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Respiratory Infections in Coal Miners Exposed to Nitrogen Oxides

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Includes the Report of the Institute's Health Review Committee

Research Report Number 18

HEALTH EFFECTS INSTITUTE

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HEALTH REVIEW COMMITTEE'S REPORT Health Effects Institute

ABBREVIATIONS

FEV_1	forced expiratory volume in one second
gh/m^3	grams of dust × hours of exposure per cubic meter of sampled air
HCHO	formaldehyde
NO	nitric oxide
NO_2	nitrogen dioxide
NO_x	nitrogen oxides
OG	occupational group
ppm•shifts	exposure in ppm multiplied by number of shifts
$C_i(t)$	mean concentration of NO_x experienced by miner i during period t
c_j	concentration of NO_x estimated for occupational group j
$E_i(t)$	exposure to NO_x of miner i during period t
$P_{ik}(T)$	proportion of time miner i worked in job category k during period T
$s_{ij}(t)$	number of shifts worked by miner i during period t in occupational group j
$s_{ik}(T)$	number of shifts worked by miner i during period T in job category k

INVESTIGATORS' REPORT

Respiratory Infections in Coal Miners Exposed to Nitrogen Oxides

Michael Jacobsen, Tom A. Smith, J. Fintan Hurley, Alastair Robertson, and Ralph Roscrow

ABSTRACT

Coal miners working underground may be exposed chronically to low levels of nitric oxide and nitrogen dioxide from diesel engine emissions and from the use of explosives for blasting. The aims of this study were to establish whether long-term exposures to low concentrations of these gases at nine British coal mines had been associated with increased susceptibility to respiratory infections and, if so, to estimate the relative risks for different levels of exposure. The nine mines concerned had been involved, since 1954, in a prospective epidemiological study of coal miners' health.

Median levels of nitrogen oxides in 4,933 pairs of full-shift samples, taken at the mines during the years 1976 through 1982 were 0.2 ppm nitric oxide and 0.03 ppm nitrogen dioxide; 10 percent of the concentrations exceeded 1.1 ppm nitric oxide and 0.08 ppm nitrogen dioxide. Multiple regression estimates of concentrations associated with different underground locations, types of work, and mining conditions at each mine were combined with detailed records of miners' attendance at work at similar locations in earlier years. These retrospective estimates of individuals' underground exposures to nitrogen oxides referred to between five- and 16-year periods of exposure. Also available for study were records of the men's exposures to respirable mine dusts and information from five-yearly medical surveys about their smoking habits, respiratory symptoms, and questionnaire-elicited reports of sickness absences attributed, among other things, to respiratory infections.

The reliability of the latter reports was examined in a sample of 471 of the men by comparing the answers to the questionnaire with physicians' diagnoses on certified sickness absence records. Miners' references to bronchitis, influenza, or colds as the cause of prolonged sickness absence during the three years preceding the surveys did, in general, reflect real spells of absence from work, lasting at least seven days, that had been diagnosed by doctors as due to respiratory infections. But only about 20 percent of the men whose colliery records indicated that there had been such an absence acknowledged them in the survey as due to a "chest illness". Most of the under-reporting was of absences certified as due to influenza, colds, or "upper respiratory tract infection", and this under-reporting was not related to the men's ages or smoking habits.

The main analyses referred to 5,408 reports of colds, influenza, or bronchitis at a total of 40,071 interviews involving nearly 20,000 miners. Changes in 11,000 of these miners' responses between consecutive medical surveys were studied in relation to exposures that occurred in the corresponding approximately five-year intervals. Responses from 7,463 of the men were examined in relation to estimates of exposures to nitrogen oxides accumulated over periods averaging seven years, and extending to 15 years or more for 750 of them. Reports of infections were related positively to age and cigarette smoking, to earlier reports of similar illnesses, to evidence of chronic bronchitic symptoms, low lung function, pneumoconiosis, and to relatively long periods of underground, as opposed to surface, work. The latter contrast was particularly clear for work involving shot firing and, to a lesser extent, for diesel driving. However, there were no consistent associations between the chosen indicators of respiratory infections and estimates of occupational exposures to nitric oxide or nitrogen dioxide in any of the subsets of data studied, including those from nonsmokers and from men whose responses indicated enhanced susceptibility to respiratory infections.

We conclude that long-term exposures to the levels of nitrogen oxides found in British coal mines during the 1970s do not detectably increase the chances that miners will absent themselves from work because of chest infections. The range of concentrations of nitrogen oxides to which the miners had been exposed occupationally were similar to those recorded in some cities polluted by motor vehicle exhaust emissions. The results suggest that similar concentrations of these gases in urban environments are unlikely to cause complaints in manual workers that would be diagnosed by family doctors as respiratory infections.

