	17	3	0	2594
105	2585	9	0	0	2594
106	2582	9	3	0	2594
112	2578	12	4	0	2594
<b>Total</b>	<b>12912</b>	<b>47</b>	<b>11</b>	<b>0</b>	<b>12970</b>

**Table 4.9** Distribution of numbers of radiographs by calculated values of median profusion of small opacities as assessed by panel readers, by survey.

Median profusion	Survey				Total
	4th	5th	6th	1980	
0/-	0	0	0	0	0
0/0	442	501	400	243	1586
0/1	232	164	98	82	576
1/0	148	96	59	32	335
1/1	192	81	39	48	360
1/2	50	15	7	25	97
2/1	17	4	5	7	33
2/2	22	9	6	7	44
2/3	2	1	4	1	8
3/2	0	0	0	0	0
3/3	0	0	0	0	0
3/+	0	0	0	0	0
<b>Total</b>	<b>1105</b>	<b>871</b>	<b>618</b>	<b>445</b>	<b>3039</b>

**Table 4.10** Distribution of proportions of radiographs at each survey by calculated values of median profusion of small opacities as assessed by panel readers; numbers tabulated are percentages, to nearest integer.

Median profusion	Survey			
	4th	5th	6th	1980
0/-	0	0	0	0
0/0	40	58	65	55
0/1	21	19	16	18
1/0	13	11	10	7
1/1	17	9	6	11
1/2	5	2	1	6
2/1	2	0	1	2
2/2	2	1	1	2
2/3	0	0	1	0
3/2	0	0	0	0
3/3	0	0	0	0
3/+	0	0	0	0





Table 4.11 continued.

Reader : 010

P r o f u s i o n s  a t  '80 Survey	Profusions at 6th survey												Total
	0-	00	01	10	11	12	21	22	23	32	33	3+	
0-	0	0	0	0	0	0	0	0	0	0	0	0	0
00	0	256	2	0	0	0	0	0	0	0	0	0	258
01	0	4	19	1	0	0	0	0	0	0	0	0	24
10	0	0	3	2	1	0	0	0	0	0	0	0	6
11	0	0	0	4	8	0	0	0	0	0	0	0	12
12	0	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	1	1	0	0	0	0	0	2
22	0	0	0	0	0	0	1	3	0	0	0	0	4
23	0	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0	0
3+	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	260	24	7	9	1	2	3	0	0	0	0	306

Reader : 011

P r o f u s i o n s  a t  '80 Survey	Profusions at 6th survey												Total
	0-	00	01	10	11	12	21	22	23	32	33	3+	
0-	0	0	0	0	0	0	0	0	0	0	0	0	0
00	0	133	1	0	0	0	0	0	0	0	0	0	134
01	0	5	9	0	0	0	0	0	0	0	0	0	14
10	0	0	3	3	0	0	0	0	0	0	0	0	6
11	0	0	3	4	11	0	0	0	0	0	0	0	18
12	0	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	1	0	0	0	0	0	1
22	0	0	0	0	0	2	0	0	0	0	0	0	2
23	0	0	0	0	0	1	0	0	0	0	0	0	1
32	0	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0	0
3+	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	138	16	7	11	3	1	0	0	0	0	0	176

Table 4.12 Numbers of radiograph pairs from consecutive surveys yielding data for logistic analysis of progression.

Period	Reader	Steps of progression on 12-point profusion scale										Total
		-3	-2	-1	0	+1	+2	+3	+4	+5	+6	
4th - 5th	010	0	0	3	306	12	1	1	0	0	0	323
	011	0	1	0	162	13	6	0	0	0	0	182
Total		0	1	3	468	25	7	1	0	0	0	505
5th - 6th	010	0	0	5	367	10	6	5	1	1	0	395
	011	0	0	1	178	19	14	1	2	1	1	217
Total		0	0	6	545	29	20	6	3	2	1	612
6th - 1980	010	0	0	4	289	13	0	0	0	0	0	306
	011	0	0	1	157	12	5	1	0	0	0	176
Total		0	0	5	446	25	5	1	0	0	0	482

## APPENDIX 1

## Detailed Results of Analyses of Assessments of Radiographs by IOM Panel

## A1.1 Between-reader Differences in Assessments of Profusion

The simplest way to investigate differences in the frequencies with which the IOM panel readers assessed the presence and profusion of small opacities is by examining the two-way tables of marginal totals obtained by comparing the assessments of pairs of readers. With five readers, there are  ${}^5C_2 = 10$  such pairwise combinations.

Table A1.1 summarises pairwise reader agreement between all 10 possible pairs of readers for the assessments of exercise XRLV, as an example. Although assessments were made on the 12-point scale of profusion, for these tables they have been collapsed to the 4-point scale, to reduce the effect on agreement of different patterns of usage of the side categories relative to the central categories.

These tables show both the extent and the nature of both the agreement and the disagreement regarding the major categories of profusion assigned to individual radiographs. Numbers lying on the diagonals of these square tables are counts of radiographs where the two readers concerned both assigned the same major category, and counts off the diagonals are of cases where the readers assigned different categories. In an obvious sense, the extent of any disagreement increases with distance from the diagonal.

In some instances, for example in the table comparing readers 101 and 106, the differences in levels of assessed profusion are clearly apparent. In others, that is amongst the readers with similar marginal frequencies for the levels of profusion, it is clearer that there is considerable evidence of association between the readers' assessments. For example, in the table comparing 101 and 105, there is a clear concentration of the values towards the diagonal, with complete agreement on the major category of  $1078 + 573 + 57 = 1708$  radiographs, representing 66% of the total.

This figure, the percentage of radiographs to which the readers assigned the same category, is sometimes known as a "consistency coefficient". These can be calculated for each of the 10 two-way tables, and they are tabulated together in Table A1.2, ranging from 56% to 75%.

The consistency coefficient measures only one aspect of the extent of agreement between readers; consistency can be low when one reader assesses profusions at a higher level than another, even if their overall ranking of the amounts of abnormality on each radiograph is the same, because then the counts in the two-way marginal tables will tend to lie just off the diagonal. Other aspects of between-reader agreement are not pursued here.

## A1.2 Within-reader Variations in Assessing Profusion

The independent randomised radiograph-reading exercise XRVL was designed to be a duplicate re-reading of the first exercise XRLV. Data from a very few radiographs were lost by their omission from the first exercise, and a few more

from the second, as detailed in 3.1. Apart from these, every radiograph was read by each of the readers on two separate occasions many months apart. The data from these readings therefore provide important information on the repeatability of each reader's classifications.

Table A1.3 shows, for each reader, a cross-classification of the major category of profusion of small opacities, on the ILO 4-point scale, assigned to each radiograph at each of the two exercises. For all the readers, it is clear that the data values cluster towards the diagonals, showing agreement between the categories assigned at the two occasions; the agreement is more readily apparent for those readers who recorded appreciable numbers of radiographs in categories other than 0. Reader 112 tended to assign higher categories to the same radiographs in the second reading exercise than in the first. None of the other readers showed quite so obvious evidence of a shift in reading level over the intervening time period.

Consistency coefficients were calculated from these tables, to summarise the proportion of radiographs for which the classifications assigned to each radiograph were the same, on the 4-point scale, at the two occasions. Table A1.4 displays these. These confirm the general impression of a reasonable level of agreement; for the different readers, however, they are obviously affected in part by the different frequencies with which those readers recorded the presence of opacities. Most obviously, the tendency of reader 106 to read few radiographs as showing abnormalities has resulted in a high self-consistency compared with those of the other readers, who all recorded more abnormalities.

### A1.3 Logistic Regression Analyses of small opacities profusion

#### A1.3.1 The Form and Presentation of the Logistic Regression Analyses

The form of the analyses which were carried out on the data from the radiograph-reading exercises was motivated by the desire to discover whether the assessed profusions of small opacities bore any relation to the variables describing the individuals' occupational exposures; whether any such relationships differed for the quartz and non-quartz components of the dust, or according to the time elapsed between exposure and response; and whether allowance for any nuisance factors for which data were available altered conclusions concerning these relationships.

Attempts to answer these questions were made by the application of logistic regression methods, which offer a convenient way of describing expected values of observed frequencies as probabilities which are functions of linear regression relationships in explanatory variables, whose parameters, or regression coefficients, have to be estimated from the data (Cox, 1970; Dobson, 1983). Logistic regression is appropriate to binary responses, that is those which are equivalent to a classification which distinguishes only between presence or absence of some characteristic. Two separate sets of analyses were undertaken. In the first, a positive response was defined as the presence, in the variable holding the median profusions, of a median profusion of category 1/0 or greater; in the second, a positive response was defined as the presence of a median profusion of category 2/1 or greater (which are, by definition, a subset of those of 1/0 or higher). In both cases, the profusion scale was divided at a point which separated the major categories of the equivalent 4-point scale. Although other points of division would have been possible, their use would have been less desirable in the light of the

differences, apparent in Table 4.6, in the relative frequencies with which the readers used the middle and side categories within each major category.

Separate analyses were performed on the data from readings of radiographs from the 4th, 5th and 6th PFR surveys and from the 1980 PXR survey. The results are summarised in tables which adopt a standardised format, and which are included here as Tables A1.5 to A1.12. Looking for example at A1.5, it will be seen that each column of tabulated values contains the results of fitting one regression model to the data. Because this report necessarily contains a number of similar tabulations, the models have been labelled in a manner which helps to identify their nature. Each column is labelled with a code containing three elements separated by obliques: the first element represents the content of the response variable, here 1+ to show that the variable represents categories of 1 or higher on the 4-point ILO scale; the second identifies the survey, here the 4th; and the third is a sequential distinction between the different models applied.

The values in the body of the table show the estimated regression coefficients against those variables included in each model, and are blank where a variable was not included. Shown in parenthesis below each estimated coefficient is the absolute value of the calculated ratio of the estimate to its estimated standard error. This ratio may be taken as a partial t-statistic for testing the significance of including that term last, where such a test is valid. A more flexible method for testing differences between models is given by the deviance statistics. These are log-likelihood statistics measuring the distance of the fit of the model from a model which fits the data exactly (Nelder and Wedderburn, 1972). Under the null hypothesis that a term introduced does not improve the fit of the model, or equivalently that its true regression coefficient(s) is zero, the reduction in deviance is distributed approximately as chi-squared, with degrees of freedom equal to the number of additional parameters fitted for the term. Changes in the deviances at the foot of each column can thus be compared with critical values of the chi-squared distribution with degrees of freedom given by differences in the total available degrees of freedom tabulated below. Single degree of freedom tests based on the deviance are asymptotically equivalent to those based on the partial t-statistics, but may give different results when based on sparse data.

In this and all the regression analyses presented here, the variables for estimates of exposure to respirable dust are those for the non-quartz fraction. They were obtained by subtracting the estimates of quartz exposure during each period from the estimates of exposure to whole respirable dust, of which the quartz was a constituent fraction. Since age was included as a continuous variable, accounting for a single degree of freedom, it was always possible to examine the effect of including age last in the model, by inspection of the partial t-statistic as tabulated.

Particularly for the models for the later surveys, the choice of exposure variables for inclusion was from amongst several, and to display the results for all possible models would have used more space than was justified. All the logistic regression analyses were performed with the package GENSTAT (Alvey *et al.*, 1977), and the sequences of models were often investigated using the facilities of that package for altering models interactively at the computer terminal. The results presented here are thus from models selected during that process, and many other possible models by implication have been found less interesting and omitted from the tabulations.

### A1.3.2 Logistic Regression Analyses of 4th Survey Radiographs

Table A1.5 presents some results from a logistic analysis of the binary variable constructed to have a value of 1 when the median profusion took the category 1/0 or higher on the ILO (1980) 12-point scale. Included in this analysis were 1104 radiographs from the 4th PFR survey, in 1970. These were the radiographs for which it was possible to calculate a median profusion, less one man who was excluded from all the logistic regression analyses because certain values of the variables estimating his dust exposures were not credible (see 4.1.4 above). The median profusion was of at least category 1/0 on the 12-point scale for 431 of these radiographs.

The values in Table A1.5 show that, on its own, age was a very highly significant predictor of the probability of a 4th survey radiograph achieving a median profusion of 1/0 or greater. The exposure variables considered for inclusion in these models were estimated exposures to respirable dust and to its quartz fraction, in two time periods: inter-survey period (ISP) 3, which was the period between the 3rd and the 4th survey; and the individual's whole working life (if any) up to the time of 3rd survey, which is labelled "previous". The greatest decrease in deviance arose from the inclusion of the previous dust exposure, with a deviance change of  $1285.1 - 1279.1 = 6.0$  with 1 degree of freedom. The 2.5% critical point of the chi-squared distribution is 5.02, so this term is statistically significant. (The same conclusion would be drawn from the partial t-statistic 2.43.) The equivalent deviance change for previous quartz exposure was somewhat smaller at 4.4, again for 1 degree of freedom, and neither of the variables for dust and quartz exposure during ISP 3 made a useful contribution to the fit of the model. Thus, exposure to dust up to 3rd survey appeared the best predictor, amongst those considered, of median profusion 1/0 or greater. With age and previous dust exposure in the model, none of the other exposure variables gave a further significant reduction in the deviance; these additional model fits are not shown here.

Results of similar analyses are shown in Table A1.6, where the response variable this time is the binary variable taking the value 1 if the median profusion at 4th survey achieved a category of 2/1 or greater; this is indicated by the first component of each column label, 2+. There were 41 positive responses at this level. In contrast to the analysis above of the less severe response, none of the variables considered, other than age, made a significant contribution to the response of category 2/1 or greater. This did not seem to be due to confounding of long-term exposure with age, because inclusion of the exposure variables did not much alter either the estimated value or the statistical significance of the age coefficient; the correlation between age and, for example, the previous dust exposure was only 0.76. No combination of exposure variables improved the fit over that of the models with the variables taken singly, and results from these fits are not shown. It was concluded that none of the exposure variables available was a useful predictor of median profusions equal to or greater than category 2/1 at this survey.

### A1.3.3 Logistic Regression Analyses of 5th Survey Radiographs

The median profusions calculated for the radiographs from the 5th PFR survey, in 1974, were analysed by logistic regression, and the results are presented as described in A1.3.1. Exposure variables containing estimates of exposure to respirable dust and its quartz fraction were available for ISP 4, which was the

period between the 4th and 5th surveys, and these variables were considered for inclusion in regression models, along with the ISP 3 and previous dust and quartz exposure variables.

Table A1.7 presents some results from the logistic regressions of the binary variable taking the value 1 if the median profusion of the 5th survey radiographs was category 1/0 or greater. Of the 870 radiographs included in this analysis, 206 had median profusions qualifying them as positive responses on this classification. Neither of the previous exposure variables yielded much improvement when added to the model with only a constant and age, and these fits are not shown. Of the other exposure variables, the ISP 4 quartz exposures made the greatest contribution to the fit, with a highly significant deviance reduction of 27.4 on 1 degree of freedom. The ISP 4 dust exposure variable gave almost as large a contribution, with a deviance reduction of 23.4. The ISP 3 variables were much less significant, with deviance reductions of 6.3 for the dust and 8.7 for the quartz variables respectively. Models 1+5/6 and 1+5/7 show the results of adding the previous and ISP 3 quartz variables to the model containing age and ISP 4 quartz. Inclusion of ISP 3 quartz made no useful contribution to the fit. Adding previous quartz gave a deviance reduction of 2.8, which with 1 degree of freedom exceeds the formal 10% critical point of the chi-squared distribution; its inclusion reduced the magnitude and increased the standard error of the age term, while the ISP 4 quartz coefficient was almost unchanged. It was concluded that there was no strong evidence that previous quartz was a useful predictor of median profusion of category 1/0 or greater, when ISP 4 quartz was already in the model.

Similar analyses, not shown, showed that previous and ISP 3 dust exposure variables made even less useful contributions, in the presence of ISP 4 quartz, than their quartz counterparts.

Table A1.8 presents results from logistic regression analyses of the binary variable taking the value 1 when the median profusion calculated for a 5th survey radiograph was of category 2/1 or greater, indicated in the column labels as 2+. There were only 14 radiographs from 870 so classified. The results were similar to those from the analysis of the 1+ variable, although there was hardly any difference between the deviance reductions for the ISP 4 dust and quartz variables, at 4.4 and 4.6 respectively. Neither the previous exposures (not shown) nor the ISP 3 exposures gave a significant deviance reduction, whether the ISP 4 quartz (or dust) exposure was in or out of the model.

#### A1.3.4 Logistic Regression Analyses of 6th Survey Radiographs

The median profusions calculated for the radiographs from the 6th PFR survey, in 1978, were analysed by logistic regression, and the results are presented as described in A1.3.1. Exposure variables containing estimates of exposure to respirable dust and its quartz fraction were available for ISP 5, which was the period between the 5th and 6th surveys, and these variables were considered for inclusion in regression models, along with the ISP 4, ISP 3 and previous dust and quartz exposure variables.

Table A1.9 presents some results from the logistic regressions of the binary variable taking the value 1 if the median profusion of the 6th survey radiographs was category 1/0 or greater. Of the 617 radiographs included in this analysis, 120 had median profusions qualifying them as positive responses on this classification. Neither of the previous exposure variables yielded much improvement when added

to the model with only a constant and age, and these fits are not shown. Of the other exposure variables, the ISP 4 quartz exposures made the greatest contribution to the fit, with a highly significant deviance reduction of 27.3 on 1 degree of freedom. The ISP 4 dust exposure variable gave a smaller contribution, with a deviance reduction of 19.8. ISP 3 dust and quartz exposures gave reductions of 15.4 and 19.8, and ISP 5 dust and quartz gave reductions of 14.2 and 16.2 respectively. All of these reductions exceeded the 0.1% significance point of the chi-squared distribution with 1 degree of freedom. Models 1+/6/8 to 1+/6/10 show the results of adding the previous, ISP 3 and ISP 5 quartz variables to the model containing age and ISP 4 quartz, chosen as a baseline because it gave the largest reduction of any single variable. The largest additional reduction in deviance was only 1.8 for either ISP 3 quartz or ISP 5 quartz, and this was well short of the 10% significance point of the chi-squared distribution. Similar analyses (not shown) adding previous, ISP 3 and ISP 5 dust exposures showed that they made even less useful additional contributions than their quartz counterparts. It was concluded that the other variables were not useful additional predictors when age and ISP 4 quartz exposure were already in the regression model.

Table A1.10 presents results from logistic regression analyses of the binary variable taking the value 1 when the median profusion calculated for a 5th survey radiograph was of category 2/1 or greater, indicated in the column labels as 2+. There were only 15 radiographs from 617 so classified. The results were similar to those from the analysis of the 1+ variable, with reductions in deviance of 19.8 for ISP 4 dust and 18.4 for ISP 4 quartz. Models 2+/6/8 to 2+/6/10 show the results for adding other variables to the model with age and ISP 4 dust; the smallest deviance, 110.5 with ISP 3 quartz added, gave a deviance reduction of 3.3 over the value of 113.8 achieved by the model with age and ISP 4 dust, which was less than the conventional 5% significance level of the chi-squared distribution with 1 degree of freedom.

In Table A1.10 it is notable that, for all the models 2+/6/2 to 2+/6/4, 2+/6/9 and 2+/6/10, the partial t-statistic for the age coefficient was less than the formal 5% significance point of the t-distribution. For these models, the question of whether age is an essential term is less clear than in the previous analyses of Tables A1.5 to A1.9.

#### A1.3.5 Logistic Regression Analyses of 1980 Survey Radiographs

The median profusions calculated for the radiographs from the NCB Medical Service's PXR survey in 1980 were analysed by logistic regression and the results are presented as described in A1.3.1. As for the radiographs from the 6th survey, the exposure variables available for inclusion in the regression models were those estimating individuals' exposures to previous, ISP 3, ISP 4 and ISP 5 respirable dust and quartz.

