WORKING FOR A HEALTHY FUTURE

HISTORICAL RESEARCH REPORT

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The effects of exposure to diesel fumes, low-level radiation, and respirable dust and quartz, on cancer mortality in coalminers

Miller BG, Buchanan D, Hurley JF, Hutchison PA, Soutar CA, Pilkington A, Robertson A

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INSTITUTE OF OCCUPATIONAL MEDICINE

The effects of exposure to diesel fumes, low-level radiation, and respirable dust and quartz, on cancer mortality in coalminers

by

BG Miller, D Buchanan, JF Hurley, A Robertson, PA Hutchison,
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FINAL REPORT ON RESEARCH CONTRACT FOR BRITISH COAL

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Report no. TM/97/04

INSTITUTE OF OCCUPATIONAL MEDICINE

The effects of exposure to diesel fumes, low-level radiation, and respirable dust and quartz, on cancer mortality in coalminers

Final report on CEC contract 7280/01/044

by

BG Miller, D Buchanan, JF Hurley, A Robertson, PA Hutchison,
MW Kidd, A Pilkington, CA Soutar

SUMMARY

The British National Coal Board's Pneumoconiosis Field Research (PFR) was a major research programme into respirable coal mine dust and its health effects. Data collection began in the 1950s and ran for 30 years. Initial investigations focused on pneumoconiosis, and the findings were influential in the setting of exposure limits for coal mines in Britain and elsewhere. Subsequently, the scope of the research was widened to include respiratory symptoms, lung function and, from the 1970s, cause-specific mortality.

The earliest analyses of PFR mortality data had been principally concerned with quantifying the effects on mortality risks of exposure to respirable coal mine dust, and primary interest had been in deaths from non-malignant respiratory diseases, with some limited analyses of deaths from malignancies. Although these had been limited to some extent by the methods of analysis available at the time, increased mortality risks from higher exposures to respirable dust had been clearly demonstrated. Risks of lung cancer had been shown to be lower than in the general population, but an increased risk of stomach cancer had been demonstrated, both results consistent with other studies.

Over the years since the study of mortality in the PFR began, there has been increased interest in risks of malignancy, in relation to certain hazards expected to be present in coal mines. It has been suggested that radiation exposures from the decay products of radon and thoron gases could increase lung cancer risks; that diesel exhaust particulates from underground vehicles could increase risks of lung and other cancers; and the International Agency for Research on Cancer has published an opinion that quartz, a component of many coal mine dust clouds, should be classified as a probable human carcinogen. Of these, only the radiation hypothesis had been examined in the PFR data (and no relationship had been found). A major new programme of work was therefore set up, seeking to identify and quantify any relationships between mortality from lung, stomach and other cancers, and exposure to respirable dust and quartz, diesel exhaust, and radon and thoron daughters.

The first phase of the PFR had been founded on three rounds of health surveys of the industrial workforce of each of 24 collieries selected to represent the diversity of the post-war British coalfields. In the first round, only chest radiographs and occupational histories were taken. At the second round, questionnaires on smoking habits, respiratory symptoms and chest illnesses were introduced, along with simple spirometry to measure lung function. A programme of

exposure characterisation had been set up, so that, from the first survey a man attended, the time he spent in each of a range of occupations was routinely recorded, with the same occupations used as the sampling frame for regular sampling of respirable dust concentrations; the dust collected was subsequently analysed for its mineral composition. These detailed data linking times worked and conditions in working locations had provided the framework for estimation of exposures to respirable dust and quartz for all the PFR work, and their use could be extended to estimate exposure to any hazard for which concentrations could be assigned to the occupations, singly or in groups.

The earliest collection of mortality data for PFR subjects had been for those attending the first round of surveys, at which time the collection of data on smoking habits and respiratory symptoms had not begun. For the later investigations of radiation risks, additional subjects, who had joined the research at surveys at the second or third round, had been traced and added to the mortality database. For the present study, it was considered essential that data should be available on smoking, and that it should be possible to estimate exposures to diesel exhaust and to underground radiation. The requirement for new exposures limited consideration to the 10 collieries in which the PFR extended to fourth and (and in two cases sixth) rounds of surveys. To maximise the numbers in the cohort, all men who had attended any survey at any of these 10 pits, and who were not already included in the PFR mortality database, were added to the database and sent for vital status tracing and flagging in the national systems. Of nearly 9000 men sent for tracing, less than 4% could not be traced, which was similar to results in earlier tracing exercises.

After omission of men with inadequate or unreliable occupational time records, the cohort for analysis was 18,166 men, entering follow-up at various surveys from the 2nd to 6th rounds. These contributed over 408,000 person-years at risk up to the end of 1992, the cut-off point chosen for the analyses, and 7002 deaths in this period.

Exposures to respirable dust and quartz, and the times in different occupations on which these were based, were available from PFR records, summarised in inter-survey periods (ISPs) of around five years. Estimates of exposure to radon and thoron daughters were also available from previous work which characterised concentration levels in pits, or in some cases seams within pits, and linked these concentrations with times worked, cumulated at the same level. Estimates of exposure to diesel fumes were based on estimates, from the occupational time records and records of the geology of each pit, of the total time in each ISP spent travelling on diesel-drawn vehicles.

Mortality rates for all internal causes and for all cancers, for cancers at specific sites, and for chronic bronchitis, were compared with regional reference rates for males, standardised for age and for year of death. Comparisons were summarised as Standardised Mortality Ratios (SMRs) in percentage units, with 95% confidence intervals (95% CIs). Mortality from all internal causes was lower than in the reference population, with an SMR of 91% (95% CI 89-93), interpreted as evidence of "healthy worker" effects, whereby men had to be relatively fit to gain and retain employment. The SMR for lung cancer was 86% (95%CI 80-93), but stomach cancer had increased risks, with an SMR of 124% (95% CI 110-141). No other cancer site investigated showed increased risks, but deaths from chronic bronchitis showed an SMR of 120% (95% CI 110-132).

Analyses to investigate exposure-response relationships for specific causes of death were based on comparisons within the cohort, using the general framework of Cox's proportional hazard regression models to adjust for age, smoking habits at entry to the cohort, different calendar periods of cohort entry, and (in some analyses) regional differences in background cause-specific

modeled as time-dependent.

Mortality from pneumoconiosis showed a very clear relationship with exposure to respirable dust, which was a better predictor of risk than respirable quartz. This was consistent with all the published PFR results on respiratory morbidity. Neither bladder cancer or leukaemia showed a significant relationship with any of the exposures. Stomach cancer risks were not related to dust or quartz exposure, nor to time spent in the industry, suggesting that the explanation for the raised SMR lies elsewhere than in the conditions of work. In most of the analyses of lung cancer, there was no strong evidence of exposure effects. In one series of analyses, when lagged by 25 years, and after adjusting risks for background regional lung cancer death rates, exposure to respirable quartz was related to lung cancer mortality at conventional levels of statistical significance, but the effect was strongly confounded with pit differences and could not be demonstrated between men of different exposure within the same pits. A similar but somewhat weaker effect was observed with radiation exposures. These findings are not considered evidence of occupational exposure effects, since they could be artefacts of other factors which differed between the working practices or surrounding environments of the collieries involved.

These analyses were based on a large cohort with detailed occupational records, and therefore had considerable power to identify occupational risks. This is exemplified by the strong relationship between dust exposure and pneumoconiosis. It is unlikely that a consistent association betwen exposure to quartz (present in relatively low concentrations in mixed coalmine dust) and lung cancer would have been missed. Power to detect the effects of radiation may have been limited by the sparsity of concentration data, but there is no way of obtaining further data for these pits. Further work is in progress to create alternative estimates of diesel exposure for these men, and the regression analyses of mortality will be repeated once these become available. Given the relatively recent introduction of underground diesel-drawn travel, and the likely long latency of risks for lung cancer, we recommend reanalysing the database once more years of follow-up have accrued, since death events within the cohort continue to be accrued. Similar considerations apply to quartz exposures at some collieries. Investigation of the raised stomach cancer risks may require new research programmes on social factors and exposures other than airborne dust.

Rapport N° TM/97/04

INSTITUTE OF OCCUPATIONAL MEDICINE
(INSTITUT DE LA MEDECINE DU TRAVAIL)

Les effets de la fumée de diesel, des radiations à faible niveau et des poussières et du quartz inhalés sur la mortalité due au cancer dans les mines de charbon

Rapport final sur le contrat CEC 7280/01/044

par

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SOMMAIRE

Le British National Coal Board's Pneumoconiosis Field Research (PFR) (Recherche sur la pneumoconiose entreprise sur le terrain par les charbonnages britanniques) était un programme majeur de recherche sur les poussières de charbons et leur effet sur la santé. Le rassemblement des données a commencé dans les années 50 et a continué pendant 30 ans. Les premières enquêtes étaient concentrées sur la pneumoconiose et leurs résultats ont servi à établir les limites d'exposition dans les mines de charbon en Grande-Bretagne et ailleurs. Par la suite, on a étendu la recherche pour qu'elle comprenne les symptômes respiratoires, les fonctions pulmonaires et, à partir des années 70, la mortalité et ses causes précises.

Les premières analyses des données de mortalité du PFR se sont principalement adressées à quantifier les effets sur les risques de mortalité de l'exposition aux poussières de charbon, et elles se sont intéressées à la mortalité résultant de maladies respiratoires non cancéreuses avec quelques analyses limitées de morts dues au cancer. Bien que ces analyses aient été quelque peu limitées par les méthodes d'analyse en vigueur à l'époque, elles démontrent clairement les risques accrus des niveaux d'exposition plus élevés aux poussières inhalées. Elles démontrent que, si le risque de cancer des poumons était plus faible que dans la population en général, le risque de cancer de l'estomac était plus élevé, ces deux résultats étant conformes aux résultats d'autres études.

Pendant la période correspondant à celle de l'étude sur la mortalité du PFR, on s'est de plus en plus intéressé aux risques accrus de cancer liés à certains risques présents dans les mines. Il a été suggéré que l'exposition aux radiations des déchets de radon et de thoron pouvaient augmenter les risques de cancer ; l'Agence internationale de recherche contre le cancer a publié une opinion avançant que le quartz, un élément de bien des poussières dans les mines de charbon, devrait être classifié comme un cancérigène probable pour les humains. Dans les données du PFR, on a seulement étudié l'hypothèse portant sur les radiations. Un nouveau programme majeur de travail a donc été établi avec pour objectif d'identifier et de quantifier tout rapport entre la mortalité due aux cancers des poumons, de l'estomac et autres, et l'exposition à l'inhalation de poussière, quartz, fumées de diesel et substances de filiation du radon et du thoron.

La première phase du PFR a été basée sur trois vagues d'études sur la santé des travailleurs industriels de chacune des 24 mines sélectionnées pour représenter la diversité des terrains carbonifères de la Grande-Bretagne après la guerre. Dans la première vague, on s'est limité aux radios des poumons et à l'expérience du travail des sujets. Dans la seconde vague, on a introduit des questionnaires sur les fumeurs/non fumeurs, leurs symptômes respiratoires et leurs maladies pulmonaires ainsi qu'une spirométrie élémentaire pour mesurer le degré de fonctionnement des poumons. On a établi un programme de caractérisation des expositions de manière à ce que, dès la première étude d'un homme, on inscrivait régulièrement le temps qu'il passait dans chacune des activités dans une gamme, les mêmes activités étant utilisées pour établir un cadre d'échantillons pour procéder à un échantillonnage régulier de la concentration des poussières inhalées ; la poussière était ensuite analysée pour établir son contenu minéral. Ces données détaillées, établissant un rapport entre le temps de travail et les conditions dans les lieux de travail, ont fourni le cadre d'évaluation de l'exposition aux poussières et au quartz inhalés pour tout le travail du PFR et leur utilisation pourrait être étendue pour une évaluation de l'exposition à toutes sortes de risques pour lesquels les degrés de concentration pourraient être imputés aux activités, isolément ou par groupes.

Les premières données sur la mortalité pour les sujets du PFR étaient les données sur les participants à la première vague d'études qui ne comprenait pas encore de données sur le fait que le sujet fumait ou non et ses symptômes respiratoires. Pour les enquêtes faites plus tard sur les risques de radiation, on a dépisté d'autres sujets, dont la participation avait débuté avec la seconde ou la troisième vague d'étude, et les informations les concernant ont été ajoutées aux banques de données sur la mortalité. Pour l'étude actuelle, on a considéré qu'il était essentiel que les données sur les fumeurs soient disponibles et qu'il devrait être possible d'estimer les expositions aux fumées de diesel et aux radiations souterraines. Les besoins de nouvelles expositions ont limité l'étude à 10 mines de charbon et le PFR a élargi son enquête à quatre vagues d'études (et dans deux cas à six). Pour atteindre le maximum de sujets, on a ajouté tous les hommes qui avaient participé à une étude dans ces 10 mines, et n'avaient pas été inclus dans les données sur la mortalité. ils ont été envoyés pour un dépistage et une signalisation de statut vital dans les systèmes à l'échelon national. Sur presque tous les 9.000 hommes envoyés pour un dépistage, moins de 4% n'ont pas pu être dépistés ce qui est un résultat similaire à celui des précédents exercices de dépistage.

Après avoir omis les hommes dont les informations sur le temps de travail n'étaient pas exactes ni sures, le groupe analysé comportait 18.166 hommes participant au suivi dans les différentes études de la 2ème à la 6ème vague. Ils ont donné un total de plus de 408.000 homme-années en situation de risque jusqu'en 1992, la date choisie pour conclure l'analyse, et 7.002 morts pendant cette période.

L'exposition aux quartz et poussières inhalés, et les temps passés dans les différentes activités sur lesquelles ils étaient basés, étaient disponibles dans les dossiers du PFR, condensés en périodes inter-études (PIE) d'environ cinq ans. Les évaluations des expositions aux dérivés de radon et de thoron étaient aussi disponibles dans des travaux antérieurs qui caractérisaient les niveaux de concentration dans les puits de mines, ou dans certains cas dans les filons de certains puits et faisaient un rapprochement entre les concentrations avec le temps de travail, cumulés au même niveau. Les évaluations d'exposition aux fumées de diesel étaient basées sur des évaluations - à partir des données de temps et des données sur la géologie de chaque puits - du temps total dans chaque PIE passé à se déplacer sur des véhicules fonctionnant au diesel.

Les taux de mortalité pour toutes les causes internes et pour tous les cancers, pour les cancers sur des sites spécifiques et pour les bronchites chroniques, ont été comparés avec les taux de référence régionaux pour les hommes, standardisés par âge et année de mort. Ces comparaisons ont été condensées en taux de mortalité standardisés (TMS) en unités de pourcentage, avec 95%

d'intervalles de sûreté (95% IS). La mortalité due à toute cause interne était inférieure à celle de la population de référence, avec un TMS de 91% (95% IS 89-93), interprété comme évidence des effets 'travailleur en bonne santé', par lesquels les hommes devaient avoir une santé suffisamment bonne pour obtenir et conserver leur emploi. Le TMS pour les cancers des poumons était de 86% (95%IS 80--93) mais les cancers de l'estomac avaient des risques accrus avec un TMS de 124% (95% IS 110-141). Aucun autre site de cancer étudié n'indiquait de risques accrus, mais les morts dues à la bronchite chronique avaient un TMS de 120% (95% IS 110-132).

Les analyses faites pour étudier les rapports exposition-réaction pour les causes spécifiques de mort étaient basées sur des comparaisons dans le groupe de sujets, en utilisant le cadre général des modèles de régression proportionnelle des risques de Cox pour ajuster les âges, les fumeurs/non fumeurs, les différentes dates du commencement de participation et, dans certaines analyses, les différences régionales dans les taux de mortalités liés à des causes spécifiques. La modélisation avait un fort pourcentage de calculs car âge et les expositions étaient donnés comme dépendant du facteur temps.

La mortalité due à la pneumoconiose a démontré un rapport net entre l'exposition à la poussière inhalée qui était un meilleur facteur de prévision de risque que le quartz inhalé. Ceci était conforme à tous les résultats publiés par le PFR sur la mortalité due aux problèmes respiratoires. Ni le cancer de la vessie ni la leucémie n'avaient de rapport notoire avec ces expositions. Les cancers de l'estomac n'étaient pas liés à l'exposition à la poussière et au quartz ni au temps passé à travailler dans l'industrie, ce qui suggère qu'on ne trouve pas d'explication pour un TMS élevé dans les conditions de travail. Dans la plupart des analyses de cancers des poumons, il n'y avait pas d'évidence d'effets d'exposition. Dans une des vagues d'analyses, vue sur une période de 25 ans et après un ajustement régional pour les taux de mortalité due au cancer des poumons, l'exposition au quartz inhalé était liée à la mortalité due au cancer des poumons à des niveaux conventionnels de signification statistique, mais l'effet était fortement dilué avec les différences de puits et on ne pouvait le démontrer entre les hommes exposés à différents degrés dans les mêmes puits de mine. On a observé un effet similaire mais moins prononcé dans les expositions aux radiations. Ces résultats ne sont pas considérés comme évidence des effets d'exposition au travail car ils pourraient être le résultat d'autres facteurs qui diffèrent entre pratiques de travail ou environnement dans les mines étudiées.

Ces analyses étaient basées sur un large groupe de sujets avec des dossiers détaillés de leurs activités et offraient donc un puissant moyen d'identification des risques liés au travail. Ceci est illustré par le fort rapport entre l'exposition à la poussière et la pneumoconiose. Il est peu probable qu'on ait manqué de remarquer un lien durable entre l'exposition au quartz (présent à une concentration relativement faible dans les poussières mélangées des mines de charbon) et le cancer des poumons. Il est possible que les moyens de détecter les effets des radiations aient été limités par la pauvreté des données de concentration mais il n'existe aucun moyen d'obtenir plus d'information dans ces mines. D'autres travaux sont actuellement faits pour obtenir des évaluations autres sur l'exposition de ces hommes aux fumées de diesel et on fera à nouveau des analyses de régression de la mortalité quand ces données seront disponibles. Etant donné l'introduction relativement récente des déplacements utilisant le diesel et la nature latente prolongée des risques de cancer du poumon, nous recommandons une nouvelle analyse des banques de données après l'accumulation de plusieurs années de suivi, car la mortalité des sujets est continue. Les mêmes considérations peuvent s'appliquer à l'exposition au quartz dans certaines mines. Il est possible que l'étude des risques élevés des cancers de l'estomac nécessite un nouveau programme de recherche sur les facteurs sociaux et les expositions à des facteurs autres que les poussières dans l'atmosphère.

Bericht-Nr. TM/97/04

INSTITUTE OF OCCUPATIONAL MEDICINE
(INSTITUT FÜR ARBEITSMEDIZIN)

Die Auswirkungen der Gefährdung durch Dieselabgase, niedrige Strahlung und respirablen Staub und Quarz auf die Krebsmortalität der Grubenarbeiter

Schlußbericht des CEC-Vertrages 7280/01/044

von

BG Miller, D Buchanan, JF Hurley, A Robertson, PA Hutchison,
MW Kidd, A Pilkington, CA Soutar

ZUSAMMENFASSUNG

Die British National Coal Board's Pneumoconiosis Field Research (PFR) war ein bedeutendes Forschungsprogramm über respirablen Kohlengrubenstaub und dessen Auswirkungen auf die Gesundheit. Die Sammlung von Daten begann in den 50er Jahren und wurde 30 Jahre lang fortgesetzt. Die ersten Untersuchungen wurden auf die Pneumokoniose konzentriert, und die Befunde hatten Einfluß auf die Festsetzung von Gefährdungsgrenzen in britischen Kohlengruben und anderswo. Später wurde der Forschungsumfang erweitert, denn man wollte auch respiratorische Symptome, die Lungenfunktion und ab der 70er Jahre die ursachenspezifische Mortalität untersuchen.

Die ersten Analysen der PFR-Mortalitätsdaten haben hauptsächlich die Quantifizierung der Auswirkungen auf das Mortalitätsrisiko wegen Gefährdung durch respirablen Kohlengrubenstaub betroffen. Man war besonders an den Todesfällen durch nichtmaligne Respirationskrankheiten interessiert und hat ein paar Analysen der Todesfälle durch Malignitäten durchgeführt. Obwohl diese Arbeit wegen der damals vorhandenen Verfahren in gewisser Weise limitiert war, konnte man das größere Mortalitätsrisiko wegen größerer Gefährdung durch respirablen Staub deutlich nachweisen. Es wurde gezeigt, daß das Lungenkrebsrisiko niedriger als in der allgemeinen Bevölkerung war, aber ein größeres Magenkrebsrisiko wurde nachgewiesen. Beide Ergebnisse stimmen mit denen aus anderen Untersuchungen überein.

Seit Beginn der Untersuchung über die Mortalität in der PFR hat man im Laufe der Zeit zunehmendes Interesse am Risiko der Malignität in Beziehung zu bestimmten Gefahren gezeigt, die man in Kohlengruben erwarten kann. Einerseits hat man nahegelegt, daß die Strahlungsgefahr durch die Zerfallsprodukte der Radon- und Thorongase das Lungenkrebsrisiko erhöht. Andererseits hat man vorgeschlagen, daß die Dieselabgaspartikel aus den Untertagefahrzeugen das Risiko von Lungen- und anderen Karzinomen steigern. Die Internationale Agentur für Krebsforschung hat ein Gutachten darüber veröffentlicht, daß Quarz, ein Bestandteil vieler Kohlengrubenstaubwolken, als mögliches humanes Karzinogen klassifiziert werden sollte. Von diesen Gefahren hat man nur die Strahlungshypothese in den PFR-Daten untersucht (und keine Beziehung gefunden). Aus dem Grunde wurde ein wichtiges neues Forschungsprogramm eingeleitet, denn man wollte alle Beziehungen zwischen der Mortalität durch Lungen- Magen- und andere Karzinome identifizieren und quantifizieren sowie auch die Gefährdung durch respirablen Staub, Quarz, Dieselabgase, Radon- und Thoronzerfallsprodukte.

Die erste Phase der PFR wurde auf drei Prüfungen der Gesundheit der Belegschaft in je 24 ausgewählten Gruben gestützt, die die Vielfalt der britischen Kohlenreviere nach dem Kriege repräsentieren sollten. Während der ersten Prüfung wurden nur der Brustkorb geröntgt und der Berufswerdegang festgehalten. Während der zweiten Prüfung wurden Fragebogen über Gewohnheitsrauchen, respiratorische Symptome und Brustkrankheiten verteilt, das wurde von einer einfachen Spirometrie der Lungenfunktion begleitet. Ein Programm zur Charakterisierung der Gefährdung wurde eingeleitet. Nachdem ein Mann an der ersten Prüfung teilgenommen hatte, wurde die von ihm an verschiedenen Arbeitsplätzen verbrachte Zeit regelmäßig aufgezeichnet. Dabei wurden die selben Arbeitsplätze als Rahmen für regelmäßige Stichproben der respirablen Staubkonzentrationen benutzt. Die Mineralzusammensetzung im gesammelten Staub wurde anschließend analysiert. Diese detaillierten Daten zum Verknüpfen der Arbeitszeit und Arbeitsplatzbedingungen lieferten den Rahmen, mit dem man die Gefährdung durch respirablen Staub und Quarz während aller PFR-Arbeiten abschätzen konnte. Die Verwendung dieser Daten könnte erweitert werden, um die Gefährdung durch alle Risiken abzuschätzen, denen dann Konzentrationen an den Arbeitsplätzen zugewiesen werden könnten und zwar einzeln oder nach Gruppen.

Die zuerst gesammelten PFR-Mortalitätsdaten haben die Männer betroffen, die an der ersten Prüfung teilgenommen haben, während der aber keine Daten über Gewohnheitsrauchen und respiratorische Symptome erfaßt wurden. Bei späteren Untersuchungen über die Strahlungsgefahr ist man anderen Männern aus der zweiten bzw. dritten Prüfung nachgegangen, die in der Mortalitätsdatenbank aufgenommen wurden. Bei der vorliegenden Studie war es unbedingt erforderlich, daß man einerseits Daten über Rauchen hatte, und es andererseits möglich war, die Gefährdung durch Dieselabgase und Untertagestrahlung abzuschätzen. Die Notwendigkeit neuer Gefährdungen hat die Forschung auf 10 Kohlengruben limitiert, in denen vier (und in zwei Fällen sechs) Prüfungen für PFR-Zwecke gemacht wurden. Zur Maximierung der Anzahl der Gruppen wurden alle Männer, die an irgendeiner Prüfung in irgendeiner dieser 10 Gruben teilgenommen hatten, aber noch nicht in den PFR-Mortalitätsdatenbank erfaßt waren, darin aufgenommen und zur entscheidenden Statusweiterverfolgung und Markierung an die Landessysteme geschickt. Von den fast 9000 zur Weiterverfolgung geschickten Männern konnten weniger als 4% nicht erforscht werden, das war den Ergebnissen aus früheren Weiterverfolgungen ähnlich.

Männer ohne zureichende bzw. zuverlässige Arbeitszeitaufzeichnungen wurden nicht aufgenommen. 18.166 Männer wurden in der Analyse erfaßt und anschließend von der 2. bis zur 6. Prüfung überwacht. Das resultierte in 408.000 gefährdeten Personen-Jahren bis Ende 1992, dem für die Analyse gewählten Ende. 7002 Todesfälle wurden in diesem Zeitraum aufgezeichnet.

Gefährdung durch respirablen Staub und Quarz sowie die Zeit an verschiedenen Arbeitsplätzen, auf die diese gestützt wurden, waren aus den PFR-Aufzeichnungen ersichtlich, die in Berichten zwischen den Prüfungen (ISP) von ca. fünf Jahren zusammengefaßt wurden. Abschätzung der Gefährdung durch Radon- und Thoronzerfallsprodukte war auch aus früheren Arbeiten ersichtlich. Sie charakterisierten die Konzentrationen in den Gruben und zuweilen in den Flözen innerhalb der Gruben und verknüpften diese Konzentrationen mit der Arbeitszeit und zwar auf dem gleichen Niveau zusammengezählt. Abschätzung der Gefährdung durch Dieselabgase wurde auf Schätzungen der Arbeitszeit- und geologischen Aufzeichnungen in jeder Grube sowie auf die Gesamtzeit aus jedem ISP gestützt, während der Dieselmotorfahrzeuge gefahren wurden.

Man hat die Mortalitätsraten aller internen Ursachen, aller Karzinome an bestimmten Plätzen und chronischer Bronchitis mit den regionalen Kontrollraten für Männer verglichen und nach Alter und Jahr des Todes normiert. Die Vergleiche wurden als normiertes Mortalitätsverhältnis (SMR) in prozentualen Einheiten in einem 95%. statistischen Sicherheitsintervall (95% CI)

zusammengefaßt. Die Mortalität durch alle internen Ursachen war niedriger als in der Kontrollbevölkerung, d.h. bei einem SMR von 91% (95% CI 89-93). Dies wurde als ein Beweis der "gesunden Arbeiter"-Effekte ausgelegt, weil die Männer verhältnismäßig gesund sein mußten, um angestellt und nicht wieder entlassen zu werden. Das SMR für Lungenkrebs war 86% (95% CI 80-93), aber Magenkrebs hatte ein höheres Risiko mit einem SMR von 124% (95% CI 110-141). Keine andere untersuchte Krebsstelle zeigte ein größeres Risiko, aber Todesfälle durch chronische Bronchitis wiesen ein SMR von 120% (95% CI 110-132) auf.

Die Analysen zur Untersuchung der Beziehung Gefährdung/Reaktion bei bestimmten Todesfällen wurden auf Vergleiche innerhalb der Gruppe gestützt. Dabei hat man den allgemeinen Rahmen der Coxschen Modelle der proportionalen Risikoregression benutzt, um das Alter, Gewohnheitsrauchen beim Beitritt der Gruppe, verschiedene Beitrittstermine der Gruppe und (in manchen Analysen) den Hintergrund regionaler Unterschiede der ursachenspezifischen Mortalitätsraten zu regulieren. Die Modellanpassung war rechnerisch intensiv, weil Alter und Gefährdungen als zeitabhängig modelliert wurden.

Die Mortalität durch Pneumokoniose zeigte eine sehr deutliche Beziehung zwischen Gefährdung und respirablem Staub, mit dem das Risiko besser als mit respirablem Quarz vorhergesagt werden konnte. Dies stimmte mit allen veröffentlichten PFR-Ergebnissen von respiratorischer Morbidität überein. Weder Blasenkrebs noch Leukämie zeigten eine signifikante Beziehung zu irgendeiner der Gefährdungen. Das Magenkrebsrisiko stand weder in Beziehung mit Gefährdung durch Staub oder Quarz noch mit der im Kohlenrevier verbrachten Zeit. Das deutete an, daß die Erklärung für das höhere SMR nicht in den Arbeitsplatzbedingungen sondern anderswo gesucht werden mußte. Bei den meisten Analysen des Lungenkrebses gab es keinen bedeutenden Beweis der Gefährdungseffekte. In einer Analysenserie wurde die Gefährdung durch respirables Quarz untersucht. Als die Daten um 25 Jahre zurückverlegt wurden, und das Risiko wegen des Hintergrundes regionaler Todesfälle durch Lungenkrebs reguliert wurde, bestand eine Beziehung mit Lungenkrebsmortalität bei herkömmlichen Niveaus der statistischen Signifikanz. Die Auswirkung wurde aber stark durch Grubenunterschiede gestört und konnte nicht zwischen unterschiedlich gefährdeten Männern in den selben Gruben gezeigt werden. Man hat einen ähnlichen aber etwas schwächeren Effekt bei der Gefährdung durch Strahlung beobachtet. Diese Befunde beweisen die Auswirkungen von beruflichen Gefährdungen nicht, weil sie durch andere Faktoren verursacht werden könnten, die zwischen dem Arbeitsverfahren oder Umfeld der betroffenen Kohlenreviere schwanken.

Diese Analysen wurden auf eine große Gruppe mit detaillierten Arbeitsplatzaufzeichnungen gestützt. Folglich haben sie das Vermögen, berufliche Risiken zu identifizieren. Dies wird durch die starke Beziehung zwischen der Gefährdung durch Staub und Pneumokoniose veranschaulicht. Es ist unwahrscheinlich, daß uns eine konsistente Beziehung zwischen der Gefährdung durch Quarz (das in relativ geringer Konzentration im gemischten Kohlengrubenstaub vorliegt) und Lungenkrebs entgangen wäre. Das Vermögen für den Nachweis der Strahlungsauswirkungen war vielleicht wegen der spärlichen Daten über die Konzentration limitiert. Es gibt aber keine andere Methode, weitere Daten aus diesen Gruben zu gewinnen. Weitere Arbeiten werden derzeit durchgeführt, um alternative Abschätzungen über die Gefährdung durch Dieselabgase für diese Männer zu erarbeiten. Wenn diese vorliegen, kann man die Regressionsanalysen der Mortalität wiederholen. In Hinsicht darauf, daß Dieselmotorfahrzeuge noch nicht lange unter Tage eingesetzt werden und das Lungenkrebsrisiko wahrscheinlich sehr latent ist, empfehlen wir, daß die Datenbank nochmals analysiert wird, wenn man mehr Daten im Laufe der Zeit gewinnt, weil Todesfälle in der Gruppe weiterhin vorkommen. Ähnliche Überlegungen treffen auf die Gefährdung durch Quarz in manchen Kohlenrevieren zu. Die Untersuchung des Magenkrebsrisikos kann vielleicht neue Forschungsprogramme über soziale Faktoren und die Gefährdungen verlangen, die nicht aus Staub in der Luft herrühren.

1. INTRODUCTION

1.1 The Pneumoconiosis Field Research programme

1.1.1 Aims and strategy

The Pneumoconiosis Field Research (PFR) programme of the then National Coal Board began in the early 1950s. The aims were "to determine how much and what kinds of dust cause pneumoconiosis, and to establish what environmental conditions should be maintained if mineworkers are not to be disabled by the dust they breathe during the course of their work".

The strategy adopted to achieve these aims comprised the following principal steps:

- carry out a detailed epidemiological study of lung disease in working coalminers;
- estimate the amount of respirable coalmine dust to which each of the studied miners had been exposed;
- estimate quantitative relationships between exposure and various measures of respiratory health and disease, including pneumoconiosis;
- estimate the risks to miners' health that might be associated with various standards for respirable dust underground, by evaluating exposure-response relationships with estimates of individuals' lifetime exposures given various standards.

The target population for the PFR surveys was all industrial workers at 24 representative British collieries. In the initial round of surveys (PFR 1: 1953-58) characterisation of health effects was limited to a full-sized chest radiograph, focussing on pneumoconiosis. In subsequent rounds, the scope was widened to include a questionnaire on smoking habits and respiratory symptoms, and simple spirometry. Exposure characterisation was given great attention, the strategy being to link detailed and extensive environmental measurements with similarly detailed records of time worked, within a structure of jobs grouped into occupational groups similar in location and conditions. Information on exposures prior to joining the research programme was obtained by taking an occupational history. The first phase of the research programme comprised three rounds of surveys, and was reported in a series of reports and papers demonstrating that risks of pneumoconiosis and of chronic bronchitis, and loss of lung function, increased with cumulative exposure to respirable dust (see for example Jacobsen *et al.*, 1971; Rae *et al.*, 1971; Rogan *et al.*, 1973). These results were highly influential in the setting of dust standards to be maintained in British coal mines (Jacobsen *et al.*, 1970), and were used to inform similar decisions in the United States.

The second phase of the research programme retained the same methodology, but was restricted to ten of the 24 collieries, partly because some had closed, and partly because similar collieries had produced similar results in the first phase. Analyses from this phase had the advantage that a greater proportion of the men's exposures had been estimated from the ongoing programme of exposure characterisation rather than from questionnaire-based histories. Again, several publications confirmed and refined the previously observed exposure-response relationships of

respiratory health effects with cumulative exposures to respirable dust (see for example Hurley *et al.*, 1982; Soutar and Hurley, 1986; Hurley *et al.*, 1987; Love and Miller, 1985; and a review by Soutar, 1987).

1.1.2 PFR studies of mortality

An extension of the PFR programme to include the study of coalminers' mortality was instituted in 1970. A total of over 31,000 men had been surveyed during the first round of surveys (PFR 1), and the study was set up to follow the mortality experience of a sample of nearly 18,000 of those, comprising all with signs of pneumoconiosis and 50% of the remainder. This cohort, followed up from PFR 1 to the end of 1972 and yielding nearly 4,000 deaths, formed the basis for mortality analyses reported in a PhD thesis by Jacobsen (1976). In 1977, the study was extended to include all of the men examined during PFR 1. There were some problems (since resolved) with the tracing for Scottish pits, and Miller and Jacobsen (1985) reported on mortality of 25,000 men from the 20 English and Welsh collieries, strengthening and extending the results of Jacobsen (1976). Mortality rates were shown to be increased in those with severe pneumoconiosis at the start of follow-up. Exposure-response relationships with estimates of exposure before PFR 1 were shown for mortality from pneumoconiosis and from chronic bronchitis and emphysema. Lung cancer showed an expected influence of smoking (in the subset for whom smoking data were available from PFR 2), but no association with dust exposure. Evidence for a link between dust exposure and digestive cancers was weak.

A further extension of the PFR mortality studies was begun in 1988, and was focussed on investigating any relationship between mortality, particularly from lung cancer, and exposure to low-level radiation from radon and thoron daughters underground. Estimates of radiation levels were available only for the ten pits which continued in the second phase of the PFR studies, and smoking habits were known only for those men of the cohort who had also attended the PFR 2 surveys. This limited the available sub-cohort to about 15,000 men. These were augmented by a fresh tracing exercise for over 4,000 men who attended PFR 2 but not PFR 1.

Maclaren (1992) reported on mortality amongst over 12,000 of these men who had reliable data on vital status, exposure and smoking, followed up from PFR 2 to the end of 1989. This study showed no clear evidence of a relationship between cumulative exposure to radon daughters (lagged by 10 years) and lung cancer mortality risks. A case-referent analysis of a subset of the men suggested weakly an increased exposure-related risk among non-smokers and lighter smokers, but no association with exposure in the larger group of regular smokers.

The current study further extends the investigation of deaths from cancers within the 10 collieries in the second phase of the PFR programme. The cohort has been augmented with men previously not included, for whom data exist from surveys later than PFR 2, and the analyses use statistical methodology developed relatively recently for the analysis of individual mortality data with covariates such as exposure which vary with time.

More detailed descriptions of the methodology of the PFR, and the implications for the availability and quality of different types of data, are given in chapter 2. The next section summarises current scientific opinion on the carcinogenicity of various potential coal mine exposures, which informs the specific objectives of the work reported here.