INTRODUCTION

Gases that are emitted from motor vehicle exhausts include nitrogen oxides (NO_x), in particular nitric oxide (NO) and nitrogen dioxide (NO_2). The acute respiratory effects of inhaling high concentrations of these materials are well recognized. More controversial is the question of possible long-term effects of subacute levels, of the kind that may occur in polluted urban environments. The issues involved are described by Lee (1980), including a critical account of evidence that laboratory animals, chronically exposed to low levels of NO_2, are less resistant to respiratory infections than are control animals

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(Gardner 1980). As noted by Shy and Love (1980), some epidemiological studies suggest that this finding may also be applicable to humans (Pearlman et al. 1971; Florey et al. 1979; Melia et al. 1979; Goldstein et al. 1979; Speizer et al. 1980), but other studies of human populations have failed to substantiate the idea (Speizer and Ferris 1973; Keller et al. 1979).

Possible reasons for such conflicting epidemiological findings include difficulties in reliably estimating the time-weighted concentrations of pollutants to which people are exposed. Errors in such estimates may obscure real exposure-response gradients, or they may generate spurious relationships if the errors happen to be correlated with some other factor that is associated with the response. Equally important are the problems of reliably identifying, in an epidemiological setting, the biological endpoints that are thought to be indicators of respiratory infections, and of measuring exposures to other pollutants that may lead to the same measure of response.

One possible approach to reducing the uncertainties is to concentrate attention on a group of people who are known to be at risk of chronic exposure to low levels of NO_x by virtue of their occupation. In principle, it should be easier to measure individuals' exposures in a well-defined occupational setting than in a complex and varying cycle of daily activity within which exposure to motor vehicle exhaust emissions is only one component.

For instance, coal miners may be exposed to varying levels of NO_x while working underground. The gases are generated as a result of the use of explosives for blasting (shot firing), and they arise also from diesel engine exhaust emissions underground. Thus, Robertson and colleagues (1984) have described measurements made at nine British coal mines during a four-year period in the 1970s. They reported low concentrations of NO and NO_2 in ranges similar to those that may be found in the atmosphere of some American cities. Using those measurements, and taking advantage of detailed records of precisely where, underground, the miners employed at those collieries had been working, these authors identified 126 men who were likely to have had relatively high occupational exposures to NO_x over several years. Other miners working at the same nine collieries were similarly identifiable as having worked during the same periods primarily at places where the concentrations of NO_x were very low or zero. An analysis of data from several medical surveys at the mines showed no significant differences between the contrasted exposure groups in their prevalence rates of bronchitic symptoms or in their standardized five- and 10-year mean rates of loss of respiratory function (Robertson et al. 1984).

We report now on a more extensive investigation of occupational exposures to NO_x among nearly 20,000 men who were employed at the same nine coal mines, and we attempt to relate estimates of those exposures to information about the occurrence of respiratory infections among the miners. The latter information is based on responses to a questionnaire that was applied in a standardized manner at a series of quinquennial epidemiological surveys at the mines. The reliability of the questionnaire-elicited data about respiratory infections has been examined in a sample of the men.

AIMS

The aims of the work were to establish whether or not British coal miners' occupational exposures to nitrogen oxides are associated with increased susceptibility to respiratory infections, and to estimate the relative risks of such infections at different levels of exposure. A subsidiary objective was to assess the usefulness, as an epidemiological tool, of survey responses to standardized questions about chest illnesses.

METHODS

DATA SOURCES

All the data used were acquired as part of a long-term epidemiological study of British coal miners known as the Pneumoconiosis Field Research (Fay 1957; Fay and Rae 1959). That research began in 1953. The aims, and the methods that were used, have been described in many publications about relationships between coal miners' exposures to respirable dust and various measures of damage to the lung (see, for instance, Jacobsen et al. 1971; Rae et al. 1971; Rogan et al. 1973; Hurley et al. 1982, 1987). The main design and methodological features of the project were reviewed by Jacobsen (1981) and are summarized below, with emphasis on those aspects that are pertinent to this study of the effects of exposures to nitrogen oxides.

DESIGN OF THE PNEUMOCONIOSIS FIELD RESEARCH AND THE MINERS STUDIED

Twenty-five coal mines were selected for study in 1952. They represented the wide range of geological and environmental conditions that were to be found at that time in the various British coal fields. Medical surveys were conducted at the mines at approximately five-year intervals, starting in 1953. By the end of 1968, three such surveys, covering 10-year periods of observation, had been completed at 24 mines. (The 25th colliery closed soon after the initial survey.) A fourth and fifth survey took place at 10 of the mines, providing 20-year periods of observation; a sixth survey, at two of the latter 10, was completed during 1978. All men employed at the collieries at the times of the surveys were invited to participate. (No women are employed underground in British coal mines.) Response rates were around 90 percent throughout. The observations made included chest radiography on each occasion and, at the second and subsequent surveys, spirometry and the recording of responses to a questionnaire about respiratory symptoms and smoking habits.