Table A1.11 presents some results from the logistic regressions of the binary variable taking the value 1 if the median profusion of the 1980 survey radiographs was category 1/0 or greater. Of the 444 radiographs included in this analysis, 119 had median profusions qualifying them as positive responses on this classification. Neither of the previous exposure variables yielded much improvement when added to the model with only a constant and age, and these fits are not shown. Of the other exposure variables, the ISP 3 quartz exposures made the greatest contribution to the fit, with a highly significant deviance reduction of 18.9 on 1 degree of freedom. The ISP 4 dust and quartz exposure variable each gave almost as large

a contribution, with deviance reductions of 18.1 and 16.3 respectively. ISP 3 and ISP 5 dust and ISP 5 quartz exposures gave reductions of 10.3, 10.2 and 10.4 respectively. These reductions were all well in excess of the 1% significance level of the chi-squared distribution with 1 degree of freedom. Models 1+/80/8 and 1+/80/9 show the results of adding the previous, ISP 4 and ISP 5 quartz variables the model containing age and ISP 3 quartz, which was the exposure variable which gave the greatest individual deviance reduction. The additional reductions were 1.1, 2.3 and 1.5 respectively, all of which were well short of the 10% significance level of chi-squared with 1 degree of freedom. Similar analyses fitting other combinations of variables produced even smaller deviance reductions. It was concluded that the other variables were not useful additional predictors when age and ISP 3 quartz exposure were already in the regression model.

Table A1.12 presents results from logistic regression analyses of the binary variable taking the value 1 when the median profusion calculated for a PXR 1980 survey radiograph was of category 2/1 or greater, indicated in the column labels as 2+. There were only 15 radiographs from 444 so classified. The results showed the greatest deviance reduction at 10.8 for ISP 4 dust, followed by 9.2 for ISP 4 quartz. Reductions due to ISP 5 dust and quartz variables were only slightly smaller, at 6.9 and 5.1, while the reductions for ISP 3 dust and quartz were also close at 5.4 and 6.8 respectively. Models 2+/80/8 to 2+/80/10 show the results of adding other variables to the model with age and ISP 4 dust. The smallest deviance, 110.5 with the addition of ISP 3 quartz, gave a deviance reduction of 3.3, which is well below the 10% significance level.

In Table A1.12, even more than in A1.10, the age coefficient is seen to be of dubious necessity for the models, as evidenced by the small values of the partial t-statistics. However, conclusions from both of those tables concerning the effects of age or of exposures must be considered suggestive rather than conclusive, because of the small numbers of positive responses on which the analyses were based.

#### A1.3.6 The Effects of Smoking on Profusions of Small Opacities

All of the analyses shown in Tables A1.5 to A1.12 were from logistic regression models in which variables representing the individuals' smoking habits had not been included. Indeed, the analyses were based on all men for whom a median profusion could be calculated and for whom, in addition, apparently reliable exposure estimates were available, and availability of data on smoking habits was not taken into account. It has already been noted that the tabulation of age and smoking habits in Table 4.1 showed the loss of questionnaires including smoking data from a few attendances at the 4th and 5th surveys, and the less trivial loss of a batch of questionnaires from the 6th, representing about 7% of those attending then. As a result, any analysis which includes smoking as a nuisance variable must necessarily be based on a subset of those already analysed; and the difference in the numbers for the 6th survey data is considerable.

Table A1.13 shows a breakdown of the numbers of radiographs available for analysis from each survey, by smoking habits where known and by grouped profusion categories. Although each man makes at most one contribution within each survey, many men attended more than one survey, and thus contribute to more than one section of the exhibit. Each man's classification by smoking habit is, for the 4th, 5th and 6th surveys, based on his answers at that survey, so for example the same man may be a smoker at one survey and an ex-smoker at a

later survey. The classifications by median profusion of small opacities have been grouped into the major categories 0 (0/-, 0/0, 0/1), 1 (1/0, 1/1, 1/2) and 2 or higher (2/1 and higher).

No questionnaire data were collected at Medical Service's PXR surveys, so the 1980 radiographs had no corresponding smoking data. Of the 444 radiographs for which analyses of median profusions have already been presented, 363 were from men for whom data on smoking habits were available from their 6th survey questionnaires. Because the elapsed time between the 6th and 1980 surveys was only about two years, the 6th survey smoking data were used for the analyses of the corresponding 1980 radiographs.

All of the regression models which were fitted to the median profusion variables, from which the most interesting results have been presented in the preceding sections, were also fitted in alternative versions which included variables representing the individuals' smoking habits as well as the variables for age and dust and quartz exposures. For the most part, these expressed the smoking effects as differences between groups of men classified by their responses at the relevant survey as current smokers, ex-smokers, and lifelong non-smokers. Such comparisons can only be estimated as differences, and it is necessary to make an arbitrary choice of one of the groups to act as a reference level. In these analyses, the non-smoking group was chosen as the reference, and the comparisons expressed as differences between the non-smokers and the remaining two groups. Tests of statistical significance of the differences amongst the three smoking groups are associated with two degrees of freedom.

Table A1.14 presents some results from the analyses of data from all four surveys. The variable analysed at each survey is the binary variable taking the value 1 where the median profusion of small opacities was of category 1/0 or greater on the 12-point scale. The tabulation shows direct comparisons between various parsimonious logistic regression models taken from amongst the results already presented, and the same model augmented by two parameters for the differences between the smoking groups. The column labels of the models without the smoking effects are the same as in the tables in which these results were first presented, and the labels for the models with the smoking effects are the same, except for the addition of the suffix S indicating that smoking effects are included.

In the model for median profusion 1/0 or greater at 4th survey, predictor variables were age at survey and dust exposure prior to 3rd survey. Since only one man had no smoking data, the results are almost identical to those for the same model in Table A1.5. The addition of smoking effects produced a deviance reduction of 4.7, which just exceeds the 10% significance level of the chi-squared distribution with two degrees of freedom. The estimated coefficients suggested that most of the difference, if real, was concentrated in a contrast between the non-smokers on one hand and the smokers and ex-smokers on the other, with little difference between these two groups. With smoking in the model, the age coefficient was reduced by about 5%, while the coefficient of previous dust was increased by under 9%.

For median profusion 1/0 or greater at 5th survey, the baseline model had predictor variables age and ISP 4 quartz exposure. Again, the results were very similar to those already presented in Table A1.7, because the data sets differed by only two men. Addition of smoking effects gave the highly significant deviance reduction of 11.1. The estimates of group differences, in contrast to those for the 4th survey, had the most extreme difference between the ex-smokers and the

smokers, with the non-smokers roughly halfway between the two groups. Inclusion of the smoking effects increased both the age and the ISP 4 quartz coefficients by about only 3%.

At 6th survey, the baseline model again included age and ISP 4 quartz exposure, and the addition of smoking terms here gave a deviance reduction of 3.8, which is well short of the 10% significance level. Again, the estimated coefficients showed the highest risk in the current smokers, but the ex-smokers' risk estimate was little greater than that of the non-smokers. Inclusion of the smoking effects had negligible influence on the age coefficient, and decreased the ISP 4 quartz coefficient by less than 4%. However, comparison of model 1+6/5 with the same model in Table A1.9 shows that the estimated ISP 4 quartz coefficient was 21% smaller when calculated from the subset of the attendances for which smoking data were available.

For the analysis of the data from the 1980 survey, results are shown with the baseline model which includes age and ISP 3 quartz exposure. The deviance reduction due to smoking effects was only 2.2, well short of conventional significance levels. Even for the contrast between the smokers and non-smokers, the estimated effect was less than its standard error. Inclusion of smoking once more made little difference to the age and exposure coefficients. As for the 6th survey data, however, the estimate of the exposure coefficient was considerably smaller when based on the subset of the data which included smoking habits.

Results from many other models gave similar results, but are not shown here. The estimates of the smoking effects were almost constant for a particular set of data, regardless of the baseline model chosen or of which exposure variables were included or excluded, as were the sizes of the corresponding reductions in deviance. Furthermore, the inclusion or exclusion of smoking effects made hardly any difference to the estimates of the regression coefficients for age or exposure variables. In particular, no difference was observed in the ranked order of the deviances with different choices of exposure variables, in models with and without smoking effects. Additional models were fitted in which different estimates of the coefficients for the age and exposure variables were made in each of the three smoking groups. None of these produced any significant improvement in model fit over the models with parallel coefficients. There was therefore no evidence that the effects of age or occupational exposures on small opacities was influenced by the individuals' smoking habits.

It was not clear why smoking should appear to be a highly significant contributor to the models for the 5th survey data but not for the data from the other surveys. Nor was there an obvious interpretation of the magnitudes of the estimated coefficients, which suggested that the ex-smokers had a lower prevalence of small opacities than the non-smokers. However, for the present purposes, the most important conclusion from these analyses was that there was little or no partial confounding between smoking habits and exposures to dust or quartz, in that the conclusions to be drawn from the analyses already presented would not be altered by the inclusion of smoking variables.

The radical changes, on exclusion of men with unknown smoking habits, to the exposure estimates from the 6th and 1980 surveys strongly suggest some sort of selection effect in the lost batch of questionnaires. It can be seen from Table A1.13 that those for whom smoking habits are now unknown had a much higher proportion of radiographs for which the median profusion was 1/0 or greater, than the remainder whose data were analysed in relation to smoking. It was concluded

that estimates of the effects of dust and quartz exposure from the reduced data set with questionnaires were subject to some distortion due to this selection effect, and that since smoking made little difference to the estimates in the reduced data set, it would be safer to base conclusions on the earlier analyses of the larger data set, without allowance for smoking.

#### A1.3.7 The Adequacy of the Median as a Summary of Readings

All the regression results in the previous section have been derived from analyses of summaries of the radiograph readings, obtained by calculating a median from the available assessments of profusion of small opacities. In general, the readers did not record identical profusions for the same radiographs, nor identical rankings for the profusions. And, although in general the agreement between the duplicate readings performed by each of the readers was better than between different readers, even the same reader did not produce identical rankings of the profusions at different readings. These observations are consistent with experience of data from the subjective assessment of radiological abnormality, but they raise the question of the adequacy of the chosen method of summarising these data by a median. It is legitimate to enquire whether the use of the median has a stabilising effect over the variation in the data, or whether its use incurs an important loss of information over what might be retrieved by analysis of the separate assessments made by the individual readers.

Table A1.15 is designed to shed some partial light on this question. To produce this tabulation, data were extracted for the five readers' assessments of small opacities profusion on the radiographs from the 5th survey, which were read on two separate occasions. Attention was focussed on the 617 radiographs for which duplicate readings existed from all five readers, and the ten individual assessments, along with their median, were converted into binary variables by dichotomising between categories 0/1 and 1/0. Regression analyses similar to those reported in Table A1.7 were performed on each of the binary responses; the initial model containing just a constant and a term for age at survey was augmented by the quartz and non-quartz dust exposure variables from ISPs 3,4,5 and the previous period, taken one at a time in turn. Table A1.15 contains the residual deviances obtained from each of these models, organised in columns labelled with the identity of the response variable being analysed, so that 101/1 labels reader 101's first set of readings. The deviances are not readily comparable within rows, because they are in part a function of the number of positive responses, and these numbers differed widely between readers. It is possible, however, to compare across columns the pattern of the deviances within each column, and the conclusions which would be drawn from them, about the relative importance in the regression models of the various exposure variables.

The strongest impression from Table A1.15 is how well the pattern within each column resembles that for the median. Firstly, the addition of either previous dust or previous quartz produced only a little improvement in the regression model, with the exception of that for the assessments made by reader 101 at her second reading. And, again with that single exception, the ISP 3 and ISP 4 dust and quartz variables made rather more substantial contributions to the models than the previous dust and quartz. There was no clear unanimity in the choice between the ISP 3, 4 and 5 and previous exposure variables, in the matter of which produced the greatest reduction in the deviance. The only column in which the best model choice was from ISP 5 exposure was 101/1, and of the remainder the best fit was obtained by ISP 3 quartz in five of the columns, ISP 4 quartz in three, and ISP

non-quartz dust in two. In the majority of the columns, the quartz variables performed better than the corresponding non-quartz dust variables. Comparison of data from the same readers at different occasions showed that for readers 104, 105 and 106 the same variable appeared best at both occasions, which provides some general reassurance about the consistency of the panel members' reading habits over time. Even where the same variable was not the best both times, there appears close similarity between the rankings of the deviances, given that the results from different readers were based on widely differing numbers of positive responses.

It was concluded that, at least on the present subset of the data, the median had preserved and summarised the principal features of the individual readings, in the strength of their relationships with the exposure variables. This conclusion was drawn in the knowledge that, as with all summary measures, the use of the median may clarify any relationship underlying the joint distribution of the readings, but at the expense of the loss of information about the individual readings' deviations from that relationship.



## APPENDIX 2

## Detailed Results of Analyses of Assessments of Radiographic Progression

## A2.1 Between-reader Differences in Assessments of Profusion and Progression

Table A2.1 shows, for the 445 radiographs in the four batches which both medical readers examined, a comparison of the categories of profusion recorded by the two readers on the same radiographs. As before, radiographs assigned the same category by both readers appear on the diagonal. Since reader 011's classifications index the rows of the tabular sections, radiographs enumerated below the diagonal are those where reader 011 recorded a higher category than 010, and vice versa.

The radiographs for which reader 011 recorded higher categories than reader 010 considerably outnumbered those for which the reverse was true. The same category was recorded by both readers in 367 radiographs, while reader 011 recorded a higher category for 60 radiographs, and reader 010 was higher for only 18 radiographs. Further, although reader 011's classification was at times as much as four categories in excess of 010's, reader 010 never exceeded 011 by more than one category. On the basis of the limited information from these four overlapping batches, then, it is concluded that, during this reading exercise, reader 011 tended to record higher categories for the same radiographs than reader 010.

The information available on the readers' agreement on progression within series of radiographs is necessarily even more limited. Table A2.2 compares the results for the pairs of radiographs from consecutive surveys which the readers had in common, each radiograph pair being classified by the number of steps of progression on the ILO (1980) 12-point scale represented by the difference between the categories recorded for the earlier and later radiograph by each reader. As in Table A2.1, reader 011's results index the rows, and numbers below the diagonal represent radiograph pairs where reader 011 recorded categories showing more profusion than did reader 010.

The last section of this Table shows the total numbers of radiograph pairs, accumulated over the three inter-survey periods. Just as reader 011 read higher categories on individual radiographs, so too did this reader record more progression than reader 010. For 252 of the 289 pairs of radiographs, neither reader observed progression. Of the remainder, there were 26 pairs for which only reader 011 observed progression, 3 pairs where only reader 010 observed progression, and 8 pairs where both readers recorded progression.

Although the readers did not always record progression to the same extent, nor even on the same radiographs, their agreement was much better than would be predicted by chance. Reduction of the last section of Table A2.2 to a table of dimension 2x2, according to whether each of the readers recorded any progression, yielded a Pearson chi-squared statistic with one degree of freedom, for the test of independence between the readers, with a value of 41.1, which is very highly significant. It was concluded that the readers did tend towards agreement on whether progression was present, even although such agreement was not complete.

## A2.2 Differences in Assessments of Progression of Large Opacities

Table A2.3 displays, for each of the two medical readers separately, comparisons between the categories of large opacities recorded for the radiographs within pairs from consecutive surveys. As with the tabulations of small opacities, there is some overlap of the batches read by the two readers, and the same radiograph can be the second of a pair spanning one ISP and the first of a pair spanning the next ISP.

Tabulated are the numbers of pairs by the category of large opacities recorded for the first and second radiograph in each pair. Here the classification is only by the recorded profusion of large opacities, and ignores information on profusions of small opacities, or on any other abnormalities, present on the same radiographs. Film pairs where the classification of large opacities profusion was the same for both radiographs are enumerated along the diagonals of these tables, while entries below the diagonals signify pairs where the profusion was assessed to have increased.

Overall, there were hardly any recordings of the presence of large opacities, and none at all were recorded by either reader for radiographs from the 4th or 5th surveys. Reader 010 recorded 2 radiographs with a profusion of A and one with a profusion of B appearing from 5th to 6th survey, while reader 011 recorded only one instance of the appearance of a profusion of A over the same period. In the period between 6th survey and the 1980 PXR survey, reader 011 recorded one change of profusion from B to C and no other large opacities, and reader 010 recorded a change from B to C, one from 0 to A and one apparent regression from category A to 0 over the same period.

## A2.3 Logistic Regression Analyses of Serial Readings

### A2.3.1 The Form and Presentation of the Analyses of Progression

The rationale for the analyses of progression between pairs of the medical readings was similar to that for the independent readings by the IOM panel, described in Appendix 1. The choice of explanatory variables was also similar, except that it was necessary here to include a dummy variable to summarise differences between the two readers' levels. The remaining variables considered were age, taken arbitrarily as at the later survey, and the variables summarising the individual's exposures to respirable coalmine dust and its quartz fraction, in the inter-survey periods 3, 4 and 5, and before the 3rd survey. Variables for the estimates of exposure to respirable dust were for the non-quartz fraction obtained by subtracting the estimates of quartz exposure from those for whole respirable dust.

The tabular layout of results is also similar to that employed earlier, as may be seen in Tables A2.4 to A2.10. Each column contains the result of fitting one regression model to the data, and is labelled with a code containing three elements. The first element identifies the content of the response variable, here 1+ to show that the positive response represents one or more steps of progression; the second identifies the inter-survey period between the pair of surveys from which the radiographs came, where 14 stands for ISP 4, between 4th and 5th survey; and the third element is a sequential distinction between the different models applied.

The values in the body of the table show the estimated regression coefficients against those variables included in each model, and are blank where a variable was not included. Shown in parenthesis below each estimated coefficient is the absolute value of the calculated ratio of the estimate to its estimated standard error, which may be taken as a partial t-statistic for a test of significance where valid. At the foot of each column is given the residual deviance and its degrees of freedom. For nested models, differences in the deviance provide statistics, distributed as chi-squared under an appropriate null hypothesis, for testing the significance of terms introduced to the model.

All the logistic regressions were fitted using the package GENSTAT (Alvey *et al.*, 1977), often interactively. The results presented here are not exhaustive, but omit many from models judged to be less interesting and omitted from the tabulations.

#### A2.3.2 Regression Analysis of Progression 4th to 5th Survey

Table A2.4 presents some results from a logistic regression analysis of the binary variable constructed to have a value of 1 when the reader's assessment of the profusion of small opacities on the 5th survey radiograph was higher by one or more category on the 12-point ILO (1980) scale than the same reader's assessment of the 4th survey radiograph, and a value of 0 otherwise. As already noted, some radiograph series were read once each by both readers, and these series contribute twice to the data set.

Of 505 assessments of radiograph pairs contributing to the analyses in Table A2.4, 33 implied progression of at least one step. There was a highly significant contribution from the term for the difference between readers, and this term has been included in all the models. The age coefficient was also significant.

With a base model containing reader and age effects, inclusion of dust or quartz exposure previous to 3rd survey produced small deviance reductions, not shown here. The largest reduction was achieved with the inclusion of quartz exposure in ISP 3, with the highly significant deviance reduction of 11.9 on 1 degree of freedom. The equivalent deviance change for ISP 3 dust was 7.3, while those for ISP 4 dust and quartz were 6.2 and 9.1 respectively. With ISP 3 quartz in the model, none of the other candidate exposure variables gave a significantly improved model. Model 1+/I4/8 shows, for example, the model with both ISP 3 and ISP 4 quartz, which gave a deviance reduction of only 1.2 with 1 degree of freedom, over the model with ISP 3 quartz alone. Other model fits, which showed even smaller deviance changes, are not shown here.

Although age was significant in model 1+/I4/1, the age coefficient was smaller and less significant in other models, notably those which included ISP 3 quartz. To ensure that conclusions about the exposure variables were not being distorted by the presence of age in the models, other models including the exposures but excluding age were also fitted. The estimated coefficients for the exposure variables were similar to those shown in Table A2.4, and the deviances retained the same rank order.