1.2 Current thinking on the possible carcinogenicity of coal mine exposures

1.2.1 Respirable coal dust

Previous studies into the carcinogenicity of exposure to coal mine dust have tended to concentrate specifically on mortality due to lung cancer and stomach cancer.

There are inconsistencies in the evidence regarding whether or not coalminers experience excess mortality from lung cancer. Thus, several British studies (Goldman, 1965; Liddell, 1973; Kennaway and Kennaway, 1953; Stocks, 1962) have shown lower than expected mortality from lung cancers in miners; and Costello *et al.* (1974) obtained similar results in a study of Appalachian miners in the US. Enterline (1972) and Rockette (1977), however, have both described elevated lung cancer rates in American coalminers. More recently, Ames *et al.* (1984) described a matched case-control study in American miners. They concluded that length of time worked underground did not predict lung cancer rates, irrespective of whether the rates were adjusted for smoking habits.

In the above studies and many others, no direct estimates of exposure to coal dust were analysed in relation to mortality. Instead, external comparisons of cause-specific mortality were made between cohorts of coalminers as a whole and the general population, or, in some cases, length of time worked underground was used for internal comparisons. In the course of their work underground, coalminers may nevertheless be exposed in varying degrees to several other agents known to be, or suspected of being, implicated with the occurrence of lung cancer in humans. These include silica, or other components of the airborne dust, as well as low-level radiation and diesel exhaust fumes. In an exposure-response analysis of US coalminers, Kuempel *et al.* (1995) estimated cumulative exposures to respirable coal mine dust up to the start of follow up for a cohort of 8788 men. An external analysis showed a deficit of lung cancer deaths in the cohort, while internally there was a negative relationship between coal dust exposure and lung cancer deaths.

Miller and Jacobsen (1985) reported results of a long-term PFR mortality study using a cohort of some 25,000 British coalminers. This showed that mortality from all non-violent causes over a 22-year period increased systematically with cumulative exposure to respirable mixed coal mine dust estimated up to the start of follow up. Principally, this trend was attributable to cause-specific exposure-response relationships for deaths due to pneumoconiosis and deaths due to bronchitis and emphysema. The authors found no evidence of an association between lung cancer deaths and dust exposure up to the start of follow up, even among miners who had already developed symptoms of pneumoconiosis.

Many studies have pointed to an association between coalmining and cancers of the digestive organs (e.g. Stocks, 1962; Ashley 1969; Matolo *et al.*, 1972; Rockette, 1977; Meijers *et al.*, 1991). In an early PFR mortality study, Jacobsen (1976) reported an increased incidence of deaths certified as due to stomach cancer in miners with radiological signs of pneumoconiosis at the first survey. Moreover, Jacobsen described an exposure-effect type of relationship between estimates of prior exposure to respirable dust and cancers of the digestive organs in those with no pneumoconiotic signs at the first survey. Miller and Jacobsen (1985), also reported some evidence that over a 22-year follow up period those with the highest exposures to dust at the start of follow up were more likely to die from cancer of the digestive system.

Stakanis and Doll (1969) had earlier demonstrated an increase in gastric cancer mortality over a range of occupations involving heavy physical activity, and suggested that a partial explanation might be the higher food intake likely in men doing heavy work. Other explanations have been hypothesised. For instance, coal dust might be ingested, either during food intake underground, or after clearance from the mucociliary tract during work. Equally, there may be some unknown biological mechanism associated with dust-induced pathological changes in the lung that leads to cancer in the lung that leads to cancer in the digestive system. It has been suggested that since there has been no consistent evidence of an exposure-response relationship with underground exposure, the excess of stomach cancer deaths among coal miners is a consequence of social or environmental factors related to living in mining communities (Coggon *et al.*, 1990). Indeed, in a mortality follow up study of residents of such a community in South Wales, Atuhaire *et al.* (1985; 1986) found an excess of stomach cancer mortality in non-miners as well as miners and ex-miners, but no clear difference in mortality between the three groups.

A recent review of the carcinogenic effects of coal dust by IARC (International Agency for Research on Cancer, 1997) noted that there were very few studies that related the carcinogenic risks directly to coal dust exposure, and therefore made separate evaluations for coal dust exposure and "occupation as a coal miner". The authors concluded that there was inadequate evidence for the carcinogenicity of coal dust in humans, but limited evidence that occupation as a coal miner resulted in exposures that were carcinogenic.

1.2.2 Respirable Quartz

Epidemiological evidence for the carcinogenicity of quartz remains controversial. The recent IARC assessment (1997) concluded that there was sufficient evidence in humans for the carcinogenicity of inhaled crystalline silica, and classified crystalline silica as a known human carcinogen. However this assessment includes the qualification that "Carcinogenicity may be dependent on inherent characteristics of crystalline silica or on external factors affecting its biological activity or distribution of its polymorphs". This admits the possibility that exposure to silica under certain circumstances may not be carcinogenic.

Exposure data is a limiting factor in currently available epidemiological studies, and so far no study has demonstrated an increased risk of lung cancer in the absence of silicosis. This suggests that exposures which cause lung cancer, have to be high enough to first cause silicosis. It therefore follows that a threshold may exist below which silicosis does not occur, and cases of lung cancer would not be anticipated. Inflammation is a precursor of silicosis, and a chronic inflammatory process is also thought to be a pre-requisite for carcinogenesis. It is also likely that a similar threshold exists for inflammatory changes, thus preventing these changes occurring, by limiting quartz exposure, would be expected to reduce the risk of quartz-induced lung cancer.

In the 1997 IARC review there was no consistent evidence of a relationship between silica and lung cancer in studies of ore miners when confounders were accounted for (e.g. McLaughlin *et al.*, 1992; Hessel *et al.*, 1990; Carta *et al.*, 1994). Foundry studies also yielded conflicting results (e.g. Andjelkovich *et al.*, 1994). Although studies of quarry and granite workers showed a lung cancer excess (e.g. Costello and Graham, 1988; Guenel *et al.*, 1989; Koskela *et al.*, 1994), no study directly quantified silica dust exposure in relation to lung cancer risk.

The results of the quarry and granite workers were considered of relevance by the IARC team. It is often assumed by study authors that results from these groups of workers are not

confounded by factors such as radiation or diesel fume, which have limited the reliability of studies of other quartz workers. However, diesel fume exposure would have to be considered in this group, in addition to smoking history. Many of the studies included in the IARC review use historical data with estimated exposures considerably higher than current levels (e.g. Guenel *et al.*, 1989), which will affect risk estimates of disease.

The IARC review also makes no distinction between studies of workers exposed to cristobalite, and those exposed to quartz. Workers exposed to cristobalite showed consistent evidence of increased lung cancer with overall relative risks of 1.5. Cristobalite which is formed from crystalline silica at high temperatures (>1400°C) has different structural activity than quartz, and is likely to have greater biological reactivity (Guthrie, 1995). This factor has implications for disease outcome. It is our opinion that the carcinogenicity of cristobalite should be considered separately from quartz.

Studies of registered silicotics showed lung cancer excess with relative risks ranging from 1.5 to 6.0 (eg. Zambon *et al.*, 1987). However registers of silicotics do not provide information on the level of exposure to quartz, and thus do not allow an assessment of a dose-response relationship. Registration is dependent on disability, and smoking related disability may increase the probability of becoming registered. Smokers are also at increased risk of developing lung cancer. There was also no convincing evidence for silica acting as a genotoxin (directly damaging to DNA) within the data presented in the IARC review.

For the purposes of determining whether exposure to quartz *per se* is related to lung cancer in man, exposure-response studies are desirable, since reports of small differences in the mortality experience of occupational groups can be the result of factors other than dust exposure (smoking habits, other occupational exposures). In a recent IOM review, Pilkington *et al.* (1996) highlighted two exposure-response studies which claimed to show an exposure-response relationship for silica exposure and lung cancer. Hnizdo and Sluis-Cremer (1991), in an exposure-response study of South African gold miners, did not take account of exposure to radon which would have been particularly high in gold mines prior to the mid 1950's.

Checkoway *et al.* (1993), in a study of diatomaceous earth workers, mainly considered exposure to cristobalite, which as previously stated is mineralogically distinct from quartz. Within this study there were doubts about possible confounding from asbestos exposure. However, a follow up study by the same author in 1996 suggested that exposure to asbestos alone did not account for the lung cancer excess reported in this group of workers. The dose-response relationship demonstrated in this population applies to cristobalite and not to quartz.

Pilkington *et al.* (1996) also reviewed other studies which suggest an elevated lung cancer risk (Amandus *et al.*, 1992; Koskela *et al.*, 1987; Merlo *et al.*, 1991). All of these studies had limitations in terms of quality of exposure data, limited consideration of confounders, or lack of data on the presence of silicosis. In addition, papers reviewed suggesting no association (Carta *et al.*, 1994; Davis et al.1983; Meijers *et al.*, 1990) are limited by small study populations and short follow up periods, which do not adequately allow for the latency of silicosis and lung cancer.

Silicosis studies conducted following the introduction of improved industrial hygiene measures in the Vermont granite industry suggest a steady fall in the number of cases of silicosis, and no new cases reported allowing for latency. Cases of lung cancer have also fallen, and so far in

those cases which have occurred, the individuals have been smokers (Costello and Graham, 1988).

Most of the studies of silicotics using historical data or silicotic registers have concluded that there is a significant association between silicosis and an excess of lung cancer. This excess could not be explained by tobacco smoking alone (Forastiere *et al.*, 1986; Zambon *et al.*, 1987; Amandus *et al.*, 1992; Hessel *et al.*, 1990; Hnizdo and Sluis-Cremer, 1991; McLaughlin *et al.*, 1992; Hua *et al.*, 1994) after statistical adjustment for the percentage of smokers in the population studied. However, in the absence of reliable exposure data, it cannot be concluded reliably from these studies that quartz itself is the agent responsible for lung cancer.

It is therefore reasonable to consider that, even if silica *per se* is not carcinogenic, the development of lung cancer is strongly dependent on exposures of crystalline silica high enough to induce a silicotic fibrogenic process, possibly in conjunction with other cofactors. Therefore, it is possible that lung cancer in association with silica, is occurring by a secondary mechanism of action, for example lung cancer may occur due to prolonged residence time of other carcinogens in lung tissue, as a result of areas of chronic inflammation and fibrosis induced by quartz exposure.

This possibility is highlighted within the EU classification for carcinogens, which considers "the existence of a secondary mechanism of action with the implication of a practical threshold above a certain dose level". Within the IARC classification final categorisation is dependent on the strength of evidence that a substance is carcinogenic and not to its potency as a carcinogen nor to the mechanism involved. This classification may change as new information becomes available.

A recent review by Weill and McDonald (1996) which concentrated on available human evidence, concluded that in the absence of lung fibrosis, the evidence that exposure to crystalline silica itself induces lung cancer remains scanty and inconsistent, but biologically plausible.

Evidence from current epidemiological studies is insufficient to support a causal relationship between crystalline silica *per se* and lung cancer. Excesses of lung cancer in subjects with silicosis have been reported, though the direct role of quartz has not been established.

It is still reasonable to conclude that exposure limits for quartz which prevent silicosis will reduce the risk of quartz related lung cancer in humans.

1.2.3 Diesel fume

Diesel exhaust contains a complex mix of gases and particulates, including CO, NO_x, SO_2, and polycyclic aromatic hydrocarbons (PAHs). The composition varies considerably dependent on a number of factors, including engine type, fuel and operating conditions. Diesel emissions undergo atmospheric transformation which alters the constituents, and the nature of emissions has also changed dramatically over the last 30 years. Recent industrial hygiene surveys of miners, truck drivers and railroad workers indicate a wide range of daily occupational exposures to diesel particulate matter (4 - 1700$\mu g/m^3$).

Animal and epidemiological evidence concerning the carcinogenicity of diesel particulates has recently been reviewed comprehensively by the Health Effects Institute (Nauss *et al.*, 1995). The

weakness of the estimates of exposure is a key difficulty in estimating health risks from the results of numerous studies which are available.

Prospective epidemiologic studies of populations exposed to diesel exhaust are not available. Retrospective occupational studies are hindered by poor exposure data and limited consideration of confounders, for example tobacco smoke and socioeconomic factors. None of the studies include measurements of diesel emissions during the time the study population was exposed. Exposure classification tends to be on the basis of job-title or company records.

The results of the studies published over the past 15 years consistently show a weak association between exposure to diesel exhaust and lung cancer. Prolonged exposure to diesel exhaust over at least 20 years in railroad workers and truckers, appears to be associated with a 1.2 to 1.5 times increase in the relative risk of lung cancer mortality in male workers. Cohen and Higgins in the HEI report (Nauss *et al.*, 1995) found that controlling for smoking, which reduced the relative risk in some studies, could not fully explain the associations between exposure to diesel exhaust and lung cancer. In general, the largest relative risks were seen in the categories expected to have the greatest cumulative exposure to diesel exhaust (Garshick *et al.*, 1988; Boffetta *et al.*, 1990; Steenland *et al.*, 1992). In general underground miners have not been included in studies due to exposure to other pollutants such as radon progeny.

Garshick *et al.* (1988) found a small but significantly elevated risk for lung cancer in a cohort of 55,407 railroad workers. They used contemporary measures of soot associated with different jobs to classify past exposures, and incorporated some adjustment for smoking. A relative risk of 1.45 (95%CI 1.11-1.89) for lung cancer was obtained in the group with the longest duration of diesel exposure.

Studies considering lung cancer rates within the general population suggest a small increase in rate among individuals whose work involves exposure to diesel exhaust. The positive associations are reported in the context of broader cancer surveys, and in many cases confounding from cigarette smoking is not adequately considered, and the number of reported cases is small.

Three studies have been identified which include more than 50 lung cancer cases and also adjust for smoking. These include the study by Risch *et al.* (1988), a case-control study considering several industries. After adjustment for smoking the odds ratio for lung cancer for those in contact with traffic fumes was 1.69 (p=0.008). Jensen *et al.* (1987) in their case-referent study after adjustment for confounders found a relative risk of 1.3 (95% CI 1.04-1.45) in transport related industry with at least 10 years in that employment.

Some epidemiological studies have also suggested an elevated risk of bladder cancer linked with occupational exposure to diesel exhaust. The evidence for bladder cancer is not as consistent. Retrospective cohort studies in railroad workers suggest little or no increase in bladder cancer risk.

Cancer risk for diesel particulates can be described in terms of a "Unit risk estimate". This is the estimated probability that a person of standard weight (70kg) will develop cancer (in this case lung cancer) due to exposure by inhalation to a concentration of 1 $\mu g/m^3$ of pollutant over a 70 year lifetime.

As discussed by Nauss *et al.* (1995), in 1990 the Environmental Protection Agency (EPA) in the USA based its risk calculations for diesel particulates on the benzo[a]pyrene component, as scientific opinion at that time considered organic constituents of diesel exhaust were responsible for observed carcinogenicity in rats. The US EPA has since decided to use the non-organic carbon core of particles as the basis for potency factor calculations based on evidence suggesting that carbon black and diesel exhaust particulate matter were equally effective in inducing lung tumours in rats (Heinrich *et al.*, 1992).

For diesel particulates, the US Environmental Protection Agency (1994) unit risk estimate derived using a linearized multistage model is 3.4×10^{-5} based on a lifetime exposure to $1 \mu g/m^3$ diesel particulate matter. The unit risk estimates based on animal data, vary by a factor of two, depending on the assumptions made about exposure and the extrapolation models selected. Risk estimates based on the epidemiological data from Garshick *et al.* (1988) vary by more than one order of magnitude, and although they are within the range of animal based estimates they tend to be higher than estimates based on animal data (Environmental Protection Agency, 1994). However, the animal data for diesel emissions are probably better than most other environmental pollutants.

1.2.4 Radon and thoron daughters

Radon is a known human carcinogen (IARC Category I), which is genotoxic (direct damage to DNA) and therefore no safe level of exposure can be assumed. Animal studies have shown that lung cancer can be induced down to radon exposures of about 20WLM, which corresponds to a lifetime exposure of 60 Bq/m^3 (Cross, 1994). The potential alpha energy exposure of workers is often expressed in terms of WLM (Working level month). One WL is an airborne alpha particle energy concentration of 1.3×10^5 MeV per litre of air, and for occupational purposes one month is 170 hours.

Epidemiological studies of many groups of miners, and various ores, have identified the association between radioactive decay products of radon gas (known collectively as radon daughters) and lung cancer (Lundin *et al.*, 1969; Muller *et al.*, 1985; Lubin *et al.* 1990). As reported in WHO Air quality Guidelines for Europe (1996) a linear relative risk model seems to fit the data over a wide range of exposure (International Commission on Radiological Protection, 1993; Lubin *et al.*, 1994). Combined analyses of the miner cohorts have indicated excess relative risks per WLM of about 0.5 to 1.5 per cent. The excess relative risk per WLM decreased with age and time since exposure. Over a broad range of total cumulative dose, a higher lung cancer risk was found to be associated with underground exposures received at low rates, suggesting that either low exposure rates, long durations of exposure, or both may be especially hazardous. Most of the miners were smokers, but a clear increase in lung cancer risk with exposure was demonstrated also among non smokers. The joint effect of radon exposure and smoking showed no clear pattern in the different cohorts, although the data were consistent with an interaction ranging between additive and multiplicative. However, exposure estimates in most of these cases have been high.

The magnitude of risk at low-level radon exposures is less well documented. Although there have been several studies of residential radon exposure, quantitative risk assessment has often been limited by imprecise exposure estimates and poor control of confounding factors (Axelson *et al.*, 1988; Schoenberg *et al.*, 1990). A recent large residential study (Pershagen *et al.*, 1994) showed an association between estimated radon exposure and lung cancer risk, which was in

general agreement with most other residential studies as well as risk estimates derived from underground miner studies. The survey was carried out in Sweden on 1360 lung cancer cases, 1424 population controls and 1360 controls matched on vital status and excluding deaths from smoking-related disease. Radon measurements were performed over a three month period, during the winter months in nearly 9000 homes occupied for more than 2 years by study subjects. The relative risk of lung cancer increased with both time weighted exposure and cumulative exposure. The relative risks for time-weighted exposures of 140-400 Bq/m^3 and >400 Bq/m^3 compared to <50 Bq/m^3 were 1.3 (95%CI 1.1-1.6) and 1.8 (1.1 - 2.9). The data was also consistent with a multiplicative effect between radon exposure and smoking.

Surveys of radon gas in British coalmines have shown levels several magnitudes lower than levels in other mines, and of a similar level to those found indoors. Measurements of radon gas in 12 British coalmines (Duggan *et al.*, 1968) gave an estimated median exposure of 20mWL. At this level a man working underground for one year would acquire a cumulative exposure of 0.2WLM, in comparison with 4.8WLM as the average annual exposure for Swedish iron-ore miners.

Maclaren (1992) assessed the effects of low level exposures to radon and thoron daughters in relation to the mortality of 19418 coal mine workers who had attended medical surveys in the 1950s and early 1960s as part of the PFR. Cumulative exposures to radon and thoron were calculated for a sub-group of 14956 men using 146 measurements of radon and thoron daughters made at 10 collieries during the 1970s, and information from the PFR database on time worked underground and on the surface. An overlapping group of 14145 men were categorized by smoking habit, using questionnaire data form medical surveys performed during the same decades. Of the complete study group 3.3% were excluded because of unknown vital status.

The SMR for all causes was 96 based on 5822 deaths in the study group of 12361 men. For lung cancer the SMR was 87 based on 521 deaths. Person-years analysis did not show any relationship between lagged cumulative exposure to radon daughters and lung cancer death rate. Case referent analysis showed a joint effect of smoking and radon daughter exposure upon mortality. However, relative risks were elevated for non-smokers, and those smoking up to 10 cigarettes a day, but declined to less than unity for heavier smokers. The negative association among heavy smokers is biologically implausible and may be due to the effect of as yet an unidentified bias. However the positive association remains in light smokers, between lung cancer mortality and radon daughter exposure.

No relationship was identified between thoron daughter exposure and mortality. The same pattern of interaction between smoking and exposure was present but was not statistically significant. Neither person-years analysis or the case-referent study showed any relationship between stomach cancer and radon or thoron daughter exposure. In general, much less is known about the health effects of thoron daughters, although the associated risk of lung cancer is reckoned to be about one-fifth that of radon daughters (James, 1988).

Recent surveys of low level radon exposure in domestic populations suggests a low risk of lung cancer at exposures currently experienced in British coal mines. However, evidence from other mining studies suggests that over a broad range of total cumulative dose, a higher lung cancer risk is associated with underground exposures received at low rates. Although this effect may be due to interaction with other co-factors occurring in these mines, it is perhaps prudent to acknowledge excess relative risks per WLM of about 0.5 to 1.5 per cent.

1.3 Aims of the present study

The objectives of the project were to answer the following questions:

- To what extent are occupational exposures to diesel fumes and to the quartz content of coalmine dust related to the occurrence of lung cancer in coalminers?

- Does exposure to coalmine dust increase the risk of death from cancers of the stomach and other digestive organs? If so, by how much?

- Is any other cancer, and specifically nasal cancer, related to occupational exposures of coalminers?

- If occupational effects are found, to what extent are they independent of the effect of smoking?

2. METHODS

2.1 Chronology and methods of PFR surveys

The objectives of the Pneumoconiosis Field Research (PFR) programme were to understand the relationships between respiratory health problems and exposure to respirable coalmine dust; and to establish how conditions should be controlled to minimise health risks to the workforce of the industry. The design of the programme was based on a series of surveys of coalworkers at a group of collieries chosen to span the range of coal types and working environments then prevalent in the British coal industry.

Throughout this report, we will refer to data collected at PFR surveys, and to measurements of exposure experienced in periods defined as falling between those surveys. The nomenclature of these surveys and periods is summarised in Table 2.1. Thus, for example, the period between 1st and 2nd PFR surveys is referred to as Inter-Survey Period 1, or ISP 1. Lengths of particular ISPs differed by pit. By convention, the period before 1st PFR survey is referred to as ISP 0, although the length of this period, from recruitment to survey, differs by individual worker.

Table 2.2 summarises the chronology of the PFR surveys at the 24 selected collieries (pits). (Since the surveys could last several weeks, the month shown for each survey is that in which most of the work was carried out.) At each survey, the target study group was all men currently working in manual and skilled employments (i.e. not management or office staff). Response rates throughout the PFR were generally high. For example, contemporary records of the surveys at pit P show that the 4th and 5th PFR surveys were attended by 88% and 91% of the eligible population; and that these responses included 91% and 95% respectively of underground workers.

All 24 pits were surveyed during the first three rounds of surveys. Thereafter, partly because of colliery closures and partly exploiting the success of the earlier work, ten of the collieries continued to a fourth and fifth survey, and two of these were visited a sixth time in 1978.

At the first round of surveys, the only record made of health status was a full-size chest radiograph (X-ray film). From the 2nd survey onwards, this was augmented by a clerk-administered questionnaire on respiratory symptoms and smoking habits, and the measurement of lung function (forced expiratory volume in one second, FEV_1; and forced vital capacity, FVC). The questionnaire used is reproduced here in Appendix 1.

The objectives of the PFR implied a need to relate the measured health effects to measures of men's exposures to respirable dust, and prospective systems were set up to monitor exposures at a level of fine detail. The strategy was to characterise the typical airborne concentrations of dust in a wide variety of colliery occupations, and to record the time men spent in these occupations. For the concentrations, a detailed programme of sampling was followed throughout the life of the research programme. The design of the sampling programme rested on splitting the working environment into a number of "occupational groups", whose definition depended on a combination of proximity, similarity of tasks, and comparability of exposure concentrations at any one time. From the many regular samples taken throughout each of the research collieries, average concentrations were then derived for each occupational group and time period, originally in terms of particle counts per volume sampled, and later by weighing. The times spent in these occupational groups were extracted from the detailed attendance record

systems used for payroll calculations. Concentrations and times were later brought together to characterise the patterns of each worker's exposures.

Men coming into the research for the first time could have a considerable history of periods of employment in that or other pits, for which times had not been recorded and/or concentration measurements were not available. The data from the attendance records system were augmented by an occupational history obtained at survey, and recorded on a standard form by a trained clerk. Concentrations for work before the research, and at other pits in the vicinity of a research colliery, were assigned from values for comparable combinations of occupational groups and periods. The contributions of these periods (often referred to as "unmeasured" as opposed to "measured", i.e. based on the recordings of conditions and times spent in occupational groups within the research colliery) to an individual's exposure estimates were thus subject to a set of assumptions of comparability; and the extent to which these assumptions were appropriate will have a bearing on the reliability of these contributions.

Men were identified throughout the research by a unique five-character identifier. The first character was the pit letter, as in Table 2.2; and the remaining four digits were a sequential number, unique within the pit, which was assigned on the first occasion on which a man attended a survey. Thereafter, all survey and exposure data for that individual were indexed by the same identifier, allowing linkage and comparison between different surveys, and between health effects, personal characteristics, and estimated exposures.

2.2 Definition of study cohort

The study of mortality within the PFR reported by Miller and Jacobsen (1985) was based on almost 32,000 coalworkers, who had all attended the first round of PFR surveys. Maclaren (1992) extended this work, with particular attention to the relationship between radiation exposures underground and mortality from lung cancer. Because smoking is an important risk factor for lung cancer, and because smoking habits were collected only from the 2nd round onwards, that extension began by adding to the mortality database men who had attended 2nd but not 1st survey. In addition, because the PFR research had been continued into its second phase only at ten of the collieries (see Table 2.2), and measures of radiation levels within mines were during that period, Maclaren's (1992) study was based on only those ten pits.

The present study required quantification of exposures to diesel fumes and to radiation levels, and there was no information on concentrations of these pollutants in the 14 pits which did not receive a 4th survey; as in Maclaren (1992), we were confined to studying the ten continuing pits. The mortality database (see 2.3.2) included all men attending either 1st or 2nd PFR survey. To increase the power of the study, it was decided to add all men who had attended any subsequent survey at any of these pits.

The target cohort was thus based on the population attending any of the PFR surveys from the 2nd onwards, at any of the 10 continuing PFR collieries. However, as in Maclaren (1992), there were requirements for the availability of data which meant that some men within that population would not qualify to enter an analysis cohort.

There were several aspects of data availability which were systematic, and the main ones are summarised in Table 2.3, which summarises which types of data were collected at each of the PFR surveys at the continuing pits. As we have already noted, the first round of PFR surveys

had no questionnaires, and thus provided no data on smoking habits. Therefore, we do not know anything about the smoking habits of any man who attended only the first survey, and could not include any such man in an analysis which required smoking data. Smoking data were collected from the second survey, but at pit P the amount smoked was not recorded; thus any analysis which required account to be taken of the amount of tobacco consumption could not be based on 2nd survey smoking data from pit P. Table 2.3 also shows that there were systematic absences of lung function data at several pits' 2nd surveys; this was due to teething problems with the measurement apparatus and technicians, which led to the earliest collected data being classed as unreliable.

Other data losses were less systematic. Attendance at the surveys was voluntary, and sometimes a man would have a radiograph taken but refuse to answer the questionnaire; an occasional radiograph might not be of sufficient quality for reliable interpretation; a man might be judged as not trying while lung function was being measured, and the measurement rejected. These outcomes are not reflected in Table 2.3, but would affect the exact numbers available for analysis, depending on what data were required.

A further loss of data was caused by a decision, taken during the processing of attendance records and occupational histories from the first two surveys, not to use data from men who had attended only one of those surveys. The decision was taken because the data processing was proving unmanageable with the then existing computer resources, but not before the data for several pits had in fact been processed. For many men, it was possible partially to retrieve this information by taking a fresh occupational history at a later survey, but men for whom this was not possible cannot be included in analyses which require data on the history of exposure.

In a mortality analysis, time-dependent availability of data has an important bearing on when follow-up is considered to start for an individual. For example, if nobody at pit P has the required full smoking information until 3rd survey, follow-up at pit P cannot begin before 3rd survey. If a man at pit P is missing other essential data from 3rd survey, but those data are available at 4th survey, we cannot begin the follow-up for that man until the time of 4th survey. Thus availability for study and time of entry to the study cohort are dependent on data availability for each individual, which as described above differed both systematically and, to a lesser extent, also at the individual level.

2.3 Determining vital status

2.3.1 Tracing strategy

From previous mortality work (Miller and Jacobsen, 1985; Maclaren, 1992) vital status tracing had already been carried out for over almost 36,000 men, including over 19,000 who had attended 1st or 2nd PFR surveys at any of the ten continuing pits. This tracing had involved identifying men by name and date of birth to the Office of Population Censuses and Surveys (OPCS) in England and Wales, and the Registrar General's Office (RGO) in Scotland. The IOM was notified of the details of deaths which had already occurred. Men not recorded as dead were "flagged" in the record systems, so that details of subsequent deaths would be forwarded as they occurred. Those not traced (typically around 5% or lower) were also notified to the IOM. This system has remained active.

It was planned to augment the existing mortality study cohort by tracing and flagging all men not already flagged in the national registers, who attended 3rd or subsequent PFR survey at a continuing pit. Interrogation of the PFR data files led to the identification of 9061 such men. So that this exercise would have maximum value for any future analyses, selection of these men was not dependent on having complete data for any particular PFR survey. Of these men, 140 did not have sufficient identifying information (i.e. no date of birth or NHS number) to be sent for tracing. Starting in April 1994, details of the remaining 8921 men were sent in three large batches to OPCS, who had agreed to carry out the tracing and to liaise with RGO on Scottish tracing and flagging.

2.3.2 Processing mortality data

The information on mortality for men in the PFR research are held in a database constructed using the facilities of SIR (SIR, 1987). Records for the new members of the target cohort sent for tracing were added to the database. As the results of the tracing were received, notification of deaths or of inability to trace for various reasons were used to updated the relevant database record. In the case of a death, the IOM received a copy of the details on the death certificate, with the underlying cause of death coded according to the International Classification of Diseases and Causes of Death (ICD) published by the World Health Organisation (WHO) Three revisions of the ICD cover the period of the study: the 7th (World Health Organisation, 1957), 8th (World Health Organisation, 1967) and 9th (World Health Organisation, 1977) revisions were introduced in 1958, 1968 and 1979 respectively. Deaths were treated as confirmed if both a date and ICD code and revision number were available; without a certificate and/or ICD code, the date of death was treated as unconfirmed. Other untraced outcomes which were given specific codes were: Embarked, Query outstanding, Not traced.

Once all 8921 men had been through the tracing exercise and OPCS had indicated that all deaths and no-traces had been communicated, the remainder of these men were assumed flagged in the OPCS systems, and were marked as "Alive" in the PFR mortality database.

As men who have been flagged die, their death details will be sent to the IOM in the same way. It is intended that these will be used to update the database, allowing future analyses with increased lengths of follow-up.

2.3.3 External reference mortality rates

Part of the planned programme of analyses was to consist of standardised comparisons of observed cohort mortality rates for chosen causes of death, with the mortality rates experienced by the general population. Data are available on numbers of deaths from specific causes by sex, age and calendar year, for each of the administrative regions of Britain; and on the corresponding populations of those regions, which would form the denominators for the calculation of rates. In fact, many of these were already held at the IOM, for regions which contained PFR collieries, from the previous mortality analyses. Periods and causes were identified for which these data files required to be augmented.

The required data came from two sources. For England and Wales, data on numbers of deaths and population sizes were supplied by OPCS in spreadsheet format on floppy disks, and were manipulated as necessary to reconcile their format with that of data already held. For Scotland,

GRO supplied a computer file of all male deaths between 1963 and 1993. These were tabulated by age group and year using the tabulation facilities of the statistical program Genstat (Genstat 5 Committee, 1993). Tabulated population data, and death data for the period before 1963 additional to that already held, were obtained by a clerk from published sources and added to the data files.

At the end of the processing, a set of data files was held, containing populations and numbers of deaths covering combinations of the following (and taking account of changes in regional boundaries and in revisions of the ICD classifications systems for coding causes of death):

Calendar years:	1958 - 1993 (1992 England and Wales)
Age groups:	15-24; 25-34; 35-44; 45-54; 55-64; 65-74; 75+
Regions (1958-1964)	Scotland, North, East and West Riding, North Midland, Midland, North Wales, South Wales.
Regions (1965-1973)	Scotland, North, Yorkshire and Humberside, East Midlands, West Midlands, North West, North Wales, South Wales.
Regions (1974-1993)	Scotland, Northern, Yorkshire and Humberside, East Midlands, West Midlands, North West, Wales.

Table 2.4 shows the correspondence between regions and the pits analysed in the current report. Table 2.5 shows the list of causes of death for which SMRs were calculated (see 2.6.2), and the corresponding ICD codes for the different revisions. In the analyses, North and South Wales were pooled pre-1974.

2.4 Exposure estimation

2.4.1 Available PFR exposure data

One of the principal strengths of the PFR was the huge sampling effort which was applied to sampling environmental conditions in each occupational group, in order to characterise the typical exposures of that group. These were then combined with data on times worked by each individual in each occupational group, to create estimates of individual exposure, in units of time-weighted total concentrations, or, equivalently, concentration-weighted total times. Those exposures had been calculated for earlier studies in terms of respirable dust and quartz, and had been stored as cumulative totals for each inter-survey period (ISP: see 2.1). Data on the times worked were stored in a computer file. It was therefore possible, for the present study, to create new exposure estimates for other contaminants, provided that a set of concentrations could be estimated which was indexed by pit, occupation and calendar time.

The data on times were stored in two parts. The first concerned times which had been extracted routinely from the attendance records system in each pit, and the second concerned time which had been collected from the individual, when an occupational history was taken at a PFR survey. The attendance record ("measured") data were stored by individual and by occupational group, and for this project were used summarised as totals over each ISP. (The original data were collected by quarter-year. They are stored in the main database of the PFR as totals for ISPs 0, 1 and 2; and by quarter for ISPs 3 onward.)

The occupational history ("unmeasured") time data were stored by individual, ISP and one of six broad working environments (each of which would cover several occupational groups): coal getting, preparation, development in coal, development in stone, elsewhere below ground, surface.

The sections below describe how these time data were used to calculate estimates of the exposures relevant to the present study.

2.4.2 Estimating exposure to respirable dust and quartz

As part of previous PFR research work, individual estimates of exposure to respirable dust and to respirable quartz had been calculated and stored by individual and ISP. The components from measured and unmeasured time were kept separate. These data were in principle ready to use for the present study. However, the tape storing the computer file of quartz exposures from unmeasured time was found to be corrupt, and it proved necessary to recalculate them.

Data were extracted on reported total times worked by each individual in each of the six broad working environments (2.4.1) and each ISP, at the 10 relevant pits. These were then multiplied by existing data on average quartz concentrations within each environment and ISP, and cumulated to create individual exposures.

The measured and unmeasured components were added together to create a single estimate of quartz exposure for each individual and ISP, prior to analysis. This format was then the same as was used for the already available respirable dust exposures.

2.4.3 Estimating exposure to diesel fume

Diesel transport was very rare in British coal mines before the early 1950's. Thereafter, diesel vehicles for man transport were introduced gradually in many mines, but there were also many where such transport was unsuitable. Of the ten pits included in the current study, four (C, F, P, V) had no diesel manriding, while the remaining six (K, Q, T, W, X, Y) used diesel vehicles at various times.

There were no data on the concentrations of particulate emissions from diesel engines experienced in different coalmine occupations for the relevant periods. We have chosen, as a surrogate measure, to assume that exposure was proportional to the time spent travelling by diesel locomotive, between the pit bottom and the place of work. Since these times had not been recorded either, they were estimated from known distances travelled. A more recent study is attempting to estimate concentrations retrospectively, but results were not available for the analyses reported here.

Many of the recorded occupational groups implied a particular place of work within the colliery: occupational groups for face workers, for instance, were face specific. From colliery plans, the distance between each face and the pit bottom was estimated. The estimated travelling distances are shown, separately for each of the six pits with diesel vehicles, in Figure 2.1. Data from the same face in each year of operation have been joined by straight lines, and it can be seen that in most instances the distance to the face stayed constant over time. Only three faces in pit K involved longer travel as they were developed. For the rest, Pit Q was the only pit with faces

involving regular diesel travel above 10 km, and Figure 2.1W shows the late introduction of diesels in pit W. For underground workers away from the face, an average was assigned across relevant faces, taking account of the known layout and operating conditions of each pit. Exposure in occupations on the surface was ignored.