The questionnaire (Appendix A) was similar to, but not identical with, that published by the British Medical Research Council (BMRC 1966). The questions were asked by trained nonmedical staff from the research team. The interviewers' reliability and consistency in the way that they administered the questionnaire was monitored at intervals during the course of the research, and corrective action was taken as necessary to improve consistency in interviewing practice (Attfield 1971).

One of the questions (question 9 in Appendix A) was: "In the last three years have you had a chest illness that has kept you off work for more than a week?" A positive response prompted the rider: "What did the doctor say it was?" Interviewers were instructed (Appendix A) to classify responses to the latter question into one of the following: asthma, bronchitis, cold, bronchitis and asthma, influenza, some other chest illness, not a chest illness. The coded answers to these questions, from miners in repeated surveys at nine of the 24 mines (Figure 1), were used to define response variables for the present study of respiratory infections.

Four partially overlapping subgroups of men who had worked at the nine mines were considered (Figure 2). Records were available for 21,490 miners who had each provided at least one set of answers to the respiratory-symptoms questionnaire, and whose cumulative exposures to respirable coal mine dust had also been recorded. Questionnaire responses from 649 men at one colliery were not usable. (The men concerned had been interviewed only once, in 1958, soon after the questionnaire was first introduced. Errors in administering the questionnaire are known to have occurred on that occasion.) Another 940 men were excluded from consideration because records of their occupational histories were not sufficiently detailed to permit retrospective estimation of their occupational exposures to NO_x.

About half (51 percent) of the other 19,901 men (group C in Figure 2) worked at mines where diesels were used (Figure 3). Group C provided 40,071 man-surveys for analysis, with valid questionnaire responses that were linkable, in principle, with estimates of exposures to NO_x during at least five years preceding the surveys (Table 1). The 40,071 responses were generated at 37 medical surveys at the nine mines during a 25-year calendar period, from February 1954 through November 1978. More than half (58 percent) of the 19,901 men in Group C provided answers to the questionnaire on at least two occasions, most of them (group D in Figure 2) at two or more consecutive surveys.

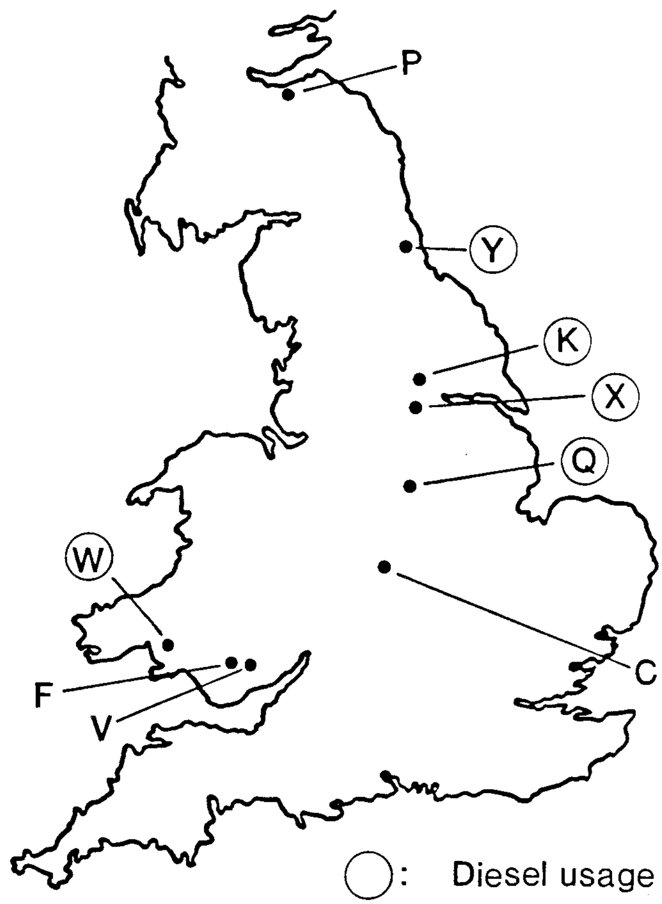

Figure 1. Locations of the nine coal mines studied.