Table A2.5 shows the results of logistic regression analyses where the response variable was the binary variable taking the value 1 if the progression over the radiograph pair spanning ISP 4 was assessed to be two or more steps on the 12-point scale; this is indicated by the first element of each column label, 2+. Of the 33 assessments showing one or more steps of progression in the 505

radiograph pairs, 7 of these showed two, and 1 three, steps of progression, so that this analysis is based on only 8 positive responses.

None of the dust or quartz exposure variables made a significant contribution to the base model containing terms for reader and age. The largest deviance change was 1.41, for quartz exposure in ISP 4, but this fell well short of any conventional significance levels. No improvement was gained by fitting models with combinations of age and exposure variables, or with exposure variables without age, and these fits are not shown here.

### A2.3.3 Regression Analysis of Progression 5th to 6th Survey

Logistic regressions for the variables representing the change in small opacities profusion in radiograph pairs spanning inter-survey period 5, between 5th and 6th survey, were performed in a similar manner to those for ISP 4. Variables estimating the coalminers' exposures to dust and quartz during ISP 5 were considered for inclusion in these models, along with the ISP 4, ISP 3 and previous dust and quartz exposure variables.

Table A2.6 presents some results from the logistic regression analysis of the variable taking the value 1 if a pair of radiographs spanning ISP 5 was assessed as showing one or more step of progression on the 12-point scale. Of 612 assessments, 61 were positive. The labelling of the columns of this table follows the same scheme as in Table A2.4.

Both reader differences and the age coefficient were highly significant. Over a base model including age and reader, previous dust and quartz exposures did not produce a significant deviance reduction, whereas all the other dust and quartz exposure variables did. The largest reduction was 48.4, highly significant with 1 degree of freedom, and due to ISP 4 quartz exposure. ISP 4 dust and ISP 3 quartz gave almost as large reductions, of 47.4 and 45.2 respectively. With ISP 4 quartz in the model, and considering the remaining dust and quartz exposure variables for inclusion, the best improvement in the fit was from the addition of ISP 3 quartz, giving a further deviance reduction of 9.7, which exceeds the 1% significance point of the chi-squared distribution with 1 degree of freedom. The partial t-statistics of 3.13 and 3.53 shown in model 1+15/8 for ISP 3 and ISP 4 quartz respectively imply that each variable made a significant independent contribution to the model.

As for progression in ISP 4, inclusion of ISP 3 quartz reduced the estimated age coefficient, but fitting models without age did not alter the conclusions regarding the exposure variables. No further inclusions or alterations to the model yielded an improvement in fit, and none of the alternatives are shown here.

Table A2.7 shows the results of similar analyses for the variable which took the value 1 when the progression assessed on the radiograph pair spanning ISP 5 was 2 or more steps on the 12-point scale. This variable had 32 positive values from the 612 assessments.

Over a base model containing reader and age terms, the introduction of previous dust and quartz exposures did not give significant deviance reductions. The largest deviance reduction was for ISP 3 quartz, at 19.7, closely followed by ISP 3 dust and ISP 4 dust and quartz at 17.0, 18.7 and 17.4 respectively. Addition of ISP 4 quartz to the model with ISP 3 quartz produced a further deviance reduction of

only 3.3, which is less than the 5% significance level of the chi-squared distribution with one degree of freedom.

Except in the models with only ISP 5 dust or quartz, the age coefficient was in general not significant. Again, models fitted without age gave very similar exposure coefficients and the same ranking of deviances.

#### A2.3.4 Regression Analysis of Progression 6th to 1980 Survey

The roughly two-year period between the 6th PFR survey and the PXR survey in 1980 is here referred to for simplicity as ISP 6. Logistic regression analyses for the variables representing the change in small opacities profusion in radiograph pairs spanning this period were performed in a similar manner to those for ISP 4. As with the analyses of the changes in ISP 5, the variables estimating the coalminers' exposures to dust and quartz were those for ISPs 5, 4 and 3, and for the period prior to the 3rd survey. No additional exposure data were available to cover the period of ISP 6.

Table A2.8 presents some results from the logistic regression analysis of the variable taking the value 1 if a pair of radiographs spanning ISP 6 was assessed as showing one or more steps of progression on the 12-point scale. Of 482 assessments contributing to this analysis, 31 were positive. The labelling of the columns of this table follows the same scheme as in Table A2.4.

Reader differences were again highly significant, and the age term was significant in all models. Over a base model including terms for age and reader differences, the largest deviance reductions from the exposure variables were 14.2 for ISP 4 dust, and 13.7 for ISP 4 quartz. ISP 5 dust and quartz gave reductions of 7.7 and 5.5, while ISP 3 dust and quartz both gave reductions of 5.2. Of the models with more than one exposure variable, the lowest deviances were given by models where ISP 4 quartz was joined by either ISP 3 or ISP 5 quartz, but neither of these variables gave significant improvements to the model fit.

There were only 6 assessments where progression of more than 2 steps was recorded, all by reader 011. Since reader 010 recorded no positives on this assessment, any logistic model including reader differences would produce estimates increasing without bound. Table A2.9 presents, instead, the results of analysing only the 176 assessments made by reader 011, from which the 6 positive assessments arose.

Over a base model containing only age, ISP 5 dust produced the largest reduction in deviance, at 5.2. ISP 5 quartz gave a reduction of 4.4, while ISP 3 and ISP 4 dust gave reductions of 2.3 and 2.2 respectively. The 5% significance point of the chi-squared distribution with one degree of freedom is 3.8. No combination of exposure variables was a significant improvement on ISP 5 dust alone. The age term failed to achieve significance in any of the models, although the t-statistic for age was larger when ISP 5 exposures were in the model than when ISP 3 or 4 exposures were used. Fitting similar models without age produced the same rankings of deviances, and had little effect on the magnitudes of the exposure coefficients.

### A2.3.5 The Effects of Smoking on Progression of Small Opacities

None of the analyses described in the previous sections and summarised in Tables A2.4 to A2.9 included explanatory variables for individuals' smoking habits. In this section are described the principal results from some additional analyses intended to investigate the effects of smoking.

Table A2.10 shows the results of augmenting some of the models which proved most interesting in the analyses of progression, by adding terms to distinguish ex-smokers and current smokers from lifelong non-smokers. The analyses are restricted to the variables representing one or more steps of progression over the relevant ISP, and the columns of Table A2.10 are numbered to correspond with the column labelling of Tables A2.4, A2.6 and A2.8, with the addition of the suffix S to indicate models including smoking terms.

For each analysis, the smoking variable has been defined according to the data from the questionnaire from the survey at the start of the ISP. Thus, for example, progression in ISP 4 has been related to smoking status at 4th survey. It has already been noted that smoking data were not available for all the surveys at which radiographs were taken, but this convention means that the serious loss of smoking data from 6th survey questionnaires affected only the numbers available for analysis for ISP 6. Of 482 men entering the analysis in Table A2.8, only 446 had data on smoking. For ISP 4, the analysis was of exactly the same group as in Table A2.4, and for ISP 5 the difference from the group contributing to Table A2.6 was only 5 men.

The three smoking groups did not show significant differences in the analyses of ISP 4 and ISP 6 data. For ISP 5, inclusion of the smoking effects gave deviance reductions in excess of the 5% point of the chi-squared distribution with 2 degrees of freedom, and the estimated coefficients suggested lower progression for ex-smokers, higher for current smokers, with the non-smokers in between but nearer the smokers.

Many other models were fitted and compared with and without smoking effects, and the overall conclusions were similar to those for the panel's readings of profusion. The estimates of smoking effects were of similar magnitude and significance for a particular set of data, regardless of which exposure variables were in the model. Estimates of the magnitudes and significance of exposure effects hardly differed between models with and without smoking terms, and the inclusion of smoking made no difference to the ranking of deviances across different choices of exposure variables. As with the panel's readings, it was concluded that there was no evidence that the effect of age or of exposure to respirable dust or quartz was influenced by the smoking habits of the individual coalworkers.

## APPENDIX 3

## Detailed Results of Analyses of Lung Function

## A3.1 Background

This chapter summarises the analyses made of lung function data from the medical surveys. These data were collected for almost all of the men who attended these surveys; occasionally, a man from whom a chest radiograph had been obtained would refuse to cooperate with the completion of questionnaires and lung function testing. In a very few cases the man was physically unable to perform the forced expiration necessary for the tests. In the remainder of cases, measurements were made from the spirometer traces, yielding estimates of the Forced Expiratory Volume in one second from the start of expiration (FEV), and of the whole Forced Vital Capacity (FVC) which the individual could expel from his lungs.

After one expiration for familiarisation, when the technicians could determine that the individual was able to make a satisfactory attempt, three further expirations were performed, with reruns for any which were technically unsatisfactory, and the variables analysed here are the arithmetic means over those three expirations. In a few cases, where the man was unable to complete three expirations, the means have been calculated over the number of expirations performed. From each survey, the analyses have included only those men for whom satisfactory FEV and FVC were both available, along with reliable data on smoking and exposures.

In A3.2, the data are considered cross-sectionally, taking separately the lung function data from the 4th, 5th and 6th surveys. (The 1980 survey was not a PFR survey, and medical questionnaires and lung function tests were not applied). In A3.3, a longitudinal view is taken, and analyses are presented of the observed changes between consecutive surveys, in the lung function measurements of individuals.

## A3.2 Regression Analyses of Lung Function Data at each Survey

## A3.2.1 The Form and Presentation of the Regression Analyses

In the cross-sectional analysis of the lung function data from each survey, the principal research question was whether the levels of lung function, on average, showed any relationship with the available data on the individuals' exposures to respirable dust and/or quartz up to the time of the survey. Lung function is related to body size, declines with increasing age, and is adversely affected by tobacco use, particularly by the inhalation of cigarette smoke (Fletcher *et al.*, 1976; Cotes, 1979). Since age was known, and the medical questionnaires included a section on smoking habits, it was possible and desirable to allow for these factors in the course of the analyses, and this was done.

The dimension of the lung function measurements FEV and FVC is a volume; the unit employed throughout is litres. Analyses were performed by the application of standard multiple linear regression models (Draper and Smith, 1981), as widely used for the analysis of such variables. Initial analyses, performed interactively at a computer terminal and not shown here in detail, investigated the extent to which it

was necessary to allow for age, body size and smoking habits. The results of these investigations clearly showed that age made a highly significant contribution to the model; that (standing) height was a better predictor of lung volumes, than weight; that when height was in the model, weight never gave a significant improvement; that smoking habits made a significant contribution to explaining differences between individuals in FEV; and that, in contrast, FVC showed no evidence of being related to smoking habits. All of these findings were consistent across the three surveys.

On the basis of these results, baseline models were defined relating FEV to age at survey, height and smoking habits (expressed as the mean differences between groups of ex-smokers and current smokers from the group of lifelong non-smokers); and FVC to age and height only. In addition, analyses of the data from the 5th survey included terms to allow for differences between measurements performed by two different technicians. Tables A3.1 to A3.6 show these baseline models, and the effects of adding to them dust and quartz exposure variables singly and in combinations.

The tabular layout of these tables is similar to that employed for the logistic analyses of the radiological data, as described in Appendix 1. Each column is from the fitting of a different model, and is labelled with a combination of the variable being analysed (FEV or FVC), the survey number (4, 5 or 6), and a sequential number to differentiate the models. The entries in the tables are the estimated regression coefficients, quantifying the change in the response variable corresponding to a unit change in the explanatory variable, with all the other explanatory variables in the model held constant. Beneath each is the absolute value of the ratio of the coefficient to its estimated standard error, which in some cases is also appropriate for use as a partial *t*-statistic for the significance of the inclusion of the variable while all the other variables are included. In linear regression, these tests are algebraically identical with those using *F*-statistics obtained by testing partial mean squares against the residual mean square.

As in the earlier analyses, the exposure variables for ISPs 3 and 4 and prior to the 3rd survey were the sums of estimates calculated from "measured" and "unmeasured" time records. For all periods, the dust variable used was that representing the non-quartz fraction, obtained by subtracting the quartz exposure from the whole respirable dust exposure.

#### A3.2.2 Regression Analyses of 4th Survey Lung Function Data

Table A3.1 presents some results from the linear regressions of FEV for 1090 men attending the 4th PFR survey. The initial baseline model included statistically significant contributions from linear terms in age and height, and differences between smoking groups. To this model were added in turn dust and quartz variables for the period prior to 3rd survey (previous), and between 3rd and 4th survey, that is inter-survey period (ISP) 3.

The estimates of the age, height and smoking effects varied little as different exposure variables were included. The average age effect was less than 40ml reduction for each year, while the height effect was a little over 40ml increase per cm. Ex-smokers and non-smokers did not differ significantly, but current smokers showed a significant deficit of around 130ml.

Neither previous dust nor previous quartz exposures made a significant contribution to the model. Both of the ISP 3 variables did bring highly significant improvements, but the model labelled FEV/4/6 shows that the inclusion of ISP 3 quartz was not an improvement over the model containing ISP 3 dust, which made the greater single contribution.

Both ISP 3 dust and quartz had positive estimated coefficients, which would suggest that lung function was better in those who had been more heavily exposed to dust. The direction of this effect goes against expectation.

Table A3.2 shows results of similar analyses of FVC at 4th survey for the same group of 1090 men. The baseline model included age and height, since smoking had been found not to make a significant contribution. Estimates of the average age effect were relatively constant in all the models, at about 30ml reduction per year, and the height effect was estimated at about 60ml difference per cm.

As with FEV, the inclusion of previous exposure variables produced negative estimates which were not statistically significant. Both ISP 3 exposure variables produced highly significant improvements, with dust the greater, and quartz not yielding an improvement when dust was in the model. Again, the estimated coefficients were positive, against expectation.

#### A3.2.3 Regression Analyses of 5th Survey Lung Function Data

Table A3.3 presents some results from the linear regressions of FEV for 854 men attending the 5th PFR survey. The initial baseline model included statistically significant contributions from linear terms in age and height, and differences between smoking groups. Also included was a term to differentiate the results obtained by an experienced technician and a new technician, who had not previously performed these tests on survey. Examination of the completed questionnaires, on which the lung function measurements were recorded, had identified 100 where the experienced technician had performed the test, and 724 performed by the new technician. There were 45 questionnaires without indication, and these have been kept separate as a distinct group in the analyses. Of course, if both technicians contributed to the measurements of this group, their heterogeneity will slightly inflate the residual in the regression analyses. However, this option was chosen as preferable to the most obvious alternative, omission of the entire group and the potentially useful information it contained regarding the other relationships of interest.

To the baseline model were added in turn dust and quartz variables for the period prior to 3rd survey (previous), and those for inter-survey periods (ISPs) 3 and 4. Estimates of the effects in the baseline changed little when exposure variables were included. The age effect was about 36ml per year, and the height effect about 38ml per cm. Current smokers differed significantly from non-smokers, with an estimated deficit of around 170ml on average, while the ex-smokers differed from the non-smokers by about 100ml. The new technician's measurements were on average about 200ml lower than those of the experienced (=old) technician, while those for whom the technician was not known were on average about 130ml higher than those of the new.

Previous dust and quartz made no significant contributions to any of the models tried, and are not included in Table A3.3. Estimated coefficients for both dust and quartz from ISP 3 were positive, but failed to reach conventional levels of

statistical significance. ISP 4 dust made a highly significant contribution, as did ISP 4 quartz, although not quite as strongly. With ISP 4 dust in the model, neither ISP 3 dust nor ISP 4 quartz gave a significant improvement, while ISP 4 dust remained significant in the presence of the others.

The estimated coefficients of ISP 4 dust and quartz were positive, indicating better lung function in those with higher dust exposure. While this finding was against expectation, it was consistent with the results above for the data from 4th survey.

Table A3.4 shows results from the regression analyses of FVC at 5th survey for the same group of men. The baseline model included age and height and a term for differences between the technicians, as described above. Smoking habits were not included.

Again, the estimates of effects in the baseline model changed little when the exposure variables were included. The age effect was about 32ml reduction per year, and the height effect about 51ml increase per cm. The difference between the old and new technicians was about 300ml, about 50% greater than for the FEV data. The FVCs for whom the operating technician was not known were on average similar in level to those from the old technician, other things being equal.

Variables representing the men's previous dust and quartz exposures did not make a significant contribution to the fit of the models, and are not shown. However, the associations with the ISP 3 and 4 dust and quartz variables were somewhat stronger for FVC than for FEV, and all were highly significant. ISP 4 dust showed the strongest effect, and when this variable was in the model none of the others gave a significant improvement, although ISP 4 dust remained significant in their presence. As in the other analyses reported so far, the regression coefficients showed an association of higher lung function with higher exposures.

#### A3.2.4 Regression Analyses of 6th Survey Lung Function Data

Table A3.5 presents results from the linear regressions of FEV for 569 men attending the 6th PFR survey. The initial baseline model included age, height and smoking habits, and the estimates of these effects changed little when exposure variables were added to the models. The age effect was about 36ml reduction per year, and the height effect about 37ml per cm. Smokers had a significantly lower lung function than non-smokers, by about 250ml on average. Ex-smokers differed from non-smokers by about 90ml.

Addition of the previous (not shown), ISP 3, 4 and 5 dust and quartz exposure variables failed to demonstrate any significant relationships of FEV with these variables. The largest improvement was with ISP 4 dust, but this was well short of even the 10% point of statistical significance. However, when ISP 3 quartz and ISP 4 dust were simultaneously added to the baseline model, the partial t-statistics indicated that each made a contribution after allowing for the other, although the overall reduction in the sum of squares was not significant; the coefficient of ISP 4 dust was positive, and that of ISP 3 quartz negative. ISP 4 dust and ISP 3 dust as a pair produced a similar but less pronounced pattern. The model with ISP 4 dust and quartz fitted less well, and other combinations, which are not shown, less well yet. It was concluded that there was little evidence of a dust or quartz effect on the 6th survey FEV data, in contrast with the strong positive relationships found in the equivalent 4th and 5th survey data.

Table A3.6 shows results from the regression analyses of the 6th survey FVC data for the same men. The baseline model here included only age and height, and once more the estimates of their effects differed little, whether dust or quartz variables were included or not. The age effect was about 33ml reduction per year, and the height effect about 54ml increase per cm. Looking over Tables A3.1 to A3.6, the consistency of these results is notable. In particular, the age effects seem particularly stable, at about 36ml per year for FEV and 32ml per year for FVC. The age effects varied a little more, from 37ml to 42ml per cm for FEV and from 51ml to 61ml per cm for FVC.

Neither ISP 3 dust nor quartz gave a significant reduction to the sum of squares, nor did those from the previous period, which are not shown. None of the ISP 4 and 5 dust and quartz variables made a contribution which exceeded the 5% level of statistical significance, but all except ISP 4 quartz exceeded the 10% point, with ISP 4 dust just ahead of ISP 5 dust. Addition of ISP 4 quartz or ISP 5 dust or quartz to a model including ISP 4 dust did not improve the fit. The model including ISP 3 quartz and ISP 4 dust produced a similar result to that for 6th survey FEV, in that the partial t-statistics indicated a significant negative association with ISP 3 quartz and a positive one with ISP 4 dust; but in this case the overall test for the inclusion of both variables over the baseline was significant at better than the 2% level.

One additional observation on the tables of results concerns the similarity of the residual mean squares, which hardly varied between surveys, although that for FVC was somewhat higher at about 0.38 than for FEV at about 0.31. This, coupled with the stability of the age and height coefficient estimates, suggests some inherent comparability of the data from the different surveys, as might be expected for data from (subsets of) the same men. The differences in the findings regarding lung function and exposures at 6th survey, from those at the 4th and 5th surveys, is thus more likely to be due to differences over time with regard to the working environment, in a way not directly related to age or height.