The travelling distance associated with each occupational group was linked with attendance records to create a surrogate exposure, as follows. Times worked were converted to numbers of shifts worked at 7.5 hours per shift prior to 1 January 1973, and 7.25 hours per shift after this. One return journey to place of work was assumed per shift, except for men identified as drivers, who were assumed to be exposed for a whole shift. Other than drivers, travelling distances in different occupational groups were cumulated to give totals by individual and ISP, and then converted to travelling time assuming an average speed of 5 miles (8 km) per hour. For drivers, travelling time was taken as the appropriate length of shift, and cumulated in the same way.

Times recorded for periods before the PFR research started (ISP 0), and for periods spent at other collieries, were ignored. Unmeasured times at the research colliery were assigned a colliery average travelling time and this component was added to that calculated from the attendance system times.

2.4.4 Estimating exposure to radon and thoron daughters

The approach used for estimating exposures to radiation from radon and thoron daughters has been described by Maclaren (1992). Measurements of radiation levels from both radon daughters and thoron daughters were made between 1972 and 1980, in the different seams of the 10 research collieries (Crawford and Edlin, 1982; Maclaren, 1992). The data are summarised as seam mean concentrations in Table 2.6 (extracted from Table 3.1 of Maclaren, 1992).

For the estimation of individual exposures, radiation levels in each seam were typified by the seam means in Table 2.6. Seams where no measurements had been made were assigned the colliery average. Occupational groups were identified, wherever possible, with specific seams, and the appropriate radiation levels assigned. Underground occupational groups which were not seam-specific were assigned the colliery average. Surface groups were assigned estimated outdoor concentrations of radon and thoron daughters, supplied by the National Radiological Protection Board (NRPB), the same value of each being used at all 10 collieries. These levels were multiplied by times recorded in the attendance record systems as worked in the occupational groups, and cumulated.

For the unmeasured time collected as occupational histories at survey, colliery average concentrations were assigned to all time worked in the underground environments, and the outdoor concentrations were used for the surface environment. The same approach was used for periods spent working at other collieries, on the basis that many men migrating into PFR collieries would have come from neighbouring collieries working the same coal seams. These concentrations were multiplied by the corresponding unmeasured times and cumulated to ISP and individual. The resulting exposure component was then added to the component estimated from the measured times.

The measurements of radiation from radon and thoron daughters were made in units of mWL, so that exposures were in units of WL.hr. One "Working Level" (WL) is an airborne alpha-particle concentration of 1.3×10^5 MeV per litre of air. It is considered more appropriate to re-

express these values as equivalent doses to tissue, in milli-Sieverts (mSv). The measured values were converted at rates of 19.2 and 57.6 WL.hr per mSv for radon and thoron respectively, and added to derive a single estimate of radiation exposure.

2.5 Smoking habits

The questions on smoking habits are shown in detail in the questionnaire reproduced in Appendix 1. These data were extracted from the PFR data files, and summarised for use in the analyses. On the basis of the responses, it was possible to classify men, at each survey for which a questionnaire was taken, as lifelong non-smoker, ex-smoker, pipe smoker only, cigarette smoker only, or cigarette and pipe smoker. The last three categories were combined into one group of current smokers. Amounts smoked were treated differently from different phases of the research. At 2nd and 3rd surveys, cigarette and pipe tobacco consumption were recorded in categories. The midpoints of these categories were taken (using 55.5 as midpoint for the >50 cigarettes per day category, and 6 ounces to represent the >5 ounces pipe tobacco per week category). A total amount of tobacco consumption in equivalent cigarettes was calculated, treating one ounce of pipe tobacco per week as equivalent to 5 cigarettes smoked per day. At 4th, 5th and 6th surveys, actual reported numbers of cigarettes per day, rather than in categories, were recorded separately for weekdays and weekends, and a weighted average (with weights of 5/7 and 2/7) was calculated. Pipe tobacco was again added at the same conversion rate, to give a total amount of tobacco consumed in equivalent cigarettes.

2.6 Statistical analysis

2.6.1 Descriptive summaries.

It was considered essential, for the interpretation of the formal analyses, to prepare summaries of the data on which these were based. Tabular summaries of the numbers of men entering the analysis cohort, and their patterns of ages, smoking habits, exposures and mortality experience, were prepared using the facilities of the statistical package Genstat (Genstat 5 Committee, 1993). Graphs were prepared on a PC, using the package Sigmaplot (Kuo and Fox, 1993).

2.6.2 Comparisons of mortality with regional reference populations

Comparisons of the mortality experience of the study cohort with those of the external reference regional populations were carried out by standard arithmetical methods which calculate a Standardised Mortality Ratio (SMR) (Breslow and Day, 1987). Standardisation was by calendar year, age in standard 10-year age groups, and region (taking account of regional boundary changes: see 2.3.3 above). To avoid possible part-year biases from the dates of the surveys at which men entered the cohort follow-up, each man was considered to be at risk from the 1st of January of the year following the date of the survey defining cohort entry. A table of person-years at risk was constructed classified by calendar year, age groups, and pit. For each year between a man's entry and his death or end of follow-up (end 1992), his age at mid-year was calculated and allocated to an age-group. The appropriate cell of the table was augmented by one year's risk-time if he survived that year, or a fraction of a year if his follow-up was

terminated by death in that year. Corresponding tables of numbers of deaths were constructed, one for each cause of interest.

The SMRs were calculated as follows: for each cause of death, the reference tables of numbers of deaths were divided by the populations, to give death rates by calendar year, age group and region. Assigning collieries to regions as shown in Table 2.4, the death rate in each cell was multiplied by the cohort person-years at risk, to produce an estimate of the average number of deaths to be expected in the cohort if the population rates applied. Marginal totals of observed and expected deaths were calculated, and the ratio of the total observed to the total expected expressed as a percentage ratio, the SMR. Standard errors of the calculated SMRs were derived, from the assumptions that counts of numbers of deaths observed in the cohort were likely to behave as Poisson variates, and that the reference populations were large enough that it was not necessary to take account of sampling variation in the reference rates.

All the calculations were carried out using the table manipulation facilities of the statistical package Genstat (Genstat 5 Committee, 1993).

2.6.3 Analyses of exposure-response relationships for mortality

Exposure-response relationships were investigated using the methodology introduced by Cox (1972), that is a regression model for survival data. The basic format of the model assumes that the instantaneous risk of mortality can be described by a *hazard function* (which generalises the idea of a mortality rate); and that this function can be parameterised as the product of a time-dependent baseline hazard function $h_0(t)$, and a regression expression involving terms for explanatory variables such as exposure, age, etc. (Collett, 1994; Clayton and Hills, 1993). A typical formulaic expression of the model is

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

where $h_i(t)$ is the hazard function for the ith individual; x_{ij} (j=1...p) are the covariates; β_j are regression coefficients representing logarithms of relative hazard; and $h_0(t)$ is a baseline hazard function shared by any individuals for whom all covariates are zero. Analysis under this model framework requires the estimation of the unknown regression coefficients $\{\beta\}$, and their variance-covariance matrix, which is done by iterative computations maximising a partial likelihood function involving the regression terms but eliminating the baseline hazard. Each β_j quantifies the effects of the relevant covariate on mortality, on the log scale, so that its exponential (or antilog) is interpreted as a ratio between mortality rates. Considerations of how to parameterise variables representing group membership ("dummy" variables), and how to examine the joint and separate effects of confounded variables and their interactions, are similar to those in ordinary regression situations.

The model allows explanatory variables to vary with time, i.e. during the follow-up. This may be expressed as

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

This seemingly small change from x_{ij} to $x_{ij}(t)$ gives immense extra capabilities to the analyses. For example, it allows us to model the effect on risk of the accumulation of exposure over different periods of a working life. It also increases hugely the amount of computation necessary to estimate the coefficients.

The models fitted to the data in the present study took as their basic time axis the time on study. As with the external analyses (2.6.2), that time was calculated beginning from 1 January following the survey attendance by which he qualified for entry to the cohort (2.2). Follow-up was to death, or to 31 December 1992.

For each cause of death analysed the analysis began with the search for a baseline model, to contain possible effects of age and of smoking habits. Because the availability of smoking data during the follow-up was variable, the analyses were performed purely in terms of the smoking habits at the qualifying survey just prior to cohort entry. Non-smokers, ex-smokers and current smokers were distinguished, and for the smokers equivalent number of cigarettes was also considered for inclusion in the baseline model. Age was modelled as increasing through the follow-up, i.e. as a time-dependent covariate, and a quadratic term was considered in case a single linear coefficient was insufficient to describe the dependency on age. In addition, since the cohort entry dates were not all simultaneous, a term was included for the date of beginning follow-up, to absorb any secular trend in mortality over the period spanned by the entry dates.

To the baseline model was added each relevant exposure. For each cause studied, deaths from other causes were treated as censoring events. Exposures were included as time-dependent covariates, calculated for time points between surveys by linear interpolation between survey dates. In addition, the analyses were carried out with exposures lagged by 15 years, by interpolating to a time 15 years previous to each time of death. Lagged exposures in ISP 0 were linearly interpolated between 1st survey and age 15 years, before which exposure was assumed to be zero. Exposures were fitted with and without pit effects, to examine the extent of confounding between pit differences and exposure effects.

The analyses were carried out on a powerful PC, using the PC version of BMDP with dynamic memory allocation (Dixon, 1992) to allocate enough memory for the very large data sets. The program BMDP2L was used, which is designed specifically to analyse survival data using regression models with time-dependent covariates, and which includes facilities for the calculation of the time-dependent covariates at each time of death.

3. POPULATION CHARACTERISTICS AND EXPOSURES

3.1 Results of tracing exercise

As described in 2.3.1, it was desired to extend the population of coalworkers for whom mortality was to be determined and monitored, to include all men who had attended any PFR survey from 2nd survey onwards, at any of the 10 continuing pits. From the data files of the PFR, this population was enumerated as 23929 men. Of these, 14868 were already included on the PFR mortality database, as a result of their inclusion in the studies reported by Miller and Jacobsen (1985) and by Maclaren (1992). Of the remaining 9061 men, 140 did not have dates of birth recorded, and were not sent for tracing, since successful unique identification was unlikely. The results at the end of the exercise, for follow-up to the end of 1992 in the remaining 8921 men, are summarised in Table 3.1.

Table 3.1 shows that, of these 8921 men, vital status could not be uniquely identified for a total of 316 men (3.5%). This table also shows the vital status of the men included in the earlier tracing exercises reported by Miller and Jacobsen (1985) and by Maclaren (1992), after which the total proportion untraced was 3.1%. The success of the extra tracing for the current study was clearly comparable with that achieved previously.

The figures in Table 3.1 represent a summary, made in January 1995, by which time the tracing exercise had produced all its returns, of the vital status held on a computer database which is updated dynamically. In particular, the distribution of numbers among those for whom vital status has been ascertained, between dead and alive, changes as mortality events are notified for men who have been flagged in the record systems. However, it is rare for the status of an individual to change between traced and untraced, or vice versa, once a tracing exercise is complete. The untraced proportions are therefore likely to remain relatively constant.

The analyses reported here used only deaths prior to 1993, providing a long enough gap to ensure that all relevant death details had passed through the tracing systems.

3.2 Cohort for mortality analysis

3.2.1 Definition of cohort for analysis

At the end of the tracing exercise, tracing had been attempted for 23789 men, and vital status established for 23009 of these. However, as described in 2.2, not all of these men had all the data necessary to qualify for inclusion in the study cohort. In fact, after excluding men for whom no valid data on smoking habits were held, and those who had insufficient data to characterise their occupational exposures, the traced men were reduced to 18166.

Table 3.2 enumerates the distribution of these men by pit; by survey at which the man first had the data required to qualify for entry; and by age at the survey defining cohort entry. There are certain sections of this table greyed out, indicating systematic patterns of omission. For example, there are no cohort entries at 2nd survey at pit P, because 2nd survey smoking data at this pit were unreliable. There were 6th surveys at only pits P and V. The other patterns depend

on the patterns of recruitment, retirement and/or redundancy at the different pits, and small numbers of men with sporadically missing data from specific surveys.

All the men in the analysis cohort were at least 15 years of age when they entered the cohort, and almost all were under 65 at entry. We have not shown separately those over 75: there were only two of these, one each at pits F and T.

3.2.2 Time at risk and deaths

Table 3.3 summarises the distribution of the men in the analysis cohort by pit and survey qualifying for cohort entry. Each row is a copy of the row from Table 3.2 showing the total over all age groups, but the data are shown again in summary for comparison with Tables 3.4 to 3.6.

For the analyses comparing observed mortality with that in reference populations, follow-up began on 1 January following the month of the survey of entry (as shown in Table 2.2). Because reference rates were available for all the relevant regions only up to and including 1992, follow-up was taken to be completed at the end of that year. Table 3.4 shows the maximum length of follow-up available for each combination of pit and survey qualifying for cohort entry; by definition, these are whole numbers of years. Thus, for example, a man who joined the cohort at 2nd survey at pit C would contribute 32 years-at risk if he remained alive throughout the follow-up period. If he died during follow-up, he would contribute the number of years he stayed alive after cohort entry.

Table 3.5 summarises the total person-years at risk accumulated for the whole cohort over the follow-up period, among the groups of men shown in Table 3.3. A related but more detailed table, broken down further by calendar year and by age-group, was used as input to the SMR calculations (2.6.2). Table 3.6 summarises the numbers of deaths observed among these groups during the follow-up period.

3.2.3 Causes of death

Table 3.7 summarises numbers of deaths experienced during the follow-up, to 31 December 1992, by the coded principal underlying cause. The groups and subgroups are defined by their codes under the 7th, 8th and 9th revisions of the ICD coding scheme. All the cause-groups analysed are present in this table, and we have included other cause-groups for information and for comparison. The relationship of groups to their subgroups is straightforward except for chronic lymphatic leukaemia, where we have implied, but not shown, the fact that the range of codes for "other leukaemia" excludes the chronic lymphatic cases; and for pneumoconiosis, which includes 7 deaths from silico-tuberculosis, which has a code outside the range conventionally labelled as "respiratory disease".

Inspection of Table 3.7 shows the usual predominance of cardiovascular causes, contributing about half the total deaths from internal causes. This is followed by lung cancer. There were 203 deaths from pneumoconiosis, which is specifically an occupational disease caused by exposure to respirable coalmine or other mineral dust.

3.3 Population characteristics of the cohort

All of the cohort were male. Table 3.8 summarises their patterns of age and smoking habits. The table distinguishes men by the survey at which they entered the cohort; and, within each survey, by age and smoking habits at that survey. Non-smokers and ex-smokers are treated as distinct single groups, but current smokers are distinguished by their tobacco consumption in "equivalent cigarettes" smoked per week, which for some men includes a contribution for pipe tobacco consumption (2.5).

In total, 13534 of the men (74.5%) were smokers at survey of entry, while the non-smokers and ex-smokers made up 17% and 8.5% respectively. These figures are typical of manual and skilled employed cohorts of the period. The proportions of non-smokers were higher in younger men, and were also higher, particularly among younger men, in the later recruited cohorts. These patterns are consistent with known population trends resulting from anti-smoking campaigns.

3.4 Exposure patterns

3.4.1 Overview

As we have described (2.6.3), the regression analyses to relate mortality to exposure were designed to take into account the cumulative accretion of exposure before and through the follow-up period. It is difficult to envisage or display a data set which is changing dynamically over time, but it is also difficult to interpret the results of a regression analysis from an observational study without a clear view of the patterns found in the explanatory variables and in their relations with each other. We have therefore chosen to summarise and present the exposure data in some detail.

The data are presented first as a series of cross-sectional summaries, at each of the PFR surveys from 2nd to 6th inclusive. Most pits did not have a sixth survey, but at some date in each pit the labelling of exposures and time recording changed from ISP 5 to ISP 6, and these dates were known. (At pit T, 5th survey was carried out early because the pit was due to close, and thus there were no increments of exposure after 5th survey. For the purposes of including this pit T in the tabulations for 6th survey, a surrogate date of five years after 5th survey was used to calculate age and time on study.) At each survey, for all of the men who were present in the cohort at that survey, various summary statistics were calculated and are tabulated in Table 3.9. Thus, for example, 9266 men joined the cohort at 2nd survey. Their ages ranged from over 15 to nearly 75 years, with a mean of almost 44 years. At that time, by definition, they all had zero follow-up time on study. Their occupational histories covered periods ranging from zero time to 102,000 hours. Also shown are the corresponding cumulative exposures to respirable quartz and dust, radiation from radon and thoron daughters, and diesel travelling time, all cumulated to 2nd survey.

At 3rd survey, the population summarised is increased by the number of men who joined the cohort at 3rd survey, and decreased by the number of those who died between 2nd and 3rd. The relatively large jump in numbers is due principally to the entry of men from pit P. The changes in numbers between subsequent surveys were less dramatic, but as before represented a combination of fresh recruitment and loss through death.

Comparison across surveys in Table 3.9 shows that the mean age changed between surveys by less than the length of the inter-survey period. This is due to a combination of the recruitment to the cohort of men who were on average relatively young, and the higher death rates among older men. Since a large proportion of those recruited during follow-up also had low or zero exposures prior to cohort entry, the means of the quartz, dust and radiation exposures do not vary much between surveys, particularly when compared with the wide variation between individuals at a particular survey.

Table 3.9 does not show to what extent high exposures to the various agents tend to occur in the same individuals, and to this end Table 3.10 shows the correlations between the same variables. The correlations at each survey have been calculated from the same data as summarised in Table 3.9, and are thus based on the same numbers of men.

Examination of the section of Table 3.10 relevant to 2nd survey shows that time on study had zero correlation with all the other variables (because all its values were identically zero at 2nd survey). The largest correlation was between age and cumulative time, the number of working hours contributing to the exposure calculations. Correlations between age and the exposure estimates themselves were considerably lower. This suggested that, for any response for which age and exposure had separate effects, the confounding between them would be only partial, so that it was possible to estimate them separately. Among the exposures, correlation was highest between respirable quartz and respirable dust, which was not surprising given that the quartz was a part of the dust. Similar patterns were observed in the other sections of Table 3.10, for the data from the remaining surveys.

Tables 3.9 and 3.10 have given a summary view of the distributions of, and relationships between, the important time-dependent variables. In the following sections, selected facets of these are shown in graphical form, highlighting differences in distributions between pits. Because the shapes of the distributions and the correlation matrices changed little between PFR surveys, we have deemed it sufficient to display data only for 3rd and 6th surveys.

Table 3.11 shows the distributions at 3rd PFR survey of the cumulative exposures to respirable dust and quartz, and the proportion (%) of quartz in the dust, by pit. The quartz proportion was calculated for each individual as the ratio of the cumulative quartz exposure to the cumulative dust exposure, and is thus an average over the period contributing to those exposures, and is not defined where the dust exposure to PFR 3 was zero.

3.4.2 Time contributing to exposures

Figure 3.1a is a summary of the distributions, by pit, of the working time accumulated up to PFR 3rd survey, and contributing to exposures up to that survey, for all cohort members alive at that time. This is a box (or box-and-whisker) plot, which displays a diagrammatic summary of the shape of a distribution. This plot displays the middle 50% of the data, from the 25th to the 75th percentile, as a box with a crossbar at the median; the lines, or whiskers, run to the 10th and 90th percentiles, and points outside this range are drawn individually as small triangles. Although there was some evidence of colliery differences, these were dwarfed by the wide range of values within each pit. Figure 3.1b is a similar plot for the accumulated times for the cohort at PFR 6th survey, and shows similar patterns to those in Figure 3.1a.

Figure 3.2 shows a scatter plot of the contributing time against age, both at PFR 6th survey. This plot, in which each triangle represents one of the 14872 men shown in Table 3.9 as in the cohort at the time of 6th survey, shows clearly how the maximum time was limited by age; and that, at any given age, there was a wide spread of times.

3.4.3 Exposure to respirable quartz and dust

Figure 3.3a is a box plot (see 3.4.2) summarising the distributions at each colliery of respirable quartz exposures cumulated to PFR 3rd survey. This shows much greater differences between collieries in the average and maximum levels of quartz exposure than was apparent in the contributing times in 3.1a. The overall pattern of the colliery differences is repeated at 6th survey, shown in Figure 3.3b.

Figure 3.4 shows the relationship between exposure to respirable quartz and age, both at 6th survey. Like Figure 3.2, this shows how the maximum attainable cumulative exposure was limited by age.

Figure 3.5a is a box plot (see 3.4.2) summarising the distributions at each colliery of respirable dust exposures cumulated to PFR 3rd survey. As with quartz, there were clearly pit differences in the average and maximum levels of dust exposure, but the pits were not all in the same rank order as for quartz. This suggested that it should be possible, in the regression analyses, to separate quartz-specific effects from those due to mixed dust. Figure 3.5b shows a very similar pattern in the respirable dust exposures cumulated to 6th survey.

Figure 3.6 shows a spread of dust exposures relative to age broadly similar to that for quartz.

3.4.4 Radiation from radon and thoron daughters

Figure 3.7a is a box plot (see 3.4.2) summarising the distributions at each colliery of estimated radiation exposures cumulated up to PFR 3rd survey. Here the differences between collieries were rather greater than for quartz, and this pattern persisted to 6th survey, as shown in Figure 3.7b. While colliery Q had the highest average levels for both respirable quartz and radiation exposures, pits did not follow the same rank order for the two exposure variables.

Figure 3.8 shows the relationship between cumulative radiation exposure and age, at 6th survey. There is some obvious banding, reflecting the markedly different levels of concentrations of radiation between collieries.

3.4.5 Exposure to diesel fumes

Figure 3.9a is a box plot (see 3.4.2) summarising the distributions at each colliery of the estimated travelling times associated with exposure to diesel fumes, cumulated up to 3rd survey. The differences between collieries were most extreme for this variable, with five collieries having no diesel travel at all up to this time. Within the other five collieries, the distributions were very skewed, with the large majority of men having relatively much lower exposures than the few with higher values, mostly due to occupations involving loco driving. Figure 3.9b shows

the pattern at 6th survey, by which time diesels had been introduced to pit W. Otherwise, the patterns were very similar to those at 3rd survey.

Figure 3.10 shows the predominance of the lower exposures. The small number of men with higher values was insufficient to show the age-limiting effect seen so clearly in the other exposures.

4. RESULTS OF STATISTICAL ANALYSES

4.1 Comparisons of mortality with reference populations

4.1.1 Form and presentation of the analyses

As described in 2.6.2, the observed death rates from a number of causes (listed in Table 2.5), based on 408375 person-years of follow-up, were compared to region-, age- and year-specific rates obtained from official UK sources. The results were expressed as Standardised Mortality Ratios (SMRs), with 95% confidence intervals (CI).

The results, for all of the causes of death analysed, are summarised in Table 4.1. For each cause of death, this table presents the number of observed deaths, the SMR and the bounds of its 95% confidence interval (in percentages), and a statistical test of the null hypothesis that the true SMR is 100%, i.e. that the observed death rates do not differ from the reference rates. This test is based on a z-statistic, which is expected to follow the Gaussian or Normal distribution. Thus for example values outside ± 1.96 are significant at the 5% level.

More detailed tabulations based on the same set of analyses are given in Appendix 2. Tables A2.1 to A2.11 each correspond to a single cause of death. Each of these tables shows SMRs, confidence interval and associated z-statistics, for the separate contribution of each pit. The pits are listed in regional order, roughly north to south (corresponding to Table 2.4). The last row of each table, for 'all' pits, is the same as the corresponding row in Table 4.1

4.1.2 All internal causes

There were 6775 deaths from internal (non-accidental) causes during the follow-up, yielding an SMR of 91% (95% CI 89-93). This low overall mortality is most easily explained as predominantly a 'healthy worker' effect. Since cohort members were all selected by being in employment at the beginning of follow-up, they would be preferentially selected from their respective age-groups, to exclude the unhealthy and less fit. SMRs of 70% to 90% for all causes are common in industrial populations, and Miller and Jacobsen (1985) produced similar figures for 20 pits in a follow-up to 1979.

Table A2.1 shows a spread of SMRs across pits from 83% at pit P to 102% at pit F, but with no suggestion of any systematic regional variations in SMR.

4.1.3 All cancers

A total of 1715 deaths during the follow-up had malignant neoplasms recorded as their underlying cause, with an SMR of 88% (95% CI 84-93). Table A2.2 shows that SMRs for individual pits ranged from 81% at pit W to 98% at pit Q, with no obvious systematic regional differences.

It thus appears that death rates from cancers were affected by healthy worker effects, although we must expect that this will differ by the type and site of the tumours. This is demonstrated below.

4.1.4 Lung cancer

Deaths from lung cancer numbered 632, with an SMR of 86% (95% CI 80-93). Table A2.3 shows a range of SMRs from 59% at pit W to 110% at pit Q, the only pit with an SMR over 100%. Again, there were no obvious systematic regional differences. The results are comparable with those of Maclaren (1992), who quoted a lung cancer SMR of 87% (95% CI 80-95) based on 278,629 person-years of follow-up in the same ten pits.

The low level of cancer mortality relative to the reference rates suggests that this population has experienced a healthy worker effect in respect of lung cancer. This may appear surprising, since we might expect such selection effects to be strongest for chronic diseases and conditions, and less evident in diseases in which expectation of survival after diagnosis is relatively short.

4.1.5 Digestive cancers

There were 249 deaths attributed to stomach cancer, with an SMR of 124% (95% CI 110-141) indicating a significant excess of mortality from this cause. Table A2.4 shows that the SMRs by pit ranged from 79% at pit W to 177% at pit Q. Seven out of the ten pits had SMRs greater than 100%. Stomach cancer was alone among all the cancer causes in having a raised SMR.

It was not possible to tell from this analysis to what extent the excess stomach cancer risks were associated with specific patterns of individual exposures or other variables. This topic is addressed in section 4.2.

Separate SMR analyses were performed for cancers of the large intestine, of the rectum, and of the oesophagus (Tables A2.5 to A2.7). All of these had SMRs around 90%, although the smaller numbers of deaths gave wider confidence intervals, and larger fluctuations between the SMRs for individual pits. None of these causes showed evidence of any excess of risks over the reference rates.

4.1.6 Other cancers

SMR for Bladder cancer was 77% (95% CI 59-99), based on 59 deaths. Because of the small numbers, individual pit SMRs were variable, but eight out of ten were below 100% (Table A2.8). The significantly low mortality suggests that bladder cancer may be subject to a healthy worker effect.

Prostate cancer deaths numbered 110, with an SMR of 86% (95% CI 72-104) (Table A2.9). Leukaemia deaths numbered only 37, with an SMR of 90% (95% CI 65-124) (Table A2.10). Neither cause thus showed strong evidence of a healthy worker effect.

4.1.7 Non-malignant respiratory diseases

Although not among the group of causes of death associated with malignant neoplasms, we have calculated SMRs for deaths from chronic bronchitis, since this condition has been demonstrated to be associated with exposure to respirable coal mine dust.

There were 436 deaths attributed to chronic bronchitis, with an SMR of 120% (95% CI 110-132) indicating a significantly raised risk for this cause, compared to the general population. Table A2.11 shows that the SMRs exceeded 100% in seven out of the ten pits, with around a 70% excess at pits K and F.

SMRs were not calculated for deaths from pneumoconioisis, since this has no causes except exposure to respirable dust, and there are no meaningful background rates.

4.2 Internal analyses of exposure-response relationships

4.2.1 Form and presentation of the results

The Cox regression models (Collett, 1994) used to investigate the relationships of cause-specific mortality with individual exposures have two primary components: an underlying hazard function which allows for changes (usually increases) in baseline hazard with the passage of time; and a log-linear regression model which expresses how changes in covariates (such as occupational exposures, smoking habits, birth cohort, etc.) affect the underlying hazard. The principal outputs of fitting such a model are estimates of the regression coefficients for covariates (estimated by maximising the partial log-likelihood function) and of their uncertainty, expressed as standard errors. The underlying hazard function is usually treated as a nuisance parameter, and is very difficult to compute where, as here, the covariates are time-dependent. Indeed, the computer program (BMDP2L: Dixon, 1992) used to fit the models for this project has no provision for printing an estimate of the underlying hazard unless all covariates are fixed.

Analyses of the different causes of death considered were carried out separately for each cause, but with similar strategic approaches to building a suitable log-linear regression model. The first step was to identify which covariates were required in the model. Covariates were selected which were expected to be important in predicting mortality from the specific cause, such as variables on smoking habits at cohort entry (grouped smokers v. ex-smokers v. non-smokers, and for the latter average tobacco consumption). Since the time axis for the underlying hazard was chosen as the time on follow-up, starting at cohort entry, it was necessary to include time-dependent regression terms for differences in age, and linear and quadratic terms in age were considered (Clayton and Hills, 1993). In addition, since cohort entry spanned a number of years, a term for differences in the date of cohort entry was included, to allow for possible secular trends in mortality rates. Models were fitted with terms for all the potential baseline covariates, and those which fell well short of significance were dropped.

To this baseline model were then added the various exposure variables, either unlagged or lagged by 15 years, both singly and in combination with terms for pit differences. Thus, for each cause, inferences about the effects of exposures, and about their confounding with covariates, were

made from comparisons of many different fitted models. We have selected the most directly informative of these to present in this report. They are presented in a series of detailed tables in Appendix 3, which share a standardised format.

An example is given by Table A3.1, which summarises the results of fitting five different models to data on deaths from lung cancer. These are labelled, so that they can be referred to in the text, by a combination of LC (for Lung Cancer) and a sequential model number. For each model, there are two columns of figures. The first is the estimated regression coefficients for the terms fitted in the model. The second is the absolute value of the ratio of the coefficient estimate to its standard error. Where the corresponding term is a single covariate or the difference between two groups, this has the interpretation of a normally distributed z-statistic for the inclusion of that term in the presence of all the others in the current model. Thus, for example, absolute values greater than 1.96 are significant at better than 5%. Note that where the term is one level of a factor dividing the data into more than two groups, the ratio term depends on the choice of baseline level, and is not an independent z-statistic, and need not on its own correspond to a valid comparison.

At the foot of the table of models is shown the value of the maximised partial log-likelihood. This is not informative in itself, but differences in this quantity between nested fitted models, multiplied by -2, yield chi-square statistics of the significance of terms by which the models differ. For a single term, this test will give similar results to that based on the z-statistic ratio; but the results are not always identical, and can differ considerably, particularly in analyses based on small numbers of deaths. The chi-square statistics calculated in this way, from the likelihood difference, are used to test the significance of grouping factors with three or more levels (i.e. with two or more degrees of freedom).

Since the model structure fitted to the hazard function is log-linear, the coefficient of any variable presented in the tables of Appendix 3 is interpreted as the logarithm of the relative risk of death attributable to a one unit increment in that variable, given that all other variables in the model remain unchanged. When interpreting these coefficients, it should be noted that terms for variables that are fixed in time, that is all baseline variables except those involving age, have been automatically included with their overall mean values subtracted, which was necessary to avoid computational problems during the iterative estimation procedure within the computer software package.

4.2.2 Lung Cancer

Baseline Model

Cox regression models for lung cancer mortality are presented in tables A3.1 to A3.5, numbered LC/01 to LC/25. Mortality from lung cancer was found to increase significantly with age, as expected, with an additional significant quadratic term indicating curvature with age. A term for amount smoked at entry was highly significant, again as expected, but when included, did not remove the need for an intercept term for current smokers at entry. These terms predicted a relative risk of almost 10 for current smokers at entry as against non-smokers, which was independent of the later addition of the exposure variables. The calendar year of entry, although not quite significant based on the z-ratio statistic, was close enough to warrant inclusion, and suggested a secular trend in mortality of decreasing risk with calendar time. Terms for the interaction between smoking status and age were significant and suggested different trends in

relative risk with age among current, ex- and non-smokers. Over the age period from 40 years to 80 years, when most deaths from lung cancer occurred, consistently the highest risks were attributable to current smokers followed by ex-smokers, with the lowest risks for non-smokers. The different trends with age between smokers and non-smokers could be interpreted as being due to the cumulative effect of smoking, if those who were current smokers at entry continued as such throughout follow up. The model predicted that in the age range from 40 to 60 years, the relative risk was rising faster for smokers than for non-smokers, while the opposite was true from 60 to 80 years. The baseline model LC/01 includes terms for year of cohort entry, smoking group (non-, ex- and current) and for amount smoked in current smokers, along with separate quadratic age trends in each of the smoking groups.

Pits

The inclusion of pit differences in model LC/10 (Table A3.3) resulted in a chi-square statistic (compared with LC/01 without pit effects) below the critical value corresponding to a 5% significance level (X^2=13.4, d.f.=9), so that there was no strong evidence for systematic pit differences. Based on the magnitude of their estimated coefficients, however, pits within the same region had similar relative risks, with pits T and Y (both North) and pit Q (East Midlands) having the highest, and pits F, V and W (all Wales) the lowest relative risk. Pits K and X (both Yorkshire and Humberside) fell between these two extremes being both slightly lower than pit P (Scotland), which in turn was slightly lower than pit C (West Midlands). This ordering of pits by their estimated coefficients did not change with the later addition of the exposure variables. (See also *additional runs* below)

Quartz and dust

Models LC/02 and LC/03 included terms for cumulative quartz exposure, unlagged and lagged respectively, after the baseline model variables, and were tested against the baseline model LC/01. The addition of unlagged quartz exposure was not significant (X^2=1.02, 1 d.f.). The 15-year lagged quartz exposure coefficient was somewhat larger, but still failed to reach statistical significance (X^2=2.04, 1 d.f.). Neither the unlagged or lagged terms for dust exposure (models L/04 and L/05) came close to statistical significance when included after the baseline model. The inclusion of each of the quartz and dust exposure variables individually had a negligible effect on the estimated coefficients for the baseline effects for smoking, age and calendar year, showing that the exposure variables were not noticeably confounded with any of the baseline variables. With pit effects in the model, both the unlagged and lagged quartz exposure coefficients were much reduced in both magnitude and significance. This suggested that the weak evidence for a lagged effect of quartz exposure could be explained by the differences in mortality at the level of pits, with no evidence of a gradient in risk with estimated quartz exposure within pits. As shown in Figure 3.3, exposures to quartz were consistently high at pits Q, T and Y and low at pits V and W and this correlates with the magnitude of their pit effects. The notable exception to this overall correlation was pit X which had, on average, high exposure, but relatively low mortality.

Radiation

Models LC/06 and LC/07 included terms for cumulative radiation exposure, unlagged and lagged respectively, after the baseline model variables, and were tested against the baseline model LC/01. The inclusion of lagged exposure was not quite significant at the 5% level

(X^2=3.26, 1 d.f.) with corresponding z-ratio of 1.85, but the unlagged term was not significant. After adjustment for pit differences, the lagged radiation term (LC/17) was greatly reduced and was not significant (X^2=0.04, 1 d.f.) when tested against model LC/10. As with quartz exposure, this suggested that the evidence of a lagged effect of radiation exposure might be explained by differences in mortality between pits alone, despite the wide range of exposures among men within the same pits. Put another way, there was considerable confounding between radiation exposure and any other factors which may affect lung cancer mortality and differ between pits. As shown in Figure 3.7, exposures to radiation were consistently high at pits T and Y and particularly at pit Q, while pits F, V and W were consistently the pits with the lowest exposure to radiation at third and sixth surveys.

Diesel exhaust

The addition of neither the unlagged nor lagged terms for exposure to diesel fumes (models LC/07 and LC/08) was statistically significant when tested against the baseline model (LC/01). Both unlagged and lagged exposure terms were also not significant when added after adjustment for pit differences (models LC/18 and LC/19). Therefore, there was no evidence of an increase in lung cancer mortality with time spent travelling on diesel locomotives, after adjusting for known confounders such as age and amount smoked.

Additional runs

Model LC/15 in Table A3.3 replaces pit differences by a single regression term for differences in published regional mortality rates. This was got by fitting a log-linear model to published lung cancer death rates, and extracting the coefficients for regional differences adjusted for age and averaged over calendar years. The logs of the inter-regional ratios were introduced as predictors in the regression model, so that their effect on the hazard would be multiplicative. Regression on these regional rate parameters was highly significant, and comparison of models LC/15 and LC/12 shows that pit differences after adjustment for regional rates were not significant (X^2=6.84, 8 d.f.). In addition, the coefficient for the lagged quartz exposure was increased in magnitude, although the z-statistic still fell short of the conventional 5% significance level.

A similar approach was applied to lagged radiation exposures, and the results are shown in Model LC/20 of Table A3.4. Here the effect of the background rates was similar, as expected; but the effect of the lagged radiation exposure increased considerably, and was now at the conventional 5% significance level.