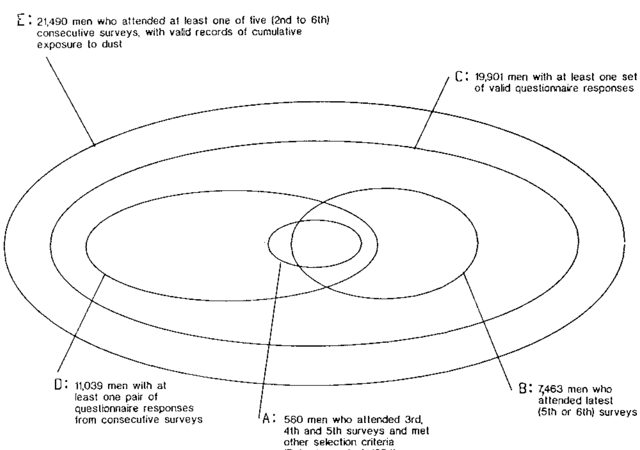

Figure 2. Schematic (Venn) diagram of the groups of men studied.

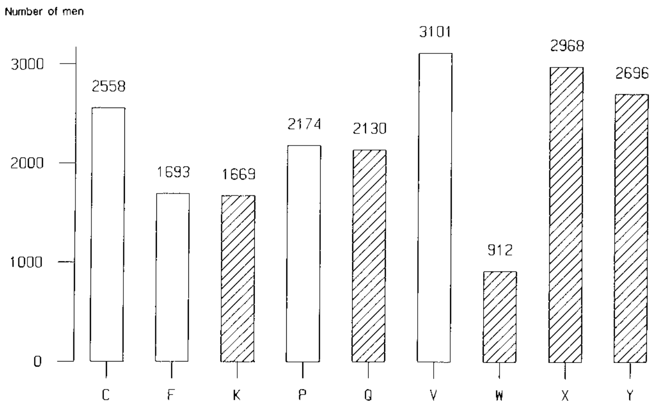

Figure 3. Distribution of 19,901 men in group C, by colliery. Hatching indicates diesel usage.

Table 1. Numbers of Surveys and Miners Contributing to 40,071 Man-Surveys

Number of Surveys at Which Questionnaire Response Was Obtained	Number of Miners	Number of Man-Surveys
1	8,446	8,446
2	5,778	11,556
3	2,887	8,661
4	2,542	10,168
5	248	1,240
Totals	19,901	40,071

The 11,039 miners in group D generated 19,515 approximately five-year intersurvey man-intervals of exposure to NO_x, with corresponding data from questionnaire responses at the start and end of those intervals. This provided an opportunity for a longitudinal study of possible relationships between changes in the chosen measure of response and approximately five-year exposures to NO_x (as distinct from the cross-sectional type of analysis of responses of the 40,071 man-surveys from group C.)

The 19,901 men in group C also included 7,463 men (group B in Figure 2) who attended the latest of the series of medical surveys at the mines, during the period from April 1975 through November 1978. Miners in group B are considered separately below, because their responses at the latest surveys could be studied in relation to the maximum possible time periods during which retrospective estimates of their cumulative occupational exposures to NO_x might be attempted.

Group A (Figure 2) refers to the 560 miners described previously by Robertson and coworkers (1984). They were selected for the earlier study as follows. All of them were required to have attended the third, fourth, and fifth of the medical surveys; records of their smoking habits on these occasions had to be complete, consistent, and to indicate that they were not exsmokers; and their occupational history records from 1972 up to the time when the NO_x measurements were made (during 1976 through 1979) had to justify their inclusion in either one of two contrasted NO_x exposure groups. Inclusion in the high-NO_x exposure group required that more than 80 percent of the time at work since 1972 had been spent in activities for which an index of combined NO_x concentration ([NO] + 7 [NO_2]) was more than 0.9 parts per million (ppm). Inclusion in the low-NO_x exposure group required that more than 80 percent of the time at work had been spent in activities where the same index was less than 0.4 ppm, and that no time had been worked in activities where the index was greater than 0.9 ppm. The analyses reported by Robertson and coworkers (1984) did not include responses to survey questions about sickness absence. Those responses, as recorded at the fifth surveys in the late 1970s, have now been studied in relation to separate estimates of individual miners' exposures to NO and to NO_2 during short (2.1 to 3.4 years) periods when the NO_x surveys were conducted underground.

THE OCCUPATIONAL GROUP DUST SAMPLING STRATEGY AND MINERS' EXPOSURES TO RESPIRABLE DUST

The field research dust-sampling strategy, instituted in 1952, was designed to provide data to estimate individual miners' long-term cumulative exposures to respirable coal mine dust (Fay and Rae 1959). Research staff permanently stationed at the collieries divided the various activities and work locations at any one time into as many "Occupational Groups" (OGs) as were necessary to ensure that each OG referred to a group of men who were working at similar jobs and in a similar environment, usually at the same location, within the same mine. Thus, any one OG is colliery- and calendar-time-specific. New OGs were opened and closed at each mine as tasks and conditions underground changed over the years.