#### A3.2.5 Checks on the Adequacy of the Regression Models

The results in Tables A3.1 to A3.6 were from regression models in which the relationship between lung function and the continuous variables representing age, height and exposure were assumed to be linear. There is no particular reason to expect linearity in these relationships, and indeed other studies have often shown a slightly curved relationship of lung function to age.

The validity of the assumption of linearity was checked in a similar manner to that described in Appendix 1 for the logistic regression models. Each of the variables age and height was split into six equal-sized groups, and a separate regression constant fitted for the level of each group; the residual sums of squares from these models were compared with those from the models which assumed linearity. The overwhelming conclusion from these tests was that a degree of non-linearity was present in the relationship with age, but not with height. It was decided to investigate the effect of non-linearity in age in a little more detail.

Table A3.7 shows comparisons between models for FEV at the three surveys; each of these consists of the appropriate baseline model plus the exposure variable which made the greatest individual contribution. They bear the same column labels as in the tables from which they were extracted. Each is compared with a model containing the same terms, augmented by quadratic and cubic terms in age. To

minimise arithmetic problems, the mean age at each survey was subtracted before the squares and cubes were calculated; these values were 44.5, 44.6 and 43.0 years at 4th, 5th and 6th survey respectively.

The results from each survey showed a significant improvement in the fit, largely due to the cubic term. Little change was observed in the estimates of the height and smoking effects, nor did the technician effects at the 5th survey alter much. However, there was a considerable drop in the estimates of the dust exposure effects for the 4th and 6th surveys, although that for 5th survey dropped by only about 10%.

Table A3.8 shows results for a similar investigation of the effects of non-linearity in age on the analyses of FVC. The results were broadly similar, with a significant improvement due to the cubic term, and little difference in height or technician effects. Again, the estimates of the exposure effects at 4th and 6th survey were reduced considerably when the non-linear age terms were included, and this time the same was observed for the 5th survey as well.

Inclusion of non-linear terms in age, then, has been seen to reduce the estimates of most of the exposure effects. However, for 4th and 5th survey FEV and FVC, the reduced estimates were still highly significant and still positive, in the opposite direction to that expected.

### A3.3 Regression Analyses of Change in Lung Function between Surveys

#### A3.3.1 The Form and Presentation of the Analyses

The cross-sectional analyses of lung function data at each survey, described in 8.1, showed, at least for the 4th and 5th survey data, a relationship between increasing exposure and increasing lung function which seemed implausible as a dose-response relationship. An alternative explanation may be that the relationship was a feature of the structure of the study population, perhaps due to selection effects during or prior to the period over which these surveys took place. We would expect such selection effects to have less influence on changes observed over time within individuals.

Tables A3.9 to A3.12 show results from fitting regression models to changes in lung function, obtained by calculating the difference between the values obtained at two consecutive surveys. Throughout, the difference has been calculated by subtracting the later from the earlier survey; the unit of the response is thus the drop (or gain, if negative) in FEV or FVC over a period of about four years. The regressions were carried out in the same way as the cross-sectional analyses reported in 8.1. Age, height and smoking habits were always taken from the earlier survey. Only men for whom changes in both FEV and FVC could be calculated were included in the analyses.

The labelling of the columns of results is similar to that employed in earlier tables; the response variables are labelled dFV for difference in FEV, and dVC for difference in FVC. The periods over which the differences were calculated were ISPs 4 and 5, and these are labelled I4 and I5 respectively.

### A3.3.2 Changes in Lung Function from 4th to 5th Survey

Table A3.9 presents results from the regression analysis of the change in FEV for 639 men with lung function data at both 4th and 5th surveys. The initial baseline model included age, height, smoking and a term for the differences between technicians which affected the lung function measurements at 5th survey.

The age coefficient was positive and significant, indicating a greater rate of loss in older men. Taller men also lost at a greater rate, presumably in some functional way as a result of their greater lung volumes. Smokers lost on average about 20ml per year (80ml per 4 years) more than non-smokers, from whom ex-smokers did not significantly differ. The estimates of these effects changed little when the exposure variables were added to the model.

None of the exposure variables for previous, ISP 3 or ISP 4 dust or quartz made a significant contribution to the model, either singly or in combinations. The largest reduction in the residual sums of squares was due to ISP 3 dust, but even this failed to reach the 10% significance level. However, it was notable that all the estimated coefficients for ISP 3 and 4 exposures were positive. Because the positive values of the response indicate a drop, any positive relationship with an exposure would, if real, indicate an association of greater loss of lung function with greater exposure.

Table A3.10 shows results from similar analyses of change over ISP 4 in FVC. The same baseline model was employed as for change in FEV, since the initial investigations had indicated that smoking made a (just) significant contribution to FVC change, which had not been the case for cross-sectional FVC. Conclusions regarding the effects of height, age and smoking were qualitatively similar to those for FEV in the same period, and changed little on the inclusion of exposure variables.

None of the exposure variables included made a significant contribution to the model. In contrast to the position with FEV change, the greatest contribution was from the previous exposures, with previous quartz just reaching the 10% significance level. The coefficients of the previous exposures were negative, which is the direction of smaller losses of lung function in association with higher previous exposures; this seems implausible, although consistent with some of the findings from the cross-sectional analyses.

### A3.3.3 Changes in Lung Function from 5th to 6th Survey

Table A3.11 shows results of regression analyses of the change in FEV for 457 men with lung function data at both 5th and 6th surveys. The baseline model included the same terms as for the changes over ISP 4, that is age, height, smoking and a term for the technician differences at 5th survey.

Obviously, the analyses of ISP 5 and ISP 4 data were not based on the same men, although they overlapped by about 350. The estimate of the age coefficient was smaller than the corresponding estimate from ISP 4 by between 30% and 50% in the various models, while the height coefficient was larger than the ISP 4 estimate by about the same margin. Smoking effects also differed, with the coefficient for ISP 5 about one quarter that for ISP 4, and nowhere near statistical significance. The ex-smokers appeared to be losing lung function less quickly in ISP 5 than the non-smokers, although this difference was below the 10%

significance level. The estimated difference between the old and new technicians was similar to that in ISP 4 (but of opposite sign, since the difference was at the start of ISP 5 but the end of ISP 4). The difference for those for whom the technician was not known looked very dissimilar from the ISP 4 value at a casual glance, but was in fact very poorly determined, since only three such men contributed to the ISP 5 analyses, compared to 39 for ISP 4.

The addition to the baseline model of the previous exposure variables made no useful contributions to the models, and they are not shown here. The addition of ISP 3, 4 and 5 dust and quartz variables gave estimates which were in all cases positive. Those for ISP 3 just exceeded the 10% level of significance, and were accompanied by the largest drop in the age coefficient. The largest individual contribution to the model was from ISP 5 dust, followed by ISP 4 dust, both of which were significant at better than the 1% level. In the models with two exposure variables, when both ISP 4 and ISP 5 dust variables were included, neither was significant in the presence of the other. However, model dFV/I5/10 shows that when ISP 5 dust and quartz were both included, quartz was not significant while dust was.

Table A3.12 shows results of similar regression analyses of the change in FVC in the same men over ISP 5. As with FEV, the estimated age effect was smaller than for ISP 4, but unlike FEV the height effect in ISP 5 was also smaller, and in fact not statistically significant. Smoking effects were again not significant, but of similar magnitude to those for FEV. The estimated difference between the old and new technicians was also similar.

As in ISP 4, addition of the dust and quartz variables produced stronger evidence of associations in FVC change than in FEV change. Previous quartz and dust were not significant, and are not shown. However, each of the ISP 3, 4 and 5 dust and quartz variables made a significant contribution, and all of them had positive estimated coefficients. The largest contributions were from ISP 4 and ISP 5 dust, both of which exceeded the 0.1% significance level.

In the models which included more than one exposure variable at a time, the ISP 3 variables were not significant in the presence of ISP 4 dust or ISP 5 dust. When ISP 4 dust and quartz were included together, the quartz effect was not significant, but the dust effect was still significant. With the inclusion of both ISP 4 and ISP 5 dust variables, both effects became not significant, although neither was entirely eliminated. However, none of the two-variable models was a significant improvement on the one-variable models with only ISP 4 or ISP 5 dust.

#### A3.3.4 Checks on the Adequacy of the Regression Models

The results in Tables A3.9 to A3.12 were from analyses in which the effects of age, height and exposure were assumed to be linear. As with the cross-sectional analyses, there was no intrinsic reason why linearity should be a better description of any relationship found than might be given by some other curve. Non-linearity, particularly in the age-dependence, had already been observed in the cross-sectional analyses of lung function, and this provided an additional justification for examining the question for the longitudinal analyses.

In earlier analyses, the question of linearity in a variable had initially been investigated by forming a grouped version of the variable and examining the pattern of the estimates for the different groups. Since in this case there was

ample justification, this process was omitted, and the analyses proceeded by examining the effects on regression models which had already been fitted, of including quadratic and cubic terms in age and in height.

In all cases, the inclusion of non-linear terms in height failed to improve the fit of the regression models. Linear adjustment for height was therefore accepted as adequate in the present data, and none of the results shown here includes any non-linear terms in height.

In contrast, the non-linear terms in age were significant in most of the models, and Tables A3.13 and A3.14 show the results of including both quadratic and cubic terms in models which have already appeared in earlier tables of results. The column labelling uses the earlier model identifier, with the suffix A for the models in which the non-linear age terms have been included.

Table A3.13 shows examples of comparisons from analyses of change in FEV over ISPs 4 and 5. In the first, the inclusion of the non-linear terms in one of the models fitted to FEV change was significant, but had little effect on the estimates of the effects of smoking or technician. The height effect was reduced by about 25%, and the ISP 3 dust effect, which had been positive but had not achieved significance, was annihilated.

The remaining four columns show similar comparisons between models for the change in FEV over ISP 5, with ISP 4 and ISP 5 dust variables respectively. With a linear term in age, ISP 4 dust was highly significant, and the addition of the non-linear terms gave a reduction in the residual sum of squares which fell short of the 5% significance level. With the non-linear terms added, there was some reduction in the height and technician terms, while the dust effect was reduced by over 20%, but was still significant.

In the model containing ISP 5 dust, the addition of the non-linear terms produced a reduction in the residual which was significant at the 5% level, although the partial t-statistics suggested that it was not necessary to include both quadratic and cubic terms. However, their inclusion reduced the height and technician coefficients, as well as that for ISP 5 dust, although this remained significant.

Table A3.14 shows similar comparisons in models for FVC changes over ISPs 4 and 5. Non-linear age terms were highly significant in the model for change over ISP 4, and their inclusion again reduced the estimated height effect, but had only a small influence on the smoking and technician effects.

In model dVC/I4/3, with only a linear age term, the term for previous quartz exposure had produced a reduction in the residual which lay just on the 10% significance level. The estimate was negative, which is in the direction of less severe loss of lung function being associated with higher exposure. With quadratic and cubic terms in age in the model, however, the estimate was reduced by over a half, and no longer approached conventional significance levels. In model dVC/I4/4, where the ISP 3 dust variable was positive although not reaching significance, the estimate in the presence of non-linear age was near zero.

The non-linear terms were also highly significant in both models for the change in FVC over ISP 5, again producing only modest influences on the height, smoking and technician effects. The estimates of the ISP 4 and ISP 5 dust effects were reduced by around 20%, but both remained significant.

It was concluded that, at most, only a minor part of the significant effects of dust exposure variables on the changes in FEV and FVC over ISP 5 could conceivably be ascribed to confounding with non-linear effects of age differences. For ISP 4, however, the weak evidence from earlier models, of possible associations with exposures in ISP 3 and earlier, could just as readily be explained as an artefact caused by the omission of significant non-linear age effects.

#### A3.4 Small Opacities and Lung Function

All the analyses so far have treated separately the radiographic evidence of pneumoconiotic shadows and the measures of individuals' lung function. Although the patterns of the relationships have not been identical, both responses have shown associations with estimates of the amounts of dust and quartz to which the individuals had been exposed in the workplace. It is obviously appropriate to inquire whether these responses are independent, or whether they are manifestations of the same disease process, and this section describes a set of analyses directed at this question.

Care is always needed in the joint assessment of separate but possibly associated responses, particularly where they represent changes which take place over a period or periods of time. In the present data, it is reasonable to assume that, if the responses are directly and causally associated, the appearance of pneumoconiotic shadows will be accompanied or followed by a consequent loss of lung function. The possibility that the loss of lung function, or the damage mechanism underlying that loss, may cause pneumoconiotic shadows, is a much less plausible hypothesis. This investigation therefore adopted the strategy of including an indicator of pneumoconiotic status amongst the explanatory variables in regression analyses of the lung function variables. It was believed that useful insights into the nature and extent of any relationships would be obtained by examination of the regression coefficient for such a variable and its statistical significance, plus any effect of its inclusion on the regression coefficients of the other variables also present in the regression models.

##### A3.4.1 Small Opacities and Lung Function at Individual Surveys

Regression analyses which had already been performed, and reported in Tables A3.1 to A3.6, were rerun with the inclusion of an extra explanatory variable which took the value 1 if the median category assigned to an individual's radiograph was 1/0 or higher, and 0 otherwise. In the analyses of small opacities profusions already reported, this was of course a response variable; but here, it was designed to represent any difference between the average values of lung function variables for men with and without small opacities of at least category 1/0.

Some of the results are shown in Table A3.15, with the columns labelled as for the corresponding models in Tables A3.1 to A3.6, with the suffix P to indicate that the model includes the variable for profusion of small opacities. Typical results are presented for both lung function variables, from each of the surveys. Numbers of men are very slightly smaller than in the earlier tabulations; median categories were not calculable for a few men for whom lung function data were analysed earlier.

The conclusions from each of these analyses were similar. After allowance for age, height and, where relevant, smoking habits and technician effects, the men with small opacities on their radiographs had lower FEV by between 100ml and 160ml, and lower FVC by between 180ml and 230ml. These differences were statistically significant in each of the models concerned. The inclusion of these differences made little difference to the estimates of age, height, smoking and technician effects. The estimates of the coefficients for dust and quartz exposure were also little changed; they remained positive, which as noted above was implausible in any directly causal sense; the likelihood that this was due to a large selection effect made it difficult to draw any useful inferences regarding the joint responses from these cross-sectional analyses. Models fitted with quartz instead of dust exposure variables led to very similar conclusions, and are not shown.

#### A3.4.2 Small Opacities and Changes in Lung Function

Similar supplementary analyses were performed on the variables representing change in lung function over inter-survey periods 4 and 5. Here, because non-linear terms in age had made a significant contribution to the fit of the regression models, with a noticeable effect upon the regression coefficients of the exposure variables, the baseline model included polynomial terms up to the cubic in age, as well as terms for height, smoking habits, technician differences, and exposure variables. To these models was added the variable taking the value 1 if the median category of small opacities was of profusion 1/0 or greater, and the value 0 otherwise.

Selected results are shown in Table A3.16. These may be compared to the relevant columns of Tables A3.13 and A3.14, in which the models with the cubic terms in age have column labels suffixed with A. (The analyses in Table A3.16 were based on slightly fewer men, but reruns of the earlier models on the reduced subgroups produced almost identical results.)

The reduction in the residual due to introducing the small opacities variable exceeded the 5% significance point only for the drop in FEV over ISP 4, although it exceeded the 10% point for the drop in FVC over both ISPs 4 and 5. In all cases, the estimated coefficient was negative; if real, this would suggest that the group showing small opacities on their radiographs had a lower rate of loss of lung function on average than those with no such radiological signs, but this does not seem plausible as a causal effect. Estimates of other terms in the models changed little in the presence of the small opacities variable, although the dust exposure effects increased slightly in all the models. Models fitted with quartz instead of dust showed similarly little change in the presence of the small opacities variable.

If loss of lung function were a sequel to parenchymal damage visible radiographically, and assuming that such damage were due to exposure to coalmine dust and/or quartz, we should have expected to observe in these analyses both a significant predictive role for the variable representing the observation of opacities, and a sizeable decrease in the coefficients of the exposures which preceded the damage. Therefore it was concluded that, while the effects observed might be due to population selection artefacts, these analyses had provided no evidence of a causal association between radiographic small opacities and level or loss of lung function in these men.



Table A1.1 Agreement between pairs of readers on profusion of small opacities on the 4-point scale, for all radiographs seen in exercise XRLV.

Rdr	Reader 101 Profusions				Total
	0	1	2	3	
104					
P 0	1262	495	49	0	1806
r 1	190	399	132	0	721
f 2	1	33	28	0	62
n 3	0	1	4	0	5
s					
Total	1453	928	213	0	2594

Rdr	Reader 101 Profusions				Total
	0	1	2	3	
105					
P 0	1078	292	19	0	1389
r 1	368	573	136	0	1077
f 2	7	63	57	0	127
n 3	0	0	1	0	1
s					
Total	1453	928	213	0	2594

Rdr	Reader 104 Profusions				Total
	0	1	2	3	
105					
P 0	1285	104	0	0	1389
r 1	519	537	121	0	1077
f 2	2	80	40	5	127
n 3	0	0	1	0	1
s					
Total	1806	721	262	0	2594

Rdr	Reader 101 Profusions				Total
	0	1	2	3	
106					
P 0	1445	870	163	0	2478
r 1	7	36	124	0	67
f 2	1	19	15	0	35
n 3	0	3	11	0	14
s					
Total	1453	928	213	0	2594

Rdr	Reader 104 Profusions				Total
	0	1	2	3	
106					
P 0	1803	660	15	0	2478
r 1	2	48	17	0	67
f 2	1	12	20	2	35
n 3	0	1	62	3	14
s					
Total	1806	721	62	5	2594

Rdr	Reader 105 Profusions				Total
	0	1	2	3	
106					
P 0	1386	1030	62	0	2478
r 1	2	41	24	0	67
f 2	1	6	28	0	35
n 3	0	0	13	1	14
s					
Total	1389	1077	127	1	2594

Table A1.1 continued.

Rdr	Reader 101 Profusions				Total	Rdr	Reader 104 Profusions				Total
	0	1	2	3			0	1	2	3	
112						112					
P 0	1142	489	65	0	1696	P 0	1479	216	1	0	1696
r 1	296	369	98	0	763	r 1	318	425	20	0	763
f 2	15	66	44	0	125	f 2	9	78	34	4	125
n 3	0	4	6	0	10	n 3	0	2	7	1	10
s						s					
Total	1453	928	213	0	2594	Total	1806	721	62	5	2594

Rdr	Reader 105 Profusions				Total	Rdr	Reader 106 Profusions				Total
	0	1	2	3			0	1	2	3	
112						112					
P 0	1220	472	4	0	1696	P 0	1690	4	2	0	1696
r 1	165	539	59	0	763	r 1	710	44	7	2	763
f 2	4	64	57	0	125	f 2	77	17	22	9	125
n 3	0	2	7	1	10	n 3	1	2	4	3	10
s						s					
Total	1389	1077	127	1	2594	Total	2478	67	35	14	2594

Table A1.2 Pairwise consistency coefficients summarising agreement between pairs of readers on major category of small opacities profusion. Tabulated is the proportion (%) of radiographs seen in exercise XRLV which both readers classified to the same category of the 4-point scale.