Since these models seemed to be offering results which could be interpreted as weak or borderline evidence of effects of lagged quartz and radiation exposures on lung cancer mortality, it was decided to fit further models, to examine the dependence of the results on the degree of lag. These models included the regional differences in background lung cancer mortality rates, as described above for models LC/15 and LC/20; and either quartz or radiation exposures, lagged by 5, 10, 20 or 25 years.
Figure 4.1 summarises the results for all the lags used for quartz exposure. The estimated quartz coefficient, the magnitude of its z-statistic, and the overall model fit all increased steadily with increased lag. The full models for the 20 and 25 year lags are shown as models LC/21 and

LC/22 in Table A3.5, which also show that the coefficient for the regional mortality differences was also rising. The other terms, for age, smoking and cohort entry date, changed little.

Figure 4.2 shows a similar pattern for the effects of different lags in the radiation exposure variables. The increase in significance and model fit were not as steep as for the quartz, but they and the coefficient continued to rise as the lag increased to 25 years. Models LC/23 and LC/24 of Table A3.5 give the complete fitted models for the 20 and 25 year lags.

Finally, model LC/25 shows the effect of fitting a model including both quartz and radiation exposure variables, lagged at 25 years. Here both exposure coefficients are much reduced, as is their statistical significance, when compared with their addition singly. This suggests that there is confounding between these apparent effects, induced by some correlation between them. We have noticed earlier that neither quartz exposure nor radiation was significant after adjustment for pit effects. But both the average percentage of quartz in coalmine dust and the levels of underground radiation vary strongly between pits, and it is plausible that the apparently significant effects in, for example, LC/22 and LC/24 are artefacts of pit effects which are not wholly related either to quartz or to radiation.

Figure 4.3 shows the relationship between the pit differences and the mean PFR 3 quartz exposure. PFR 3 was chosen because of the apparent increased significance of quartz exposures when lagged up to 25 years; the values were those summarised in Table 3.11. The adjusted pit effect on the y-axis was obtained from the pit effects of model LC/10 of Table A3.3. These terms, representing differences on the log scale between lung cancer rates at different pits, were already adjusted for age, smoking and date of cohort entry, but not for regional differences in the background lung cancer mortality rates. For regional adjustment, the estimated log-ratio differences, as fitted for example in models LC/20 to 25, were subtracted from the pit effects; the mean level is thus arbitrary, but the differences are the adjusted logs of ratios between the pits. Figure 4.3 shows that the largest part of any evidence of a trend of lung cancer with pit mean quartz exposure arises from the separation of pits Q and W from the remainder, which show no real evidence of a consistent relationship. For confirmation, model LC/22 was rerun, using data only from the eight pits excluding Q and W. While all the coefficients changed slightly, the principal effect was to reduce the coefficient of the 25-year lagged quartz exposure to 0.0173, and its z-statistic ratio to 1.51, which corresponds in the Normal distribution to a significance level of about 13%, i.e. far short of what would be customarily accepted as statistically significant. In the absence of any evidence of an effect of exposure within pits, and lacking a really convincing and consistent relationship at the level of pit means, we conclude that this study provides no strong evidence that the pit differences observed can be ascribed to differences in quartz exposure.

In passing, we present Figure 4.4, which compares the adjusted pit effects with the pit-specific SMRs, both for lung cancer. Whereas the pit effects are adjusted for region, age, smoking and date of cohort entry, the SMRs are adjusted only for region, age and calendar date. This demonstrates that the adjustments for differences between distributions in smoking habits between pits were very small, compared to the pit differences; implying that the explanation of the pit differences cannot be based on smoking effects. Finally, Figure 4.5 compares the SMRs for lung and stomach cancer, which show a perhaps surprising measure of association, dominated by the high SMRs of pit Q and the low values for pit W. Recall however that differences between pits were not statistically significant, either for lung or stomach cancer, after regional adjustment.

Summary for lung cancer

Before fitting any exposure variables, lung cancer mortality was found to increase markedly with age and with amount smoked at cohort entry, with slightly different trends with age for the different categories of smoking status. These results were consistent with known trends. There was also some evidence of a secular decrease in lung cancer mortality through calendar time. Independently of these effects, there was evidence of differences in mortality among pits which were consistent with variation in published regional rates. Also independent of the baseline effects, but not of pit effects, a gradient in risk was found with increased exposure to quartz, and to radiation from radon and thoron daughters, when both were lagged by periods of 15 to 25 years. However, supplementary analyses have indicated that these effects were not independent of each other, and could be artefacts due to confounding with other, unmeasured, pit differences. The results cannot be considered strong evidence for effects of exposure on lung cancer mortality. No significant increase in risk was found for either dust exposure or diesel exposure, both when unlagged or lagged by fifteen years.

4.2.3 Stomach Cancer

Baseline Model

Cox regression models for stomach cancer mortality are presented in tables A3.6 to A3.9, numbered SC/01 to SC/19. Mortality from stomach cancer was found to increase significantly with age, with an additional significant quadratic term indicating curvature with age. There was a significant decrease in mortality with cohort entry date, pointing to a general secular trend similar to that for lung cancer, but with a markedly steeper gradient through time. This trend, which appeared independent of the exposure variables added later, translated to a 7% decrease in relative risk with each calendar year difference in date of entry. Doll (1996) notes that, although cigarette smoking is now believed to be a cause of at least some kinds of lung cancer, its probable mode of action is synergistic with diet, and some studies have failed to show a smoking effect. In the present study, there was no significant relationship between mortality from stomach cancer and smoking habits, and the following analyses have not been adjusted for smoking.

Pits

The increase in the chi-square statistic from the baseline model with the inclusion of the pit effect terms (SC/10) was close to its expected value (X^2= 7.34, 9 d.f.), indicating no significant differences in overall stomach cancer mortality among the ten pits. Unlike for lung cancer, the ordering of pits on the magnitude of their estimated coefficients did not cluster by region, giving no evidence of a strong underlying regional mortality effect.

Quartz and dust

Models SC/02 and SC/03 included terms for cumulative quartz exposure, unlagged and lagged respectively, and were tested against the baseline model SC/01. The addition of neither the unlagged or the lagged quartz exposure terms was significant. Models SC/04 and SC/05 show that neither the unlagged (X^2=0.12, 1 d.f.) or the lagged (X^2=0.06, 1 d.f.) dust exposure terms

differed significantly from zero. None of the exposure variables became significant when the models were augmented with pit effects, as shown by models SC/11 and SC/12 (for quartz), and SC/13 and SC/14 (for dust) in Table A3.8. Therefore, there was no evidence of any increase in stomach cancer mortality with increased dust exposure, or quartz exposure, after adjusting for the effects of age and cohort entry date.

Radiation

Models SC/06 and SC/07 in Table A3.7 included terms for cumulative radiation exposure, unlagged and lagged respectively, after the baseline model variables, and were tested against the baseline model SC/01. The increase in the chi-square statistic from the baseline model to the unlagged model was no greater than expected by chance ($X^2 = 1.32$, 1 d.f.). The increase to the lagged exposure model was similar, and again not significant, ($X^2 = 1.08$, 1 d.f.) although the z-ratio was only slightly over 1.0 and not suggestive of a strong effect. With adjustment for pit differences, the inclusions of unlagged and lagged radiation exposure (SC/16, SC/17, Table A3.9) were again not significant. Therefore, there was no clear evidence of an increase in stomach cancer mortality with increased radiation exposure.

Diesel exhaust

The inclusion of terms for diesel exhaust exposure, both unlagged and lagged as in SC/08 and SC/09 respectively of Table A3.7, were not significant and the coefficients were little different for the lagged and unlagged exposure terms. Similarly, after the inclusion of pit effects, the addition of terms for diesel exposure as in models SC/18 and SC/19 of Table A3.9, for unlagged and lagged exposure respectively, was not significant. Therefore, there was no evidence that increased exposure to diesel exhaust fumes resulted in an increase in risk of mortality from stomach cancer.

Additional runs

As for lung cancer, the published regional mortality rates for stomach cancer were analysed, and coefficients extracted for the logs of between-region differences. These differences were considerably less marked than those for lung cancer. The results of fitting a model including this term and lagged dust exposure is shown as model SC/15 in Table A3.8, where it can be seen that adjustment for regional differences was not significant.

Summary for stomach cancer

Looking at all the model results together, there appeared to be no evidence of any increase in mortality from stomach cancer related to an increase in exposure to dust, quartz, radiation due to radon and thoron daughter products or diesel exhaust fume, after adjustment for the known increase in mortality with age and after allowing for an underlying secular decrease in mortality with calendar time. This was despite the power provided by the Cox models being based on 249 stomach cancer deaths in the cohort during follow up and despite evidence from the external comparisons, that the miners in this cohort experienced a raised incidence of stomach cancer deaths in relation to their regional populations.

To investigate to what extent the raised mortality from stomach cancer could be due to one or more factors linked to the amount of time men spent working as coalminers, two additional Cox models were fitted. The first included, with the baseline model variables, time contributing to exposures, and the second, the same variable lagged by 15 years. In both cases the addition of the time variable had negligible effect, with estimated coefficients very close to zero (models not shown). This indicated that mortality from stomach cancer was not related to overall time spent working in coalmining. Along with the generally negative results from the analyses described above, the overall conclusion is that this study provides no strong evidence for an effect of occupational exposures on risks of mortality from stomach cancer.

4.2.4 Leukaemia

Baseline Model

The results of the Cox models for leukaemia mortality, based on 37 deaths, are shown in tables A3.10 and A3.11 in Appendix 3. The only significant baseline variables were an increase in risk with age and a decrease with cohort entry date as shown in baseline model LK/01. On *a priori* grounds, no models were fitted with quartz or dust exposures.

Pits

The inclusion of terms for pit differences, as in model LK/06 in Table A3.11, gave a chi-square statistic close to its expectation (X^2=10.16, 9 d.f.). Therefore, there was no evidence of differences among pits in relative risk of mortality from leukaemia. However, the inclusion of pit differences produced a more markedly negative relationship with cohort entry date. This may indicate some instability in the model fitting, given the small numbers of deaths from leukaemia.

Radiation

The addition of terms to the baseline model for exposure to radiation, both unlagged and lagged (models LK/02, LK/03 in Table A3.10) were not significant. The addition of these terms after adjustment for pit differences (LK/07, LK/08 in Table A3.11) was also not significant. Therefore, there was no evidence that an increase in exposure to radon and thoron daughters was associated with an increase in mortality from leukaemia.

Diesel exhaust

Models LK/04 and LK/05 (Table A3.10) show the fit of terms for exposure to diesel fumes, unlagged and lagged respectively, to the baseline model LK/01. These effects were not significant. The estimated coefficients, and their z-statistics, changed little when included after adjustment for possible pit differences in mortality (models LK/09, LK/10 in Table A3.11). Therefore there was no evidence that risk of mortality from leukaemia increased with exposure to diesel exhaust fumes.

Summary for leukaemia

With only 37 deaths, the study was obviously limited in its power to identify exposure-response relationships. In analyses of these deaths, there was no evidence that those dying from leukaemia had higher exposures to radon and thoron daughters than those who survived, after adjusting for an increase in mortality with age and a secular trend in mortality with cohort entry date. Similarly, there was no evidence that those dying from this condition had higher exposures to diesel exhaust fumes, as they were estimated in this study using diesel travelling times. These two results held whether exposures were unlagged or lagged by fifteen years to allow for a latency period between exposure and death.

4.2.5 Bladder Cancer

Baseline Model

The Cox model results for bladder cancer mortality are presented in tables A3.12 to A3.13 in Appendix 3. The baseline model, BC/01, shows that both linear and quadratic terms in age were significant. As with all the other causes of death investigated here, there was evidence of a secular trend in mortality, decreasing with cohort entry date. This trend was independent of the later inclusion of exposure variables. Additionally, a positive gradient in log relative risk with increased amount of equivalent cigarettes smoked at entry was significant. Silverman *et al.* (1992) report that smoking is well established as a cause of human bladder cancer, with most studies demonstrating an increase in risk with increasing consumption. In the models fitted here, smoking has been allowed for by fitting the single variable representing intensity of smoking consumption. The only occupational exposure considered potentially relevant on *a priori* grounds was diesel exhaust exposure.

Pits

The addition of terms for pit differences to the baseline model, as shown in model BC/04, was not significant, being close to its expected value (X^2=10.78; 8 d.f.). Only eight terms could be fitted since there were no deaths recorded at pit W.

Diesel exhaust

To the baseline model were added terms for diesel exposure, both unlagged and lagged, and these are shown in Table A3.12, in models BC/02 and BC/03 respectively. The estimated coefficients were little different in magnitude from the lagged to the unlagged models. Neither lagged nor unlagged diesel exposure was significant. After adjustment for pit differences, the addition of terms for diesel exposure, both unlagged and lagged as in models BC/05 and BC/06 of Table A3.13, were still not significant. Although there was no evidence of a gradient in relative mortality with diesel exposure within pits, when the pit effects were placed in rank order of the magnitude of their coefficients from positive to negative, almost exclusively, the highest ranked pits were the pits where diesel locomotives were used for travel. This was true whether diesel exposure was included in the model or not. The exception was pit V, with no diesel travel but which was ranked third in terms of relative mortality. Also, pit W with no deaths could not

be ranked but this suggested it had relatively low mortality. Although pit W was a diesel pit, diesel locomotives were only introduced in the mid-1970's, late in follow up, when the pit was merged with a neighbouring colliery and this resulted in generally lower exposures than for other diesel pits (figure 3.9).

Summary for bladder cancer

With only 59 deaths occurring during follow up, the exposure-response analysis of mortality due to bladder cancer had less power to detect positive associations compared with the analyses of mortality due to lung and stomach cancers. The direct estimate of exposure to diesel exhaust fume was not a significant predictor of mortality but there was some slight suggestion that pits where diesels were used for manriding were associated with a higher risk of mortality. This was most particularly true for pit Q with the highest estimated risk of mortality, which was significantly higher than three of the non-diesel pits, the exclusion being pit V. At pit Q, the long travelling distances to and from the pit bottom to the coal faces meant exposure to diesel fume while travelling was higher than at all other pits (figure 3.9). However, pit W stands as a counter-example, and the observed pit differences could just as readily be explained by chance.

4.2.6 Pneumoconiosis

Baseline Model

The Cox model results for mortality due to pneumoconiosis are shown in tables A3.14 and A3.15 in Appendix 3. The baseline model PN/01, shows that both linear and quadratic terms for age were significant. As before, the year of cohort entry was associated with a decrease in mortality, which was independent of later added exposure variables. Neither amount smoked or smoking status at entry were significant predictors of mortality due to pneumoconiosis, and they are not included in these models.

Pits

When added to the baseline model as in model PN/06, terms for pit differences were highly significant (X^2=78.26, 9 d.f.). The magnitude of the coefficients and their z-ratios indicated that mortality was greatest at pits W and F, with pit Q being the lowest. These individual difference terms changed considerably on the introduction of variables for quartz and dust exposure (see below).

Quartz and dust

When added separately to the baseline model as in models PN/02 to PN/05 in Table A3.14, the terms for quartz and dust exposure were highly significant, predicting higher mortality from pneumoconiosis with higher quartz exposures and, separately, higher dust exposures. Since these two exposures were highly correlated (Table 3.10), it was not surprising that if one was a significant predictor, the other would be also. The higher overall likelihood values indicated that the lagged exposures, in both cases, provided a better model fit. After adjustment for pit differences, the inclusion of both exposures separately was again highly significant, with the

lagged exposures for both quartz (X^2= 66.56, 1 d.f.) and dust (X^2= 82.42, 1 d.f.) proving to be the strongest predictors. The confounding between the pit difference terms and quartz exposure, in particular, meant that the coefficient for lagged quartz exposure, which translated to a relative risk of 3% per mg.hr.m^{-3} of exposure before adjustment, became 17% after adjustment. Therefore, when the quite different mean levels in quartz exposure across pits were accounted for, an increase in mortality was still predicted with increased quartz exposure among men within the same pit. Due to the correlation between quartz and dust exposure the same was also true for dust exposure, with the lagged model (PN/11) predicting a 0.7% increase in risk with every mg.hr.m^{-3} of dust exposure.

Models PN/06 and PN/12 include both lagged dust and lagged quartz exposures, with and without pit effects respectively. Model PN/12 shows that when pit effects and lagged dust exposure are in the model, the addition of lagged quartz is not an improvement, so that model PN/11 would be preferred. Without pit effects, the lagged dust exposure coefficient is increased, while the lagged quartz exposure is significant but negative. Comparison of PN/06 with PN/12 shows that pit effects are still highly significant when both lagged dust and lagged quartz exposures are in the model. Since the proportion of quartz in coalmine dust differs widely between pits, this suggests that the negative quartz coefficient in PN/06 is an artefact due to not including pit effects.

Summary for pneumoconiosis

It is well established that exposure to respirable coalmine dust in underground mining can cause pneumoconiosis; and that this condition, in its severe form of progressive massive fibrosis, can lead to premature death. The analyses here of mortality due to pneumoconiosis are entirely consistent with previous observations, which have pointed to cumulative exposures to respirable dust as the single most important risk factor for the development of radiological abnormalities in coalworkers. The inability to explain all of the pit differences by the amount of quartz in the dust is also consistent with all published PFR work on radiological surveys.

Mortality from pneumoconiosis was not the focus of this study, and these analyses have been included for comparison with the analyses of deaths from cancer. The strength of the association of pneumoconiosis deaths with exposure to respirable dust confirms the reliability of the exposure estimates, and gives a pointer as to the power of the analyses of other causes of death, such as lung and stomach cancer, with at least the same number of cohort deaths, to detect significant exposure-response relationships. Further investigation of the pit differences would be possible, in terms of more detailed distinctions between types of quartz and temporal patterns of exposure.

5. DISCUSSION

5.1 Summary of principal findings

5.1.1 Summary of mortality

The cohort analysed contributed over 408,000 man-years of follow-up to the end of 1992. There were over 7000 deaths in the cohort during the follow-up period.

5.1.2 Comparisons of mortality with reference populations

For the purposes of this report, we have compared the death rates from various causes, up to the end of 1992, with the corresponding rates in males in the regions of England, Wales and Scotland in which the pits were situated. Results of these comparisons have been expressed as Standardised Mortality Ratios (SMRs), as is customary.

SMRs for all-cause mortality were generally low (averaging 91%: 95% CI 89 - 93), as is often found in occupational studies. In almost all cases, the pit-specific SMRs were slightly higher than those reported by Miller and Jacobsen (1985) and Miller *et al.* (1981) for a follow up to 1979. This is to be expected as the cohort ages, and the healthy worker effects wear off (although it should be noted that the comparison is not exact, since the cohort for the present study was augmented by men joining the PFR research at later surveys, and omitted men present only at the earliest surveys because they lacked smoking or other data essential to the present analyses).

Elevated SMRs were found for stomach cancer (124; 95% CI 110-141), but not for any of the other cancers studied, i.e. lung, large intestine, rectum, oesophagus, bladder, prostate and leukaemia. Deaths from chronic bronchitis also displayed a raised SMR (120; 95% CI 110-132).

5.1.3 Exposure-response relationships

Exposure-response relationships were explored by regression methods designed for data from mortality studies. These were limited to causes with sufficient numbers of deaths, viz. lung, stomach and bladder cancers, leukaemia and pneumoconiosis. Exposures considered were respirable dust and quartz, diesel fume (as indicated by underground travelling time) and exposure to radiation from radon and thoron daughters combined.

Mortality from pneumoconiosis showed a very clear relationship with exposure to respirable dust, which was a better predictor of risk than respirable quartz. None of stomach cancer, bladder cancer or leukaemia showed a significant relationship with any of the exposures.

In the analyses of lung cancer, there was no strong evidence of exposure effects. When lagged by 25 years, and after adjusting risks for background regional lung cancer death rates, exposure to respirable quartz reached conventional levels of statistical significance, but the effect was strongly confounded with pit differences and could not be demonstrated between men of different exposure within the same pits. A similar but somewhat weaker effect was observed

with radiation exposures. These findings are not considered strong evidence of occupational exposure effects, since they could be artefacts of other factors which differed between the working practices or surrounding environments of the collieries involved.

5.2 Representativeness of cohort

In the original design of the PFR, the 24 collieries which contributed to the first phase of the analyses were selected specifically to cover the range of types of coal and of working practices typical of their day, and this principle was maintained in deciding which pits would be retained in the second phase of the research. Thus the 10 pits studied here are representative of the British coalfields as they existed.

The target population for the PFR surveys was all industrial workers, at the coal face, elsewhere underground, and above ground. Thus the only employees who were not included were management, office staff, and auxiliary workers such as canteen staff. Those who were included covered the whole range of exposure conditions from the face to the open spaces of the pithead.

These surveyed populations were the basis for the mortality tracing, which has now been widened to include all men who ever attended any survey at any of the 10 continuing pits; almost 24,000 men. Tracing of these men in the national registers has been very successful, with less than 4% untraced. The follow-up continues, as all traced survivors have been flagged in the national systems.

The analyses reported here were based on over 18,000 men. The principal exclusions were of men who had attended only the first round of PFR surveys, and for whom there were therefore no smoking data. Of the remainder, the principal systematic exclusions were men attending only the second survey at pit P, who were excluded for lack of smoking data; and men whose occupational histories had been judged, at the survey at which they had been recruited, to be unreliable.

Overall, the study group is considered to be representative of employees in the British coalfields through about twenty years from the end of the 1950s.

5.3 Reliability of exposure estimation

In many epidemiological studies, exposure is characterised by classifying individuals according to where they worked (at time of survey, or at entry to cohort); and this may be supplemented by a time since first employed in the industry. Often this is all that is practically possible in a retrospective situation. In the PFR, however, the need for detailed and differential characterisation of exposures to dust was established from the start. Men had a full occupational history taken when they joined the research programme. There was an on-going programme of sampling in a wide range of underground and surface jobs, with a sampling strategy based on occupational groups; and times worked, recorded in the payroll systems, were allocated by colliery staff to these same occupational groups. Thus times worked could be linked with summaries of measured concentrations, to produce elements of exposure; and these elements then summed over occupations to give estimates of total exposure in particular time periods. Indeed, the dust exposures were based on a level of detail which, at the time, was unequalled in coalmining or any other industry (except workers continually monitored by badge for exposure

to radiation). The method of quantifying the concentrations was changed to gravimetric after some years of particle counting, but the earlier data were converted using factors which were estimated separately by pit, and the conversion is not considered to be a serious source of distortion.

The same level of detail was not, of course, available for work in the period before the research started. Estimation of exposures from occupational histories attempted to maintain important distinctions in intensity of concentration, but the mean concentrations used applied to broad categories of work such as face work, elsewhere underground, etc., rather than to specific occupational groups; and the concentrations used were estimated from means observed during the first ten years of the PFR research, under the assumption that these were appropriate to describe conditions before the 1950s. Similar assumptions and methods were used to assign exposures to periods spent in other, non-PFR collieries. Thus each man's exposure was made up of varying proportions of the 'unmeasured', i.e. based on occupational histories, and the 'measured', i.e. based on the ongoing sampling and time-recording systems of the PFR. Those with the highest unmeasured contribution would, on average, be those older men who already had a history in mining when the PFR started, while men recruited straight into the research collieries could have exposures based entirely on the measured data. The analyses of Miller and Jacobsen (1985) relied solely on data from the occupational histories, yet found that these predicted mortality better than simply time in the industry. The cohort for the present study was more weighted towards those with higher proportions of measured exposures, and the statistical methods used allowed their accumulation over time to be taken into account in the analysis.

The derivation of quartz concentrations was based on compositional analyses of the dust samples. Those for the earlier periods of the research were obtained much later, from the samples which had been retained, while quartz determination for later periods became a routine part of the analysis of the dust samples. Again, there was a change in methodology from an interference microscopy technique to ashing and infra-red spectroscopy, but both methods estimated the proportion of quartz in the sample, which was combined with the dust estimate to produce a quartz mass estimate. Sometimes dust samples within an occupational group were pooled to provide enough dust to allow the compositional analyses by the ashing method, but at most these would cover a single year rather than the quarter-years by which the dust was summarised. The greatest uncertainties in the quartz exposures were, as for the dusts, in the unmeasured portions before the start; here, the assumptions regarding constancy of dust concentrations were supplemented by similar assumptions about constancy of composition.

A consequence of these observations is that mortality analyses which assume lags of many years, by ignoring that period in the calculation of time-dependent exposures, will still be based quite heavily, perhaps even predominantly, on unmeasured exposures, and will be as reliable as the untestable assumptions on which these were based. The longer the follow-up period, the greater will be the influence of measured exposures, and for this reason the value of the data set will increase as deaths continue to accrue.

Exposures to diesel fumes and to radiation were also based on the PFR time-recording systems, but the assessment of concentrations was based on much sparser information. There were no direct measures of diesel exhaust particulate concentrations, but they were assumed to be constant while travelling, and there were detailed records of travelling times, distances and methods for each occupational group. Total exposure for most men was therefore based on estimates of travelling time to different faces in different periods, linked to the occupational

groups in the time-recording systems. We believe therefore that cumulated travelling time is a good surrogate for diesel exposure. A project running as this report is finalised is using retrospective exposure estimation techniques to estimate actual concentrations to diesel fumes, and will reestimate exposures and reanalyse lung cancer mortality. Diesel vehicles were used only very occasionally, if at all, prior to the start of the PFR programme, and there were therefore no significant underground exposures to diesel exhaust particulates before this time.

There is only limited data available on concentrations for radiation from radon and thoron daughters. The study reported by Crawford and Edlin (1982) produced limited numbers of measurements, taken at a single point in time. These are in some cases common to a whole pit, in others split by seam, but not by occupational group or even by face. These data will not be supplemented now that the pits concerned are closed.

In summary, the exposure estimates are all based on uniquely strong work history information collected prospectively in the course of a 25 year research programme. Direct measurements of respirable dust and quartz were collected throughout the research and it is difficult to conceive of better exposure information than exists for dust and quartz. The information on diesel and radiation exposures is based on much less direct measurement, but the exposures still make use of the working histories, and are based on sound relationships between exposure and the working environment.

5.4 Adequacy of statistical models

Analysis of mortality data at the level of individual subjects has always seemed more difficult than dealing with data from cross-sectional studies, because of the complex processes involved: deaths take place throughout the follow-up; men can each die from at most one cause during the follow-up, so that the data on cause specific mortality can be heavily censored; each member of the cohort ages during follow-up; risks change with age; and exposures are accumulated over periods of time, including throughout the follow-up. Methods for regression analysis of epidemiological data sets were laid out in the pioneering paper of Cox (1972), but the computational burden of estimating parameters within the framework meant that the application of these methods to studies of large groups of subjects has become practicable only with the power of modern computers, and the development of efficient estimation algorithms.

Previous analyses of PFR mortality data (Miller *et al.*, 1981; Miller and Jacobsen, 1985; Maclaren, 1992) have analysed the data after grouping them into tables. In situations where an outcome or risk may depend simultaneously on several continuous predictors, such grouping reduces the power to detect both main effects and interactions, and does not yield straightforward quantification of exposure-response relationships. We have avoided these disadvantages by using up-to-date software on fast modern computers, to fit many regression models to our data. The software used has allowed the risks to be modelled as a function of exposures accumulated over time, rather than at one fixed point; adjustment has been made, in some models and for some causes, for regional differences in background mortality; dependence on age has been modelled as time-dependent; allowance has been made for secular trends in mortality rates, relevant to the differences in cohort entry dates; and, where necessary, dependence of risk on age has been modelled with quadratic rather than just linear terms, and with separate coefficients depending on smoking habits.

Thus, in a number of ways, the modelling of cause-specific mortality in the present study used methods which were modern improvements on more approximate methods used in the past. The relationships with background variables were largely as expected: the strong dependence of risks on age, and of lung cancer risks with smoking, were entirely in line with prior expectations of these data. In addition, the relationships of mortality from pneumoconiosis with exposure to dust were very consistent with relationships of exposure with prevalence and incidence of radiological abnormalities, derived from analysis of radiological data from the PFR (see 5.5). We therefore have no serious caveats about the ability of the statistical methods used to identify and quantify exposure-response relationships, if they existed.

5.5 Comparison with other studies

5.5.1 Pneumoconiosis

The analyses of mortality ascribed to pneumoconiosis in men who had been part of the PFR produced results entirely consistent with the results of the PFR's studies of the development of pneumoconiosis in life as characterised from survey radiographs. Hurley *et al.* (1982) published results from the second phase of the PFR research which showed very clear relationships with cumulative exposures to dust, differences between pits in the relative risks of the same amounts of dust exposure, and no clear explanation of these patterns in terms of the contribution of quartz within the respirable dust. Such a summary would suit well the results shown in models PN/10-12 in Table A3.15. In both studies, pit Q had by far the lowest relative risks. Hurley *et al.* (1982) identified pit T as having unusually high relative risks; for mortality, the relative risk at pit W was rather higher than that at pit T, which nevertheless occupied second place (model PN/11).

5.5.2 Stomach cancer

This study has identified a raised SMR for stomach cancer, consistent with several other studies (Stocks, 1962; Enterline, 1972; Matolo *et al.*, 1972; Rockette, 1977; Logan, 1982). However, a suggestion of a weak relationship with dust exposure, in earlier PFR analyses reported by Miller and Jacobsen (1985), has not been confirmed in the present study, which has evinced no evidence of an exposure-response relationship, even with time worked in the industry. This, in turn, is consistent with the negative results from some other, smaller (principally case-control) studies (Swaen *et al.*, 1987; Atuhaire *et al.*, 1986; Weinberg *et al.*, 1985). This leaves us with the task of explaining why coalminers should be at increased risk of stomach cancer, if not directly from the inhalation and deposition of respirable coal mine dust or other directly occupational exposure. In part, this may be labelled a phenomenon of social class; miners are characterised in official publications as belonging to Social Class III, although it is arguable that this is justified only on grounds of income, and that their lifestyles are more typical of Class IV or V. Logan (1982) quotes stomach cancer SMRs for 1971 as 109 for Social Class III (118 if restricted to the sub-Class of manual workers, IIIM), 125 for Class IV, and 147 for Class V (Logan, 1982; Table 5A). Our observed SMR of 124 is certainly in this range. Logan also quotes relative SMRs (RSMRs), which provide a comparison to all-cause mortality. For stomach cancer in 1971, these are 104, 111, 110 and 107 for III, IIIM, IV and V respectively. But our all-cause SMR was low, giving an RSMR of 124/91=136. This suggests that miners may have increased risks over those of the same Social Class.

Even if it is accepted that part of the excess stomach cancer risk is a social class effect, this begs the question of what risk factors for stomach cancer preferentially affect members of the social classes III to V. Smoking habits differ across the classes, but smoking is at best a weak predictor for stomach cancer mortality, and in fact was not a statistically significant predictor in the analyses reported here. Mechanistically, it has been suggested that eating while underground may lead to the ingestion of coal dust, which may be carcinogenic or become so in reaction with, for example, digestive acids. If so, one might have expected more evidence of a relationship with time worked. It is possible that general diet may be a factor, as may alcohol consumption, or the use underground of chewing tobacco, but we have no data on any of these. It also seems possible that the heavy use of domestic coal typical of mining communities might generate local atmospheric pollution with potentially carcinogenic properties, but again we have no data to investigate such an hypothesis; and one might expect such effects to be manifest in lung cancer rates as well as for stomach cancer.

5.5.3 Lung cancer

The debate on whether quartz causes cancer in humans continues (International Agency for Research on Cancer, 1997; McDonald, 1989; Pilkington *et al.*,1996). Because of the strength of the exposure estimates, among other factors, this study had great power to detect any increased risk of lung cancer which may be related to quartz exposure, and was therefore in a position to make an important contribution to the debate. There was no evidence of any exposure-response relationship, with any of the exposures, when comparisons were made within collieries. There were, however, differences in risk between collieries, which appeared to show a small degree of association with heavily lagged quartz exposures, but which could better be explained as being due to the effects of the two pits with the highest and lowest risks. While colliery differences include quartz concentrations, they may also include local population differences, or exposure to other, unknown, local hazards. Lung cancer mortality rates are well known to vary by region and social class, (Logan, 1982). Our attempts to standardise by geographical region may not have adjusted sufficiently for the small scale geographical variations associated with individual collieries.

In the context of the general debate on quartz and lung cancer, these negative findings apply to situations where the quartz content of the dust is generally less than ten percent (Dodgson *et al.*, 1971). The lung is therefore responding to a much larger amount of coal and other minerals, and this could conceivably modify the response to quartz. All other exposure-response studies of quartz and lung cancer have given negative results (as distinct from cristobalite, where the evidence is equivocal), while several incidence studies of quartz-exposed workers have demonstrated increased frequencies, so the question is still open. Resolution of this uncertainty requires exposure-response studies with high quality exposure data, in populations exposed to dust containing higher proportions of quartz in the dust than in the present study.

An important subsidiary question in the quartz debate, particularly in the arena of statutory classification and labelling, is whether any lung cancer risks associated with quartz exposures are limited to men who have already developed silicosis, as has been suggested by some studies of members of silicosis registers (International Agency for Research on Cancer, 1997; McDonald, 1989; Pilkington *et al.*, 1996). In the absence of an exposure-response relationship for quartz, the present study is unlikely to shed any light on this question. However, any inclination to treat the increased risk at pit Q as quartz-related must be tempered by the observation that pit Q had the lowest risks of radiological abnormalities, and the lowest relative

mortality from pneumoconiosis, which seems to argue against its quartz exposures being singularly pathogenic. This once more raises the possibility that the quartz in different pits or occupational situations may differ in its ability to affect health (Miller *et al.*, 1993). Such differences have been clearly demonstrated with regard to risks of radiological progression (Miller *et al.*, in press), although the precise characteristics which differentiate quartz exposures are not known. Further analyses to investigate the risks specifically in men with and without pneumoconiosis would be helpful.

Review of the epidemiological literature suggests that heavy exposure to diesel exhaust fumes possibly does increase the risks of lung cancer, though the evidence is not conclusive (Steenland, 1986; International Agency for Research on Cancer, 1989; Jacobsen *et al.*, 1988). The present work demonstrates no increased risks in coalminers, in response to the generally low concentrations found in British mines. Given the relatively late introduction of diesels and the likelihood of long latency for lung cancer, it may be prudent to re-examine the relationship at some point in the future, to obtain greater power to detect what may be a small effect if it exists at all.

No convincing evidence was found for a dose-response relationship between lung cancer mortality and exposure to radiation from radon and thoron daughters. Finkelstein (1996), using similar methods of statistical analysis, found a relationship with radon exposures accumulated between four and 14 years before diagnosis. His data, however, included cancer registrations with non-fatal outcomes, and conversion of his dose rates shows that the uranium miners studied were experiencing average radon exposure concentrations some ten times higher than even the highest concentration in Table 2.6. Our failure to show a relationship is more likely to be due to the differences in exposure magnitudes.

5.6 Potential for further analyses

The mortality database from the PFR provides the ability to investigate cause-specific mortality, in relation to conditions of work in the coalmining industry. All deaths are recorded by cause, so that there is scope to analyse causes not previously examined, much as the present study and that of Maclaren (1992) focused on cancer, moving away from the previous emphasis (Miller and Jacobsen, 1985) on non-malignant respiratory disease. Thus other types of cancer, or other non-malignant disease, could be investigated.

There has been a recent upsurge in interest in chronic bronchitis, in respect of various legal cases over compensation for disability. Much of the debate has been fuelled by PFR studies of lung function loss, such as those of Marine *et al.* (1988) and Love and Miller (1982). The newly augmented cohort contains a higher proportion of men from whom data on smoking habits and lung function were taken in life. Analyses to refine earlier observations (Miller *et al.*, 1981) of a relationship between lung function loss and subsequent mortality could be carried out, and extended to specific causes of death rather than just all-cause mortality. Such analyses could inform the debate over the seriousness of, and prognosis for, early changes in lung function.

A coalworker attending a PFR survey always had a chest radiograph taken, and the readings made of these, regarding presence or absence of radiological signs, have not been taken into account in our analyses. There is scope to incorporate these data, probably in suitable subsets of the cohort, to address questions such as whether radiological signs are an early indicator of

subsequent risk for lung cancer or other causes of death; or whether there is any evidence of quartz-related risks in the subset of men already showing radiological signs.

We note here that the unusually high quartz exposures experienced in the one Scottish colliery (P) (Miller *et al.*, in press) might conceivably express themselves in an increased lung cancer risk. However, the population exposed was not large, and the follow-up since exposure only about twenty years, so it is perhaps not surprising that no effects were detected here. All traced cohort members are flagged in the national registers, so that deaths will continue to accrue, and should be examined further at points in the future.

Such investigations might be extended to other collieries, if it were possible to differentiate the quartz exposures experienced by source (dirt bands, roof and floor, etc.) and type. Any differentiation would likely be on the basis of the recorded characteristics of the various faces worked, and could be linked into exposure estimation by the fact that face occupational groups in the PFR system were face-specific.