Records were accumulated of the number of shifts (including overtime) worked by each miner in various OGs, from the start of the research until the late 1970s. Average respirable dust concentrations characterizing the OGs were calculated from measurements made close to where a randomly selected member of a group happened to be working on the day that sampling was scheduled. These measurements began at the time that the chosen miner arrived at pit bottom at the start of a shift, and continued until he left pit bottom at the end of the working shift, including traveling time underground ("portal-to-portal" sampling). The frequency with which any one OG was sampled was determined by a formula designed to distribute the available sampling resources between OGs at any one colliery in a way that would minimize the mean variance of dust exposure estimates for individuals within a group (Ashford 1958). The exposures were calculated by summing the products, for any one miner, of the mean OG dust concentrations and the number of shifts that he worked in them. The units of exposure are, therefore, the products of time and the concentrations of respirable dust in the air; they are expressed here as (grams of dust) × (hours of exposure) per cubic meter of sampled air (gh/m^3). Dodgson and colleagues (1971) give further details of how the mean dust concentrations were obtained, and Hurley and associates (1982, 1987) elaborate on the methods used to calculate the exposures.

MEASUREMENT OF CONCENTRATIONS OF NITROGEN OXIDES UNDERGROUND

Nitric oxide and NO_2 concentrations were measured during the years 1976 through 1979 for all underground OGs that were then in existence at the nine mines (Figure 1). A total of 3,422 full-shift measurements were made in 459 OGs (including 35 surface groups), by a method developed specifically to satisfy electrical safety regulations in coal mines (Dodgson et al. 1976). At least five complete-shift-average measurements of NO and of NO_2 were made for most of the underground OGs at each colliery.

Similar methods were used during the period 1980 through 1982 at four of the same nine mines, yielding 1,511 more underground measurements. Two of the latter four collieries were studied again in 1985. On that occasion, 54 full-shift samples were taken over 15 working days during a three-week calendar period at 11 and 13 locations, respectively, at two of the mines where measurements had been made during the 1976 through 1979 surveys.

The latter measurements of NO_x, in 1985, were accompanied by simultaneous assessments of airborne formaldehyde concentrations. These were determined by chemisorption of formaldehyde on Amberlite XAD-2 coated with 2-4-dinitrophenylhydrazine (Andersson et al. 1979). Laboratory analyses used gas chromatography-mass spectrometry with selected ion monitoring.

ESTIMATES OF CONCENTRATIONS OF NITROGEN OXIDES IN OCCUPATIONAL GROUPS THAT WERE NOT IN EXISTENCE WHEN MEASUREMENTS WERE MADE

The OG-specific mean concentrations of NO_x, as measured during the period 1976 through 1979, were regressed on explanatory variables that represented various colliery-specific mining factors and underground conditions that would be identifiable from computer files and manuscript records about OGs that had closed before 1976. The explanatory variables referred only to conditions underground, because very few measurements of NO_x had been made for surface jobs, and they did not include conditions associated with hand-filled coal extraction. The latter, premechanization, hand-filling methods had been phased out at all nine mines during the 1960s. The regression models chosen (Appendix B) explained 68 percent and 86 percent of the variation in the measured NO and NO_2 concentrations, based on 829 and 821 residual degrees of freedom, respectively (Table 2).

Table 2. Regression of Nitrogen Oxides Concentrations on Mining Variables: Analyses of Variance

	Nitric Oxide			Nitrogen Dioxide		
Source of Variation	SS[a]	DF[b]	MS[c]	SS	DF	MS
Regression	625.9	38	16.471	16.56	38	0.4358
Residual	279.3	829	0.337	2.43	821	0.0030
Total	905.2	867[d]	1.044	19.00	859[e]	0.0221
Percentage of variance explained	67.7			86.4		

[a] SS = sum of squares.

[b] DF = degrees of freedom.

[c] MS = mean square.

[d] A total of 424 underground OGs were sampled during the years 1976 through 1979. Mean concentrations for those 424 OGs were calculated, specific to the particular calendar year in which the samples were taken. This yielded 868 values of each regressand for analysis. Weighted least squares were used to estimate 38 mining variable regression coefficients (Appendix B), with the number of samples contributing to the mean concentrations as weights.

[e] A study of residuals from preliminary analyses of the NO_2 concentrations identified eight aberrant values. These values were omitted from the analysis recorded above, which was used to estimate NO_2 concentrations for unsampled OGs (Appendix B).