Reader	101	104	105	106
104	65.1			
105	65.8	71.8		
106	57.7	72.2	56.1	
112	59.9	74.7	70.0	67.8

**Table A1.3 Agreement within each reader between assessments of profusion on the 4-point scale on the same radiographs seen on two different occasions.**

Reader : 101

Exercise	XRVL Profusions				Total
	0	1	2	3	
XRLV					
P 0	1019	390	13	0	1422
r 1	230	584	85	0	899
f 2	12	137	54	0	203
n 3	0	0	0	0	0
Total	1261	1111	152	0	2524

Reader : 104

Exercise	XRVL Profusions				Total
	0	1	2	3	
XRLV					
P 0	1573	187	1	0	1761
r 1	200	479	15	0	694
f 2	0	27	30	1	58
n 3	0	0	3	2	5
Total	1773	693	49	3	2518

Reader : 105

Exercise	XRVL Profusions				Total
	0	1	2	3	
XRLV					
P 0	1137	227	0	0	1364
r 1	123	869	46	0	1038
f 2	0	39	79	0	118
n 3	0	0	1	0	1
Total	1260	1135	126	0	2521

Reader : 106

Exercise	XRVL Profusions				Total
	0	1	2	3	
XRLV					
P 0	2341	45	24	1	2411
r 1	27	16	17	2	62
f 2	2	4	21	7	34
n 3	0	0	3	10	13
Total	2370	65	65	20	2520

Reader : 112

Exercise	XRVL Profusions				Total
	0	1	2	3	
XRLV					
P 0	1296	343	23	0	1662
r 1	131	452	147	2	732
f 2	2	29	82	6	119
n 3	0	0	5	4	9
Total	1429	824	257	12	2522

**Table A1.4 Consistency coefficients summarising the proportion (%) of radiographs classified by each reader in the same category of profusion on the 4-point scale, on two separate occasions.**

	Reader				
	101	104	105	106	112
Consistency (%)	66	83	83	95	73

Table A1.5 Results of fitting different regression models to profusion of small opacities at 4th survey. Variable analysed is median profusion dichotomised between categories 0/1 and 1/0. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models				
	1+/4/1	1+/4/2	1+/4/3	1+/4/4	1+/4/5
constant	-4.001 (12.98)	-3.661 (10.85)	-3.706 (10.9)	-3.974 (12.18)	-3.973 (12.43)
age at survey	0.07703 (12.23)	0.06266 ( 7.30)	0.0650 ( 7.6)	0.0772 (12.09)	0.07710 (12.14)
dust previous		0.00759 ( 2.43)			
quartz previous			0.1198 ( 2.09)		
dust ISP 3				-0.00252 ( 0.29)	
quartz ISP 3					-0.0218 ( 0.39)
deviance	1285.1	1279.1	1280.7	1285.0	1285.0
degrees of freedom	1102	1101	1101	1101	1101

Table A1.6 Results of fitting different regression models to profusion of small opacities at 4th survey. Variable analysed is median profusion dichotomised between categories 1/2 and 2/1. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models				
	2+/4/1	2+/4/2	2+/4/3	2+/4/4	2+/4/5
constant	-9.25 ( 7.48)	-9.36 ( 7.12)	-9.37 ( 7.12)	-9.17 ( 6.84)	-9.10 ( 6.93)
age at survey	0.1174 ( 5.29)	0.1213 ( 4.64)	0.1214 ( 4.90)	0.1170 ( 5.16)	0.1161 ( 5.11)
dust previous		-0.00178 ( 0.29)			
quartz previous			-0.033 ( 0.30)		
dust ISP 3				-0.0044 ( 0.19)	
quartz ISP 3					-0.060 ( 0.39)
deviance	307.3	307.2	307.2	307.3	307.2
degrees of freedom	1102	1101	1101	1101	1101

**Table A1.7** Results of fitting different regression models to profusion of small opacities at 5th survey. Variable analysed is median profusion dichotomised between categories 0/1 and 1/0. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models							
	1+/5/1	1+/5/2	1+/5/3	1+/5/4	1+/5/5	1+/5/6	1+/5/7	1+/5/8
constant	-5.351 (11.22)	-5.578 (11.16)	-5.550 (11.20)	-6.466 (11.38)	-6.161 (11.34)	-5.763 ( 9.87)	-6.189 (11.36)	-6.314 (10.79)
age at survey	0.08788 ( 9.43)	0.08457 ( 8.83)	0.08575 ( 8.99)	0.0982 ( 9.68)	0.0964 ( 9.51)	0.0828 ( 6.45)	0.0979 ( 9.39)	0.0976 ( 9.42)
dust previous								
quartz previous						0.1341 ( 1.67)		
dust ISP 3		0.0265 ( 2.53)						
quartz ISP 3			0.2061 ( 2.99)				-0.0570 ( 0.62)	
dust ISP 4				0.0763 ( 4.83)				0.0231 ( 0.78)
quartz ISP 4					0.3720 ( 5.18)	0.3655 ( 5.10)	0.4110 ( 4.29)	0.284 ( 2.13)
deviance	825.7	819.4	817.0	802.3	798.3	795.5	797.9	797.7
degrees of freedom	868	867	867	867	867	866	866	866

**Table A1.8 Results of fitting different regression models to profusion of small opacities at 5th survey. Variable analysed is median profusion dichotomised between categories 1/2 and 2/1. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models						
	2+/5/1	2+/5/2	2+/5/3	2+/5/4	2+/5/5	2+/5/6	2+/5/7
constant	-7.71 ( 5.05)	-8.10 ( 4.83)	-8.12 ( 4.91)	-9.60 ( 4.51)	-8.92 ( 4.78)	-8.61 ( 4.19)	-8.91 ( 4.66)
age at survey	0.0735 ( 2.56)	0.0699 ( 2.30)	0.0714 ( 2.36)	0.0938 ( 2.57)	0.0874 ( 2.61)	0.0776 ( 1.80)	0.0865 ( 2.48)
dust previous							
quartz previous						0.088 ( 0.37)	
dust ISP 3		0.0369 ( 1.12)					
quartz ISP 3			0.307 ( 1.62)				0.035 ( 0.13)
dust ISP 4				0.0996 ( 2.17)			
quartz ISP 4					0.412 ( 2.58)	0.405 ( 2.39)	0.387 (1.66)
deviance	135.4	134.2	133.2	131.0	130.8	130.6	130.7
degrees of freedom	868	867	867	867	867	868	868

**Table A1.9 Results of fitting different regression models to profusion of small opacities at 6th survey. Variable analysed is median profusion dichotomised between categories 0/1 and 1/0. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	1+/6/1	1+/6/2	1+/6/3	1+/6/4	1+/6/5	1+/6/6	1+/6/7	1+/6/8	1+/6/9	1+/6/10
constant	-5.340 ( 8.69)	-5.521 ( 8.47)	-5.421 ( 8.22)	-5.912 ( 8.61)	-5.869 ( 8.61)	-6.175 ( 9.09)	-6.371 ( 8.83)	-5.761 ( 7.87)	-5.778 ( 8.39)	-6.199 ( 8.41)
age at survey	0.0831 ( 6.88)	0.0717 ( 5.53)	0.0730 ( 5.58)	0.0794 ( 6.08)	0.0831 ( 6.35)	0.0877 ( 7.05)	0.0954 ( 7.16)	0.0794 ( 4.97)	0.0789 ( 5.83)	0.0881 ( 6.40)
dust previous										
quartz previous								0.048 ( 0.40)		
dust ISP 3		0.0496 ( 3.95)								
quartz ISP 3			0.3627 ( 4.45)						0.146 ( 1.33)	
dust ISP 4				0.0845 ( 4.41)						
quartz ISP 4					0.4310 ( 5.16)			0.4279 ( 5.10)	0.333 ( 3.00)	0.356 ( 3.56)
dust ISP 5						0.0832 ( 3.79)				
quartz ISP 5							0.425 ( 4.07)			0.175 ( 1.34)
deviance	540.7	525.3	520.8	520.8	513.4	526.5	524.5	513.2	511.6	511.6
degrees of freedom	615	614	614	614	614	614	614	613	613	613

**Table A1.10 Results of fitting different regression models to profusion of small opacities at 6th survey. Variable analysed is median profusion dichotomised between categories 1/2 and 2/1. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	2+/6/1	2+/6/2	2+/6/3	2+/6/4	2+/6/5	2+/6/6	2+/6/7	2+/6/8	2+/6/9	2+/6/10
constant	-7.15 ( 4.65)	-8.28 ( 4.12)	-7.54 ( 3.83)	-9.05 ( 4.43)	-8.35 ( 4.32)	-8.95 ( 4.85)	-9.21 ( 4.75)	-9.87 ( 4.55)	-8.69 ( 4.04)	-8.18 ( 3.96)
age at survey	0.0721 ( 2.43)	0.0520 ( 1.40)	0.0473 ( 1.24)	0.0612 ( 1.63)	0.0723 ( 2.00)	0.0815 ( 2.48)	0.0962 ( 2.77)	0.0884 ( 2.02)	0.0473 ( 1.18)	0.0565 ( 1.43)
dust previous										
quartz previous								-0.360 ( 1.13)		
dust ISP 3		0.1176 ( 3.57)								
quartz ISP 3			0.762 ( 4.05)						0.458 ( 1.88)	0.472 ( 1.97)
dust ISP 4				0.2126 ( 4.02)				0.2163 ( 4.17)	0.1529 ( 2.40)	
quartz ISP 4					0.690 ( 4.38)					0.450 ( 111.5)
dust ISP 5						0.1545 ( 3.09)				
quartz ISP 5							0.691 ( 3.20)			
deviance	133.6	120.1	116.5	113.8	115.2	124.5	124.4	112.6	110.5	119.8
degrees of freedom	615	614	614	614	614	614	614	613	613	613

**Table A1.11 Results of fitting different regression models to profusion of small opacities at 1980 survey. Variable analysed is median profusion dichotomised between categories 0/1 and 1/0. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	1+/80/1	1+/80/1	1+/80/1	1+/80/1	1+/80/1	1+/80/6	1+/80/7	1+/80/8	1+/80/9	1+/80/10
constant	-5.141 ( 7.72)	-5.239 ( 7.21)	-5.217 ( 7.17)	-5.652 ( 7.58)	-5.520 ( 7.56)	-5.826 ( 7.71)	-5.920 ( 7.73)	-4.925 ( 6.26)	-5.379 ( 7.12)	-5.533 ( 6.94)
age at survey	0.0854 ( 6.59)	0.0746 ( 5.18)	0.0748 ( 5.24)	0.0823 ( 5.84)	0.0844 ( 6.04)	0.0886 ( 6.37)	0.0941 ( 6.63)	0.0655 ( 3.86)	0.0774 ( 5.26)	0.0800 ( 5.23)
dust previous										
quartz previous								0.134 ( 1.03)		
dust ISP 3		0.0434 ( 3.20)								
quartz ISP 3			0.3839 ( 4.28)					0.3609 ( 3.91)	0.265 ( 2.22)	0.321 (3.13)
dust ISP 4				0.0766 ( 3.73)						
quartz ISP 4					0.3751 ( 3.95)				0.188 ( 1.50)	
dust ISP 5						0.0748 ( 3.19)				
quartz ISP 5							0.360 ( 3.26)			0.163 ( 1.24)
deviance	458.1	447.8	439.2	444.0	441.8	447.9	447.7	438.1	436.9	437.7
degrees of freedom	442	441	441	441	441	441	441	440	440	440

**Table A1.12 Results of fitting different regression models to profusion of small opacities at 1980 survey. Variable analysed is median profusion dichotomised between categories 1/2 and 2/1. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	2+/80/1	2+/80/1	2+/80/1	2+/80/1	2+/80/1	2+/80/6	2+/80/7	2+/80/8	2+/80/9	2+/80/10
constant	-5.12 ( 4.07)	-4.97 ( 3.31)	-4.84 ( 3.29)	-5.73 ( 3.67)	-5.35 ( 3.70)	-6.17 ( 4.00)	-6.15 ( 3.99)	-4.67 ( 2.63)	-5.46 ( 3.36)	-5.66 ( 3.58)
age at survey	0.0369 ( 1.48)	0.0101 ( 0.31)	0.0124 ( 0.40)	0.0172 ( 0.55)	0.0261 ( 0.90)	0.0362 ( 1.26)	0.0460 ( 1.61)	-0.0180 ( 0.42)	0.0102 ( 0.30)	0.0184 ( 0.58)
dust previous								0.0211 ( 1.25)		
quartz previous										
dust ISP 3		0.0731 ( 2.30)								
quartz ISP 3			0.502 ( 2.65)						0.171 ( 0.64)	
dust ISP 4				0.1536 ( 3.19)				0.1527 ( 3.16)	0.1297 ( 2.08)	0.1190 ( 1.41)
quartz ISP 4					0.525 ( 3.25)					0.155 ( 0.51)
dust ISP 5						0.1324 ( 2.67)				
quartz ISP 5							0.497 ( 2.46)			
deviance	128.8	123.4	122.0	118.0	119.6	121.9	123.7	116.5	117.7	117.8
degrees of freedom	442	441	441	441	441	441	441	440	440	440

**Table A1.13** Numbers of men included in logistic analyses of median profusion at each survey, by grouped median profusion and smoking habits. Smoking data used for 1980 survey are those collected from the same men at 6th survey.

Survey	Smoking habit	Median profusion of small opacities			Total
		up to 0/1	1/0 - 1/2	2/1 & higher	
4th	Nonsmoker	113	36	1	150
	Exsmoker	71	60	3	134
	Smoker	488	294	37	819
	Unknown	1	0	0	1
	Combined	673	390	41	1104
5th	Nonsmoker	121	21	1	143
	Exsmoker	114	25	1	140
	Smoker	428	145	12	585
	Unknown	1	1	0	2
	Combined	664	192	14	870
6th	Nonsmoker	97	7	0	104
	Exsmoker	88	15	0	103
	Smoker	292	68	6	366
	Unknown	20	15	9	44
	Combined	497	105	15	617
1980	Nonsmoker	63	11	0	74
	Exsmoker	48	14	0	62
	Smoker	164	57	6	227
	Unknown	50	22	9	81
	Combined	325	104	15	444

**Table A1.14 Results of fitting regression models with and without smoking variables to median profusions of small opacities, dichotomised between categories 0/1 and 1/0, from each survey. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models							
	1+/4/2	1+/4/2S	1+/5/5	1+/5/5S	1+/6/5	1+/6/5S	1+/80/3	1+/80/3S
constant	-3.656 (10.82)	-3.929 (10.45)	-6.198 (11.35)	-6.512 (10.90)	-6.168 ( 8.20)	-6.928 ( 8.16)	-5.344 ( 6.49)	-5.588 ( 6.49)
age at survey	0.06256 ( 7.29)	0.05956 ( 6.85)	0.0971 ( 9.53)	0.1000 ( 9.51)	0.0880 ( 6.11)	0.0884 ( 5.97)	0.0782 ( 4.81)	0.0790 ( 4.74)
dust previous	0.00760 ( 2.44)	0.00825 ( 2.63)						
quartz previous								
dust ISP 3								
quartz ISP 3							0.283 ( 2.80)	0.268 ( 2.62)
dust ISP 4								
quartz ISP 4			0.3715 ( 5.17)	0.3848 ( 5.28)	0.3416 ( 3.74)	0.3291 ( 3.57)		
dust ISP 5								
quartz ISP 5								
ex-smoker v. non		0.587 ( 2.07)		-0.483 ( 1.38)		0.408 ( 0.82)		-0.093 ( 0.19)
smoker v. non		0.407 ( 1.81)		0.319 ( 1.14)		1.021 ( 2.40)		0.373 ( 0.97)
deviance	1279.0	1274.3	794.1	783.0	441.3	437.5	347.1	344.9
degrees of freedom	1100	1098	865	863	570	568	360	358

**Table A1.15** Residual deviances obtained by fitting logistic regression models separately to each of five readers' duplicate assessments of profusion of small opacities at 5th survey, dichotomised between categories 0/1 and 1/0. Models fitted included a constant, age and the individual exposure variables one at a time.

Variables	Reader/occasion										median
	101/1	104/1	105/1	106/1	112/1	101/2	104/2	105/2	106/2	112/2	
age at survey	838.9	613.0	691.0	152.3	566.3	824.5	583.6	720.2	200.1	629.1	540.5
+dust previous	838.9	613.0	687.1	151.5	564.3	816.8	583.3	717.7	200.1	626.9	539.9
+quartz previous	838.9	613.0	687.0	151.8	563.8	817.6	582.6	716.8	200.1	624.9	539.8
+dust ISP 3	834.5	606.1	668.3	139.6	548.3	817.0	572.1	707.5	188.8	614.1	525.1
+quartz ISP 3	833.9	602.4	670.0	133.2	542.3	814.8	569.0	702.2	185.0	610.4	520.6
+dust ISP 4	832.3	602.9	666.8	140.4	545.8	817.7	568.1	700.8	190.0	613.0	520.2
+quartz ISP 4	832.9	596.6	670.2	140.9	543.6	815.9	563.8	702.5	190.2	609.9	512.3
+dust ISP 5	831.7	608.4	673.5	144.3	557.4	820.3	574.4	704.6	192.7	619.3	526.2
+quartz ISP 5	834.9	606.7	677.2	141.3	558.7	821.5	574.4	709.3	190.4	619.4	524.1





Table A2.1 continued.

6th Survey		Profusions : Reader 010												
P		0-	00	01	10	11	12	21	22	23	32	33	3+	Total
r	0-	0	0	0	0	0	0	0	0	0	0	0	0	0
o	00	0	96	5	0	0	0	0	0	0	0	0	0	101
f	01	0	7	3	0	0	0	0	0	0	0	0	0	10
u	10	0	1	1	0	0	0	0	0	0	0	0	0	2
s	11	0	6	3	0	2	0	0	0	0	0	0	0	11
i	12	0	0	1	0	0	1	0	0	0	0	0	0	2
o	21	0	0	0	0	0	0	0	0	0	0	0	0	0
n	22	0	0	0	0	0	0	1	0	0	0	0	0	1
s	23	0	0	0	0	0	0	0	0	0	0	0	0	0
Rdr	32	0	0	0	0	0	0	0	0	0	0	0	0	0
	33	0	0	0	0	0	0	0	0	0	0	0	0	0
011	3+	0	0	0	0	0	0	0	0	0	0	0	0	0
Total		0	110	13	0	2	1	1	0	0	0	0	0	127

1980 Survey		Profusions : Reader 010												
P		0-	00	01	10	11	12	21	22	23	32	33	3+	Total
r	0-	0	0	0	0	0	0	0	0	0	0	0	0	0
o	00	0	76	2	0	0	0	0	0	0	0	0	0	78
f	01	0	4	2	0	0	0	0	0	0	0	0	0	6
u	10	0	2	1	0	0	0	0	0	0	0	0	0	3
s	11	0	4	5	0	2	0	0	0	0	0	0	0	11
i	12	0	0	0	0	0	0	0	0	0	0	0	0	0
o	21	0	0	0	0	0	0	0	0	0	0	0	0	0
n	22	0	0	0	1	0	0	0	0	0	0	0	0	1
s	23	0	0	0	0	0	0	1	0	0	0	0	0	1
Rdr	32	0	0	0	0	0	0	0	0	0	0	0	0	0
	33	0	0	0	0	0	0	0	0	0	0	0	0	0
011	3+	0	0	0	0	0	0	0	0	0	0	0	0	0
Total		0	86	10	1	2	0	1	0	0	0	0	0	100

Table A2.2 Comparisons of assessments by the two medical readers of change in small opacities profusion on the same pairs of radiographs, by survey.