Knowledge of face characteristics has permitted an extension in the direction of diesel exposures. In an IOM project still running as this report is being finalised, a retrospective exposure assessment seeks to assign concentrations of diesel fume to underground occupations, to replace the travelling times used as surrogate concentrations in the present report. The analyses of relationships between lung cancer mortality and diesel exposures will be rerun with the new exposure estimates, and the results compared with those given here.

As remarked above, the confirmation of an increased stomach cancer risk among men in at least some of the pits suggests that further work to identify causes is warranted. More detailed exposure assessment within the PFR study seems unlikely to be informative, and studies in mining communities may be more useful. These might examine whether the risks are shared by wives, or by neighbours in non-coalmining employments.

5.7 Concluding remarks

Previous studies, and this, have shown that exposures to respirable dust, and to a certain extent quartz, can have health consequences which are reflected in increased mortality risks. The results of the present study provide no consistent evidence that such exposures increased risks of mortality from cancer.

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Table 2.1 Chronology and nomenclature of PFR surveys and inter-survey periods. Note that length of ISP 0 is variable, depending on date of recruitment at colliery.

PFR Survey		1st	2nd	3rd	4th	5th	6th
Inter-Survey Period (ISP)	ISP 0	ISP 1	ISP 2	ISP 3	ISP 4	ISP 5	ISP 6

Table 2.2 Dates, by convention, for PFR surveys at 24 research pits. Month given is that in which the majority of the survey work was carried out.

Pit	PFR Survey					
	1st	2nd	3rd	4th	5th	6th
A	6/56	7/62	7/67			
B	7/55	7/61	7/66			
C	5/55	6/60	7/65	10/71	10/75	
D	6/55	6/60	5/66			
E	11/53	12/57	2/64			
F	2/56	3/62	3/67	5/72	5/76	
G	10/54	10/59	10/64			
H	4/56	4/62	3/68			
I	5/54	4/59	2/65			
J	2/55	11/59	11/65			
K	5/56	5/62	5/68	11/73	11/76	
L	3/55	3/60	3/66			
M	9/54	9/59	3/65			
N	5/58	6/63	7/68			
O	6/54	6/58	6/64			
P	3/54	4/58	3/64	11/70	11/74	11/78
Q	6/54	6/59	5/65	6/71	6/75	
S	12/53	11/57	12/63			
T	4/55	4/60	4/66	3/70	6/73	
V	2/54	7/58	6/64	6/70	6/74	6/78
W	12/55	11/61	11/66	9/72	9/76	
X	11/55	6/61	5/67	4/73	3/77	
Y	11/54	6/59	6/65	3/71	4/75	
Z	3/56	11/61	11/67			

Table 2.3 Summary of data available (collected and valid for analysis) from PFR surveys at each of 10 continuing pits.

Pit	PFR Survey					
	1st	**2nd**	**3rd**	**4th**	**5th**	**6th**
C	5/55 x [redacted]	6/60 x s r *	7/65 x s r l	10/71 x s r l	10/75 x s r l	[redacted]
F	2/56 x [redacted]	3/62 x s r l	3/67 x s r l	5/72 x s r l	5/76 x s r l	[redacted]
K	5/56 x [redacted]	5/62 x s r l	5/68 x s r l	11/73 x s r l	11/76 x s r l	[redacted]
P	3/54 x [redacted]	4/58 x † r	3/64 x s r l	11/70 x s r l	11/74 x s r ‡	11/78 x s r l
Q	6/54 x [redacted]	6/59 x s r	5/65 x s r l	6/71 x s r l	6/75 x s r l	[redacted]
T	4/55 x [redacted]	4/60 x s r	4/66 x s r l	3/70 x s r l	6/73 x s r l	[redacted]
V	2/54 x [redacted]	7/58 x s r	6/64 x s r l	6/70 x s r l	6/74 x s r l	6/78 x s r l
W	12/55 x [redacted]	11/61 x s r l	11/66 x s r l	9/72 x s r l	9/76 x s r l	[redacted]
X	11/55 x [redacted]	6/61 x s r l	5/67 x s r l	4/73 x s r l	3/77 x s r l	[redacted]
Y	11/54 x [redacted]	6/59 x s r	6/65 x s r l	3/71 x s r l	4/75 x s r l	[redacted]

x Radiographs (X-ray films) taken
s Smoking data taken
r Respiratory symptoms taken
l Lung function measured
† Smoking data incomplete
* FEV, but no FVC
‡ Change of technician affected lung fn. results

Table 2.4 Relationship of 10 continuing pits to standard administrative regions.

Pit letter	Time Period		
	Up to 1964	1965 - 1973	1974 - 1993
P	Scotland	Scotland	Scotland
T Y	Northern	Northern	North
K X	East & West Ridings	Yorkshire & Humberside	Yorkshire & Humberside
Q	North Midland	East Midland	East Midlands
C	Midland	West Midland	West Midlands
F V W	Wales I (South East)	Wales I (South East)	Wales

Table 2.5 Causes of death for which SMR analyses (comparisons with reference rates) were carried out, and corresponding ICD codes under the relevant revisions.

Cause of death	ICD Revision		
	7th	8th	9th
All internal causes	000-799	000-799	000-799
Cancers:			
All cancers	140-205	140-209	140-208
Lung	162	162	162
Stomach	151	151	151
Large intestine	153	153	153
Rectum	154	154	154
Oesophagus	150	150	150
Bladder	181	188	188
Prostate	177	185	185
Leukaemia	204	204-207	204-208
Chronic bronchitis	502	491	491

Table 2.6 Summary of measurements of radiation levels in PFR pits. Table shows, for each seam sampled within 10 pits, number of measurements taken (No.), and mean radiation from radon and thoron daughters (mWL).

Pit	Seam	No.	Radon	Thoron
C	a	10	4.00	4.34
F	b	6	1.07	0.53
	c	3	0.80	0.73
K	d	4	7.60	5.15
	e	4	9.42	3.62
P	f	6	3.07	3.42
	g	3	3.63	4.30
Q	h	50	20.30	6.87
	i	3	6.93	4.33
T	j	5	5.14	3.42
	k	3	8.67	3.63
V	l	3	0.80	0.97
	m	11	2.05	1.14
	n	3	3.00	2.43
W	o	6	1.45	1.55
X	p	4	0.62	2.98
	q	2	2.50	4.05
	r	3	0.70	2.53
Y	s	2	5.90	2.30
	t	13	5.22	4.12

Table 3.1 Results of tracing exercise. Table shows numbers of men by vital status, in the sub-populations traced in earlier and current phases of the PFR mortality studies, with percentages in *italics*.

Vital status	**PFR mortality study phase**					
	Earlier studies		This study		**Total**	
Alive	5915	*39.8*	6639	*74.4*	12554	*52.8*
Dead	8489	*57.1*	1966	*22.0*	10455	*43.9*
Embarked	83	*0.6*	53	*0.6*	136	*0.6*
Not traced	319	*2.1*	250	*2.8*	569	*2.4*
Unconfirmed death	42	*0.3*	1	*0.0*	43	*0.2*
Query outstanding	20	*0.1*	12	*0.1*	32	*0.1*
Total	14868	*100.0*	8921	*100.0*	23789	*100.0*

Table 3.2 Distribution of men entering cohort for analysis, by pit, survey qualifying for cohort entry, and age at entry.

Pit	Age at survey	PFR survey					
		2nd	3rd	4th	5th	6th	Total
C	15-24	48	85	72	123		328
	25-34	106	60	49	58		273
	35-44	201	70	42	38		351
	45-54	362	81	53	31		527
	55-64	391	66	14	9		480
	65+	21	3	0	0		24
	Total	1129	365	230	259		1983
F	15-24	14	142	93	47		296
	25-34	81	69	61	53		264
	35-44	178	29	40	38		285
	45-54	212	37	45	27		321
	55-64	186	27	9	12		234
	65+	8	7	0	1		16
	Total	679	311	248	178		1416
K	15-24	41	141	83	71		336
	25-34	110	47	41	36		234
	35-44	262	24	17	18		321
	45-54	268	24	28	20		340
	55-64	205	23	9	4		241
	65+	8	0	0	0		8
	Total	894	259	178	149		1480
P	15-24		152	109	76	59	396
	25-34		207	59	22	6	294
	35-44		213	47	23	6	289
	45-54		268	66	12	3	349
	55-64		215	59	11	2	287
	65+		13	0	0	0	13
	Total		1068	340	144	76	1628
Q	15-24	222	77	85	73		457
	25-34	234	31	93	66		424
	35-44	292	38	88	32		450
	45-54	268	19	108	17		412
	55-64	157	10	100	7		274
	65+	10	0	1	1		12
	Total	1183	175	475	196		2029

Pit	Age at survey	PFR survey					
		2nd	3rd	4th	5th	6th	Total
T	15-24	75	183	18	4		280
	25-34	134	58	8	5		205
	35-44	299	51	9	3		362
	45-54	345	40	11	3		399
	55-64	272	33	6	2		313
	65+	12	4	0	0		16
	Total	1137	369	52	17		1575
V	15-24	347	295	91	52	104	889
	25-34	233	76	22	14	72	417
	35-44	415	76	33	4	48	576
	45-54	351	73	55	13	25	517
	55-64	179	46	39	2	13	279
	65+	32	0	1	0	0	33
	Total	1557	566	241	85	262	2711
W	15-24	10	61	20	4		95
	25-34	79	47	11	6		143
	35-44	191	31	9	5		236
	45-54	151	25	11	7		194
	55-64	104	12	4	12		132
	65+	0	0	0	1		1
	Total	535	176	55	35		801
X	15-24	74	255	67	71		467
	25-34	183	116	75	42		416
	35-44	247	56	109	39		451
	45-54	238	59	173	31		501
	55-64	192	33	121	12		358
	65+	12	1	0	0		13
	Total	946	520	545	195		2206
Y	15-24	81	204	112	63		460
	25-34	183	71	106	50		410
	35-44	278	67	95	28		468
	45-54	429	48	125	47		649
	55-64	226	35	63	15		339
	65+	9	1	1	0		11
	Total	1206	426	502	203		2337
Total	15-24	912	1595	750	584	163	4004
	25-34	1343	782	525	352	78	3080
	35-44	2363	655	489	228	54	3789
	45-54	2624	674	675	208	28	4209
	55-64	1912	500	424	86	15	2937
	65+	112	29	3	3	0	147
	Total	9266	4235	2866	1461	338	18166

Table 3.3 Summary distribution of men entering cohort for analysis, by pit and by survey qualifying for cohort entry.

Pit	PFR Survey of entry					
	2nd	3rd	4th	5th	6th	**Total**
C	1129	365	230	259		1983
F	679	311	248	178		1416
K	894	259	178	149		1480
P		1068	340	144	76	1628
Q	1183	175	475	196		2029
T	1137	369	52	17		1575
V	1557	566	241	85	262	2711
W	535	176	55	35		801
X	946	520	545	195		2206
Y	1206	426	502	203		2337
Total	9266	4235	2866	1461	338	18166

Table 3.4 Maximum length of follow-up in years, by pit and by survey qualifying for cohort entry.

Pit	PFR Survey of entry				
	2nd	3rd	4th	5th	6th
C	32	27	21	17	
F	30	25	20	16	
K	30	24	19	16	
P		28	22	18	14
Q	33	27	21	17	
T	32	26	22	19	
V	34	28	22	18	14
W	31	26	20	16	
X	31	25	19	15	
Y	33	27	21	17	

Table 3.5 Total person-years at risk from entry to end of follow-up at 31/12/92, by pit and by survey qualifying for cohort entry.

Pit	PFR Survey of entry					
	2nd	3rd	4th	5th	6th	**Total**
C	25260	8254	4700	4250		42463
F	14479	7190	4807	2758		29235
K	20329	5897	3294	2341		31862
P		24656	6834	2526	1026	35042
Q	32099	4435	9097	3244		48876
T	26007	8682	1125	287		36101
V	41687	14512	5063	1503	3639	66403
W	12477	4164	1068	552		18260
X	22435	12259	9713	2841		47248
Y	29212	10399	9960	3314		52885
Total	223985	100447	55662	23617	4665	408375

Table 3.6 Numbers of deaths observed in cohort to end of follow-up at 31/12/92, by pit and by survey qualifying for cohort entry.

Pit	PFR Survey of entry					
	2nd	3rd	4th	5th	6th	**Total**
C	776	142	22	20		960
F	446	57	19	14		536
K	485	31	16	8		540
P		462	75	12	4	553
Q	543	29	100	14		686
T	733	75	4	3		815
V	772	121	27	3	6	929
W	305	39	3	1		348
X	503	79	96	12		690
Y	747	105	72	21		945
Total	5310	1140	434	108	10	7002

Table 3.7 Summary of numbers of deaths during follow-up to 31/12/92, in chosen groups of causes, and the ICD codes defining those groups.

Cause of death	ICD code revisions			No. of deaths
	7th	8th	9th	
Respiratory cancers:	160-165	160-163	160-165	647
Lung	162	162	162	632
Nasal	160	160	160	1
Laryngeal	161	161	161	2
Other respiratory	Remainder	Remainder	Remainder	12
Digestive cancers:	150-159	150-159	150-159	614
Oesophagus	150	150	150	56
Stomach	151	151	151	249
Large intestine	153	153	153	113
Rectum	154	154	154	86
Other digestive	Remainder	Remainder	Remainder	110
Buccal cavity	140-148	140-149	140-149	19
Genito-urinary cancers:	170-181	180-189	180-189	194
Bladder	181	188	188	59
Prostate	177	185	185	110
Kidney	180	189	189	19
Other genito-urinary	Remainder	Remainder	Remainder	6
Lymphatic & haematopoietic cancers:	200-205	200-209	200-208	88
Chronic lymphatic leukaemia	204.0	204.1	204.1	11
Other leukaemia	204	204-207	204-208	26
Other lymphatic tissue	Remainder	Remainder	Remainder	51
Brain cancer	193	191	191	21
Other cancer	Remainder	Remainder	Remainder	132
All cancers	140-205	140-209	140-208	1715
Respiratory disease:	470-527, 240,241	460-519	460-519	1272
Chronic bronchitis	502	491	491	436
Other bronchitis	500-501	490,492	490,492	56
Pneumoconiosis (incl. 7 silico-tuberculosis)	001,523,524	010,515,516	011.4,500-505	203
Other respiratory	Remainder	Remainder	Remainder	584
Cardiovascular disease:	400-468	390-458	390-459	3342
Ischaemic heart disease	420,422	410-414	410-414	2297
Other cardiovascular	Remainder	Remainder	Remainder	1045
Other internal causes	Remainder	Remainder	Remainder	446
All internal causes	000-799	000-799	000-799	6775
All external causes	800-999	800-999	800-999	227
All causes	000-999	000-999	000-999	7002

Table 3.8 Distribution of men entering cohort for analysis, by survey qualifying for cohort entry, and by smoking habits and age at entry.

Survey of entry	Smoking habits/ equivalent cigarettes	Age at survey						
		15-24	25-34	35-44	45-54	55-64	65+	Total
2nd	Non-smoker	235	267	298	316	193	11	1320
	Ex-smoker	14	64	157	192	196	14	637
	1-10	360	353	592	748	668	54	2775
	11-20	259	497	935	997	658	28	3374
	21-30	39	139	329	319	160	4	990
	31+	5	23	52	52	37	1	170
	Total	912	1343	2363	2624	1912	112	9266
3rd	Non-smoker	402	139	70	62	52	2	727
	Ex-smoker	83	60	46	67	61	2	319
	1-10	492	154	127	141	118	11	1043
	11-20	527	341	284	293	195	12	1652
	21-30	84	77	109	103	66	2	441
	31+	7	11	19	8	8	0	53
	Total	1595	782	655	674	500	29	4235
4th	Non-smoker	258	99	74	92	61	0	584
	Ex-smoker	52	56	76	95	64	0	343
	1-10	111	72	60	109	94	0	446
	11-20	234	214	194	272	158	3	1075
	21-30	79	64	69	88	37	0	337
	31+	16	20	16	19	10	0	81
	Total	750	525	489	675	424	3	2866
5th	Non-smoker	212	78	27	20	18	0	355
	Ex-smoker	48	55	41	39	18	1	202
	1-10	48	35	22	39	12	1	157
	11-20	171	118	74	68	32	1	464
	21-30	86	50	50	34	4	0	224
	31+	19	16	14	8	2	0	59
	Total	584	352	228	208	86	3	1461
6th	Non-smoker	59	24	14	3	1	0	101
	Ex-smoker	10	11	10	9	4	0	44
	1-10	16	7	2	2	2	0	29
	11-20	53	25	16	9	6	0	109
	21-30	22	8	7	4	0	0	41
	31+	3	3	5	1	2	0	14
	Total	163	78	54	28	15	0	338
Total	Non-smoker	1166	607	483	493	325	13	3087
	Ex-smoker	207	246	330	402	343	17	1545
	1-10	1027	621	803	1039	894	66	4450
	11-20	1244	1195	1503	1639	1049	44	6674
	21-30	310	338	564	548	267	6	2033
	31+	50	73	106	88	59	1	377
	Total	4004	3080	3789	4209	2937	147	18166

Table 3.9 Summary distributions of time-dependent covariates at each survey.

Time-dependent Variable	Survey	No. of obsns.	Mean	Standard Deviation	Min	Lower Quartile	Median	Upper Quartile	Max
Age (years)	PFR 2	9266	43.9	12.4	15.7	35.3	45.1	53.9	74.8
	PFR 3	13030	44.4	14.7	15.9	32.0	45.8	56.3	78.2
	PFR 4	15053	47.0	15.0	15.4	34.5	48.5	59.0	82.4
	PFR 5	15663	48.2	15.4	16.4	35.2	49.7	60.6	85.1
	PFR 6	14872	50.5	15.3	16.3	37.6	51.7	62.5	88.8
Time on study (years)	PFR 2	9266	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	PFR 3	13030	3.9	2.7	0.0	0.0	6.0	6.0	6.0
	PFR 4	15053	7.6	4.5	0.0	5.0	10.0	12.0	12.0
	PFR 5	15663	10.3	5.4	0.0	4.0	10.0	16.0	16.0
	PFR 6	14872	13.8	5.8	0.0	8.0	14.0	20.0	20.0
Time contributing to exposures (hrs × 10^{-3})	PFR 2	9266	44.4	22.6	0.0	25.1	44.2	62.9	102.3
	PFR 3	13030	42.5	25.9	0.0	20.9	43.1	64.8	102.3
	PFR 4	15053	43.8	26.5	0.0	20.9	44.3	66.5	101.2
	PFR 5	15663	42.6	27.1	0.0	17.3	42.6	65.7	103.1
	PFR 6	14872	42.4	26.9	0.0	17.2	42.6	65.5	107.0
Cumulative respirable dust (ghm^{-3})	PFR 2	9266	154.4	119.6	0.0	56.3	129.8	224.9	840.6
	PFR 3	13030	137.1	122.0	0.0	40.6	103.5	208.1	840.6
	PFR 4	15053	139.8	120.8	0.0	41.8	107.8	211.3	840.6
	PFR 5	15663	133.5	120.1	0.0	34.3	101.1	203.2	840.6
	PFR 6	14872	129.2	117.7	0.0	32.0	96.6	197.2	834.6
Cumulative respirable quartz (ghm^{-3})	PFR 2	9266	7.01	5.96	0.00	2.60	5.35	9.86	37.24
	PFR 3	13030	6.23	5.95	0.00	1.77	4.57	8.96	41.67
	PFR 4	15053	6.67	6.16	0.00	1.90	4.99	9.73	42.68
	PFR 5	15663	6.45	6.21	0.00	1.54	4.75	9.48	42.68
	PFR 6	14872	6.29	6.14	0.00	1.44	4.58	9.25	42.68
Cumulative radiation (mSv)	PFR 2	9266	12.7	15.0	0.0	3.1	6.8	17.5	105.9
	PFR 3	13030	13.6	16.8	0.0	2.5	7.5	19.7	118.1
	PFR 4	15053	14.2	17.9	0.0	2.6	7.7	19.9	118.3
	PFR 5	15663	13.9	18.0	0.0	2.4	7.2	19.1	118.3
	PFR 6	14872	13.8	18.2	0.0	2.4	7.2	18.7	118.3
Cumulative diesel travel (hrs × 10^{-3})	PFR 2	9266	0.271	0.708	0.000	0.000	0.000	0.328	12.002
	PFR 3	13030	0.427	1.182	0.000	0.000	0.000	0.508	24.686
	PFR 4	15053	0.570	1.517	0.000	0.000	0.000	0.606	33.942
	PFR 5	15663	0.661	1.686	0.000	0.000	0.003	0.641	33.997
	PFR 6	14872	0.740	1.843	0.000	0.000	0.002	0.741	35.815

Table 3.10 Correlations between time-dependent covariates at each survey.

Survey	Variable name	No.	Correlations					
PFR 2	Age (y)	1						
	Time on study (y)	2	0.00					
	Cumulative time (y)	3	0.90	0.00				
	Cumulative respirable dust (ghm^{-3})	4	0.54	0.00	0.63			
	Cumulative respirable quartz (ghm^{-3})	5	0.51	0.00	0.58	0.85		
	Cumulative radiation (mSv)	6	0.34	0.00	0.37	0.47	0.66	
	Cumulative diesel travel (hours × 10^{-3})	7	-0.06	0.00	-0.06	0.12	0.28	0.45
		No.	1	2	3	4	5	6
PFR 3	Age (y)	1						
	Time on study (y)	2	0.44					
	Cumulative time (y)	3	0.91	0.42				
	Cumulative respirable dust (ghm^{-3})	4	0.61	0.40	0.67			
	Cumulative respirable quartz (ghm^{-3})	5	0.58	0.40	0.63	0.87		
	Cumulative radiation (mSv)	6	0.45	0.32	0.48	0.52	0.69	
	Cumulative diesel travel (hours × 10^{-3})	7	0.04	0.19	0.05	0.17	0.32	0.47
		No.	1	2	3	4	5	6
PFR 4	Age (y)	1						
	Time on study (y)	2	0.44					
	Cumulative time (y)	3	0.89	0.38				
	Cumulative respirable dust (ghm^{-3})	4	0.61	0.29	0.67			
	Cumulative respirable quartz (ghm^{-3})	5	0.55	0.22	0.61	0.86		
	Cumulative radiation (mSv)	6	0.42	0.21	0.46	0.52	0.66	
	Cumulative diesel travel (hours × 10^{-3})	7	0.05	0.19	0.08	0.18	0.30	0.49
		No.	1	2	3	4	5	6
PFR 5	Age (y)	1						
	Time on study (y)	2	0.51					
	Cumulative time (y)	3	0.88	0.42				
	Cumulative respirable dust (ghm^{-3})	4	0.63	0.32	0.69			
	Cumulative respirable quartz (ghm^{-3})	5	0.56	0.26	0.63	0.87		
	Cumulative radiation (mSv)	6	0.42	0.23	0.47	0.53	0.67	
	Cumulative diesel travel (hours × 10^{-3})	7	0.07	0.19	0.11	0.20	0.33	0.54
		No.	1	2	3	4	5	6
PFR 6	Age (y)	1						
	Time on study (y)	2	0.53					
	Cumulative time (y)	3	0.86	0.41				
	Cumulative respirable dust (ghm^{-3})	4	0.63	0.33	0.70			
	Cumulative respirable quartz (ghm^{-3})	5	0.56	0.26	0.63	0.86		
	Cumulative radiation (mSv)	6	0.41	0.23	0.46	0.53	0.67	
	Cumulative diesel travel (hours × 10^{-3})	7	0.07	0.17	0.12	0.20	0.34	0.57
		No.	1	2	3	4	5	6

Table 3.11 Summary distributions of respirable dust and quartz exposures at PFR third survey, and percentage respirable quartz in exposure, by pit.

Exposure Variable	Pit	No. of obsns.	Mean	Standard Deviation	Min	Lower Quartile	Median	Upper Quartile	Max
Cumulative respirable dust (ghm^{-3})	C	1437	82.6	54.1	0.0	34.2	79.1	126.5	207.6
	F	959	243.8	183.1	0.0	70.6	235.7	371.0	840.6
	K	1093	114.5	86.8	0.0	43.5	95.3	178.1	370.5
	P	1068	56.0	36.7	0.1	26.0	53.9	81.8	174.3
	Q	1325	180.4	156.8	0.0	42.5	142.0	290.0	651.9
	T	1436	151.9	123.7	0.0	45.3	121.8	243.6	555.2
	V	2048	142.7	118.7	0.0	32.6	120.7	227.3	508.7
	W	678	135.8	105.1	0.0	44.0	116.4	212.7	499.0
	X	1416	129.3	95.9	0.0	47.2	115.8	200.3	433.5
	Y	1570	143.2	107.9	0.0	51.1	130.0	223.5	436.9
Cumulative respirable quartz (ghm^{-3})	C	1437	3.25	2.20	0.00	1.24	3.34	5.05	8.77
	F	959	7.99	5.81	0.00	2.33	8.27	12.17	25.36
	K	1093	6.20	4.88	0.00	1.95	5.30	9.87	19.64
	P	1068	2.70	1.85	0.00	1.10	2.58	4.00	9.78
	Q	1325	11.13	9.94	0.00	2.45	8.48	17.97	41.67
	T	1436	7.83	6.11	0.00	2.58	6.63	12.85	27.14
	V	2048	4.20	3.48	0.00	0.99	3.63	6.75	17.07
	W	678	3.40	2.10	0.00	1.58	3.34	4.89	11.25
	X	1416	9.22	6.66	0.00	3.38	8.68	14.54	28.05
	Y	1570	5.84	4.13	0.00	2.60	5.27	8.80	17.39
Percentage quartz in respirable dust	C	1423	3.71	1.12	0.00	3.51	3.86	4.22	6.36
	F	904	3.33	0.87	0.00	2.92	3.24	3.75	6.47
	K	1077	5.10	0.88	0.00	4.55	5.43	5.65	6.97
	P	1068	4.72	0.77	0.62	4.25	4.72	5.13	7.43
	Q	1321	6.05	0.94	3.75	5.44	6.12	6.50	8.38
	T	1388	5.67	1.58	0.00	4.75	5.37	6.52	12.17
	V	2044	3.04	0.94	0.00	2.48	2.90	3.51	11.13
	W	648	3.25	1.83	0.00	2.15	2.67	3.51	10.66
	X	1365	7.47	2.31	0.00	6.46	6.94	7.88	13.07
	Y	1388	4.33	0.89	0.00	3.82	4.12	4.60	6.92

Table 4.1 Summary of results of comparisons of mortality in cohort with external reference rates. Table shows, for chosen groups of causes, numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Cause of death	**Observed deaths**	**SMR %**	**Confidence bounds**		**z-test**
			Lower	Upper	
All internal causes	6775	91	89	93	-8.08
Cancers:					
All cancers	1715	88	84	93	-5.29
Lung	632	86	80	93	-3.81
Stomach	249	124	110	141	3.26
Large intestine	113	90	74	108	-1.21
Rectum	86	91	74	113	-0.86
Oesophagus	56	87	67	114	-1.05
Bladder	59	77	59	99	-2.17
Prostate	110	86	72	104	-1.59
Leukaemia	37	90	65	124	-0.68
Chronic bronchitis	436	120	110	132	3.70

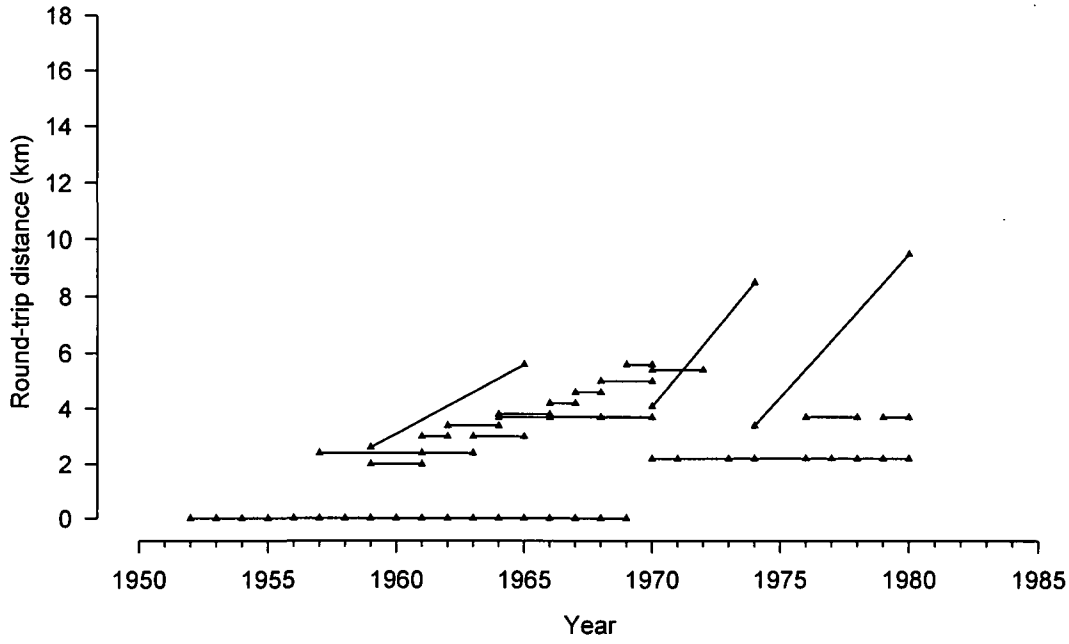

Figure 2.1K Estimated round-trip travelling distances to coalface. Estimates for the same face in different years are joined. Pit K.

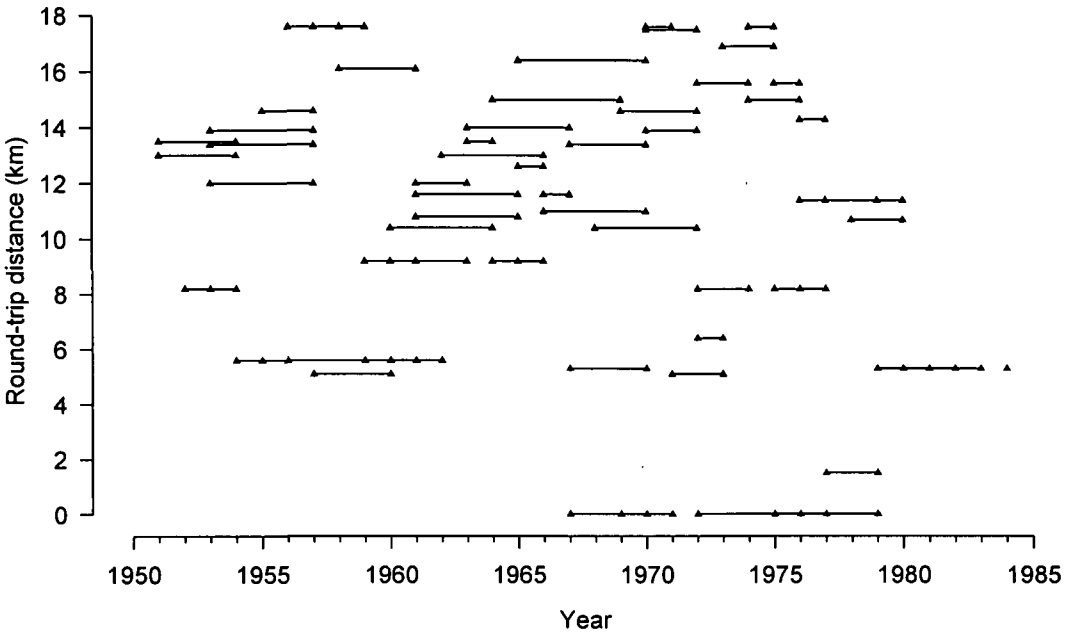

Figure 2.1Q Estimated round-trip travelling distances to coalface. Estimates for the same face in different years are joined. Pit Q.

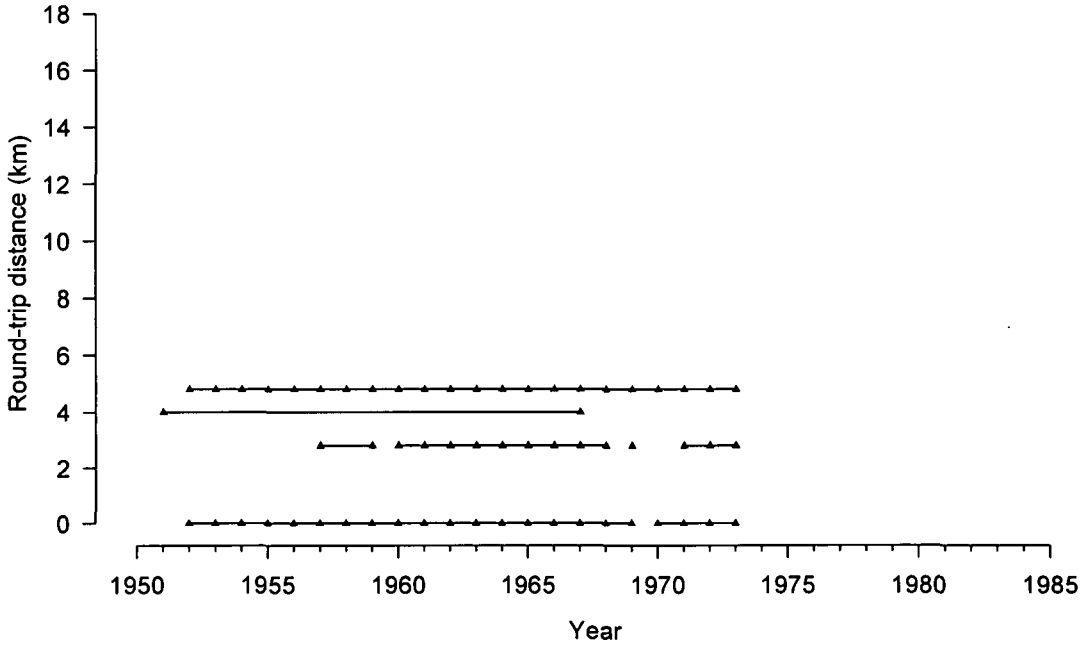

Figure 2.1T Estimated round-trip travelling distances to coalface. Estimates for the same face in different years are joined. Pit T.

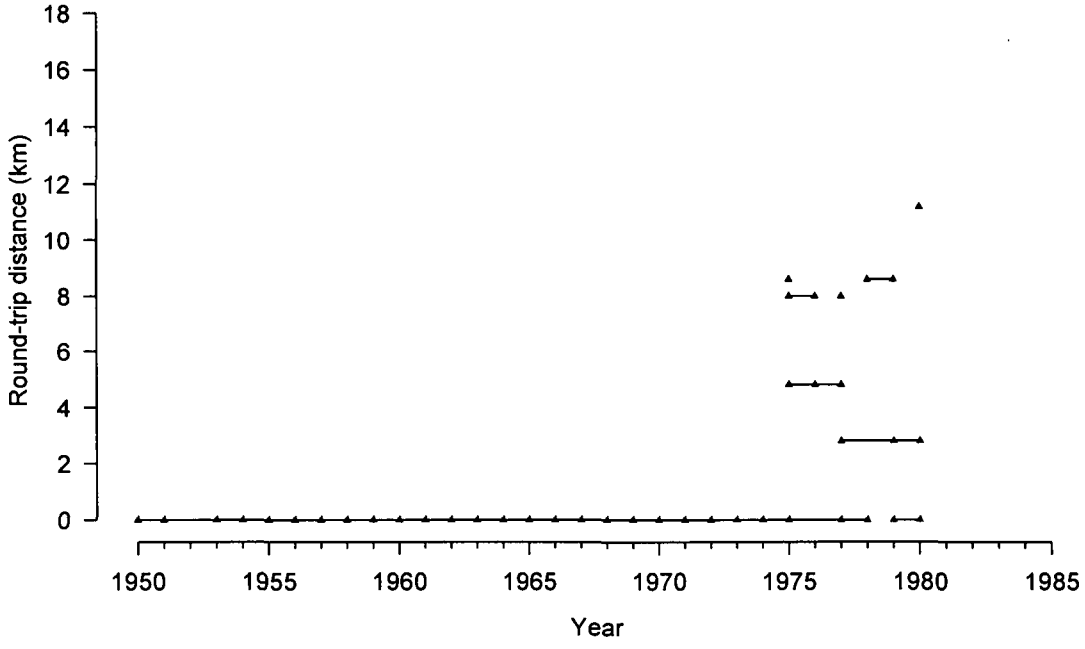

Figure 2.1W Estimated round-trip travelling distances to coalface. Estimates for the same face in different years are joined. Pit W.