Calendar dates for when mechanical mining methods were established in each colliery were determined from manuscript records and reports compiled over the years by field staff in the Pneumoconiosis Field Research (Appendix C). Postmechanization OGs that had closed before 1976 were identified and classified with respect to the explanatory variables used in the regression analysis, and the corresponding NO and NO_2 concentrations were estimated from the fitted coefficients.

ESTIMATION OF MINERS' OCCUPATIONAL EXPOSURES TO NITROGEN OXIDES

Individuals' exposures to NO and (separately) to NO_2 at the nine collieries were estimated retrospectively by applying the same principle as that described above for determining exposures to respirable dust; that is, by summing the products of concentrations of each of those gases associated with particular OGs and the number of shifts worked by a miner in those OGs during the period concerned. Symbolically,

$$E_i(t) = \sum_j c_j(t)\, s_{ij}(t)$$

where $E_i(t)$ is the exposure for an individual i during a period t; c_j is the concentration of NO_x estimated for OG_j; and $s_{ij}(t)$ is the number of shifts worked by miner i during period t in OG_j. The units of exposure are ppm multiplied by number of shifts (ppm•shifts). One shift may be taken as approximately equivalent to 7.25 hours.

Another related measure of exposure is the time-weighted mean concentration of NO or of NO_2 that a miner experienced during a period t, that is,

$$C_i(t) = E_i(t) \,/\, \sum_j s_{ij}(t)$$

The units are ppm of NO (or NO_2).

Occupational exposures at the nine collieries were first calculated for the 560 miners in group A (Figure 2), with t referring to the precise calendar period, in 1976 through 1979, when the measurements were made at the collieries concerned. Those nine values of t ranged from 2.1 to 3.4 years and averaged 2.8 years, with individual miners working variable numbers of shifts ($\sum s_{ij}$) during those periods.

Estimates of miners' occupational exposures to, and time-weighted mean concentrations of, NO or NO_2 prior to 1976 were calculated similarly, by linking the Pneumoconiosis Field Research attendance record files of the s_{ij} with OG-specific estimates of concentrations. The periods (t) over which these retrospective estimates of exposure were made corresponded to the approximately five-year intervals between medical surveys at the colliery concerned. Estimates of cumulative occupational exposures, for analyses of responses from group B, were obtained by summing over all available five-year periods.

Exposures were calculated only for periods and activities for which the corresponding values of NO_x concentrations had been estimated from the regression analyses. Work on the surface, and on hand-filled faces, was always omitted. Men who had been engaged full-time in these activities in the relevant periods were excluded from analyses; those who had also worked in other activities were included, but with underestimated exposures. It was also impossible to estimate exposures at work prior to mechanization. Analyses of groups C and D were not affected, except through reduction in the combinations of colliery and survey in which analyses were made, but omission of work prior to mechanization led to further underestimation of the lifetime occupational exposures of several men in group B. Work during all premechanization periods, and later on hand-filled faces, involved higher underground levels of NO_x than subsequently (Appendix C), but to unknown and nonestimable levels. Therefore, the calculated values $E_i(t)$ underestimate individuals' full lifetime exposures.

The sensitivity of the estimates $E_i(t)$ to temporal variations in NO_x concentrations underground was assessed by comparing them with similar estimates based on NO_x concentrations that were found at four of the collieries during 1980 through 1982 and (at one mine) in 1985.

Further quantitative indices of individuals' exposures to NO_x were calculated by considering the proportions of time worked in nine different job categories, or types of OG, during a period T, that is,

$$P_{ik}(T) = s_{ik} \,/\, \sum_{k=1}^{9} s_{ik}$$

where s_{ik} is the number of shifts worked by a miner i during a period T in job category k, and where T may include time at work before mechanization ($T \geq t$).

Seven of the nine job categories were included in the retrospective estimation of concentrations of NO_x for OGs that had closed before 1976. The $P_{ik}(T)$, for k = "work on hand-filled faces", reflects relative lengths (though not intensities) of exposures that are likely to have been relatively high but that are not included in the $E_i(t)$ or $C_i(t)$.

INVESTIGATION OF THE RELIABILITY OF QUESTIONNAIRE RESPONSES ABOUT CHEST ILLNESSES

Relevant information was gathered in two stages. First, a stratified random sample was identified, consisting of 278 men who had attended the fifth medical surveys at the mines during the years 1974 through 1977. The stratification was by colliery and by the recorded responses to the question about chest illnesses; sampling within strata was designed to generate an approximately uniform distribution with respect to collieries, and to include some examples of all possible answers to the question about sickness absence, including 60 negative responses. Colliery medical officers were asked to provide, in confidence, details of certified sickness absences during the three years preceding the surveys for the individuals sampled.