Period : 4th to 5th survey

		Steps of change in profusion, reader 010										
		-3	-2	-1	0	+1	+2	+3	+4	+5	+6	Total
C h a n g e	-3	0	0	0	0	0	0	0	0	0	0	0
	-2	0	0	0	1	0	0	0	0	0	0	1
	-1	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	83	2	0	0	0	0	0	85
	+1	0	0	0	6	1	0	0	0	0	0	7
	+2	0	0	0	0	1	0	0	0	0	0	1
	+3	0	0	0	0	0	0	0	0	0	0	0
rdr	+4	0	0	0	0	0	0	0	0	0	0	0
	+5	0	0	0	0	0	0	0	0	0	0	0
	+6	0	0	0	0	0	0	0	0	0	0	0
Total		0	0	0	90	4	0	0	0	0	0	94

Period : 5th to 6th survey

		Steps of change in profusion, reader 010										
		-3	-2	-1	0	+1	+2	+3	+4	+5	+6	Total
C h a n g e	-3	0	0	0	0	0	0	0	0	0	0	0
	-2	0	0	0	0	0	0	0	0	0	0	0
	-1	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	1	89	0	0	0	0	0	0	90
	+1	0	0	0	7	0	0	0	0	0	0	7
	+2	0	0	0	5	1	1	1	0	0	0	8
	+3	0	0	0	1	0	0	0	0	0	0	1
rdr	+4	0	0	0	0	0	0	0	0	0	0	0
	+5	0	0	0	0	0	0	0	0	0	0	0
	+6	0	0	0	0	0	0	0	1	0	0	1
Total		0	0	1	102	1	1	1	1	0	0	107

Table A2.2 continued.

Period : 6th to 1980 survey

		Steps of change in profusion, reader 010									Total	
		-3	-2	-1	0	+1	+2	+3	+4	+5	+6	Total
C h a n g e r d r 011	-3	0	0	0	0	0	0	0	0	0	0	0
	-2	0	0	0	0	0	0	0	0	0	0	0
	-1	0	0	0	1	0	0	0	0	0	0	1
	0	0	0	0	77	1	0	0	0	0	0	78
	+1	0	0	0	5	0	0	0	0	0	0	5
	+2	0	0	0	2	1	0	0	0	0	0	3
	+3	0	0	0	0	1	0	0	0	0	0	1
	+4	0	0	0	0	0	0	0	0	0	0	0
	+5	0	0	0	0	0	0	0	0	0	0	0
	+6	0	0	0	0	0	0	0	0	0	0	0
Total		0	0	0	85	3	0	0	0	0	0	88

All three inter-survey periods combined

		Steps of change in profusion, reader 010									Total	
		-3	-2	-1	0	+1	+2	+3	+4	+5	+6	Total
C h a n g e r d r 011	-3	0	0	0	0	0	0	0	0	0	0	0
	-2	0	0	0	1	0	0	0	0	0	0	1
	-1	0	0	0	1	0	0	0	0	0	0	1
	0	0	0	1	249	3	0	0	0	0	0	253
	+1	0	0	0	18	1	0	0	0	0	0	19
	+2	0	0	0	7	3	1	1	0	0	0	12
	+3	0	0	0	1	1	0	0	0	0	0	2
	+4	0	0	0	0	0	0	0	0	0	0	0
	+5	0	0	0	0	0	0	0	0	0	0	0
	+6	0	0	0	0	0	0	1	0	0	1	
Total		0	0	1	277	8	1	1	1	0	0	289

**Table A2.3 Assessments of profusion of large opacities by two medical readers in serial reading exercise.**  
Included are all radiograph pairs read for adjacent surveys.

**Reader : 010**  
Profusions of large opacities  
at 4th survey

a	0	A	B	C	Total
t 0	324	0	0	0	324
5 A	0	0	0	0	0
t B	0	0	0	0	0
h C	0	0	0	0	0
<b>Total</b>	<b>324</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>324</b>

**Reader : 011**  
Profusions of large opacities  
at 4th survey

a	0	A	B	C	Total
t 0	182	0	0	0	182
5 A	0	0	0	0	0
t B	0	0	0	0	0
h C	0	0	0	0	0
<b>Total</b>	<b>182</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>182</b>

**Reader : 010**  
Profusions of large opacities  
at 5th survey

a	0	A	B	C	Total
t 0	393	0	0	0	393
6 A	2	0	0	0	2
t B	1	0	0	0	1
h C	0	0	0	0	0
<b>Total</b>	<b>396</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>396</b>

**Reader : 011**  
Profusions of large opacities  
at 5th survey

a	0	A	B	C	Total
t 0	216	0	0	0	216
6 A	0	0	0	0	0
t B	1	0	0	0	1
h C	0	0	0	0	0
<b>Total</b>	<b>217</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>217</b>

**Reader : 010**  
Profusions of large opacities  
at 6th survey

a	0	A	B	C	Total
t 0	304	1	0	0	305
1 A	1	0	0	0	1
9 B	0	0	0	0	0
8 C	0	0	1	0	1
0					
<b>Total</b>	<b>305</b>	<b>1</b>	<b>1</b>	<b>0</b>	<b>307</b>

**Reader : 011**  
Profusions of large opacities  
at 6th survey

a	0	A	B	C	Total
t 0	175	0	0	0	175
1 A	0	0	0	0	0
9 B	0	0	0	0	0
8 C	0	0	1	0	1
0					
<b>Total</b>	<b>175</b>	<b>0</b>	<b>1</b>	<b>0</b>	<b>176</b>

**Table A2.4 Results of fitting different logistic regression models to binary variable indicating one or more steps of progression of small opacities in ISP 4. Tabulated values are estimated regression coefficients. Absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models							
	1+/I4/1	1+/I4/2	1+/I4/3	1+/I4/4	1+/I4/4	1+/I4/6	1+/I4/7	1+/I4/8
constant	-5.20 ( 4.64)	-5.80 ( 4.70)	-5.47 ( 4.51)	-6.14 ( 4.94)	-5.93 ( 4.92)	-5.69 ( 4.41)	-5.34 ( 4.29)	-5.744 ( 4.63)
reader 011	0.991 ( 2.71)	0.971 ( 2.62)	0.942 ( 2.53)	1.018 ( 2.75)	1.043 ( 2.81)	0.923 ( 2.46)	0.937 ( 2.51)	0.974 ( 2.61)
age at survey	0.0458 ( 1.99)	0.0354 ( 1.40)	0.0329 ( 1.30)	0.0474 ( 1.97)	0.0490 ( 2.03)	0.0411 ( 1.37)	0.0339 ( 1.34)	0.0372 ( 1.45)
dust previous								
quartz previous						-0.102 ( 0.51)		
dust ISP 3		0.0632 ( 2.66)					-0.0216 ( 0.45)	
quartz ISP 3			0.4501 ( 3.47)			0.461 ( 3.51)	0.548 ( 2.19)	0.340 ( 2.06)
dust ISP 4				0.0847 ( 2.46)				
quartz ISP 4					0.394 ( 3.17)			0.188 (1.153)
deviance	232.7	225.4	220.8	226.5	223.6	220.6	220.6	219.6
degrees of freedom	502	501	501	501	501	500	500	500

**Table A2.5 Results of fitting different logistic regression models to binary variable indicating two or more steps of progression of small opacities in ISP 4. Tabulated values are estimated regression coefficients. Absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models						
	2+/I4/1	2+/I4/2	2+/I4/3	2+/I4/4	2+/I4/5	2+/I4/6	2+/I4/7
constant	-5.54 ( 2.92)	-6.66 ( 3.33)	-6.48 ( 3.28)	-5.59 ( 2.84)	-5.51 ( 2.81)	-6.11 ( 3.00)	-5.94 ( 2.96)
reader 011	1.709 ( 2.13)	1.626 ( 1.98)	1.640 ( 2.09)	1.705 ( 2.08)	1.676 ( 2.11)	1.726 ( 2.16)	1.7465 ( 2.13)
age at survey	0.0102 ( 0.26)	0.0591 ( 1.24)	0.0508 ( 1.09)	0.0075 ( 0.18)	-0.0012 ( 0.03)	0.0089 ( 0.22)	0.0091 ( 0.22)
dust previous		-0.0383 ( 1.50)					
quartz previous			-0.614 ( 1.36)				
dust ISP 3				0.0114 ( 0.25)			
quartz ISP 3					0.272 ( 1.11)		
dust ISP 4						0.0633 ( 0.95)	
quartz ISP 4							0.311 ( 1.30)
deviance	77.01	74.53	75.17	76.94	75.94	76.15	75.60
degrees of freedom	502	501	501	501	501	501	501

**Table A2.6 Results of fitting different logistic regression models to binary variable indicating one or more steps of progression of small opacities in ISP 5. Tabulated values are estimated regression coefficients. Absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	1+/15/1	1+/15/2	1+/15/3	1+/15/4	1+/15/5	1+/15/6	1+/15/7	1+/15/8	1+/15/9	1+/15/10
constant	-4.862 ( 6.20)	-5.442 ( 5.97)	-4.856 ( 5.50)	-6.717 ( 7.00)	-6.151 ( 6.67)	-6.700 ( 7.12)	-7.015 ( 7.14)	-5.694 ( 5.88)	-5.85 ( 5.83)	-6.56 ( 6.56)
reader 011	1.287 ( 4.59)	1.372 ( 4.71)	1.362 ( 4.59)	1.473 ( 4.96)	1.532 ( 5.05)	1.354 ( 4.67)	1.335 ( 4.61)	1.500 ( 4.81)	1.381 ( 4.62)	1.523 ( 4.94)
age at survey	0.0429 ( 2.85)	0.0183 ( 1.03)	0.0143 ( 0.80)	0.0388 ( 2.25)	0.0443 ( 2.60)	0.0565 ( 3.48)	0.0706 ( 4.09)	0.0258 ( 1.36)	0.0298 ( 1.53)	0.0544 (2.94)
dust previous										
quartz previous										
dust ISP 3		0.1027 ( 5.69)								
quartz ISP 3			0.707 ( 6.42)					0.434 ( 3.13)	0.605 ( 5.05)	
dust ISP 4				0.1874 ( 6.40)						
quartz ISP 4					0.739 ( 6.65)			0.484 ( 3.53)		0.637 ( 4.98)
dust ISP 5						0.1339 ( 4.75)				
quartz ISP 5							0.625 ( 5.07)		0.333 ( 2.44)	0.243 ( 1.61)
deviance	367.9	332.6	322.7	320.5	319.5	344.7	342.8	309.8	317.1	317.1
degrees of freedom	609	608	608	608	608	608	608	607	607	607

**Table A2.7 Results of fitting different logistic regression models to binary variable indicating two or more steps of progression of small opacities in ISP 5. Tabulated values are estimated regression coefficients. Absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	2+/15/1	2+/15/2	2+/15/3	2+/15/4	2+/15/5	2+/15/6	2+/15/7	2+/15/8	2+/15/9	2+/15/10
constant	-4.98 ( 4.94)	-5.39 ( 4.70)	-4.82 ( 4.37)	-6.277 ( 5.36)	-5.721 ( 5.20)	-6.26 ( 5.40)	-6.66 ( 5.51)	5.25 ( 4.59)	-5.54 ( 4.49)	-6.33 ( 5.11)
reader 011	1.070 ( 2.89)	1.099 ( 2.93)	1.052 ( 2.80)	1.153 ( 3.06)	1.174 ( 3.12)	1.086 ( 2.90)	1.072 ( 2.87)	1.106 ( 2.92)	1.054 ( 2.79)	1.154 ( 3.02)
age at survey	0.0333 ( 1.70)	0.0088 ( 0.39)	0.0066 ( 0.29)	0.0270 ( 1.25)	0.0311 ( 1.48)	0.0421 ( 2.06)	0.0545 ( 2.53)	0.0130 ( 0.56)	0.0178 ( 0.73)	0.0404 ( 1.78)
dust previous										
quartz previous										
dust ISP 3		0.0927 ( 4.04)								
quartz ISP 3			0.590 ( 4.47)					0.410 ( 2.44)	0.512 ( 3.49)	
dust ISP 4				0.1496 ( 4.20)						
quartz ISP 4					0.539 ( 4.39)			0.300 ( 1.89)		0.451 ( 3.10)
dust ISP 5						0.1003 ( 2.83)				
quartz ISP 5							0.515 ( 3.36)		0.255 ( 1.49)	0.230 ( 1.24)
deviance	240.0	223.0	220.3	221.3	222.6	232.3	229.7	217.0	218.2	221.1
degrees of freedom	609	608	608	608	608	608	608	607	607	607

**Table A2.8 Results of fitting different logistic regression models to binary variable indicating one or more steps of progression of small opacities in ISP 6. Tabulated values are estimated regression coefficients. Absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	1+/16/1	1+/16/2	1+/16/3	1+/16/4	1+/16/16	1+/16/6	1+/16/7	1+/16/8	1+/16/9	1+/16/10
constant	-7.17 ( 5.27)	-7.34 ( 5.18)	-7.22 ( 5.01)	-8.31 ( 5.31)	-7.94 ( 5.26)	-8.17 ( 5.39)	-8.22 ( 5.33)	7.99 ( 5.20)	-7.87 ( 5.12)	-8.10 ( 5.04)
reader 011	0.983 ( 2.57)	1.033 ( 2.75)	1.001 ( 2.59)	1.123 ( 2.85)	1.101 ( 2.80)	1.025 ( 2.64)	1.009 ( 2.61)	1.107 ( 2.79)	1.013 ( 2.64)	1.097 ( 2.76)
age at survey	0.0815 ( 3.23)	0.0677 ( 2.51)	0.0715 ( 2.63)	0.0764 ( 2.72)	0.0811 ( 2.95)	0.0846 ( 3.14)	0.0929 ( 3.39)	0.0827 ( 2.90)	0.0815 ( 2.87)	0.0834 ( 2.90)
dust previous										
quartz previous										
dust ISP 3		0.0534 ( 2.33)								
quartz ISP 3			0.307 ( 2.33)					-0.045 ( 0.23)	0.204 ( 1.33)	
dust ISP 4				0.1323 ( 3.64)						
quartz ISP 4					0.505 ( 3.80)			0.534 ( 2.92)		0.475 ( 2.98)
dust ISP 5						0.1011 ( 2.80)				
quartz ISP 5							0.415 ( 2.46)		0.286 ( 1.47)	0.075 ( 0.35)
deviance	208.5	203.3	203.3	194.3	194.8	200.8	203.0	194.7	201.3	194.7
degrees of freedom	479	478	478	478	478	478	478	477	477	477

**Table A2.9 Results of fitting different logistic regression models to binary variable indicating two or more steps of progression of small opacities in ISP 6, using only assessments by reader 011. Tabulated values are estimated regression coefficients. Absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	2+/16/1	2+/16/2	2+/16/3	2+/16/4	2+/16/5	2+/16/6	2+/16/7	2+/16/8	2+/16/9	2+/16/10
constant	-7.52 ( 2.63)	-7.80 ( 2.30)	-7.55 ( 2.40)	-8.44 ( 2.49)	-7.74 ( 2.45)	-9.84 ( 2.84)	-10.32 ( 2.70)	-10.15 ( 2.67)	-9.67 ( 2.67)	-10.28 ( 2.64)
age at survey	0.0839 ( 1.55)	0.0623 ( 0.96)	0.0746 ( 1.25)	0.0798 ( 1.29)	0.0840 ( 1.43)	0.0965 ( 1.59)	0.1192 ( 1.78)	0.1039 ( 1.52)	0.0968 ( 1.52)	0.1061 ( 1.53)
dust previous										
quartz previous										
dust ISP 3		0.0830 ( 1.46)								
quartz ISP 3			0.280 ( 1.04)					-0.115 ( 0.29)		
dust ISP 4				0.1162 ( 1.43)						
quartz ISP 4					0.176 ( 0.54)				-0.282 ( 0.68)	
dust ISP 5						0.1841 ( 2.25)		0.1989 ( 2.02)	0.2047 ( 2.41)	0.143 ( 0.98)
quartz ISP 5							0.757 ( 2.15)			0.233 ( 0.35)
deviance	49.13	46.84	48.21	46.98	48.87	43.95	44.77	43.87	43.47	43.83
degrees of freedom	174	173	173	173	173	173	173	172	172	172

**Table A2.10 Results of fitting logistic regression models with and without smoking variables to binary variable indicating one or more steps of progression of small opacities profusion, in each ISP. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models							
	1+/14/3	1+/14/3S	1+/15/5	1+/15/5S	1+/15/8	1+/15/8S	1+/16/5	1+/16/5S
constant	-5.47 ( 4.51)	-5.77 ( 4.54)	-6.184 ( 6.66)	-6.434 ( 6.66)	-5.716 ( 5.84)	-5.98 ( 5.86)	-9.87 ( 4.94)	-11.35 ( 4.77)
reader 011	0.942 ( 2.53)	0.946 ( 2.54)	1.496 ( 4.91)	1.586 ( 5.10)	1.459 ( 4.65)	1.558 ( 4.84)	1.317 ( 2.90)	1.401 ( 3.01)
age at survey	0.0329 ( 1.30)	0.0300 ( 1.15)	0.0452 ( 2.63)	0.0474 ( 2.64)	0.0259 ( 1.35)	0.0239 ( 1.17)	0.1134 ( 3.18)	0.1160 ( 3.02)
dust previous								
quartz previous								
dust ISP 3								
quartz ISP 3	0.450 ( 3.47)	0.471 ( 3.55)			0.452 ( 3.25)	0.488 ( 3.43)		
dust ISP 4								
quartz ISP 4			0.741 ( 6.65)	0.764 ( 6.72)	0.478 ( 3.48)	0.488 ( 3.54)	0.463 ( 3.04)	0.459 ( 3.01)
dust ISP 5								
quartz ISP 5								
ex-smoker v. non		-0.445 ( 0.47)		-0.855 ( 1.38)		-0.786 ( 1.20)		1.09 ( 0.97)
smoker v. non		0.528 ( 0.82)		0.236 ( 0.52)		0.440 ( 0.91)		1.53 ( 1.45)
deviance	220.8	218.3	315.1	309.2	304.7	297.5	153.3	150.0
degrees of freedom	501	499	603	601	602	600	442	440

**Table A3.1 Results of fitting different regression models to lung function at 4th survey. Variable analysed is forced expiratory volume (FEV) in one second, averaged over three (maximum) technically satisfactory expirations. FEV is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models					
	FEV/4/1	FEV/4/2	FEV/4/3	FEV/4/4	FEV/4/5	FEV/4/6
constant	-2.118 ( 4.39)	-2.123 ( 4.40)	-2.122 ( 4.40)	-2.225 ( 4.65)	-2.202 ( 4.60)	-2.222 ( 4.64)
age at survey	-0.03676 (27.15)	-0.03583 (17.64)	-0.03638 (18.22)	-0.03834 (27.52)	-0.03766 (27.65)	-0.03819 (26.92)
height (cm)	0.04206 (15.35)	0.04198 (15.30)	0.04204 (15.33)	0.04230 (15.56)	0.04229 (15.54)	0.04231 (15.55)
ex-smokers v non	0.0005 ( 0.01)	-0.0036 ( 0.05)	-0.0011 ( 0.02)	0.0051 ( 0.08)	0.0053 ( 0.08)	0.0054 ( 0.08)
smokers v non	-0.1399 ( 2.75)	-0.1417 ( 2.78)	-0.1406 ( 2.76)	-0.1312 ( 2.60)	-0.1326 ( 2.62)	-0.1313 ( 2.60)
dust previous		-0.0005 ( 0.61)				
quartz previous			-0.0039 ( 0.26)			
dust ISP 3				0.00931 ( 4.28)		0.0067 ( 1.32)
quartz ISP 3					0.0583 ( 4.10)	0.0188 ( 0.57)
residual s.s.	337.50	337.38	337.48	331.90	332.34	331.81
degrees of freedom	1085	1084	1084	1084	1084	1083
residual m.s.	0.3111	0.3112	0.3113	0.3062	0.3066	0.3064