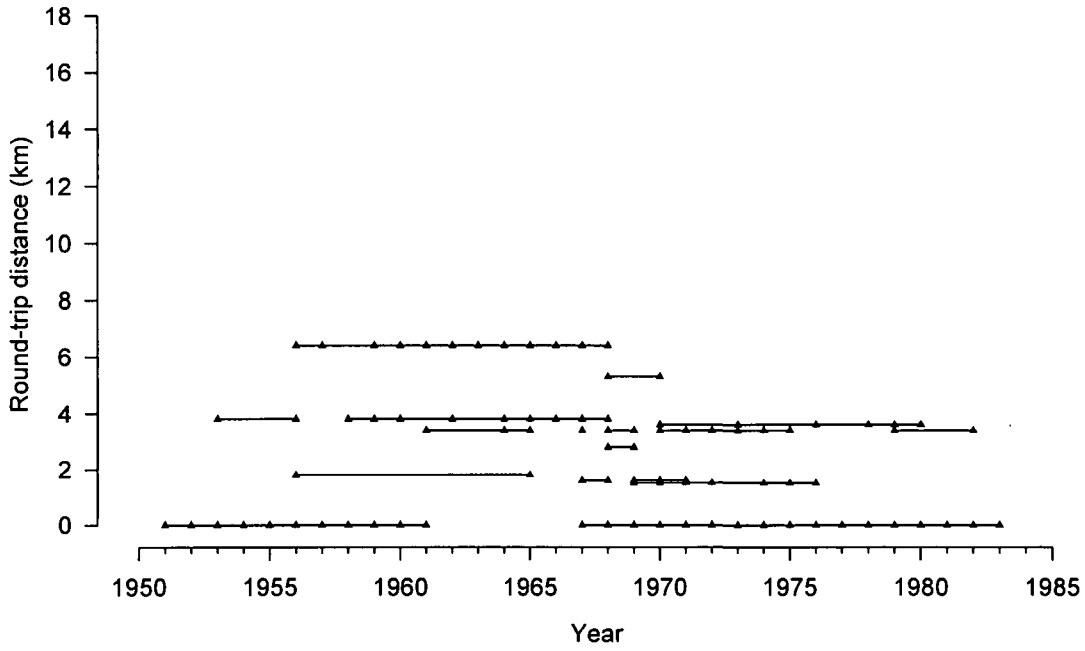

Figure 2.1X Estimated round-trip travelling distances to coalface. Estimates for the same face in different years are joined. Pit X.

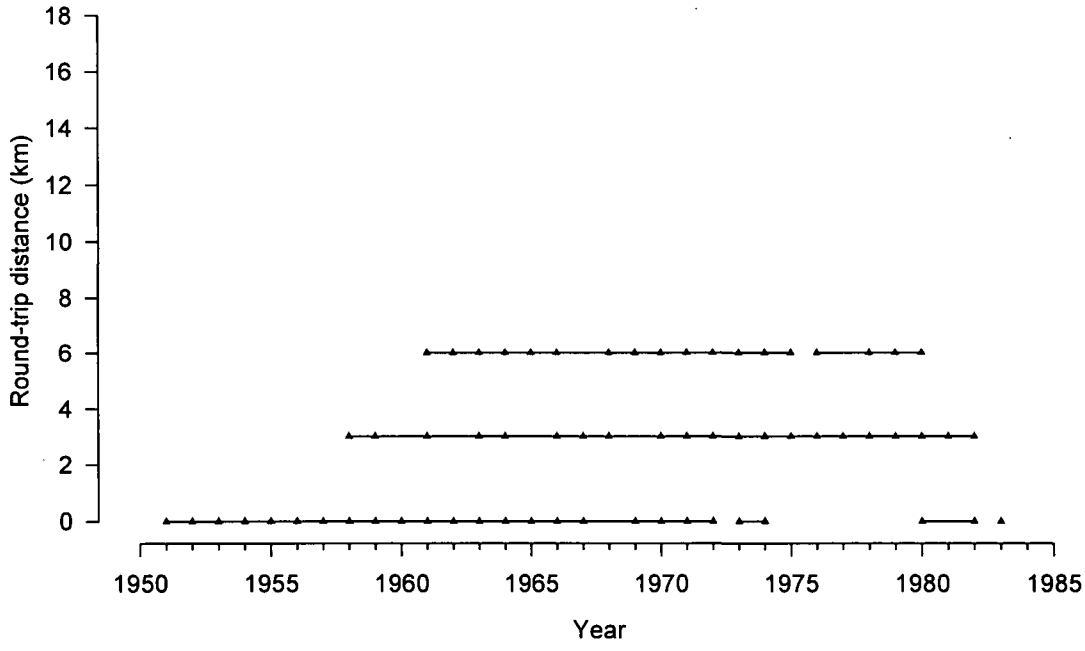

Figure 2.1Y Estimated round-trip travelling distances to coalface. Estimates for the same face in different years are joined. Pit Y.

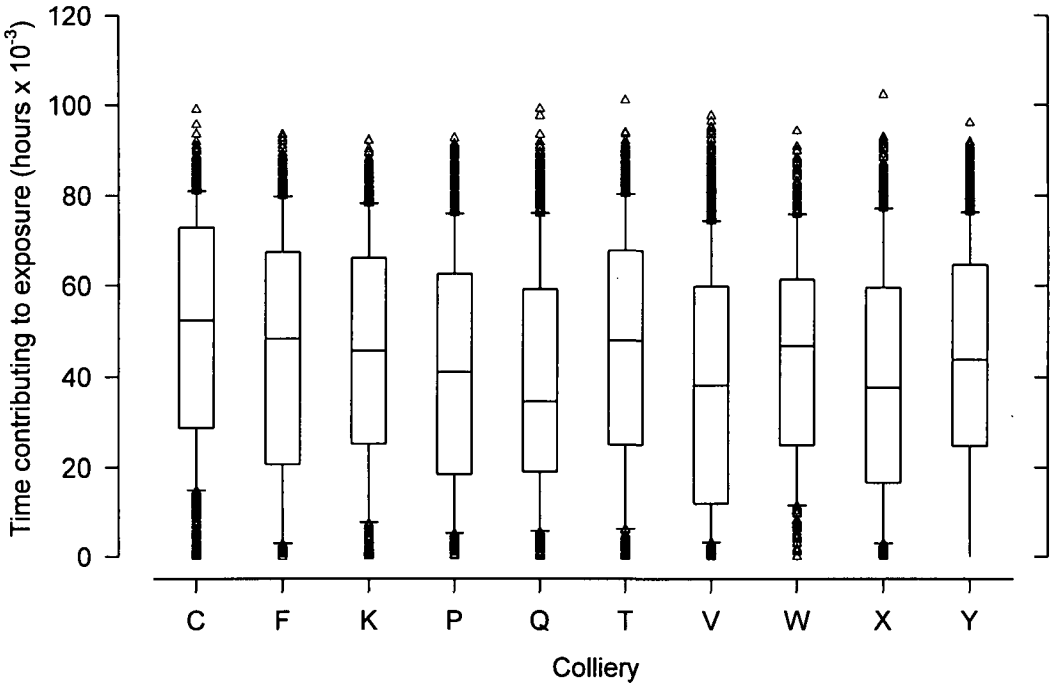

Figure 3.1a. Box plot showing distribution by colliery of total time contributing to exposure up to 3rd PFR survey, for cohort members surviving to then.

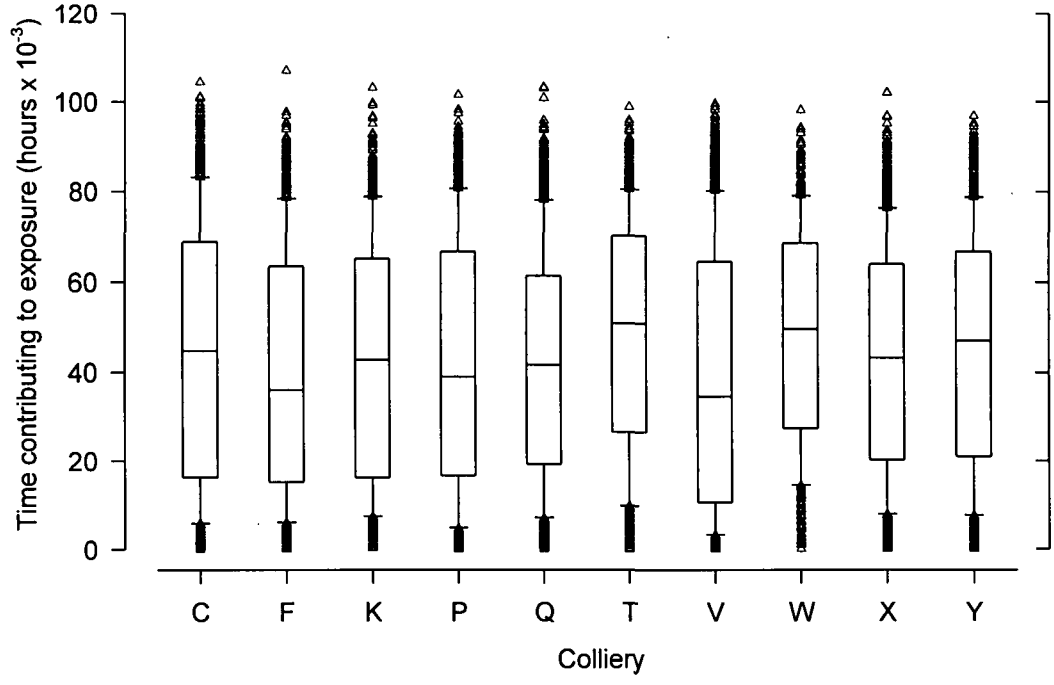

Figure 3.1b. Box plot showing distribution by colliery of total time contributing to exposure, up to 6th PFR survey, for cohort members surviving to then.

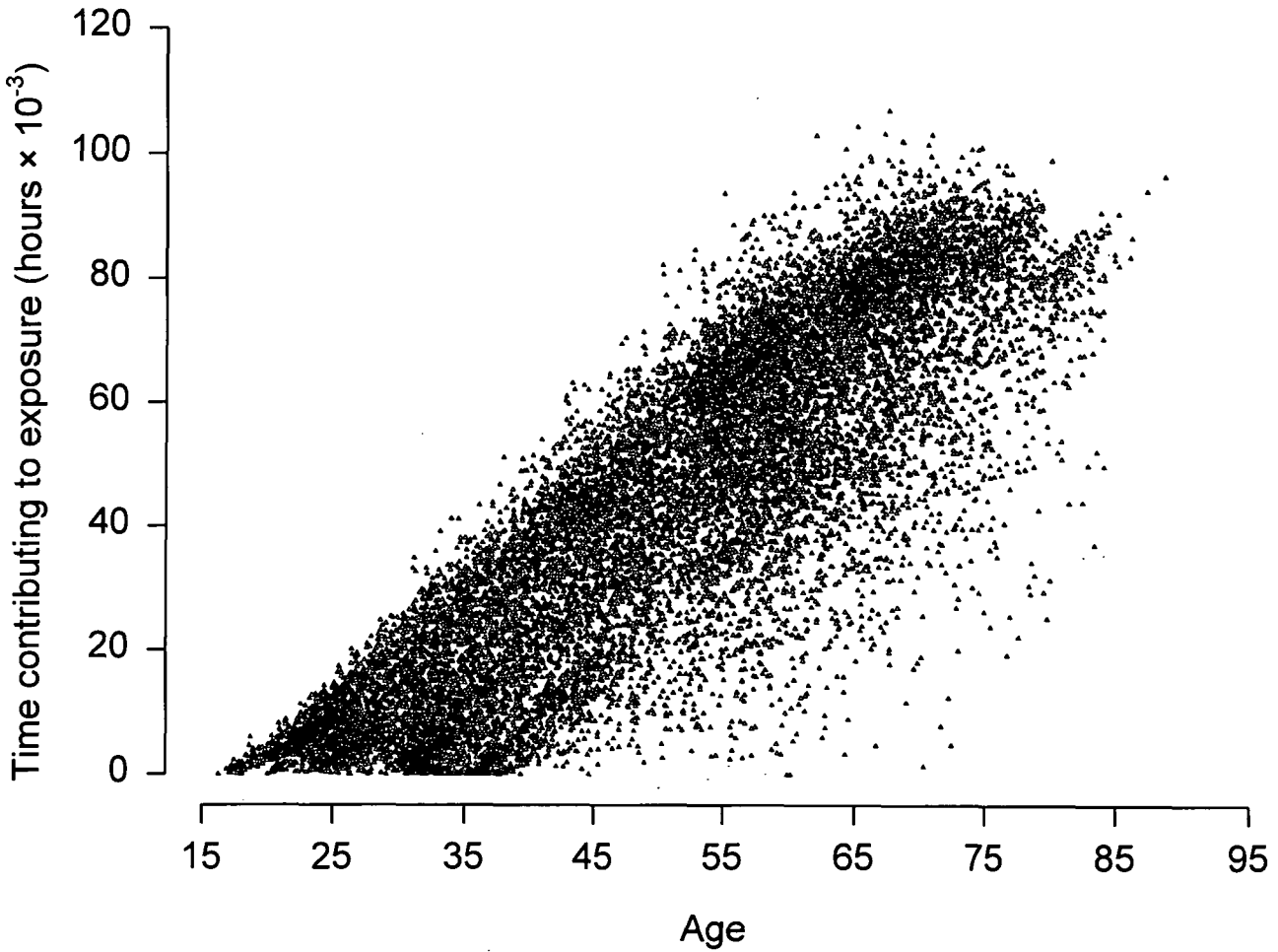

Figure 3.2. Scatter plot showing relationship between time contributing to exposure and age, at 6th PFR survey.

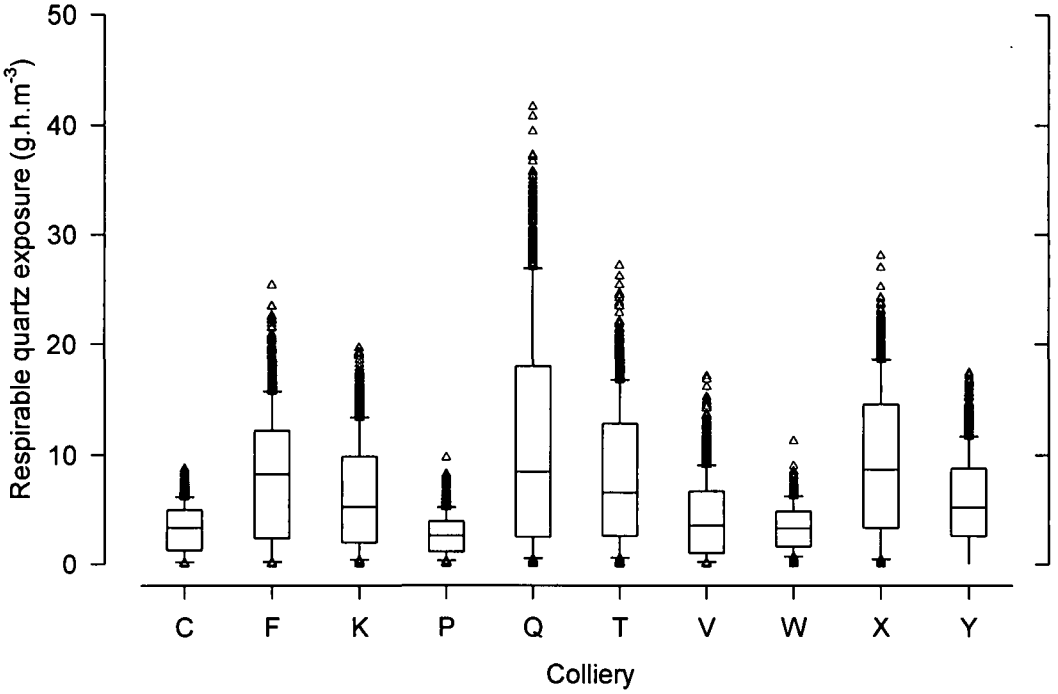

Figure 3.3a. Box plot showing distribution by colliery of cumulative respirable quartz exposure, up to 3rd PFR survey, for cohort members surviving to then.

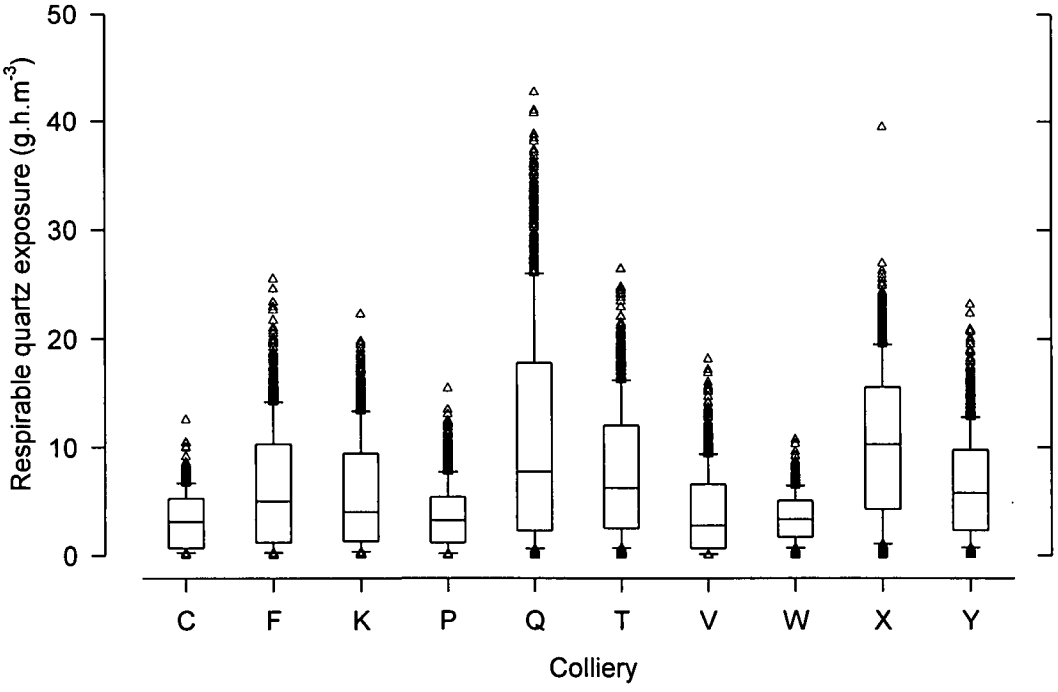

Figure 3.3b. Box plot showing distribution by colliery of cumulative respirable quartz exposure, up to 6th PFR survey, for cohort members surviving to then.

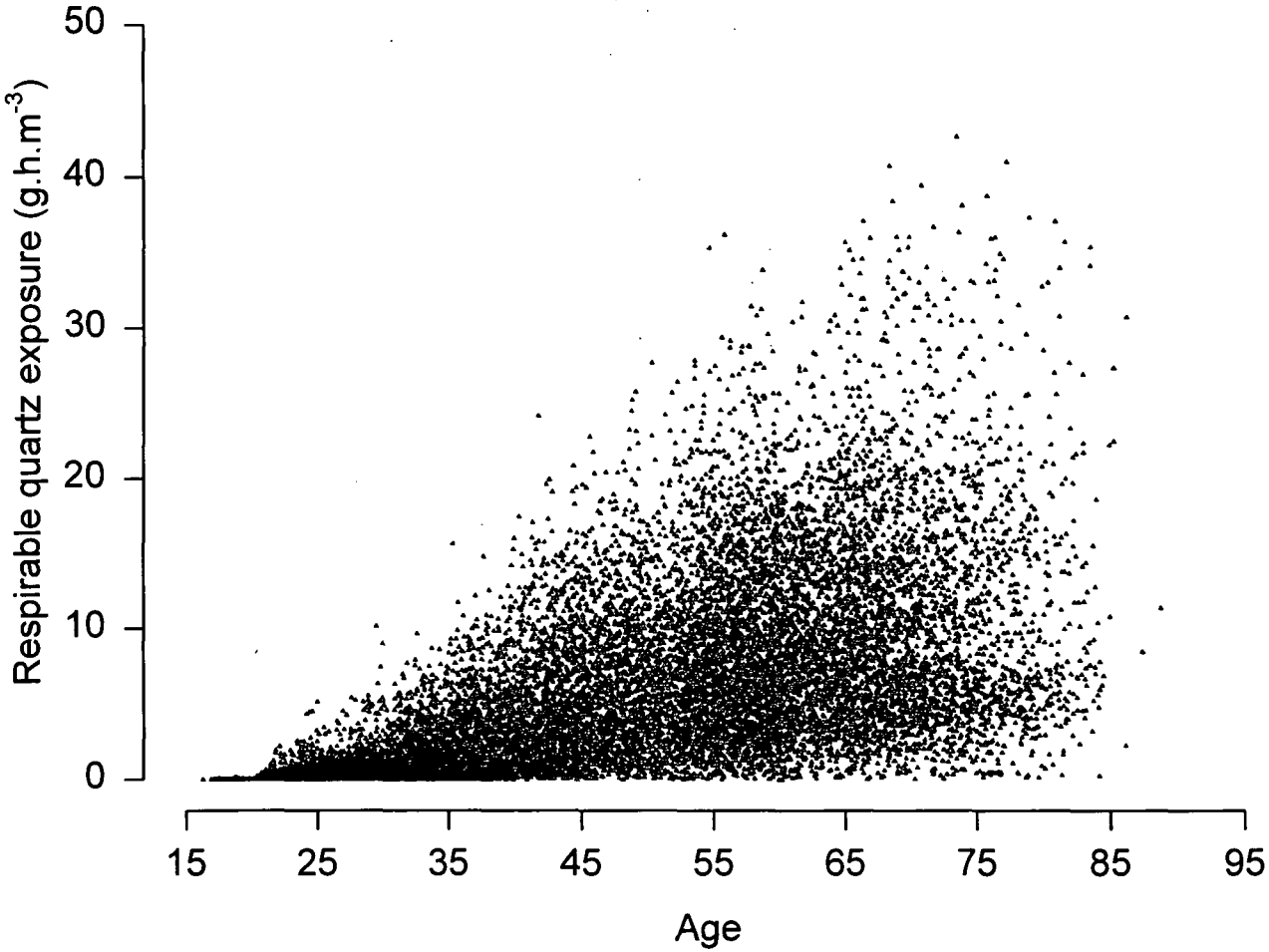

Figure 3.4. Scatter plot showing relationship between respirable quartz exposure and age, at 6th PFR survey.

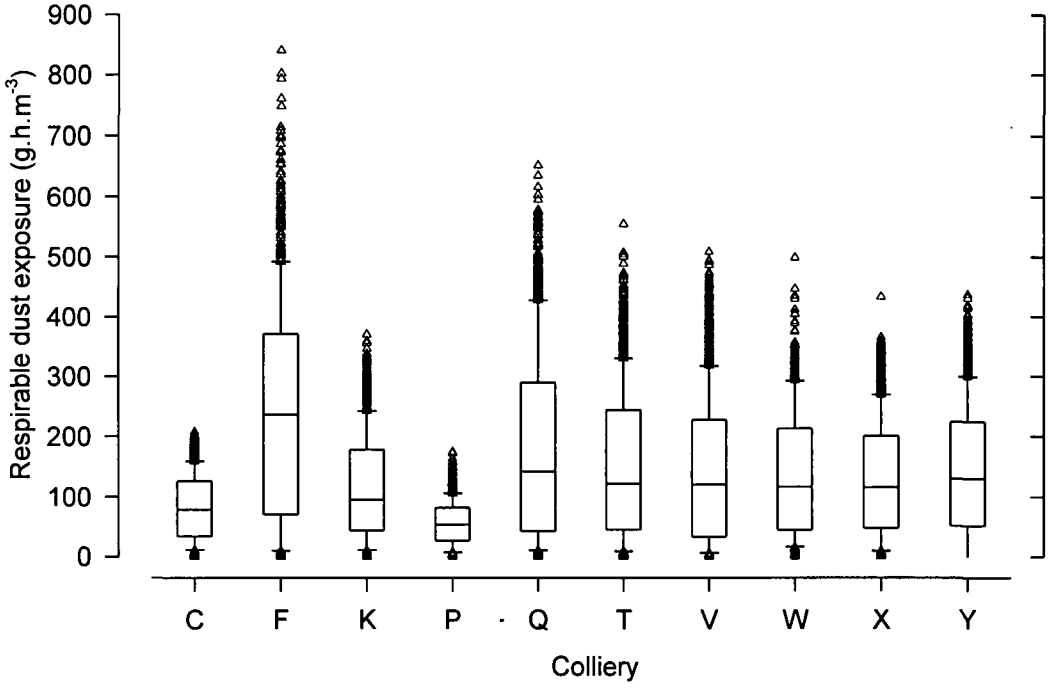

Figure 3.5a. Box plot showing distribution by colliery of cumulative respirable dust exposure, up to 3rd PFR survey, for cohort members surviving to then.

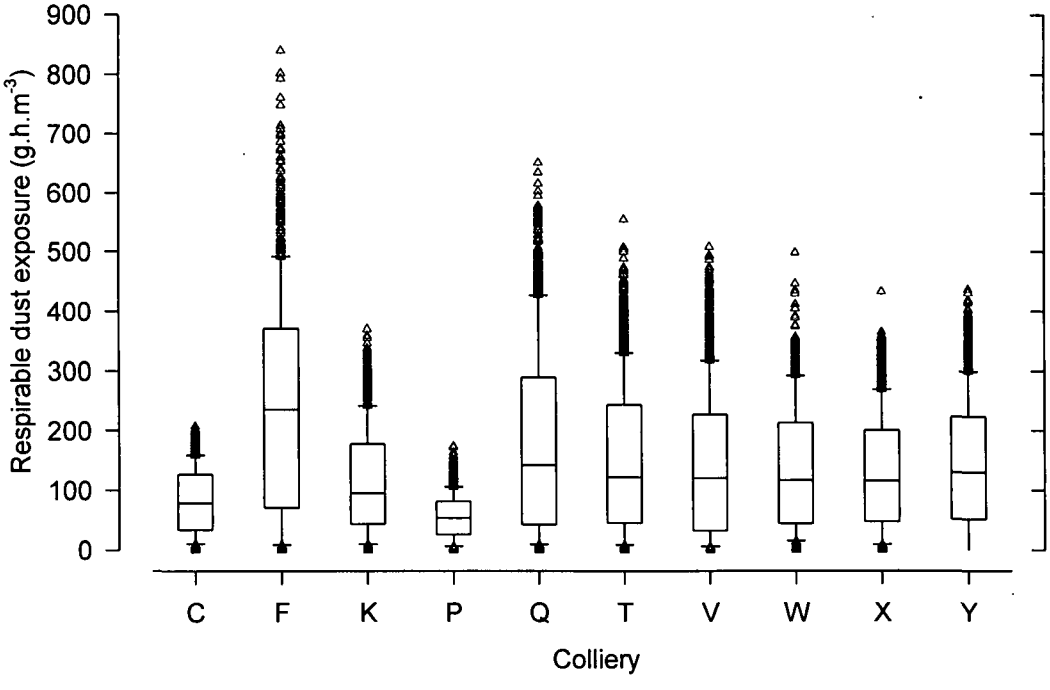

Figure 3.5b. Box plot showing distribution by colliery of cumulative respirable dust exposure, up to 6th PFR survey, for cohort members surviving to then.

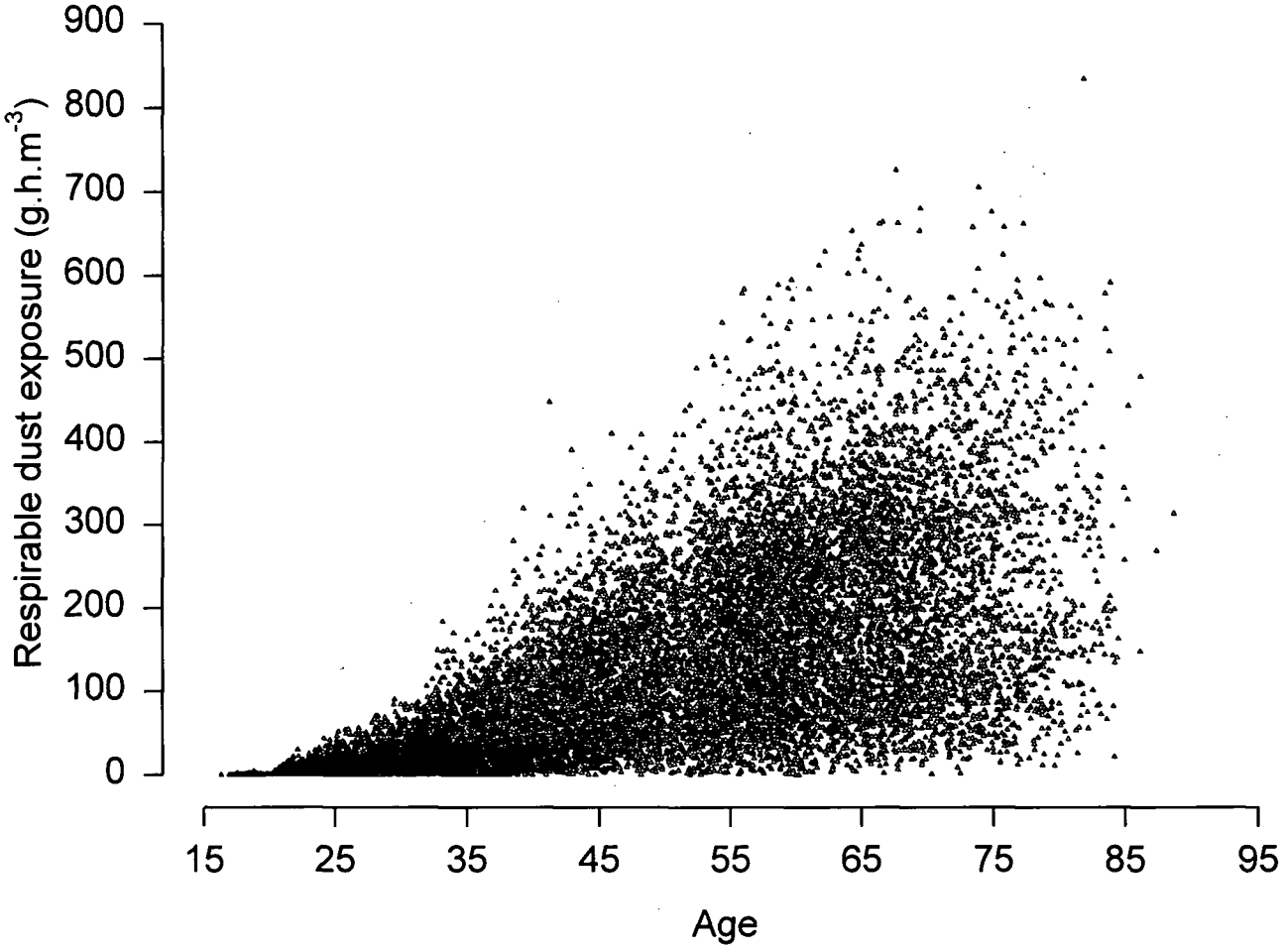

Figure 3.6. Scatter plot showing relationship between respirable dust exposure and age, at 6th PFR survey.

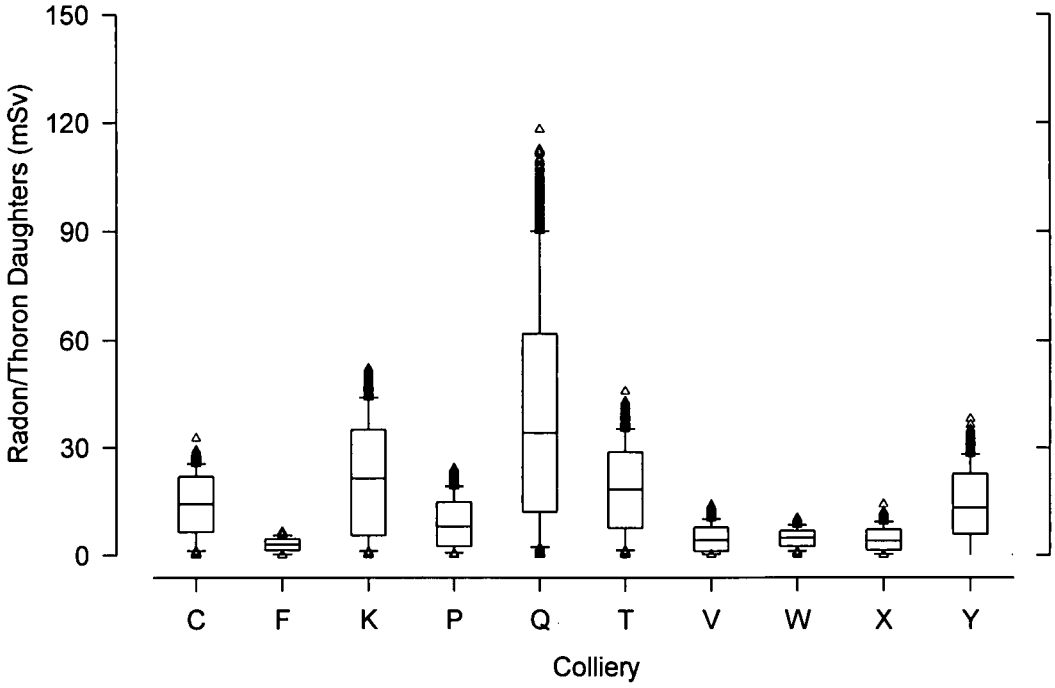

Figure 3.7a. Box plot showing distribution by colliery of cumulative radiation exposure from radon and thoron daughters, up to 3rd PFR survey, for cohort members surviving to then.

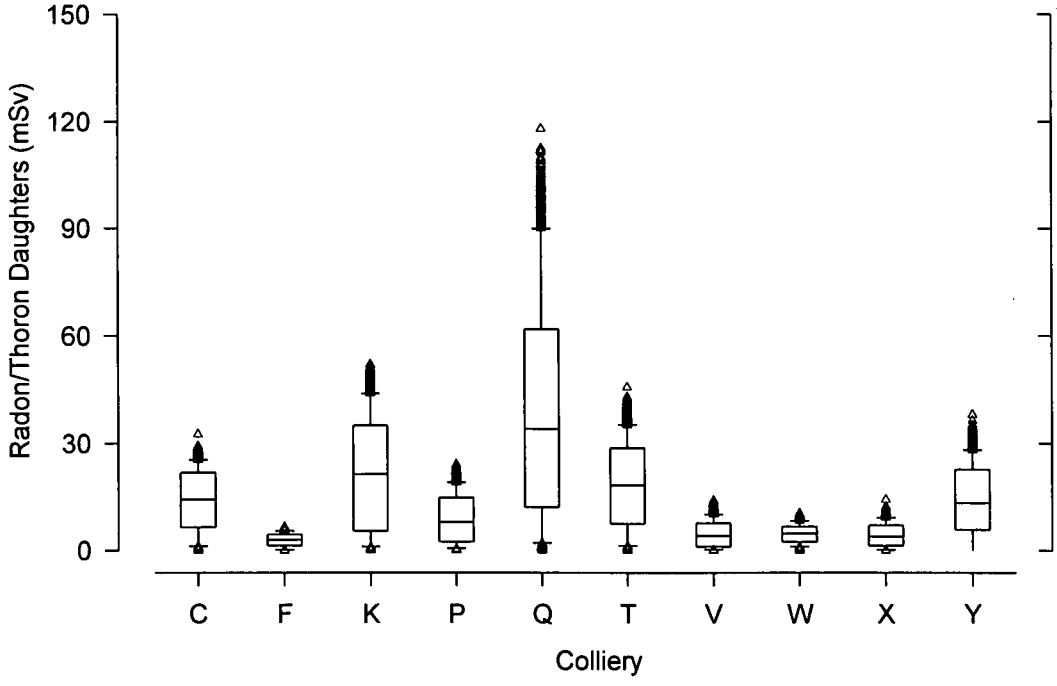

Figure 3.7b. Box plot showing distribution by colliery of cumulative radiation exposure from radon and thoron daughters, up to 6th PFR survey, for cohort members surviving to then.