Useful information was obtained from only two of the collieries. The sample sizes for those two collieries were, therefore, increased in the second stage of data collection. Similar information about sickness absence, but referring to a three-year period prior to March 1986, was also requested from one of the doctors for 432 miners who were employed in 1986 at one of the collieries. This anticipated a medical survey that had been scheduled at that mine for late February 1986, in connection with other research. The questionnaire that was to be used in this survey differed in some respects from that used at earlier surveys. Arrangements were made, therefore, to ask the standard question about chest illnesses, as in Appendix A, before any other questions about respiratory symptoms were asked.

Finally, two physicians were invited to examine independently the sampled miners' full-size postero-anterior chest radiographs that had been acquired at the surveys from which the questionnaire responses were obtained. The doctors were asked to record, in a standard manner, whether there was any obliteration of costophrenic angles, using the International Labour Organisation's (1980) convention, and to note whether there were any other radiographic signs consistent with the occurrence of a respiratory infection.

STATISTICAL METHODS

The estimates of NO_x concentrations for unsampled OGs were obtained from least squares analyses of results from the 1976 through 1979 surveys. Linear model facilities in the package GENSTAT (Alvey et al. 1977) were used, with each concentration measurement weighted equally.

Tabulations of data were produced with the facilities of the SIR data-base management system (Robinson et al. 1980), and graphical displays were made manually or with the aid of the SAS/GRAPHS package (Statistical Analysis System 1985).

The main statistical analyses of hypothesized associations between the binary response variables and the various potential risk factors were carried out with the use of the (unconditional) logistic regression programs from the BMDP statistical software package (Dixon 1983) or the generalized linear model facilities of GENSTAT. All analyses were colliery-specific and always included an intercept or constant term. Age and exposure to respirable dust were always included as explanatory variables, as were indicator variables for various smoking groups and an age-smoking interaction. One series of analyses of each data set included covariates referring only to time spent in various activities (and ignoring the available estimates of occupational exposure to NO_x). Then, in a second series, some of the covariates in time worked were replaced by estimates of occupational exposure to NO or to NO_2. Average results, over all collieries, were calculated from weighted means of fitted regression coefficients using the reciprocals of squared estimated standard errors as weights. Approximate relative risks were calculated by exponentiating regression coefficients or their weighted means.

In the cross-sectional type of analyses of responses from groups A, B, and C (Figure 2), the probability that an individual reported an infection was represented as a linear logistic function of the explanatory variables under study. For the analyses of longitudinal changes in group D, we adopted the general approach described by Muenz and Rubinstein (1985). Two independent logistic regressions were used to represent the probabilities of a change in the binary response between successive surveys. One analysis referred only to intervals that began with a denial that a relevant episode of respiratory illness had taken place. The other referred only to intervals that began with an indication that time off work with a respiratory infection had been taken during the preceding interval.

Unless otherwise specified, the term "statistically significant" in this report refers to a 5-percent level of significance.

RESULTS

RELIABILITY OF THE QUESTIONNAIRE RESPONSES ABOUT CHEST ILLNESSES

Sickness absence data were obtained for 69 men surveyed in 1975 at colliery Q, for 82 men surveyed in the same year at colliery Y, and for 404 men from colliery Y who were invited to attend the survey there in 1986. Of the latter, 78 did not attend, and the questionnaire forms for six others did not include an answer to the question about sickness absence. Thus there were available for analysis 151 pairs of data from the 1975 surveys and 320 from the 1986 survey.

The groups of data from the two surveys were considered separately because of the design-determined difference between the distributions of questionnaire responses among the men sampled. The 1975 data had been contrived to include a relatively high proportion (77 percent) of men who had replied positively to the question about chest illnesses. In contrast, only 34 (11 percent) of the 320 men seen at the 1986 survey replied positively to the same question (Table 3), a proportion unaffected by the original sampling plan.

The diagnoses on the sickness absence returns that were selected for the analysis referred to spells of absence of at least seven days' duration in the three years prior to the survey, irrespective of cause. Most men had experienced more than one such spell of absence. Results from 1975 and from 1986 referred, respectively, to 922 and to 800 spells (Table 3). Of these, 273 from 1975 and 10 from 1986 were not accompanied by a diagnosis, so they provided no information that could be compared with the responses in the survey.

In aggregate, about one-fourth (376) of the remaining 1,439 records referred to a respiratory or chest infection. Of these, 23 percent included specific reference to bronchitis. Influenza was mentioned on 41 percent of the 376 returns, and colds on 8 percent. Chest infections represented another 8 percent, and the remaining 20 percent referred to upper respiratory tract infections.