**Table A3.2** Results of fitting different regression models to lung function at 4th survey. Variable analysed is forced vital capacity (FVC), averaged over three (maximum) technically satisfactory expirations. FVC is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models					
	FVC/4/1	FVC/4/2	FVC/4/3	FVC/4/4	FVC/4/5	FVC/4/6
constant	-4.611 ( 8.64)	-4.624 ( 8.66)	-4.626 ( 8.66)	-4.747 ( 9.00)	-4.714 ( 8.92)	-4.745 ( 8.99)
age at survey	-0.03016 (20.41)	-0.02850 (12.87)	-0.02903 (13.32)	-0.03228 (21.33)	-0.03132 (21.15)	-0.03218 (20.86)
height (cm)	0.06078 (19.95)	0.06064 (19.88)	0.06072 (19.91)	0.06109 (20.29)	0.06107 (20.25)	0.06110 (20.29)
dust previous		-0.00092 ( 1.00)				
quartz previous			-0.0118 ( 0.70)			
dust ISP 3				0.01277 ( 5.30)		0.01102 ( 1.97)
quartz ISP 3					0.0776 ( 4.93)	0.0127 ( 0.35)
residual s.s.	418.58	418.19	418.39	408.01	409.42	407.97
degrees of freedom	1087	1086	1086	1086	1086	1085
residual m.s.	0.3851	0.3851	0.3853	0.3757	0.3770	0.3760

**Table A3.3 Results of fitting different regression models to lung function at 5th survey. Variable analysed is forced expiratory volume (FEV) in one second, averaged over three (maximum) technically satisfactory expirations. FEV is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models						
	FEV/5/1	FEV/5/2	FEV/5/3	FEV/5/4	FEV/5/5	FEV/5/6	FEV/5/7
constant	-1.444 ( 2.70)	-1.490 ( 2.79)	-1.471 ( 2.75)	-1.539 ( 2.89)	-1.493 ( 2.80)	-1.534 ( 2.88)	-1.545 ( 2.90)
age at survey	-0.03576 (22.60)	-0.03690 (21.36)	-0.03648 (22.02)	-0.03611 (22.86)	-0.03588 (22.71)	-0.03561 (19.80)	-0.03618 (22.87)
height (cm)	0.03740 (12.40)	0.03766 (12.49)	0.03756 (12.46)	0.03763 (12.53)	0.03754 (12.47)	0.03754 (12.48)	0.03762 (12.53)
ex-smokers v non	-0.0974 ( 1.41)	-0.0980 ( 1.42)	-0.0978 ( 1.41)	-0.1033 ( 1.50)	-0.1013 ( 1.46)	-0.1042 ( 1.51)	-0.1031 ( 1.49)
smokers v non	-0.1731 ( 3.18)	-0.1697 ( 3.11)	-0.1702 ( 3.12)	-0.1697 ( 3.13)	-0.1711 ( 3.15)	-0.1708 ( 3.15)	-0.1697 ( 3.13)
tech old v new	0.2149 ( 3.53)	0.2097 ( 3.44)	0.2123 ( 3.48)	0.1927 ( 3.15)	0.2012 ( 3.29)	0.1909 ( 3.12)	0.1928 ( 3.15)
tech not known	0.1526 ( 1.76)	0.1376 ( 1.58)	0.1376 ( 1.58)	0.1216 ( 1.40)	0.1332 ( 1.53)	0.1231 ( 1.41)	0.1220 ( 1.40)
dust ISP 3		0.00397 ( 1.64)				-0.00201 ( 0.59)	
quartz ISP 3			0.0237 ( 1.45)				
dust ISP 4				0.01045 ( 2.94)		0.01253 ( 2.51)	0.01515 ( 2.21)
quartz ISP 4					0.0356 ( 2.09)		-0.0262 ( 0.80)
residual s.s.	268.16	267.31	268.03	265.45	266.78	265.34	265.25
degrees of freedom	847	846	846	846	846	845	845
residual m.s.	0.3166	0.3160	0.3162	0.3138	0.3153	0.3140	0.3139

**Table A3.4** Results of fitting different regression models to lung function at 5th survey. Variable analysed is forced vital capacity (FVC), averaged over three (maximum) technically satisfactory expirations. FVC is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models						
	FVC/5/1	FVC/5/2	FVC/5/3	FVC/5/4	FVC/5/5	FVC/5/6	FVC/5/7
constant	-3.218 ( 5.53)	-3.285 ( 5.65)	-3.256 ( 5.60)	-3.356 ( 5.82)	-3.293 ( 5.69)	-3.351 ( 5.81)	-3.363 ( 5.83)
age at survey	-0.03169 (18.73)	-0.03353 (18.13)	-0.03285 (18.55)	-0.03227 (19.21)	-0.03191 (18.95)	-0.03150 (16.42)	-0.03235 (19.22)
height (cm)	0.05077 (15.40)	0.05117 (15.55)	0.05101 (15.50)	0.05107 (15.65)	0.05097 (15.55)	0.05094 (15.59)	0.05107 (15.65)
tech old v new	0.3367 ( 5.04)	0.3281 ( 4.92)	0.3323 ( 4.98)	0.3010 ( 4.52)	0.3134 ( 4.69)	0.2983 ( 4.47)	0.3011 ( 4.52)
tech not known	0.3150 ( 3.32)	0.2912 ( 3.06)	0.2909 ( 3.05)	0.2667 ( 2.82)	0.2830 ( 2.98)	0.2689 ( 2.84)	0.2671 ( 2.82)
dust ISP 3		0.00644 ( 2.43)				-0.00307 ( 0.83)	
quartz ISP 3			0.0390 ( 2.18)				
dust ISP 4				0.01673 ( 4.33)		0.01992 ( 3.66)	0.02208 ( 2.96)
quartz ISP 4					0.0604 ( 3.25)		-0.0299 ( 0.84)
residual s.s.	323.11	320.86	321.31	316.13	319.13	315.87	315.87
degrees of freedom	849	848	848	848	848	847	845
residual m.s.	0.3806	0.3784	0.3789	0.3728	0.3763	0.3729	0.3729

**Table A3.5 Results of fitting different regression models to lung function at 6th survey. Variable analysed is forced expiratory volume (FEV) in one second, averaged over three (maximum) technically satisfactory expirations. FEV is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	FEV/6/1	FEV/6/2	FEV/6/3	FEV/6/4	FEV/6/5	FEV/6/6	FEV/6/7	FEV/6/8	FEV/6/9	FEV/6/10
constant	-1.336 ( 2.02)	-1.336 ( 2.02)	-1.342 ( 2.02)	-1.358 ( 2.05)	-1.353 ( 2.04)	-1.377 ( 2.07)	-1.391 ( 2.09)	-1.380 ( 2.09)	-1.426 ( 2.16)	-1.357 ( 2.05)
age at survey	-0.03631 (18.82)	-0.03639 (15.72)	-0.03595 (16.61)	-0.03749 (17.92)	-0.03685 (18.50)	-0.03652 (18.74)	-0.03624 (18.77)	-0.03594 (15.51)	-0.03640 (16.82)	-0.03763 (17.66)
height (cm)	0.03731 (10.10)	0.03732 (10.08)	0.03731 (10.09)	0.03744 (10.14)	0.03741 (10.12)	0.03744 (10.12)	0.03748 (10.13)	0.03734 (10.12)	0.03758 (10.20)	0.03743 (10.13)
ex-smokers v non	-0.0968 ( 1.21)	-0.0963 ( 1.19)	-0.0991 ( 1.23)	-0.0845 ( 1.05)	-0.0921 ( 1.15)	-0.0925 ( 1.15)	-0.0943 ( 1.18)	-0.0912 ( 1.13)	-0.0850 ( 1.06)	-0.0825 ( 1.02)
smokers v non	-0.2463 ( 3.89)	-0.2461 ( 3.89)	-0.2462 ( 3.89)	-0.2422 ( 3.83)	-0.2454 ( 3.88)	-0.2424 ( 3.82)	-0.2426 ( 3.83)	-0.2429 ( 3.85)	-0.2366 ( 3.75)	-0.2411 ( 3.81)
dust ISP 3		0.00018 ( 0.06)						-0.00716 ( 1.55)		
quartz ISP 3			-0.0078 ( 0.37)						-0.0556 ( 1.90)	
dust ISP 4				0.00647 ( 1.45)				0.01426 ( 2.12)	0.01452 ( 2.36)	0.00904 ( 1.03)
quartz ISP 4					0.0228 ( 1.07)					-0.0142 ( 0.34)
dust ISP 5						0.00368 ( 0.77)				
quartz ISP 5							0.0220 ( 0.99)			
residual s.s.	178.52	178.52	178.48	177.86	178.16	178.52	178.22	177.10	176.73	177.82
degrees of freedom	564	563	563	563	563	563	563	562	562	562
residual m.s.	0.3165	0.3171	0.3170	0.3159	0.3164	0.3168	0.3165	0.3151	0.3145	0.3164

**Table A3.6 Results of fitting different regression models to lung function at 6th survey. Variable analysed is forced vital capacity (FVC), averaged over three (maximum) technically satisfactory expirations. FVC is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	FVC/6/1	FVC/6/2	FVC/6/3	FVC/6/4	FVC/6/5	FVC/6/6	FVC/6/7	FVC/6/8	FVC/6/9	FVC/6/10
constant	-3.445 ( 4.75)	-3.446 ( 4.75)	-3.450 ( 4.76)	-3.476 ( 4.80)	-3.466 ( 4.78)	-3.540 ( 4.88)	-3.540 ( 4.88)	-3.470 ( 4.79)	-3.513 ( 4.84)	-3.555 ( 4.93)
age at survey	-0.03315 (15.92)	-0.03367 (13.56)	-0.03276 (14.06)	-0.03474 (15.49)	-0.03378 (15.73)	-0.03363 (16.05)	-0.03299 (15.85)	-0.03506 (15.39)	-0.03439 (14.87)	-0.03327 (14.34)
height (cm)	0.05385 (13.25)	0.05390 (13.25)	0.05384 (13.24)	0.05404 (13.33)	0.05398 (13.29)	0.05416 (13.35)	0.05414 (13.34)	0.05401 (13.31)	0.05413 (13.33)	0.05419 (13.41)
dust ISP 3		0.00130 ( 0.39)								
quartz ISP 3			-0.0086 ( 0.37)							-0.0749 ( 2.33)
dust ISP 4				0.00918 ( 1.88)				0.01595 ( 1.67)	0.00571 ( 0.77)	0.02005 ( 2.98)
quartz ISP 4					0.0279 ( 1.20)			-0.0375 ( 0.82)		
dust ISP 5						0.00951 ( 1.83)			0.00494 ( 0.62)	
quartz ISP 5							0.0410 ( 1.67)			
residual s.s.	217.54	217.48	217.48	216.18	216.98	216.26	216.46	215.92	216.03	214.12
degrees of freedom	566	565	565	565	565	565	565	564	564	564
residual m.s.	0.3843	0.3849	0.3849	0.3826	0.3840	0.3828	0.3831	0.3828	0.3830	0.3796

**Table A3.7** Results of fitting regression models with and without non-linear terms in age to lung function at 4th, 5th and 6th surveys. Variable analysed is forced expiratory volume (FEV) in one second, averaged over three (maximum) technically satisfactory expirations. FEV is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models					
	FEV/4/4	FEV/4/4A	FEV/5/4	FEV/5/4A	FEV/6/4	FEV/6/4A
constant	-2.225 ( 4.65)	-1.370 ( 2.66)	-1.539 ( 2.89)	-1.041 ( 1.87)	-1.358 ( 2.05)	-0.609 ( 0.88)
age at survey	-0.03834 (27.52)	-0.04859 (16.68)	-0.03611 (22.86)	-0.04529 (13.87)	-0.03749 (17.92)	-0.05087 (11.18)
(age-mean(age)) <sup>2</sup>		0.000040 ( 0.30)		0.000156 ( 1.10)		0.000237 ( 1.04)
(age-mean(age)) <sup>3</sup>		0.000028 ( 3.55)		0.000026 ( 3.19)		0.000045 ( 3.07)
height (cm)	0.04230 (15.56)	0.04038 (14.75)	0.03763 (12.53)	0.03709 (12.38)	0.03744 (10.14)	0.03685 ( 9.96)
ex-smokers v non	0.0051 ( 0.08)	0.0055 ( 0.08)	-0.1033 ( 1.50)	-0.0924 ( 1.34)	-0.0845 ( 1.05)	-0.0921 ( 1.15)
smokers v non	-0.1312 ( 2.60)	-0.1310 ( 2.60)	-0.1697 ( 3.13)	-0.1575 ( 2.88)	-0.2422 ( 3.83)	-0.2353 ( 3.74)
tech old v new			0.1927 ( 3.15)	0.1928 ( 3.16)		
tech not known			0.1216 ( 1.40)	0.1287 ( 1.48)		
dust ISP 3	0.00931 ( 4.28)	0.00611 ( 2.59)				
dust ISP 4			0.01045 ( 2.94)	0.00944 ( 2.44)	0.00647 ( 1.45)	0.00393 ( 0.84)
residual s.s.	331.90	326.40	265.45	262.21	177.86	174.30
degrees of freedom	1084	1082	846	844	563	561
residual m.s.	0.3062	0.3017	0.3138	0.3107	0.3159	0.3107

**Table A3.8** Results of fitting regression models with and without non-linear terms in age to lung function at 4th, 5th and 6th surveys. Variable analysed is forced expiratory volume (FVC) in one second, averaged over three satisfactory expirations. FVC is expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models					
	FVC/4/4	FVC/4/4A	FVC/5/4	FVC/5/4A	FVC/6/4	FVC/6/4A
constant	-4.747 ( 8.92)	-3.577 ( 6.32)	-3.356 ( 5.82)	-2.405 ( 4.02)	-3.476 ( 4.80)	-2.402 ( 3.19)
age at survey	-0.03228 (21.33)	-0.04521 (14.22)	-0.03227 (19.21)	-0.04806 (13.79)	-0.03474 (15.49)	-0.05285 (10.70)
(age-mean(age)) <sup>2</sup>		-0.000163 ( 1.12)		0.000080 ( 0.53)		0.000072 ( 0.29)
(age-mean(age)) <sup>3</sup>		0.000032 ( 3.70)		0.000042 ( 4.79)		0.000056 ( 3.55)
height (cm)	0.06109 (20.29)	0.05843 (19.40)	0.05107 (15.65)	0.04994 (15.49)	0.05404 (13.33)	0.05284 (13.21)
tech old v new			0.3010 ( 4.52)	0.2960 ( 4.50)		
tech not known			0.2667 ( 2.82)	0.2669 ( 2.85)		
dust ISP 3	0.01277 ( 5.30)	0.00735 ( 2.83)				
dust ISP 4			0.01673 ( 4.33)	0.01293 ( 3.11)	0.00918 ( 1.88)	0.00409 ( 0.81)
residual s.s.	408.01	396.42	316.13	306.40	216.18	208.45
degrees of freedom	1086	1084	848	846	565	563
residual m.s.	0.3757	0.3657	0.3728	0.3622	0.3826	0.3702

**Table A3.9 Results of fitting different regression models to change in lung function between 4th and 5th survey, i.e. over about 4 years. Variable analysed is (positive) drop in FEV, expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	dFV/14/1	dFV/14/2	dFV/14/3	dFV/14/4	dFV/14/5	dFV/14/6	dFV/14/7	dFV/14/8	dFV/14/9	dFV/14/10
constant	-0.777 ( 2.04)	-0.774 ( 2.03)	-0.779 ( 2.04)	-0.813 ( 2.13)	-0.792 ( 2.07)	-0.808 ( 2.11)	-0.790 ( 2.07)	-0.824 ( 2.16)	-0.811 ( 2.12)	-0.810 ( 2.12)
age at survey	0.00587 ( 4.58)	0.00664 ( 3.59)	0.00623 ( 3.44)	0.00542 ( 4.12)	0.00567 ( 4.37)	0.00606 ( 4.67)	0.00598 ( 4.64)	0.00529 ( 4.00)	0.00636 ( 3.43)	0.00535 ( 3.77)
height (cm)	0.00434 ( 2.02)	0.00423 ( 1.96)	0.00431 ( 2.00)	0.00441 ( 2.06)	0.00437 ( 2.04)	0.00436 ( 2.03)	0.00434 ( 2.02)	0.00443 ( 2.07)	0.00428 ( 1.98)	0.00441 ( 2.06)
ex-smokers v non	0.0143 ( 0.27)	0.0107 ( 0.20)	0.0130 ( 0.24)	0.0159 ( 0.30)	0.0153 ( 0.28)	0.0138 ( 0.26)	0.0138 ( 0.26)	0.0157 ( 0.29)	0.0114 ( 0.21)	0.0161 ( 0.30)
smokers v non	0.0818 ( 2.02)	0.0803 ( 1.98)	0.0812 ( 2.01)	0.0854 ( 2.11)	0.0836 ( 2.07)	0.0818 ( 2.02)	0.0813 ( 2.01)	0.0860 ( 2.13)	0.0836 ( 2.06)	0.0856 ( 2.11)
tech old v new	-0.1089 ( 2.81)	-0.1087 ( 2.80)	-0.1086 ( 2.80)	-0.1088 ( 2.81)	-0.1085 ( 2.80)	-0.1128 ( 2.90)	-0.1119 ( 2.88)	-0.1094 ( 2.83)	-0.1085 ( 2.80)	-0.1081 ( 2.76)
tech not known	-0.0255 ( 0.46)	-0.0263 ( 0.48)	-0.0256 ( 0.46)	-0.0329 ( 0.59)	-0.0309 ( 0.56)	-0.0307 ( 0.55)	-0.0290 ( 0.52)	-0.0308 ( 0.56)	-0.0343 ( 0.43)	-0.0325 ( 0.59)
dust previous		-0.000415 ( 0.57)							-0.000528 ( 0.73)	
quartz previous			-0.0037 ( 0.28)							
dust ISP 3				0.00268 ( 1.56)				0.00572 ( 1.46)	0.00280 ( 1.62)	0.00287 ( 1.22)
quartz ISP 3					0.0110 ( 1.02)			-0.0211 ( 0.86)		
dust ISP 4						0.00240 ( 0.97)				-0.00041 ( 0.12)
quartz ISP 4							0.0093 ( 0.83)			
residual s.s.	69.740	69.704	69.731	69.472	69.625	69.636	69.664	69.390	69.414	69.472
degrees of freedom	632	631	631	631	631	631	631	630	630	630
residual m.s.	0.1103	0.1105	0.1105	0.1101	0.1103	0.1104	0.1104	0.1101	0.1102	0.1103

**Table A3.10 Results of fitting different regression models to change in lung function between 4th and 5th survey, i.e. over about 4 years. Variable analysed is (positive) drop in FVC, expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	dVC/14/1	dVC/14/2	dVC/14/3	dVC/14/4	dVC/14/5	dVC/14/6	dVC/14/7	dVC/14/8	dVC/14/9	dVC/14/10
constant	-1.523 ( 3.22)	-1.513 ( 3.21)	-1.538 ( 3.26)	-1.567 ( 3.32)	-1.540 ( 3.26)	-1.553 ( 3.27)	-1.531 ( 3.24)	-1.530 ( 3.23)	-1.592 ( 3.37)	-1.570 ( 3.31)
age at survey	0.01000 ( 6.30)	0.01263 ( 5.53)	0.01259 ( 5.63)	0.00944 ( 5.80)	0.00978 ( 6.09)	0.01018 ( 6.34)	0.01007 ( 6.31)	0.01270 ( 5.55)	0.01232 ( 5.51)	0.01282 ( 5.69)
height (cm)	0.00909 ( 3.42)	0.00871 ( 3.27)	0.00885 ( 3.33)	0.00918 ( 3.46)	0.00913 ( 3.43)	0.00912 ( 3.43)	0.00909 ( 3.42)	0.00879 ( 3.29)	0.00891 ( 3.36)	0.00887 ( 3.34)
ex-smokers v non	-0.0143 ( 0.22)	-0.0266 ( 0.40)	-0.0238 ( 0.36)	-0.0124 ( 0.19)	-0.0132 ( 0.20)	-0.0147 ( 0.22)	-0.0146 ( 0.40)	-0.0252 ( 0.38)	-0.0229 ( 0.34)	-0.0244 ( 0.37)
smokers v non	0.1002 ( 2.00)	0.0950 ( 1.90)	0.0961 ( 1.92)	0.1046 ( 2.09)	0.1022 ( 2.04)	0.1002 ( 2.00)	0.0999 ( 2.00)	0.0956 ( 1.91)	0.1007 ( 2.01)	0.0961 ( 1.92)
tech old v new	-0.2399 ( 5.00)	-0.2392 ( 4.99)	-0.2375 ( 4.96)	-0.2397 ( 5.01)	-0.2394 ( 4.99)	-0.2435 ( 5.05)	-0.2418 ( 5.02)	-0.2380 ( 4.96)	-0.2369 ( 4.95)	-0.2413 ( 5.01)
tech not known	-0.0428 ( 0.63)	-0.0458 ( 0.67)	-0.0439 ( 0.64)	-0.0519 ( 0.76)	-0.0488 ( 0.71)	-0.0478 ( 0.70)	-0.0451 ( 0.66)	-0.0446 ( 0.65)	-0.0546 ( 0.80)	-0.0492 ( 0.72)
dust previous		-0.001434 ( 1.60)						-0.00051 ( 0.22)		
quartz previous			-0.0272 ( 1.64)					-0.0185 ( 0.43)	-0.0313 ( 1.88)	-0.0276 ( 1.67)
dust ISP 3				0.00329 ( 1.55)					0.00384 ( 1.79)	
quartz ISP 3					0.0121 ( 0.91)					
dust ISP 4						0.00229 ( 0.75)				0.00243 ( 0.80)
quartz ISP 4							0.0058 ( 0.42)			
residual s.s.	106.82	106.39	106.36	106.42	106.68	106.73	106.79	106.36	105.82	106.26
degrees of freedom	632	631	631	631	631	632	631	630	630	630
residual m.s.	0.1690	0.1686	0.1686	0.1686	0.1691	0.1691	0.1692	0.1688	0.1680	0.1687