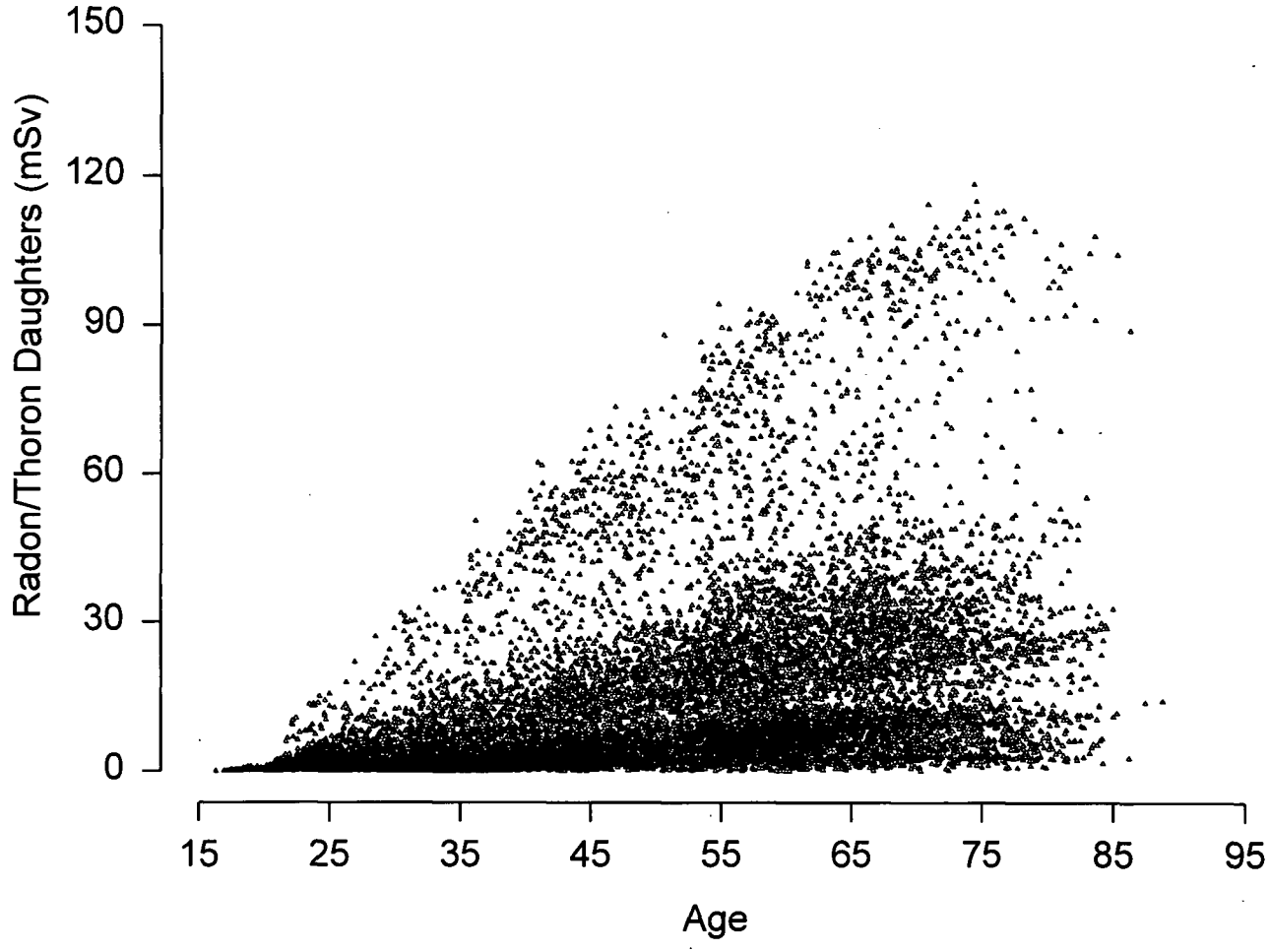

Figure 3.8. Scatter plot showing relationship between radiation exposure from radon and thoron daughters and age, at 6th PFR survey.

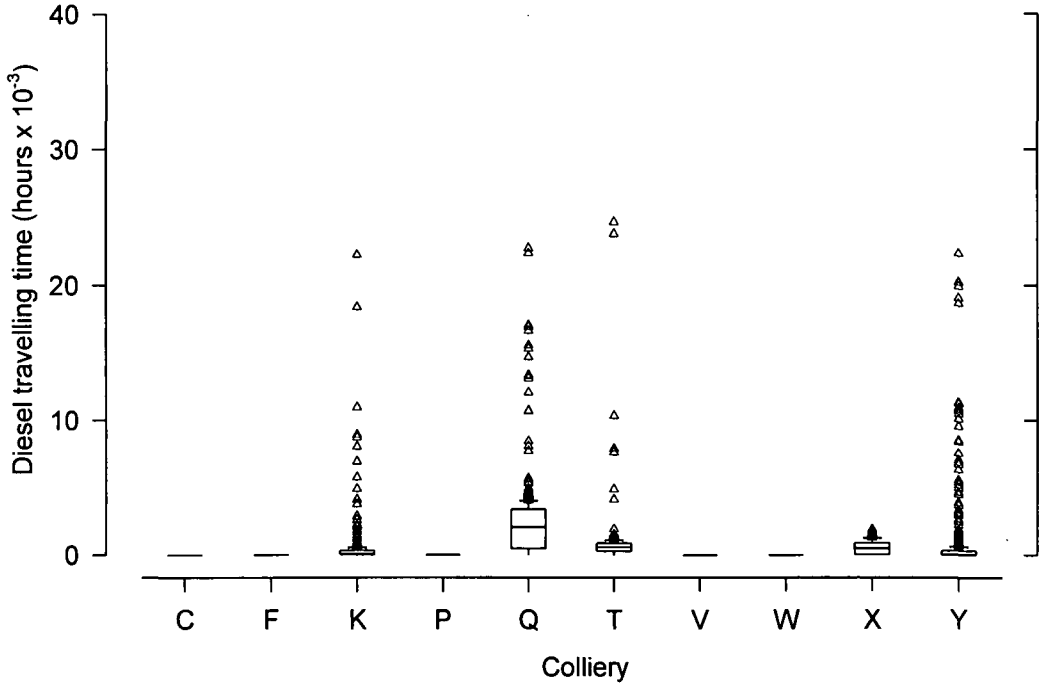

Figure 3.9a. Box plot showing distribution by colliery of cumulative time spent travelling by diesels, up to 3rd PFR survey, for cohort members surviving to then.

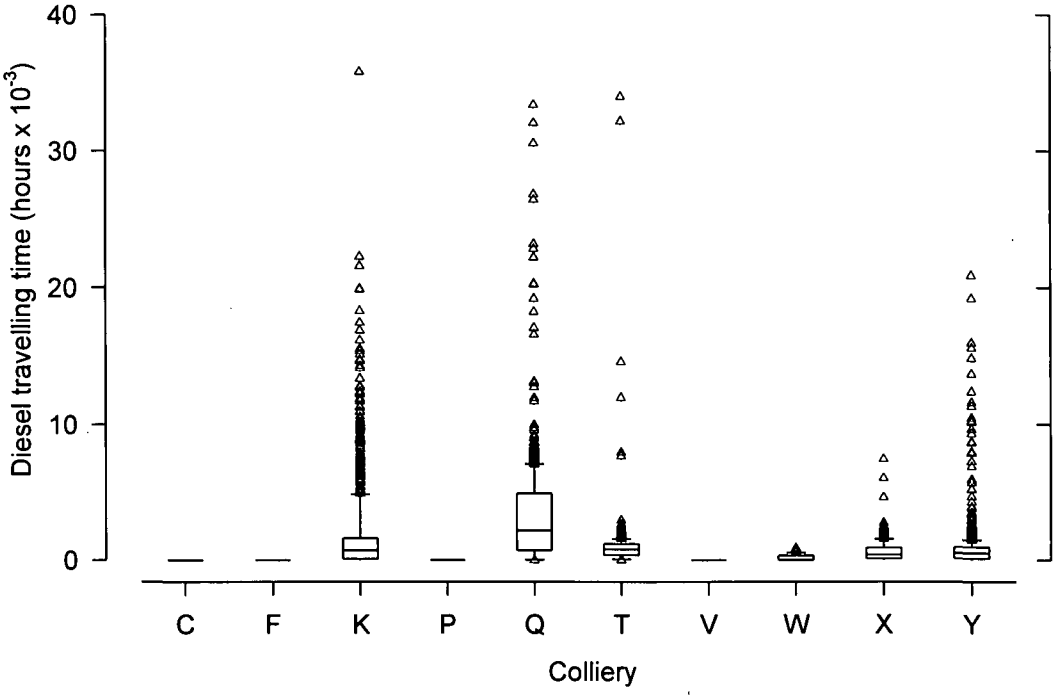

Figure 3.9b. Box plot showing distribution by colliery of cumulative time spent travelling by diesels, up to 6th PFR survey, for cohort members surviving to then.

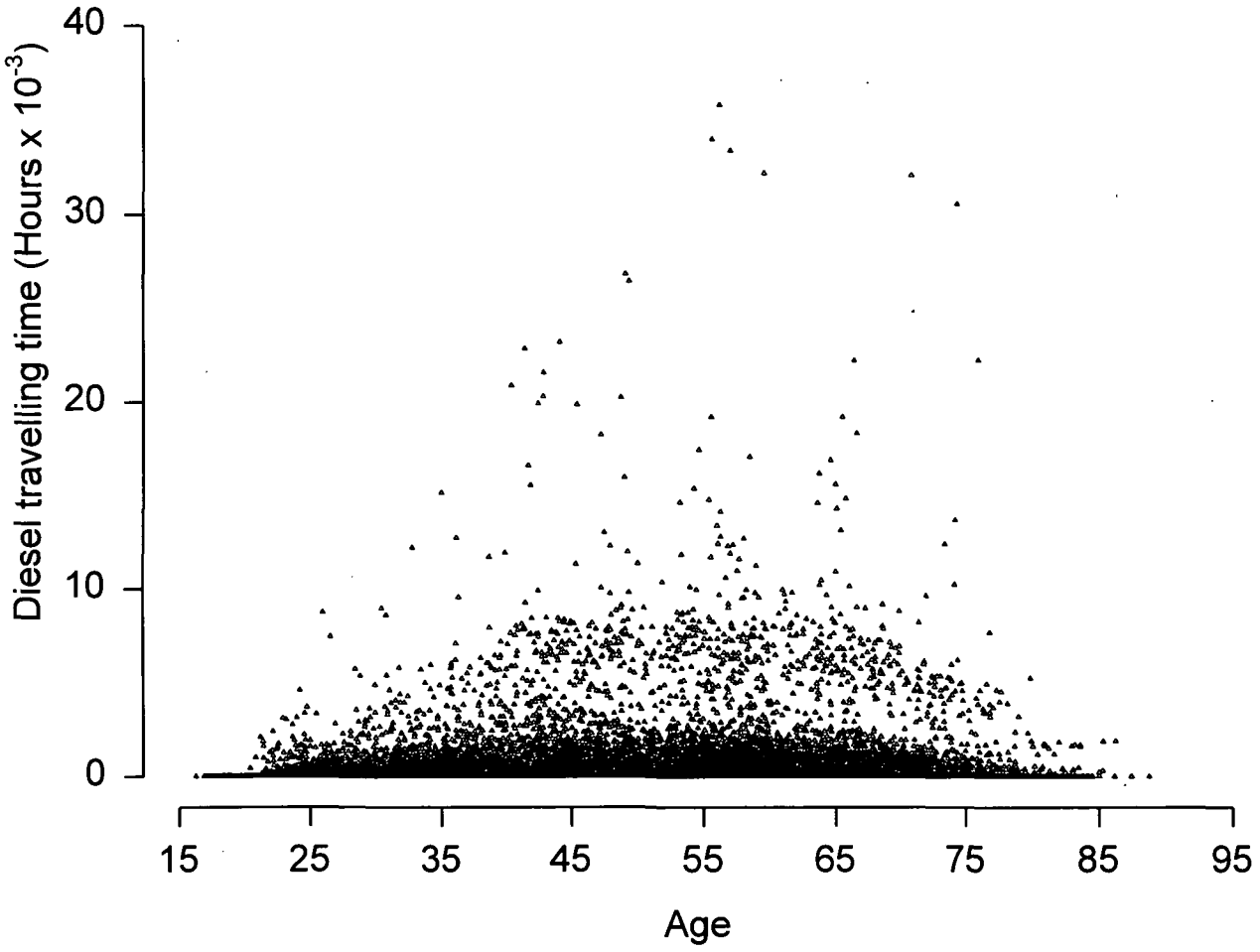

Figure 3.10. Scatter plot showing relationship between time spent travelling by diesels and age, at 6th PFR survey.

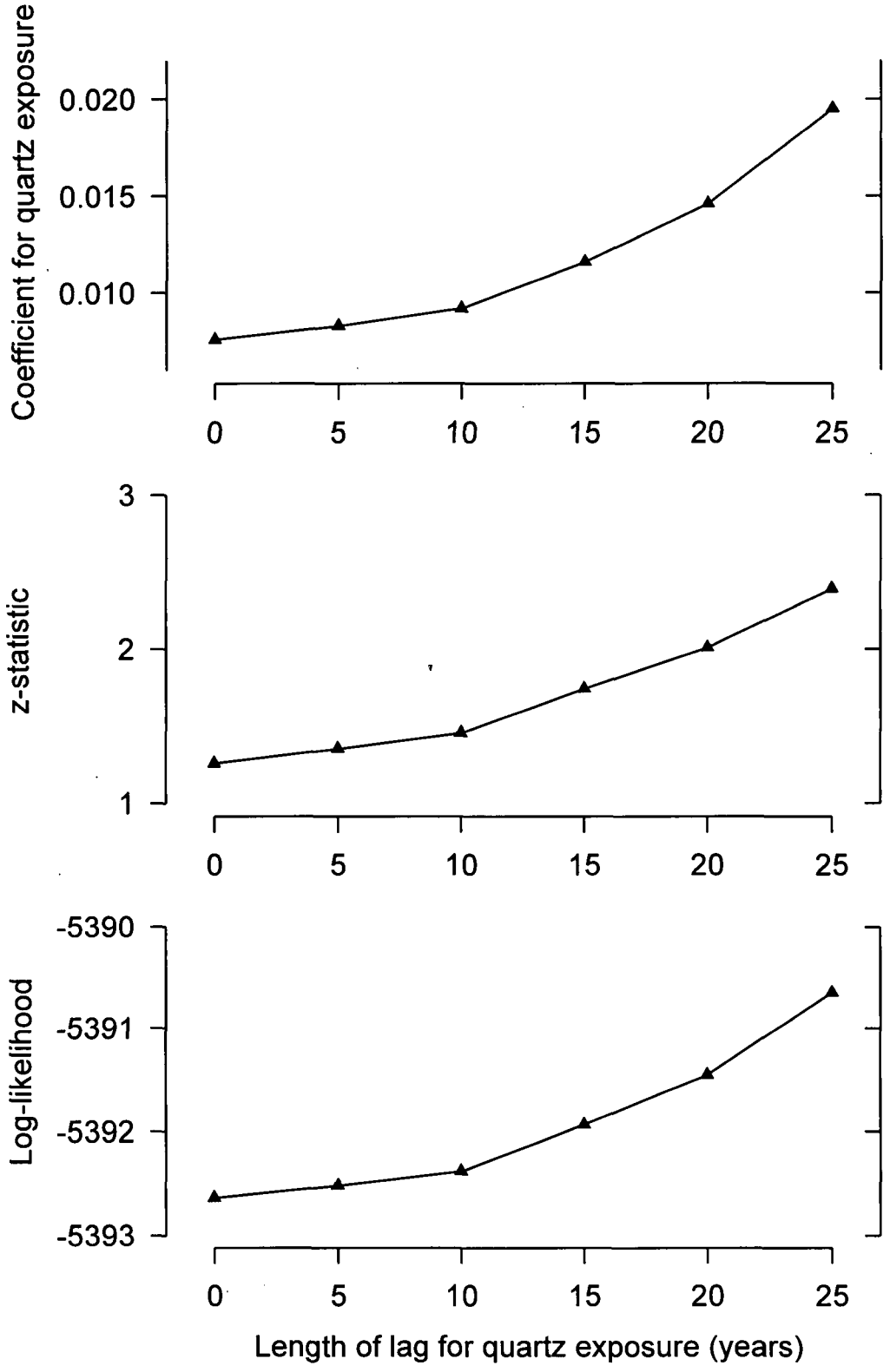

Figure 4.1 Regression modelling of lung cancer mortality: effect of different lags on quartz exposure coefficient and significance, and overall model fit.

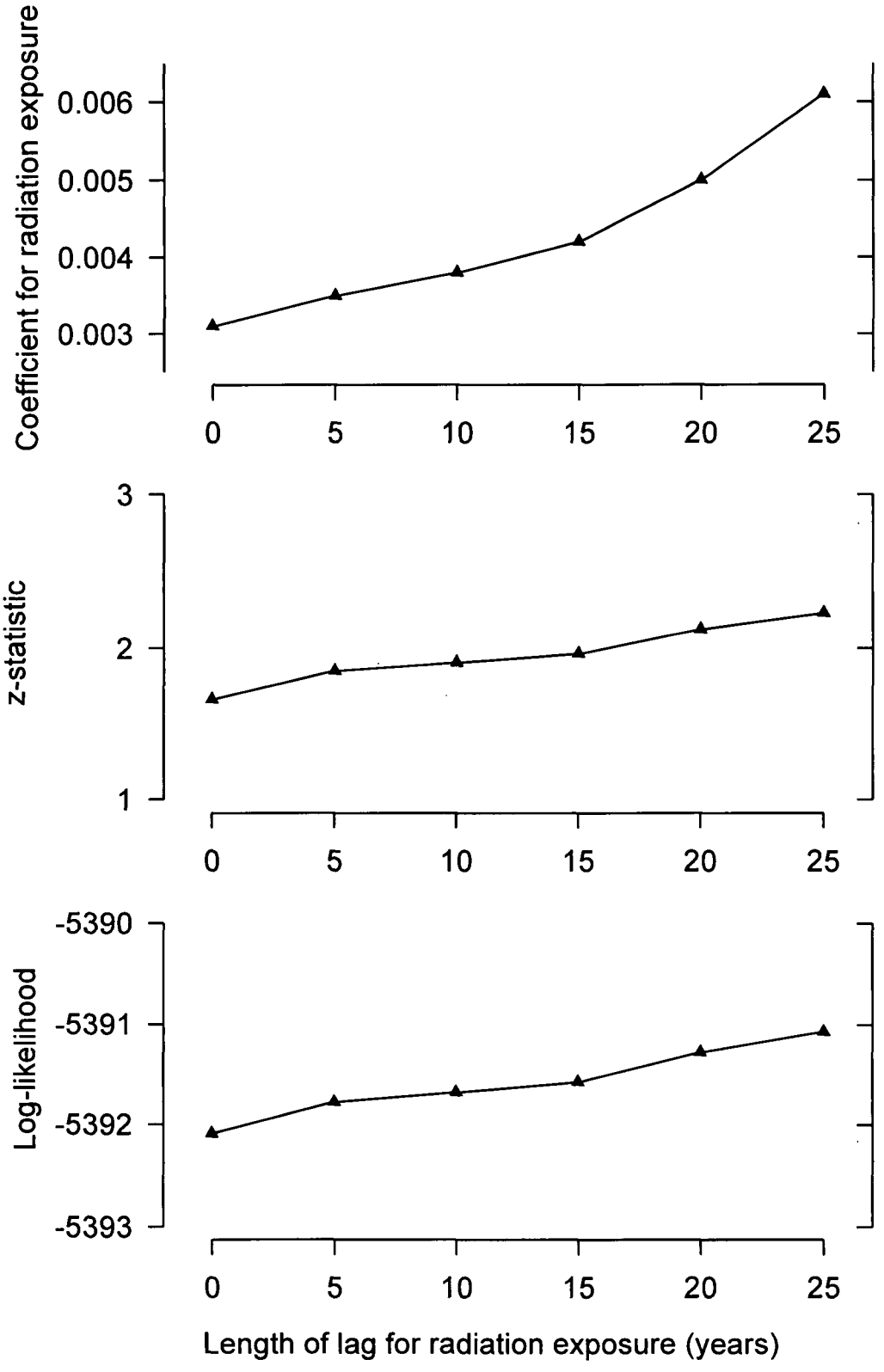

Figure 4.2 Regression modelling of lung cancer mortality: effect of different lags on radiation exposure coefficient and significance, and overall model fit.

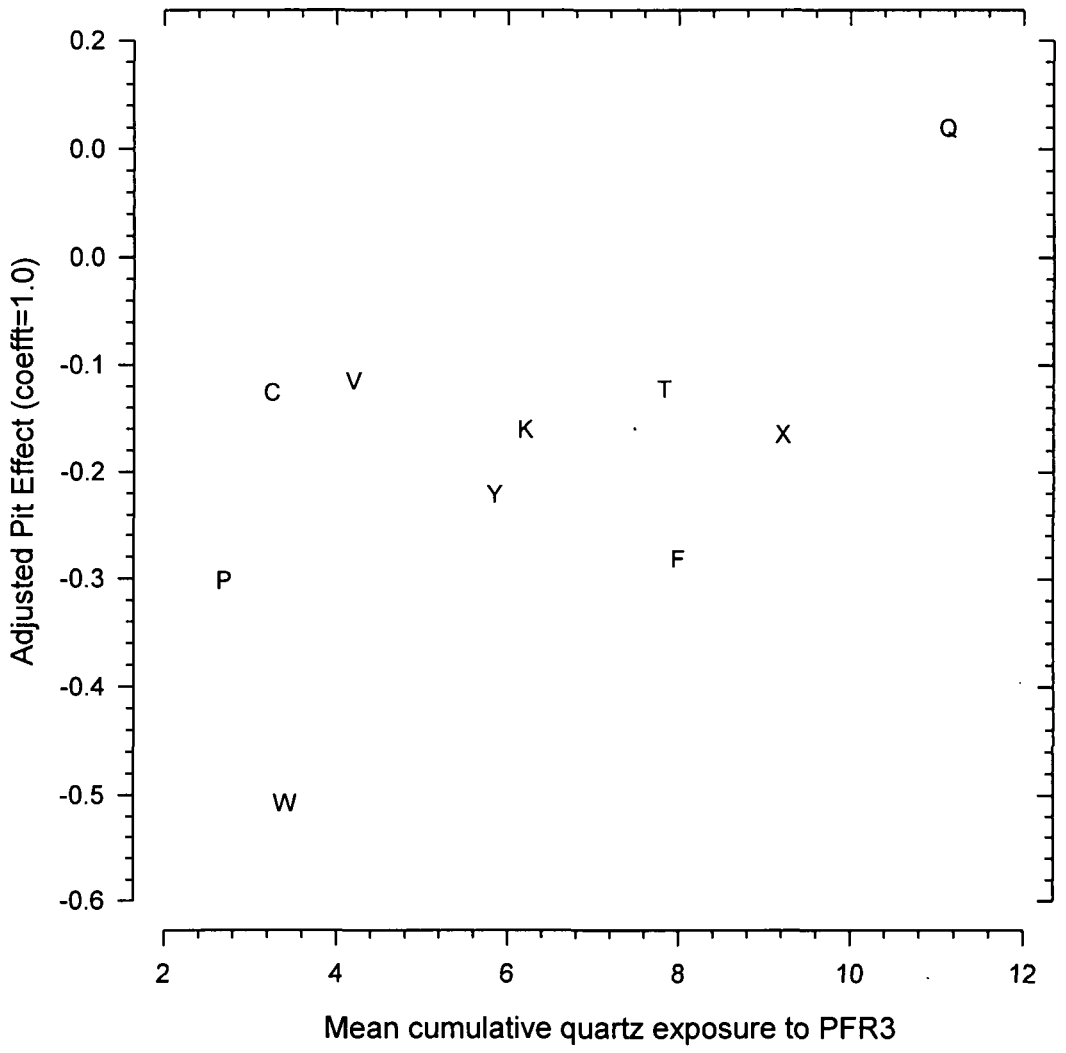

Figure 4.3 Relationship of pit differences in lung cancer mortality rates (on scale of log of mortality ratio), adjusted for age, cohort entry date, region and smoking habits, with pit mean quartz exposure at PFR 3rd survey.

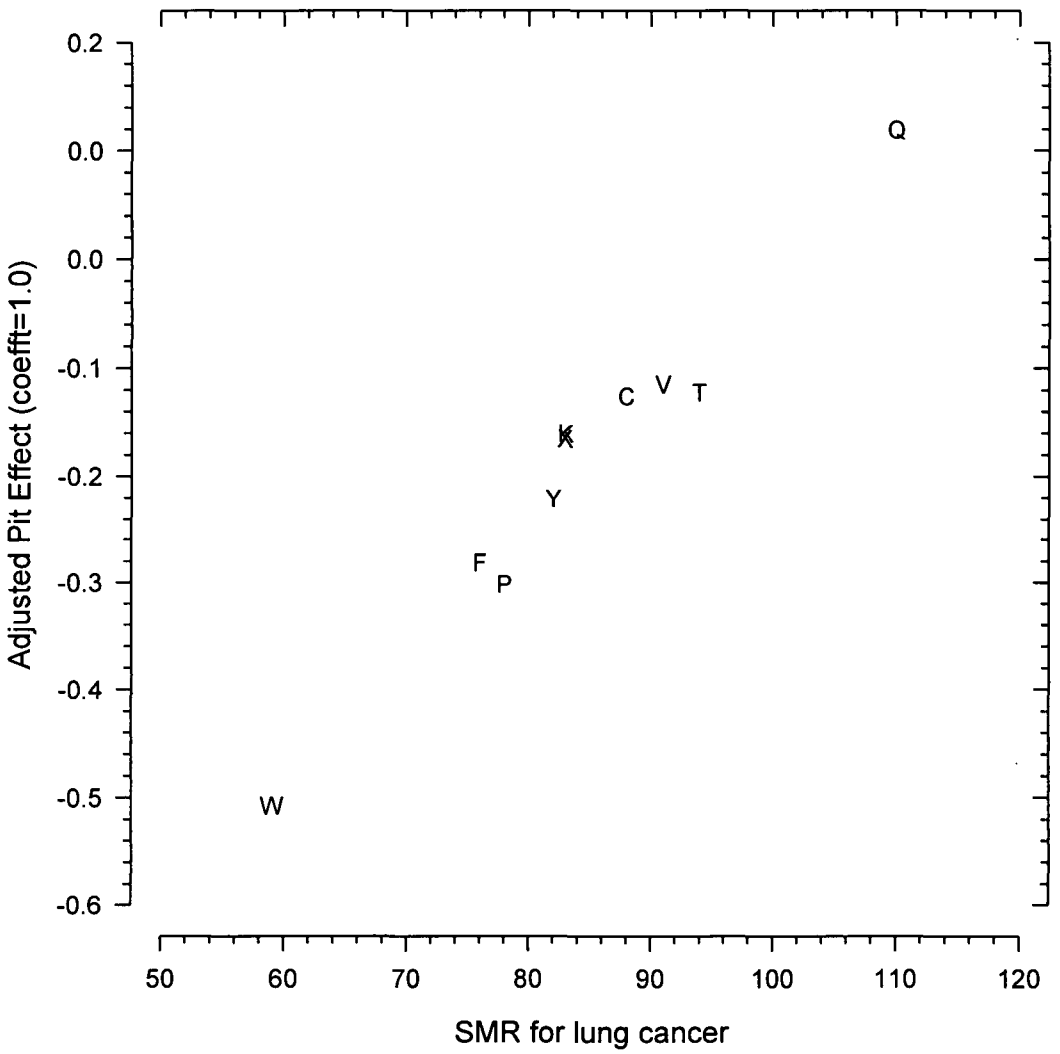

Figure 4.4 Relationship of pit differences in lung cancer mortality rates (on scale of log of mortality ratio), adjusted for age, cohort entry date, region and smoking habits, with SMR for lung cancer, adjusted for age, calendar year and region.

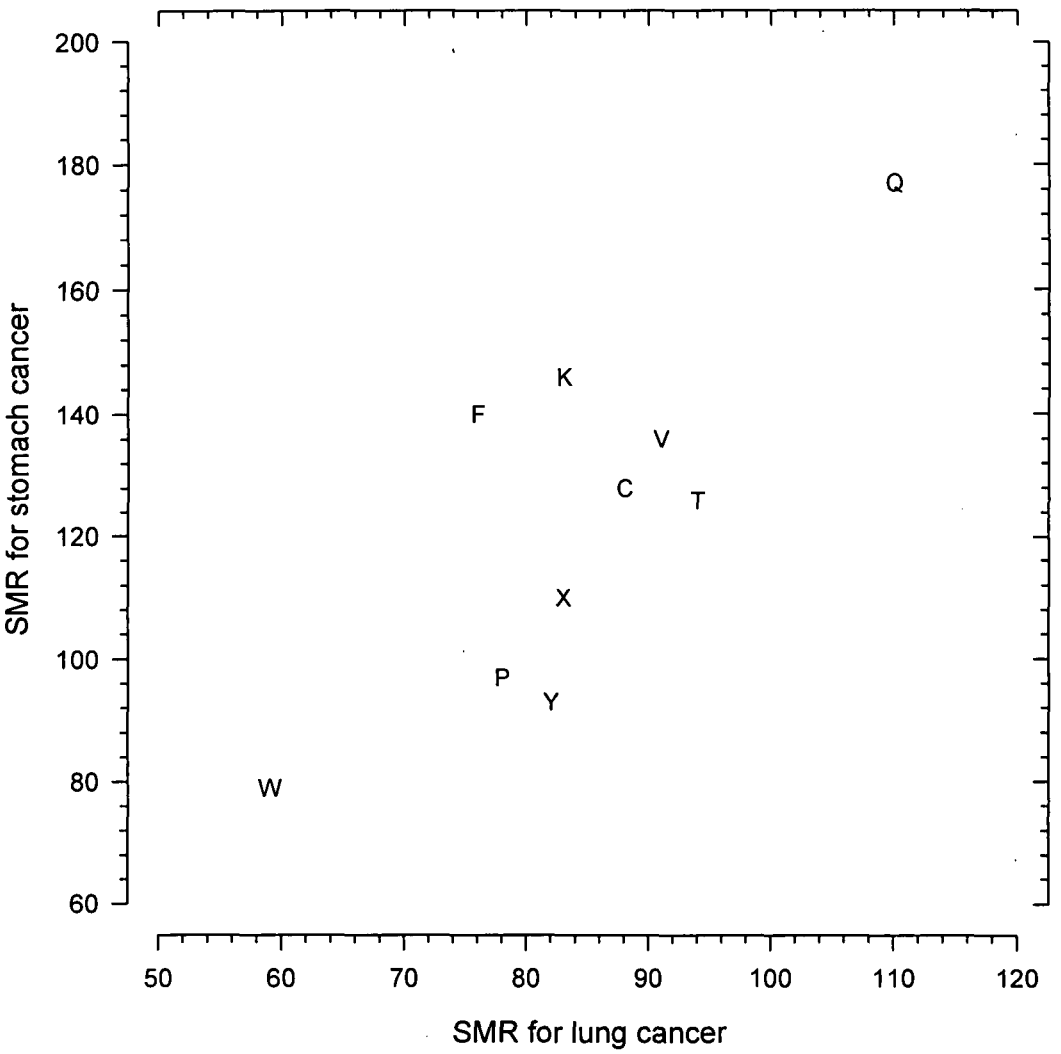

Figure 4.5 Relationship of SMRs for stomach cancer and lung cancer.

Appendix 1

Reproduction of recording form and instructions for 'Panda II' questionnaire, as used in PFR surveys.

PANDA 11

COLLIERY LETTER [ ] 1

A PERSONAL DATA

NAME ..... X-RAY NUMBER 2 [ ][ ][ ][ ] 5

DATE OF BIRTH (MONTH & YEAR) 6 [ ][ ][ ][ ] 9

B RESPIRATORY SYMPTOMS QUESTIONNAIRE

PREAMBLE: "I am going to ask you some questions about your chest - about cough and spit, for example. Please try to answer 'Yes' or 'No'. Your answers will be treated confidentially.

COUGH

Q. 1	Do you cough when you get up or first thing in the morning?	10
Q.1a	Do you cough like this on most days for as much as 3 months in the year?	11
Q. 2	Do you cough during the rest of the day? - I don't mean just at the end of your shift.	12
Q.2a	Do you cough like this on most days for as much as 3 months in the year?	13

PHLEGM

Q. 3	Do you bring up phlegm when you get up or first thing in the morning?...	14
Q.3a	Do you bring up phlegm like this on most days for as much as 3 months in the year?	15
Q. 4	Do you bring up phlegm during the rest of the day? - I don't mean just at the end of your shift. ...	16
Q.4a	Do you bring up phlegm like this on most days for as much as 3 months in the year?	17

BREATHLESSNESS

Q. 5	Do you have to walk slower than other people on level ground because of your chest?...	18

WHEEZING

Q. 6	Do you ever have wheezing or whistling in your chest? - I don't mean only when you have a cold. ...	19

WEATHER

Q. 7	Does the weather affect your chest?	20

SMOKING

Q. 8	Do you smoke? (If 'Yes', Q.8a - 8d; If 'No', Q.8e)	21
Q.8a	Do you smoke cigarettes, a pipe or both? (Record C, P or B)	22
Q.8b	How many cigarettes do you smoke per day on Mondays to Fridays? ... ... 23 [ ][ ]	24
Q.8c	How many cigarettes do you smoke per day on Saturdays and Sundays? ... ... 25 [ ][ ]	26
Q.8d	How many ounces of tobacco do you smoke per week? (Record in ounces. x = ½)...	27
Q.8e	Have you ever smoked as much as one cigarette per day for one year?	28

CHEST ILLNESSES

Q. 9	In the last 3 years have you had a chest illness that has kept you off work for more than a week?...	29
Q.9a	If 'Yes', what did your doctor say it was?	30

(A = Asthma; B = Bronchitis; C = Cold; D = Bronchitis & Asthma; F = Influenza; S = Some other chest illness; X = Not a chest illness)

C ANTHROPOMETRIC DATA

Height (cms)	31 [ ][ ][ ]	33
Sitting Height (cms)	34 [ ][ ][ ]	36
Weight (kgms)	37 [ ][ ][ ]	39

D VENTILATORY FUNCTION

Second Blow	F.E.V.	40 [ ][ ][ ]	42
	F.V.C.	43 [ ][ ][ ]	45
Third Blow	F.E.V.	46 [ ][ ][ ]	48
	F.V.C.	49 [ ][ ][ ]	51
Fourth Blow	F.E.V.	52 [ ][ ][ ]	54
	F.V.C.	55 [ ][ ][ ]	57

SERIES 700

Form B.901

INSTITUTE OF OCCUPATIONAL MEDICINE

PNEUMOCONIOSIS FIELD RESEARCH

INSTRUCTIONS FOR PANDA 11

A PERSONAL DATA

Date of birth — Month: January – December = 01 – 12
Enter code for the month with leading zero for January – September

Year: Enter the last two digits of the year (i.e. tens and units)

B RESPIRATORY SYMPTOMS QUESTIONNAIRE

Q1, 2, 3 and 4: If YES enter 'Y', if NO enter 'N'

Q1a, 2a, 3a and 4a: If answer to previous question is NO then leave blank, otherwise enter 'Y' for YES and 'N' for NO

Q5, 6 and 7: If YES enter 'Y', if NO enter 'N'

Q8: If YES enter 'Y' and ask Qs. 8a – 8d, leaving Q8e blank
If NO enter 'N' and ask Q8e, leaving Qs. 8a – 8d blank

- Q8a: Enter 'C' for Cigarettes only
  'P' for Pipe only
  'B' for Cigarettes and Pipe
- Q8b and 8c: Enter number of cigarettes with leading zero if less than 10 or '00' if none
- Q8d: Enter 'X' for ½ ounce only, otherwise enter the number of ounces or '0' for none
- Q8e: Enter 'Y' for YES and 'N' for NO

Q9: Enter 'Y' for YES and 'N' for NO

- Q9a: If answer to Q9 is NO leave blank, otherwise enter
  'A' for Asthma
  'B' for Bronchitis
  'C' for Cold
  'D' for Bronchitis and Asthma
  'F' for Influenza
  'S' for some other chest illness
  'X' for chest injury (not regarded as chest illness). Do not amend answer to Q9

C & D ANTHROPOMETRIC DATA AND VENTILATORY FUNCTION

Enter leading zeros where appropriate

ADDITIONAL QUESTIONING

If difficulty is experienced in obtaining 'YES' or 'NO' apply the following:
"I know this is difficult but please try to answer 'YES' or 'NO'
I will repeat the question"
If the answer is again equivocal, record 'NO'

Appendix 2

Tables of results of comparisons of mortality from selected causes with external reference rates, by pit.