**Table A3.11 Results of fitting different regression models to change in lung function between 5th and 6th survey, i.e. over about 4 years. Variable analysed is (positive) drop in FEV, expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	dFV/15/1	dFV/15/2	dFV/15/3	dFV/15/4	dFV/15/5	dFV/15/6	dFV/15/7	dFV/15/8	dFV/15/9	dFV/15/10
constant	-1.002 ( 2.27)	-1.047 ( 2.37)	-1.016 ( 2.30)	-1.132 ( 2.56)	-1.074 ( 2.42)	-1.193 ( 2.69)	-1.153 ( 2.59)	-1.191 ( 2.68)	-1.191 ( 2.68)	-1.171 ( 2.64)
age at survey	0.00368 ( 2.29)	0.00251 ( 1.43)	0.00273 ( 1.60)	0.00289 ( 1.79)	0.00342 ( 2.12)	0.00426 ( 2.65)	0.00462 ( 2.78)	0.00412 ( 2.20)	0.00368 ( 2.12)	0.00379 ( 2.23)
height (cm)	0.00593 ( 2.38)	0.00622 ( 2.50)	0.00607 ( 2.44)	0.00647 ( 2.61)	0.00627 ( 2.52)	0.00646 ( 2.61)	0.00637 ( 2.56)	0.00647 ( 2.61)	0.00654 ( 2.64)	0.00638 ( 2.58)
ex-smokers v non	-0.0880 ( 1.50)	-0.0863 ( 1.48)	-0.0872 ( 1.49)	-0.0874 ( 1.50)	-0.0888 ( 1.52)	-0.0915 ( 1.57)	-0.0948 ( 1.62)	-0.0912 ( 1.57)	-0.0900 ( 1.55)	-0.0878 ( 1.50)
smokers v non	0.0214 ( 0.47)	0.0236 ( 0.52)	0.0220 ( 0.48)	0.0243 ( 0.54)	0.0220 ( 0.48)	0.0285 ( 0.63)	0.0255 ( 0.56)	0.0285 ( 0.63)	0.0275 ( 0.61)	0.0290 ( 0.64)
tech old v new	0.0916 ( 1.90)	0.0867 ( 1.79)	0.0895 ( 1.85)	0.0837 ( 1.74)	0.0864 ( 1.79)	0.0868 ( 1.81)	0.0915 ( 1.90)	0.0864 ( 1.80)	0.0846 ( 1.76)	0.0843 ( 1.75)
tech not known	-0.268 ( 1.31)	-0.236 ( 1.30)	-0.238 ( 1.16)	-0.214 ( 1.05)	-0.243 ( 1.19)	-0.213 ( 1.04)	-0.236 ( 1.15)	-0.211 ( 1.03)	-0.205 ( 1.01)	-0.209 ( 1.03)
dust ISP 3		0.00341 ( 1.66)						0.00036 ( 0.15)		
quartz ISP 3			0.0231 ( 1.66)							
dust ISP 4				0.00845 ( 2.74)					0.00409 ( 0.89)	
quartz ISP 4					0.0239 ( 1.68)					
dust ISP 5						0.00991 ( 2.89)		0.00958 ( 2.35)	0.00653 ( 1.27)	0.01529 ( 2.11)
quartz ISP 5							0.0341 ( 2.13)			-0.0283 ( 0.84)
residual s.s.	55.718	55.378	55.380	54.805	55.371	54.704	55.161	54.701	54.608	54.617
degrees of freedom	450	449	449	449	449	449	449	448	448	448
residual m.s.	0.1238	0.1233	0.1233	0.1221	0.1233	0.1218	0.1229	0.1221	0.1219	0.1219

**Table A3.12 Results of fitting different regression models to change in lung function between 5th and 6th survey, i.e. over about 4 years. Variable analysed is (positive) drop in FVC, expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models									
	dVC/15/1	dVC/15/2	dVC/15/3	dVC/15/4	dVC/15/5	dVC/15/6	dVC/15/7	dVC/15/8	dVC/15/9	dVC/15/10
constant	-0.755 ( 1.43)	-0.833 ( 1.58)	-0.781 ( 1.48)	-0.957 ( 1.82)	-0.890 ( 1.69)	-1.029 ( 1.95)	-0.986 ( 1.85)	-0.961 ( 1.83)	-0.953 ( 1.81)	-1.024 ( 1.94)
age at survey	0.00595 ( 3.09)	0.00391 ( 1.87)	0.00423 ( 2.08)	0.00472 ( 2.45)	0.00545 ( 2.84)	0.00678 ( 3.54)	0.00739 ( 3.73)	0.00497 ( 2.35)	0.00458 ( 2.36)	0.00562 ( 2.72)
height (cm)	0.00261 ( 0.88)	0.00311 ( 1.05)	0.00286 ( 0.97)	0.00345 ( 1.17)	0.00325 ( 1.10)	0.00337 ( 1.14)	0.00328 ( 1.11)	0.00344 ( 1.17)	0.00340 ( 1.15)	0.00353 ( 1.20)
ex-smokers v non	-0.0816 ( 1.16)	-0.0788 ( 1.13)	-0.0802 ( 1.15)	-0.0807 ( 1.17)	-0.0831 ( 1.19)	-0.0867 ( 1.25)	-0.0920 ( 1.32)	-0.0811 ( 1.17)	-0.0797 ( 1.15)	-0.0837 ( 1.21)
smokers v non	0.0367 ( 0.67)	0.0405 ( 0.74)	0.0378 ( 0.70)	0.0412 ( 0.76)	0.0378 ( 0.70)	0.0469 ( 0.87)	0.0430 ( 0.79)	0.0409 ( 0.76)	0.0421 ( 0.78)	0.0448 ( 0.83)
tech old v new	0.2222 ( 3.84)	0.2137 ( 3.71)	0.2183 ( 3.80)	0.2098 ( 3.67)	0.2125 ( 3.69)	0.2153 ( 3.77)	0.2220 ( 3.87)	0.2102 ( 3.67)	0.2108 ( 3.68)	0.2109 ( 3.69)
tech not known	-0.213 ( 0.87)	-0.156 ( 0.64)	-0.159 ( 0.65)	-0.128 ( 0.53)	-0.165 ( 0.68)	-0.133 ( 0.55)	-0.163 ( 0.67)	-0.130 ( 0.54)	-0.125 ( 0.51)	-0.118 ( 0.49)
dust ISP 3		0.00592 ( 2.42)						-0.00101 ( 0.28)		
quartz ISP 3			0.0415 ( 2.50)							
dust ISP 4				0.01315 ( 3.58)				0.01427 ( 2.63)	0.01734 ( 2.50)	0.00819 ( 1.49)
quartz ISP 4					0.0448 ( 2.64)				-0.0226 ( 0.71)	
dust ISP 5						0.01421 ( 3.47)				0.00743 ( 1.22)
quartz ISP 5							0.0521 ( 2.73)			
residual s.s.	79.802	78.774	78.706	77.588	78.578	77.716	78.500	77.574	77.500	77.332
degrees of freedom	450	449	449	449	449	449	449	448	448	448
residual m.s.	0.1773	0.1754	0.1753	0.1728	0.1750	0.1731	0.1748	0.1732	0.1730	0.1726

**Table A3.13** Results of fitting regression models with and without non-linear terms in age to change in lung function in ISPs 4 and 5. Variable analysed is (positive) drop in FEV expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models					
	dFV/14/4	dFV/14/4A	dFV/15/4	dFV/15/4A	dFV/15/6	dFV/15/6A
constant	-0.813 ( 2.13)	-0.091 ( 0.23)	-1.132 ( 2.56)	-0.810 ( 1.76)	-1.193 ( 2.69)	-0.859 ( 1.87)
age at survey	0.00542 ( 4.12)	-0.00393 ( 1.71)	0.00289 ( 1.79)	-0.00260 ( 0.92)	0.00426 ( 2.65)	-0.00173 ( 0.61)
(age-mean(age)) <sup>2</sup>		-0.000260 ( 2.00)		0.000212 ( 0.67)		0.000147 ( 0.46)
(age-mean(age)) <sup>3</sup>		0.000023 ( 3.19)		0.000024 ( 1.68)		0.0000230 ( 0.58)
height (cm)	0.00441 ( 2.06)	0.00324 ( 1.54)	0.00647 ( 2.61)	0.00610 ( 2.47)	0.00646 ( 2.61)	0.00615 ( 0.49)
ex-smokers v non	0.0159 ( 0.30)	0.0052 ( 0.10)	-0.0874 ( 1.50)	-0.0894 ( 1.54)	-0.0915 ( 1.57)	-0.0934 ( 1.61)
smokers v non	0.0854 ( 2.11)	0.0745 ( 1.87)	0.0243 ( 0.54)	0.0253 ( 0.56)	0.0285 ( 0.63)	0.0280 ( 0.62)
tech old v new	-0.1088 ( 2.81)	-0.1224 ( 3.24)	0.0837 ( 1.74)	0.0732 ( 1.52)	0.0868 ( 1.81)	0.0752 ( 0.57)
tech not known	-0.0329 ( 0.59)	-0.0619 ( 1.14)	-0.214 ( 1.05)	-0.227 ( 1.12)	-0.213 ( 1.04)	-0.225 ( 1.11)
dust ISP 3	0.00268 ( 1.56)	-0.00044 ( 0.25)				
dust ISP 4			0.00854 ( 2.74)	0.00667 ( 2.09)		
dust ISP 5					0.00991 ( 2.89)	0.00855 ( 2.47)
residual s.s.	69.472	65.625	54.805	54.113	54.704	53.906
degrees of freedom	631	629	449	447	449	447
residual m.s.	0.1101	0.1043	0.1221	0.1211	0.1218	0.1206

**Table A3.14 Results of fitting regression models with and without non-linear terms in age to change in lung function in ISPs 4 and 5. Variable analysis is (positive) drop in FVC expressed in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.**

Variables	Parsimonious models							
	dVC/I4/3	dVC/I4/3A	dVC/I4/4	dVC/I4/4A	dVC/I5/4	dVC/I5/4A	dVC/I5/6	dVC/I5/6A
constant	-1.513 ( 3.21)	-0.747 ( 1.55)	-1.567 ( 3.32)	-0.713 ( 1.47)	-0.957 ( 1.82)	-0.398 ( 0.73)	-1.029 ( 1.95)	-0.445 ( 0.82)
age at survey	0.01259 ( 5.63)	0.00024 ( 0.07)	0.00944 ( 5.80)	-0.00109 ( 0.38)	0.00472 ( 2.45)	-0.00481 ( 1.45)	0.00678 ( 3.54)	-0.00368 ( 1.09)
(age-mean(age)) <sup>2</sup>		-0.000392 ( 2.42)		-0.000415 ( 2.58)		0.000347 ( 0.92)		0.000254 ( 0.68)
(age-mean(age)) <sup>3</sup>		0.000024 ( 2.61)		0.000024 ( 2.60)		0.0000416 ( 2.43)		0.0000400 ( 2.33)
height (cm)	0.00885 ( 3.33)	0.00769 ( 2.96)	0.00918 ( 3.46)	0.00775 ( 2.98)	0.00345 ( 1.17)	0.00282 ( 0.96)	0.00337 ( 1.14)	0.00283 ( 0.97)
ex-smokers v non	-0.0238 ( 0.36)	-0.0332 ( 0.51)	-0.0124 ( 0.19)	-0.0302 ( 0.46)	-0.0807 ( 1.17)	-0.0843 ( 1.23)	-0.0867 ( 1.25)	-0.0901 ( 1.32)
smokers v non	0.0961 ( 1.92)	0.0861 ( 1.75)	0.1046 ( 2.09)	0.0863 ( 1.75)	0.0412 ( 0.76)	0.0427 ( 0.79)	0.0469 ( 0.87)	0.0459 ( 0.86)
tech old v new	-0.2375 ( 4.96)	-0.2565 ( 5.47)	-0.2397 ( 5.01)	-0.2584 ( 5.52)	0.2098 ( 3.67)	0.1917 ( 3.37)	0.2153 ( 3.77)	0.1950 ( 3.44)
tech not known	-0.0439 ( 0.64)	-0.0909 ( 1.36)	-0.0519 ( 0.76)	-0.0908 ( 1.35)	-0.128 ( 0.53)	-0.152 ( 0.63)	-0.133 ( 0.55)	-0.155 ( 0.64)
quartz previous	-0.0272 ( 1.64)	-0.0126 ( 0.77)						
dust ISP 3			0.00329 ( 1.55)	-0.00055 ( 0.25)				
dust ISP 4					0.01315 ( 3.58)	0.01003 ( 2.67)		
dust ISP 5							0.01421 ( 3.47)	0.01183 ( 2.89)
residual s.s.	106.39	100.52	106.42	100.60	77.588	75.497	77.716	75.288
degrees of freedom	631	629	631	629	449	447	449	447
residual m.s.	0.1686	0.1598	0.1686	0.1599	0.1728	0.1689	0.1731	0.1684

**Table A3.15** Results of linear regression analyses of lung function variables at 4th, 5th and 6th surveys, including indicator for small opacities median profusion  $\geq 1/0$  as explanatory variable. Variables analyses are FEV and FVC, in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models					
	FEV/4/4P	FEV/5/4P	FEV/6/4P	FVC/4/4P	FVC/5/4P	FVC/6/4P
constant	-2.286 ( 4.77)	-1.624 ( 3.04)	-1.298 ( 1.96)	-4.791 ( 9.11)	-3.445 ( 5.98)	-3.444 ( 4.76)
age at survey	-0.03670 (24.51)	-0.03426 (20.52)	-0.03683 (17.12)	-0.02956 (18.15)	-0.02967 (16.76)	-0.03348 (14.53)
height (cm)	0.04246 (15.60)	0.03783 (12.58)	0.03690 ( 9.98)	0.06109 (20.37)	0.05115 (15.71)	0.05367 (13.23)
ex-smokers v non	0.0134 ( 0.20)	-0.1193 ( 1.73)	-0.0696 ( 0.87)			
smokers v non	-0.1250 ( 2.47)	-0.1695 ( 3.12)	-0.2197 ( 3.46)			
tech old v new		0.1957 ( 3.20)			0.3114 ( 4.68)	
tech not known		0.1476 ( 1.68)			0.2872 ( 3.02)	
dust ISP 3	0.00915 ( 4.20)			0.01245 ( 5.19)		
dust ISP 4		0.01148 ( 3.21)	0.00762 ( 1.70)		0.01840 ( 4.75)	0.01085 ( 2.22)
opacities 1/0+	-0.1080 ( 2.90)	-0.1590 ( 3.21)	-0.1502 ( 2.25)	-0.1824 ( 4.44)	-0.2289 ( 4.37)	-0.2153 ( 2.96)
residual s.s.	328.49	261.07	174.61	400.07	308.54	211.62
degrees of freedom	1077	839	559	1079	841	561
residual m.s.	0.3050	0.3112	0.3124	0.3708	0.3669	0.3772

**Table A3.16** Results of linear regression analyses of changes in lung function variables in ISPs 4 and 5, including indicator for small opacities median profusion  $\geq 1/0$  at start of ISP as explanatory variable. Variables analysed are (positive) drop in FEV and FVC, in litres. Tabulated values are estimated regression coefficients; absolute value of ratio of estimate to standard error is in parenthesis.

Variables	Parsimonious models					
	dFV/14/4P	dFV/15/4P	dFV/15/6P	dVC/14/4P	dVC/15/4P	dVC/15/6P
constant	-0.106 ( 0.27)	-0.997 ( 2.14)	-1.035 ( 2.23)	-0.702 ( 1.44)	-0.556 ( 1.01)	-0.589 ( 1.07)
age at survey	-0.00343 ( 1.45)	-0.00057 ( 0.20)	0.00029 ( 0.10)	-0.00024 ( 0.08)	-0.00305 ( 0.89)	-0.00196 ( 0.56)
(age-mean(age)) <sup>2</sup>	-0.000259 ( 1.98)	0.000194 ( 0.61)	0.000122 ( 0.39)	-0.000404 ( 2.51)	0.000340 ( 0.91)	0.000242 ( 0.65)
(age-mean(age)) <sup>3</sup>	0.000023 ( 3.15)	0.000021 ( 1.48)	0.000020 ( 1.39)	0.000024 ( 2.60)	0.000040 ( 2.29)	0.000038 ( 2.20)
height (cm)	0.00327 ( 1.54)	0.00678 ( 2.72)	0.00678 ( 2.73)	0.00759 ( 2.89)	0.00338 ( 1.15)	0.00334 ( 1.13)
ex-smokers v non	0.0049 ( 0.09)	-0.1006 ( 1.74)	-0.1049 ( 1.81)	-0.0302 ( 0.46)	-0.0962 ( 1.40)	-0.1020 ( 1.48)
smokers v non	0.0756 ( 1.87)	0.0247 ( 0.54)	0.0274 ( 0.60)	0.0863 ( 1.72)	0.0399 ( 0.74)	0.0433 ( 0.80)
tech old v new	-0.1234 ( 3.22)	0.0750 ( 1.57)	0.0773 ( 1.62)	-0.2618 ( 5.54)	0.1923 ( 3.39)	0.1958 ( 3.45)
tech not known	-0.0554 ( 1.01)	-0.242 ( 1.20)	-0.242 ( 1.20)	-0.0775 ( 1.14)	-0.164 ( 0.68)	-0.168 ( 0.70)
dust ISP 3	-0.00040 ( 0.23)			-0.00057 ( 0.26)		
dust ISP 4		0.00770 ( 2.41)			0.01091 ( 2.88)	
dust ISP 5			0.00932 ( 2.70)			0.01247 ( 3.04)
opacities 1/0+	-0.0330 ( 1.17)	-0.1129 ( 2.57)	-0.1105 ( 2.52)	-0.0600 ( 1.71)	-0.0921 ( 1.77)	-0.0879 ( 1.69)
residual s.s.	65.180	53.149	52.976	99.580	75.687	74.531
degrees of freedom	620	444	444	620	444	444
residual m.s.	0.1051	0.1215	0.1193	0.1606	0.1682	0.1679

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