Table A2.1 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

All internal causes

Pit	Observed deaths	SMR %	Confidence bounds		z- test
			Lower	Upper	
P	535	83	76	90	-4.52
T	793	99	92	106	-0.36
Y	912	89	83	95	-3.68
K	524	92	85	101	-1.83
X	672	89	83	96	-3.00
Q	662	89	82	96	-3.17
C	927	90	84	96	-3.32
F	527	102	93	111	0.39
V	893	87	82	93	-4.16
W	330	95	86	106	-0.87
All	**6775**	**91**	**89**	**93**	-8.08

Table A2.2 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

All cancers

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	144	85	72	100	-2.07
T	200	95	82	109	-0.79
Y	241	87	76	98	-2.29
K	126	84	71	100	-2.03
X	178	88	76	101	-1.83
Q	194	98	85	112	-0.33
C	228	88	77	100	-2.06
F	106	83	69	100	-2.00
V	227	89	78	102	-1.77
W	71	81	64	102	-1.90
All	**1715**	**88**	**84**	**93**	-5.29

Table A2.3 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Lung cancer

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	55	78	60	102	-1.97
T	80	94	75	117	-0.59
Y	92	82	67	100	-2.02
K	48	83	62	110	-1.36
X	65	83	65	106	-1.54
Q	78	110	88	137	0.81
C	86	88	72	109	-1.17
F	33	76	54	106	-1.72
V	77	91	72	113	-0.89
W	18	59	37	94	-2.55
All	**632**	**86**	**80**	**93**	-3.81

Table A2.4 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Stomach cancer

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	14	97	58	164	-0.10
T	28	126	87	182	1.14
Y	26	93	63	136	-0.39
K	21	146	95	224	1.57
X	21	110	72	168	0.42
Q	34	177	126	247	2.89
C	35	128	92	178	1.38
F	21	140	91	214	1.41
V	41	136	100	185	1.83
W	8	79	39	157	-0.72
All	**249**	**124**	**110**	**141**	3.26

Table A2.5 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Cancer of large intestine

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	7	63	30	133	-1.36
T	16	121	74	198	0.73
Y	17	99	62	159	-0.04
K	8	86	43	172	-0.44
X	18	143	90	227	1.40
Q	8	63	32	127	-1.45
C	13	76	44	131	-1.06
F	7	77	37	162	-0.73
V	12	67	38	117	-1.55
W	7	113	54	238	0.32
All	**113**	**90**	**74**	**108**	-1.21

Table A2.6 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Cancer of rectum

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	7	103	49	216	0.08
T	16	157	96	256	1.62
Y	11	83	46	150	-0.64
K	6	84	38	188	-0.44
X	8	83	41	166	-0.56
Q	9	88	46	170	-0.39
C	10	72	39	134	-1.11
F	8	127	63	254	0.63
V	8	64	32	128	-1.42
W	3	70	23	217	-0.68
All	**86**	**91**	**74**	**113**	-0.86

Table A2.7 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Cancer of oesophagus

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	4	60	22	159	-1.18
T	6	96	43	214	-0.10
Y	10	118	64	220	0.51
K	3	66	21	204	-0.80
X	3	47	15	144	-1.61
Q	6	91	41	201	-0.25
C	8	94	47	189	-0.16
F	6	134	60	298	0.67
V	7	78	37	163	-0.70
W	3	96	31	298	-0.07
All	**56**	**87**	**67**	**114**	-1.05

Table A2.8 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Bladder cancer

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	2	31	8	123	-2.27
T	6	72	32	159	-0.89
Y	10	93	50	173	-0.23
K	4	62	23	165	-1.08
X	8	94	47	189	-0.17
Q	11	135	75	244	0.93
C	7	66	32	139	-1.21
F	1	21	3	146	-2.42
V	10	106	57	196	0.17
W	0	0	*	*	-3.61
All	**59**	**77**	**59**	**99**	-2.17

Table A2.9 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Prostate cancer

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	11	107	59	192	0.21
T	10	83	45	154	-0.61
Y	22	141	93	214	1.47
K	5	49	21	119	-1.89
X	11	83	46	150	-0.64
Q	11	77	42	138	-0.95
C	13	67	39	115	-1.63
F	5	56	23	135	-1.49
V	17	98	61	158	-0.08
W	5	85	35	203	-0.39
All	**110**	**86**	**72**	**104**	-1.59

Table A2.10 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Leukaemia

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	4	124	46	329	0.40
T	4	99	37	264	-0.02
Y	3	56	18	174	-1.16
K	4	123	46	328	0.39
X	3	67	22	209	-0.76
Q	3	63	20	197	-0.89
C	6	106	48	236	0.15
F	3	105	34	325	0.08
V	3	52	17	160	-1.35
W	4	209	78	556	1.23
All	**37**	**90**	**65**	**124**	-0.68

Table A2.11 Results of comparisons of mortality in cohort with external reference rates, by pit. Table shows numbers of deaths, age- year- and region-standardised mortality ratio (SMR) and 95% confidence interval, and statistical test for SMR=100%.

Chronic bronchitis

Pit	Observed deaths	SMR %	Confidence bounds		z-test
			Lower	Upper	
P	17	81	51	131	-0.90
T	54	122	94	160	1.40
Y	48	95	72	126	-0.35
K	48	170	128	225	3.22
X	42	119	88	161	1.10
Q	44	140	104	189	2.07
C	62	103	80	132	0.22
F	43	166	123	224	2.94
V	71	143	114	181	2.77
W	7	44	21	91	-2.73
All	**436**	**120**	**110**	**132**	3.70

Appendix 3

Tables of results of regression analysis by Cox model.

Table A3.1 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to respirable quartz and dust. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Lung cancer

Terms in regression model	Regression models fitted									
	LC/01		LC/02		LC/03		LC/04		LC/05	
Age	0.1552	*9.04*	0.1536	*8.91*	0.1523	*8.82*	0.1557	*9.02*	0.1552	*8.97*
Age squared	-0.0019	*4.00*	-0.0019	*3.96*	-0.0019	*3.96*	-0.0019	*4.01*	-0.0019	*4.00*
Cohort entry date	-0.0173	*1.69*	-0.0170	*1.67*	-0.0172	*1.69*	-0.0177	*1.72*	-0.0173	*1.69*
Smoking effects (vs. non)										
Ex-smokers	-0.2147	*0.14*	-0.2114	*0.14*	-0.2028	*0.13*	-0.2170	*0.14*	-0.2152	*0.14*
Current smokers	2.2802	*3.68*	2.2758	*3.68*	2.2775	*3.68*	2.2818	*3.68*	2.2802	*3.68*
Equivalent cigarettes	0.0249	*4.92*	0.0251	*4.96*	0.0252	*4.98*	0.0248	*4.88*	0.0249	*4.90*
Additional age effect for ex-smokers	0.2296	*1.49*	0.2294	*1.49*	0.2285	*1.48*	0.2297	*1.49*	0.2296	*1.49*
Additional age squared effect for ex-smokers	-0.0074	*1.82*	-0.0073	*1.82*	-0.0073	*1.81*	-0.0074	*1.82*	-0.0074	*1.82*
Additional age effect for current smokers	0.0735	*1.65*	0.0733	*1.65*	0.0729	*1.64*	0.0735	*1.65*	0.0735	*1.65*
Additional age squared effect for current smokers	-0.0031	*2.23*	-0.0031	*2.23*	-0.0031	*2.22*	-0.0031	*2.23*	-0.0031	*2.23*
Quartz exposure			0.0060	*1.01*						
Quartz exposure (15 yr. lag)					0.0094	*1.44*				
Dust exposure							-0.0001	*0.33*		
Dust exposure (15 yr. lag)									0.0000	*0.03*
Log-likelihood	-5395.54		-5395.03		-5394.52		-5395.48		-5395.54	
Degrees of freedom	10		11		11		11		11	

Table A3.2 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to radiation and diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Lung cancer

Terms in regression model	Regression models fitted									
	LC/01		LC/06		LC/07		LC/08		LC/09	
Age	0.1552	*9.04*	0.1537	*8.94*	0.1531	*8.90*	0.1551	*9.03*	0.1548	*9.02*
Age squared	-0.0019	*4.00*	-0.0019	*3.98*	-0.0019	*3.99*	-0.0019	*3.98*	-0.0019	*3.96*
Cohort entry date	-0.0173	*1.69*	-0.0157	*1.53*	-0.0160	*1.57*	-0.0170	*1.66*	-0.0169	*1.65*
Smoking effects (vs. non)										
Ex-smokers .	-0.2147	*0.14*	-0.2162	*0.14*	-0.2095	*0.14*	-0.2182	*0.14*	-0.2111	*0.14*
Current smokers	2.2802	*3.68*	2.2759	*3.67*	2.2774	*3.67*	2.2803	*3.68*	2.2839	*3.69*
Equivalent cigarettes	0.0249	*4.92*	0.0254	*5.02*	0.0255	*5.03*	0.0250	*4.93*	0.0250	*4.94*
Additional age effect for ex-smokers	0.2296	*1.49*	0.2299	*1.49*	0.2294	*1.49*	0.2297	*1.49*	0.2287	*1.48*
Additional age squared effect for ex-smokers	-0.0074	*1.82*	-0.0074	*1.82*	-0.0074	*1.82*	-0.0074	*1.82*	-0.0073	*1.82*
Additional age effect for current smokers	0.0735	*1.65*	0.0734	*1.66*	0.0733	*1.66*	0.0734	*1.65*	0.0733	*1.66*
Additional age squared effect for current smokers	-0.0031	*2.23*	-0.0031	*2.24*	-0.0031	*2.24*	-0.0031	*2.23*	-0.0031	*2.24*
Radiation exposure			0.0028	*1.57*						
Radn. exposure (15 yr. lag)					0.0038	*1.85*				
Diesel travel							0.0110	*0.54*		
Diesel travel (15 yr. lag)									0.0385	*1.51*
Log-likelihood	-5395.54		-5394.36		-5393.91		-5395.40		-5394.59	
Degrees of freedom	10		11		11		11		11	

Table A3.3 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to respirable quartz and dust. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Lung cancer

Terms in regression model	Regression models fitted											
	LC/10		LC/11		LC/12		LC/13		LC/14		LC/15	
Age	0.1547	*9.02*	0.1543	*8.93*	0.1526	*8.80*	0.1548	*8.95*	0.1537	*8.86*	0.1509	*8.74*
Age squared	-0.0019	*3.99*	-0.0019	*3.98*	-0.0019	*3.96*	-0.0019	*3.99*	-0.0019	*3.97*	-0.0019	*3.93*
Cohort entry date	-0.0143	*1.32*	-0.0141	*1.30*	-0.0139	*1.28*	-0.0143	*1.32*	-0.0140	*1.29*	-0.0183	*1.78*
Smoking effects (vs. non)												
Ex-smokers	-0.2205	*0.14*	-0.2194	*0.14*	-0.2109	*0.14*	-0.2212	*0.15*	-0.2168	*0.14*	-0.1917	*0.13*
Current smokers	2.2884	*3.69*	2.2878	*3.69*	2.2888	*3.69*	2.2886	*3.69*	2.2882	*3.69*	2.2917	*3.70*
Equivalent cigarettes	0.0245	*4.77*	0.0245	*4.78*	0.0246	*4.80*	0.0245	*4.77*	0.0246	*4.78*	0.0241	*4.70*
Additional age effect for ex-smokers	0.2292	*1.49*	0.2292	*1.49*	0.2286	*1.48*	0.2293	*1.49*	0.2290	*1.49*	0.2274	*1.48*
Additional age squared effect for ex-smokers	-0.0073	*1.82*	-0.0073	*1.82*	-0.0073	*1.81*	-0.0074	*1.82*	-0.0073	*1.82*	-0.0073	*1.81*
Additional age effect for current smokers	0.0729	*1.64*	0.0729	*1.64*	0.0725	*1.64*	0.0729	*1.64*	0.0728	*1.64*	0.0723	*1.63*
Additional age squared effect for current smokers	-0.0031	*2.22*	-0.0031	*2.22*	-0.0031	*2.22*	-0.0031	*2.22*	-0.0031	*2.22*	-0.0031	*2.21*
Pit differences (vs. C)												
F	-0.3057	*1.48*	-0.3163	*1.49*	-0.3487	*1.63*	-0.3028	*1.35*	-0.3388	*1.50*		
K	-0.0249	*0.14*	-0.0333	*0.18*	-0.0574	*0.31*	-0.0240	*0.13*	-0.0345	*0.19*		
P	-0.0182	*0.10*	-0.0199	*0.11*	-0.0234	*0.13*	-0.0184	*0.10*	-0.0167	*0.09*		
Q	0.1189	*0.75*	0.0983	*0.52*	0.0364	*0.19*	0.1210	*0.71*	0.0943	*0.55*		
T	0.1440	*0.92*	0.1340	*0.82*	0.1024	*0.62*	0.1452	*0.91*	0.1288	*0.80*		
V	-0.1390	*0.87*	-0.1437	*0.89*	-0.1592	*0.98*	-0.1373	*0.81*	-0.1589	*0.94*		
W	-0.5316	*2.04*	-0.5327	*2.05*	-0.5375	*2.06*	-0.5306	*2.03*	-0.5439	*2.07*		
X	-0.0297	*0.18*	-0.0482	*0.25*	-0.1011	*0.53*	-0.0282	*0.16*	-0.0463	*0.27*		
Y	0.0452	*0.30*	0.0373	*0.24*	0.0164	*0.11*	0.0465	*0.30*	0.0304	*0.19*		
Quartz exposure			0.0016	*0.20*								
Quartz exposure (15 yr. lag)					0.0068	*0.79*					0.0116	*1.74*
Dust exposure							0.0000	*0.03*				
Dust exposure (15 yr. lag)									0.0002	*0.37*		
Regional mortality differences											0.7738	*2.27*
Log-likelihood	-5388.82		-5388.80		-5388.51		-5388.82		-5388.75		-5391.93	
Degrees of freedom	19		20		20		20		20		12	

Table A3.4 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to radiation and diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Lung cancer

Terms in regression model	Regression models fitted											
	LC/10		LC/16		LC/17		LC/18		LC/19		LC/20	
Age	0.1547	*9.02*	0.1552	*9.01*	0.1544	*8.94*	0.1547	*9.02*	0.1545	*9.01*	0.1521	*8.85*
Age squared	-0.0019	*3.99*	-0.0019	*4.00*	-0.0019	*3.99*	-0.0019	*4.01*	-0.0019	*3.97*	-0.0019	*3.97*
Cohort entry date	-0.0143	*1.32*	-0.0145	*1.34*	-0.0142	*1.31*	-0.0146	*1.35*	-0.0141	*1.30*	-0.0170	*1.65*
Smoking effects (vs. non)												
Ex-smokers	-0.2205	*0.14*	-0.2227	*0.15*	-0.2182	*0.14*	-0.2185	*0.14*	-0.2172	*0.14*	-0.2006	*0.13*
Current smokers	2.2884	*3.69*	2.2885	*3.69*	2.2887	*3.69*	2.2874	*3.69*	2.2912	*3.70*	2.2910	*3.70*
Equivalent cigarettes	0.0245	*4.77*	0.0244	*4.75*	0.0245	*4.78*	0.0244	*4.77*	0.0245	*4.77*	0.0244	*4.77*
Additional age effect for ex-smokers	0.2292	*1.49*	0.2292	*1.49*	0.2291	*1.49*	0.2292	*1.49*	0.2288	*1.48*	0.2285	*1.48*
Additional age squared effect for ex-smokers	-0.0073	*1.82*	-0.0074	*1.82*	-0.0073	*1.82*	-0.0073	*1.82*	-0.0073	*1.82*	-0.0073	*1.81*
Additional age effect for current smokers	0.0729	*1.64*	0.0730	*1.64*	0.0729	*1.64*	0.0730	*1.64*	0.0728	*1.64*	0.0729	*1.65*
Additional age squared effect for current smokers	-0.0031	*2.22*	-0.0031	*2.22*	-0.0031	*2.22*	-0.0031	*2.22*	-0.0031	*2.23*	-0.0031	*2.23*
Pit differences (vs. C)												
F	-0.3057	*1.48*	-0.3179	*1.52*	-0.2999	*1.43*	-0.3050	*1.48*	-0.3065	*1.49*		
K	-0.0249	*0.14*	-0.0110	*0.06*	-0.0317	*0.17*	-0.0045	*0.02*	-0.0353	*0.19*		
P	-0.0182	*0.10*	-0.0203	*0.11*	-0.0172	*0.10*	-0.0173	*0.10*	-0.0192	*0.11*		
Q	0.1189	*0.75*	0.1610	*0.79*	0.0976	*0.47*	0.1571	*0.90*	0.0861	*0.51*		
T	0.1440	*0.92*	0.1506	*0.96*	0.1403	*0.89*	0.1554	*0.99*	0.1332	*0.85*		
V	-0.1390	*0.87*	-0.1474	*0.91*	-0.1351	*0.83*	-0.1409	*0.88*	-0.1368	*0.85*		
W	-0.5316	*2.04*	-0.5413	*2.07*	-0.5270	*2.01*	-0.5318	*2.04*	-0.5303	*2.04*		
X	-0.0297	*0.18*	-0.0384	*0.23*	-0.0254	*0.15*	-0.0210	*0.12*	-0.0374	*0.22*		
Y	0.0452	*0.30*	0.0487	*0.32*	0.0435	*0.29*	0.0538	*0.35*	0.0392	*0.26*		
Radiation exposure			-0.0009	*0.32*								
Radn. exposure (15 yr. lag)					0.0005	*0.16*					0.0042	*1.96*
Diesel travel							-0.0135	*0.51*				
Diesel travel (15 yr. lag)									0.0187	*0.60*		
Regional mortality differences											0.7299	*2.16*
Log-likelihood	-5388.82		-5388.77		-5388.80		-5388.68		-5388.65		-5391.58	
Degrees of freedom	19		20		20		20		20		12	

Table A3.5 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to respirable quartz and radiation at various lags. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Lung cancer

Terms in regression model	Regression models fitted									
	LC/21		LC/22		LC/23		LC/24		LC/25	
Age	0.1502	*8.70*	0.1494	*8.66*	0.1519	*8.84*	0.1516	*8.82*	0.1497	*8.65*
Age squared	-0.0019	*3.95*	-0.0019	*3.98*	-0.0019	*3.99*	-0.0019	*4.01*	-0.0019	*4.00*
Cohort entry date	-0.0182	*1.78*	-0.0181	*1.76*	-0.0168	*1.64*	-0.0166	*1.61*	-0.0172	*1.67*
Smoking effects (vs. non)										
Ex-smokers	-0.1880	*0.12*	-0.1825	*0.12*	-0.1989	*0.13*	-0.1962	*0.13*	-0.1994	*0.13*
Current smokers	2.2925	*3.70*	2.2937	*3.70*	2.2910	*3.70*	2.2923	*3.70*	2.2934	*3.70*
Equivalent cigarettes	0.0242	*4.71*	0.0242	*4.71*	0.0244	*4.77*	0.0244	*4.77*	0.0244	*4.75*
Additional age effect for ex-smokers	0.2270	*1.47*	0.2262	*1.47*	0.2284	*1.48*	0.2281	*1.48*	0.2283	*1.48*
Additional age squared effect for ex-smokers	-0.0073	*1.80*	-0.0073	*1.80*	-0.0073	*1.81*	-0.0073	*1.81*	-0.0073	*1.80*
Additional age effect for current smokers	0.0721	*1.63*	0.0718	*1.62*	0.0729	*1.65*	0.0728	*1.65*	0.0720	*1.63*
Additional age squared effect for current smokers	-0.0031	*2.20*	-0.0031	*2.20*	-0.0031	*2.23*	-0.0031	*2.23*	-0.0031	*2.21*
Quartz exposure (20 yr. lag)	0.0146	*2.01*								
Quartz exposure (25 yr. lag)			0.0195	*2.39*					0.0135	*1.25*
Radiation exposure (20 yr lag)					0.0050	*2.12*				
Radiation exposure (25 yr. lag)							0.0061	*2.23*	0.0031	*0.84*
Regional mortality diffs.	0.7942	*2.32*	0.8202	*2.39*	0.7366	*2.18*	0.7421	*2.19*	0.8082	*2.35*
Log-likelihood	-5391.45		-5390.65		-5391.28		-5391.07		-5390.30	
Degrees of freedom	12		12		12		12		13	

Table A3.6 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to respirable quartz and dust. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Stomach cancer

Terms in regression model	Regression models fitted									
	SC/01		SC/02		SC/03		SC/04		SC/05	
Age	0.1411	*8.50*	0.1404	*8.38*	0.1402	*8.31*	0.1420	*8.46*	0.1419	*8.38*
Age squared	-0.0013	*2.67*	-0.0013	*2.64*	-0.0013	*2.65*	-0.0013	*2.68*	-0.0013	*2.67*
Cohort entry date	-0.0721	*4.06*	-0.0719	*4.05*	-0.0720	*4.06*	-0.0729	*4.06*	-0.0725	*4.05*
Quartz exposure			0.0029	*0.31*						
Quartz exposure (15 yr. lag)					0.0034	*0.33*				
Dust exposure							-0.0002	*0.35*		
Dust exposure (15 yr. lag)									-0.0001	*0.23*
Log-likelihood	-2154.21		-2154.16		-2154.16		-2154.15		-2154.18	
Degrees of freedom	3		4		4		4		4	

Table A3.7 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to radiation and diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Stomach cancer

Terms in regression model	Regression models fitted									
	SC/01		SC/06		SC/07		SC/08		SC/09	
Age	0.1411	*8.50*	0.1395	*8.37*	0.1392	*8.35*	0.1411	*8.51*	0.1409	*8.49*
Age squared	-0.0013	*2.67*	-0.0013	*2.63*	-0.0013	*2.65*	-0.0013	*2.61*	-0.0013	*2.63*
Cohort entry date	-0.0721	*4.06*	-0.0700	*3.94*	-0.0707	*3.98*	-0.0713	*4.02*	-0.0719	*4.05*
Radiation exposure			0.0032	*1.18*						
Radn. exposure (15 yr. lag)					0.0034	*1.06*				
Diesel travel							0.0274	*0.94*		
Diesel travel (15 yr. lag)									0.0273	*0.58*
Log-likelihood	-2154.21		-2153.55		-2153.67		-2153.82		-2154.06	
Degrees of freedom	3		4		4		4		4	

Table A3.8 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to respirable quartz and dust. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Stomach cancer

Terms in regression model	Regression models fitted											
	SC/10		SC/11		SC/12		SC/13		SC/14		SC/15	
Age	0.1419	*8.55*	0.1438	*8.51*	0.1445	*8.43*	0.1462	*8.65*	0.1470	*8.57*	0.1417	*8.36*
Age squared	-0.0013	*2.70*	-0.0013	*2.72*	-0.0013	*2.72*	-0.0014	*2.77*	-0.0014	*2.76*	-0.0013	*2.67*
Cohort entry date	-0.0694	*3.60*	-0.0705	*3.63*	-0.0702	*3.63*	-0.0720	*3.71*	-0.0710	*3.67*	-0.0734	*4.03*
Pit differences (vs. C)												
F	0.3198	*1.14*	0.3687	*1.27*	0.3712	*1.27*	0.4882	*1.61*	0.4765	*1.56*		
K	0.2160	*0.77*	0.2548	*0.89*	0.2557	*0.89*	0.2681	*0.95*	0.2645	*0.94*		
P	-0.1407	*0.43*	-0.1321	*0.41*	-0.1335	*0.41*	-0.1465	*0.45*	-0.1450	*0.45*		
Q	0.2747	*1.13*	0.3732	*1.29*	0.3768	*1.30*	0.4097	*1.57*	0.4006	*1.53*		
T	0.0823	*0.32*	0.1324	*0.50*	0.1361	*0.51*	0.1663	*0.64*	0.1633	*0.62*		
V	0.1646	*0.70*	0.1873	*0.78*	0.1895	*0.79*	0.2701	*1.09*	0.2634	*1.06*		
W	-0.2640	*0.67*	-0.2573	*0.65*	-0.2548	*0.65*	-0.2006	*0.51*	-0.1994	*0.50*		
X	-0.0263	*0.09*	0.0613	*0.19*	0.0633	*0.20*	0.0661	*0.23*	0.0596	*0.21*		
Y	-0.1966	*0.75*	-0.1601	*0.60*	-0.1616	*0.61*	-0.1125	*0.42*	-0.1226	*0.46*		
Quartz exposure			-0.0071	*0.61*								
Quartz exposure (15 yr. lag)					-0.0083	*0.63*						
Dust exposure							-0.0008	*1.36*				
Dust exposure (15 yr. lag)									-0.0008	*1.24*	-0.0001	*0.18*
Regional mortality differences											-0.2304	*0.26*
Log-likelihood	-2150.54		-2150.36		-2150.34		-2149.62		-2149.77		-2154.15	
Degrees of freedom	12		13		13		13		13		5	

Table A3.9 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to radiation and diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Stomach cancer

Terms in regression model	Regression models fitted									
	SC/10		SC/16		SC/17		SC/18		SC/19	
Age	0.1419	*8.55*	0.1404	*8.36*	0.1408	*8.34*	0.1419	*8.55*	0.1418	*8.54*
Age squared	-0.0013	*2.70*	-0.0013	*2.67*	-0.0013	*2.69*	-0.0013	*2.67*	-0.0013	*2.68*
Cohort entry date	-0.0694	*3.60*	-0.0686	*3.54*	-0.0692	*3.58*	-0.0690	*3.57*	-0.0693	*3.59*
Pit differences (vs. C)										
F	0.3198	*1.14*	0.3538	*1.23*	0.3395	*1.19*	0.3190	*1.14*	0.3194	*1.14*
K	0.2160	*0.77*	0.1788	*0.62*	0.1936	*0.68*	0.1965	*0.69*	0.2129	*0.76*
P	-0.1407	*0.43*	-0.1351	*0.41*	-0.1373	*0.42*	-0.1419	*0.44*	-0.1412	*0.43*
Q	0.2747	*1.13*	0.1512	*0.45*	0.2006	*0.62*	0.2311	*0.87*	0.2632	*1.02*
T	0.0823	*0.32*	0.0627	*0.24*	0.0696	*0.27*	0.0703	*0.27*	0.0790	*0.31*
V	0.1646	*0.70*	0.1877	*0.78*	0.1774	*0.74*	0.1675	*0.71*	0.1657	*0.70*
W	-0.2640	*0.67*	-0.2376	*0.60*	-0.2490	*0.63*	-0.2634	*0.67*	-0.2637	*0.67*
X	-0.0263	*0.09*	-0.0012	*0.00*	-0.0117	*0.04*	-0.0349	*0.12*	-0.0288	*0.10*
Y	-0.1966	*0.75*	-0.2063	*0.79*	-0.2022	*0.77*	-0.2064	*0.79*	-0.1986	*0.76*
Radiation exposure			0.0025	*0.54*						
Radn. exposure (15 yr. lag)					0.0018	*0.35*				
Diesel travel							0.0151	*0.43*		
Diesel travel (15 yr. lag)									0.0077	*0.13*
Log-likelihood	-2150.54		-2150.39		-2150.48		-2150.45		-2150.53	
Degrees of freedom	12		13		13		13		13	

Table A3.10 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to radiation and diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Leukaemia

Terms in regression model	Regression models fitted									
	LK/01		LK/02		LK/03		LK/04		LK/05	
Age	0.0728	*4.68*	0.0748	*4.73*	0.0754	*4.68*	0.0699	*4.54*	0.0712	*4.62*
Cohort entry date	-0.0877	*1.81*	-0.0910	*1.86*	-0.0897	*1.84*	-0.0919	*1.89*	-0.0894	*1.84*
Radiation exposure			-0.0053	*0.62*						
Radn. exposure (15 yr. lag)					-0.0059	*0.58*				
Diesel travel							-0.2539	*1.35*		
Diesel travel (15 yr. lag)									-0.5220	*1.36*
Log-likelihood	-327.63		-327.42		-327.45		-326.19		-325.91	
Degrees of freedom	2		3		3		3		3	

Table A3.11 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to radiation and diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Leukaemia

Terms in regression model	Regression models fitted									
	LK/06		LK/07		LK/08		LK/09		LK/10	
Age	0.0665	*4.10*	0.0679	*3.96*	0.0678	*3.80*	0.0637	*3.98*	0.0655	*4.08*
Cohort entry date	-0.1790	*2.17*	-0.1801	*2.18*	-0.1792	*2.17*	-0.1829	*2.23*	-0.1795	*2.19*
Pit differences (vs. C)										
F	0.3272	*0.45*	0.2829	*0.38*	0.2987	*0.40*	0.3330	*0.46*	0.3361	*0.46*
K	0.4071	*0.61*	0.4553	*0.66*	0.4382	*0.64*	0.6787	*1.00*	0.5827	*0.87*
P	0.7766	*1.07*	0.7695	*1.06*	0.7722	*1.07*	0.7891	*1.09*	0.8018	*1.11*
Q	-0.7427	*1.02*	-0.5965	*0.65*	-0.6459	*0.71*	-0.0166	*0.02*	-0.0604	*0.08*
T	-0.1977	*0.31*	-0.1727	*0.26*	-0.1796	*0.27*	0.0306	*0.05*	0.0532	*0.08*
V	-1.1479	*1.54*	-1.1776	*1.56*	-1.1660	*1.55*	-1.1879	*1.59*	-1.2054	*1.60*
W	0.7276	*1.11*	0.6936	*1.04*	0.7059	*1.06*	0.7361	*1.13*	0.7193	*1.10*
X	-0.1324	*0.18*	-0.1645	*0.23*	-0.1532	*0.21*	0.0519	*0.07*	0.0759	*0.10*
Y	-0.8575	*1.19*	-0.8456	*1.17*	-0.8506	*1.18*	-0.7082	*0.97*	-0.7397	*1.02*
Radiation exposure			-0.0034	*0.25*						
Radn. exposure (15 yr. lag)					-0.0028	*0.18*				
Diesel travel							-0.3078	*1.34*		
Diesel travel (15 yr. lag)									-0.5961	*1.34*
Log-likelihood	-322.55		-322.51		-322.53		-321.24		-321.01	
Degrees of freedom	11		12		12		12		12	

Table A3.12 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposure to diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Bladder cancer

Terms in regression model	Regression models fitted					
	BC/01		BC/02		BC/03	
Age	0.1856	*3.89*	0.1850	*3.89*	0.1843	*3.87*
Age squared	-0.0024	*1.88*	-0.0023	*1.82*	-0.0023	*1.84*
Cohort entry date	-0.0668	*1.68*	-0.0645	*1.62*	-0.0657	*1.66*
Equivalent cigarettes	0.0393	*2.98*	0.0395	*3.00*	0.0393	*2.99*
Diesel travel			0.0607	*1.52*		
Diesel travel (15 yr. lag)					0.0722	*1.41*
Log-likelihood	-497.85		-497.04		-497.19	
Degrees of freedom	4		5		5	

Table A3.13 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposure to diesel fumes from pit travel. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Bladder cancer

Terms in regression model	Regression models fitted					
	BC/04		BC/05		BC/06	
Age	0.1876	*3.96*	0.1874	*3.95*	0.1870	*3.95*
Age squared	-0.0023	*1.81*	-0.0022	*1.79*	-0.0022	*1.79*
Cohort entry date	-0.0465	*1.23*	-0.0454	*1.20*	-0.0461	*1.22*
Equivalent cigarettes	0.0407	*3.08*	0.0408	*3.10*	0.0407	*3.09*
Pit differences (vs. C)						
F	-0.9067	*0.85*	-0.9092	*0.85*	-0.9096	*0.85*
K	0.3579	*0.57*	0.3021	*0.47*	0.3301	*0.52*
P	-0.3391	*0.42*	-0.3436	*0.42*	-0.3446	*0.42*
Q	1.0273	*2.11*	0.9255	*1.78*	0.9459	*1.85*
T	0.3812	*0.68*	0.3478	*0.62*	0.3508	*0.63*
V	0.6949	*1.39*	0.7017	*1.41*	0.7008	*1.40*
W	*		*		*	
X	0.8084	*1.54*	0.7872	*1.49*	0.7897	*1.50*
Y	0.6678	*1.35*	0.6450	*1.30*	0.6524	*1.31*
Diesel travel			0.0330	*0.61*		
Diesel travel (15 yr. lag)					0.0408	*0.58*
Log-likelihood	-492.46		-492.30		-492.32	
Degrees of freedom	12		13		13	

* No deaths at pit W => no estimate of pit effect

Table A3.14 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to respirable quartz and dust. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Pneumoconiosis

Terms in regression model	Regression models fitted											
	PN/01		PN/02		PN/03		PN/04		PN/05		PN/06	
Age	0.2104	*7.33*	0.2049	*7.11*	0.1999	*6.94*	0.1898	*6.56*	0.1763	*6.16*	0.1814	*6.30*
Age squared	-0.0020	*2.78*	-0.0020	*2.68*	-0.0019	*2.65*	-0.0018	*2.49*	-0.0017	*2.42*	-0.0018	*2.48*
Cohort entry date	-0.1172	*5.10*	-0.1147	*5.04*	-0.1145	*5.05*	-0.0988	*4.48*	-0.1023	*4.67*	-0.1044	*4.74*
Quartz exposure			0.0210	*2.31*								
Quartz exposure (15 yr. lag)					0.0298	*3.07*					-0.0820	*4.84*
Dust exposure							0.0035	*7.41*				
Dust exposure (15 yr. lag)									0.0043	*8.34*	0.0073	*9.99*
Log-likelihood	-1682.53		-1680.01		-1678.17		-1657.10		-1650.24		-1636.85	
Degrees of freedom	3		4		4		4		4		5	

Table A3.15 Results of regression analysis by Cox model. Models show relationship between log of cause-specific mortality hazard and exposures to respirable quartz and dust. Table contains estimates of regression coefficients, with absolute value of ratio of coefficient to standard error in *italics*.

Pneumoconiosis

Terms in regression model	Regression models fitted											
	PN/07		PN/08		PN/09		PN/10		PN/11		PN/12	
Age	0.2095	*7.25*	0.1796	*6.15*	0.1595	*5.53*	0.1780	*6.07*	0.1567	*5.40*	0.1542	*5.29*
Age squared	-0.0020	*2.77*	-0.0017	*2.34*	-0.0017	*2.33*	-0.0017	*2.33*	-0.0016	*2.22*	-0.0016	*2.21*
Cohort entry date	-0.1335	*4.50*	-0.1221	*4.18*	-0.1283	*4.42*	-0.1188	*4.09*	-0.1258	*4.37*	-0.1251	*4.34*
Pit differences (vs. C)												
F	0.9373	*3.46*	-0.0628	*0.20*	-0.3359	*1.03*	-0.6329	*1.72*	-0.9802	*2.54*	-0.9651	*2.50*
K	-0.2744	*0.71*	-1.0704	*2.62*	-1.2898	*3.13*	-0.6951	*1.79*	-0.7904	*2.03*	-0.9171	*2.16*
P	-0.6960	*1.40*	-0.8033	*1.61*	-0.7783	*1.56*	-0.6168	*1.24*	-0.6044	*1.22*	-0.6341	*1.27*
Q	-2.2788	*3.12*	-4.7672	*5.55*	-5.5728	*6.27*	-3.6036	*4.75*	-3.9097	*5.11*	-4.3177	*4.60*
T	0.4866	*1.94*	-0.6154	*1.94*	-0.9630	*2.91*	-0.2879	*1.04*	-0.4907	*1.72*	-0.6387	*1.84*
V	0.1735	*0.67*	-0.2434	*0.91*	-0.3752	*1.38*	-0.6793	*2.35*	-0.8579	*2.92*	-0.8146	*2.73*
W	1.2014	*4.32*	1.1197	*4.02*	1.0559	*3.79*	0.6310	*2.16*	0.4413	*1.48*	0.5268	*1.66*
X	0.2128	*0.70*	-1.4001	*3.50*	-1.8085	*4.40*	-0.4575	*1.44*	-0.5915	*1.85*	-0.8614	*1.81*
Y	-0.2645	*0.89*	-0.9776	*3.05*	-1.0984	*3.43*	-0.9592	*3.06*	-1.0730	*3.41*	-1.1239	*3.49*
Quartz exposure			0.1205	*6.55*								
Quartz exposure (15 yr. lag)					0.1656	*7.82*					0.0318	*0.77*
Dust exposure							0.0052	*7.61*				
Dust exposure (15 yr. lag)									0.0067	*8.57*	0.0058	*4.00*
Log-likelihood	-1643.40		-1620.25		-1610.12		-1612.00		-1602.19		-1601.89	
Degrees of freedom	12		13		13		13		13		14	

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