Table 3 shows an association between the miners' responses in the survey about the causes of their sickness absences in the preceding three years, and the causes of spells of absence as recorded by their physicians at the time. Note, however, that some individuals had several spells of absence with different diagnoses, and multiple spells with the same diagnosis; the enumerations in the various columns of Table 3 are not statistically independent.

Table 4, on the other hand, summarizes the data with the miners classified into mutually exclusive groups. The nine diagnostic headings for the columns in Table 3 are summarized into three headings in Table 4. The first two are plausibly interpretable as physicians' references to respiratory infections; a man was placed under the first heading if he had at least one spell of absence recorded as due to "bronchitis", "cold", or "influenza", and under the second heading if he had no spells due to any of those three but had at least one spell recorded as due to "chest infection" or "upper respiratory tract infection". The third heading indicates men whose records showed no sickness absence, or absence only for reasons unrelated to respiratory infections. The fourth column in Table 4 identifies men whose records showed at least one spell of sickness absence lasting seven days or more but with no diagnosis noted. It is not possible to determine whether or not these men had had absences due to respiratory infections. The replies to the questionnaire are summarized into three categories in Table 4: responses putatively interpretable as references to respiratory infections (that is, "bronchitis" or "cold" or "influenza"), other positive responses (mainly those classified at interview as "some other chest illness"), and negative responses to the survey question.

Table 3. Reliability of Questionnaire Responses: Physicians' Diagnoses of Causes of Sickness Absences for Spells of at Least Seven Days in a Sample of 471 Miners Who Gave Varying Responses at Survey to Questions About Sickness Absence

		Sickness Absence Diagnosis											
Medical Survey	Questionnaire Response	Number of Men Sampled	Bronchitis	Influenza	Cold	Bronchitis & Asthma	Asthma	Chest Infection	URTI[a]	Other Chest	Not Chest Infection	No Diagnosis	Total Number of Sickness Absences
1986	Bronchitis	13	15	7	0	0	1	5	5	0	40	3	76
	Influenza	6	0	4	0	0	0	1	2	0	24	0	31
	Cold	5	0	6	1	0	0	0	1	0	14	0	22
	Bronchitis & asthma	1	1	0	0	5	3	0	0	0	0	0	9
	Asthma	0	0	0	0	0	0	0	0	0	0	0	0
	Other chest	5	0	1	0	0	0	0	0	7	10	0	18
	Not chest	4	0	1	0	0	0	0	1	4	9	0	15
	Not absent	286	8	85	9	0	0	10	36	6	468	7	629
	Total	320	24	104	10	5	4	16	45	17	565	10	800
1975	Bronchitis	32	29	9	2	0	0	2	9	2	83	58	194
	Influenza	22	1	13	2	0	1	1	3	1	81	48	151
	Cold	25	5	11	11	0	0	1	11	0	85	42	166
	Bronchitis & asthma	1	0	0	0	0	0	0	0	0	5	0	5
	Asthma	1	2	1	1	0	0	0	0	0	0	1	5
	Other chest	36	23	5	1	1	2	6	8	23	79	66	214
	Not chest	0	0	0	0	0	0	0	0	0	0	0	0
	Not absent	34	3	11	3	0	0	1	2	0	109	58	187
	Total	151	63	50	20	1	3	11	33	26	442	273	922

[a] URTI = Upper respiratory tract infection.

Table 4. Concordance Between 471 Miners' Questionnaire Responses and Certified Sickness Absence Records

Medical Survey	Questionnaire Response[b]	Certified Sickness Absence[a] Record: Bronchitis, Cold, or Influenza	Chest or URT[c] Infection	No Absence Due to a Respiratory Infection[d]	Certified Absence with No Diagnosis	Total
1986	Bronchitis, cold, influenza	17	3	3	1	24
	No absence with chest illness	64	17	201	4	286
	Other response	3	1	6	0	10
	Total	84	21	210	5	320
1975	Bronchitis, cold, influenza	47	4	9	19	79
	No absence with chest illness	9	1	10	14	34
	Other response	12	10	8	8	38
	Total	68	15	27	41	151

[a] For seven consecutive days or more.
[b] Response to question 9, Appendix A.
[c] URT = upper respiratory tract.
[d] "Respiratory infection" here includes diagnoses of bronchitis, colds, influenza, chest infection, and URT infection.

Both sets of data in Table 4 reflect the association between the grouped questionnaire responses and the groupings based on sickness absence returns. Diagnoses of respiratory infection in the preceding three years were recorded for 20 of the 24 men who in the 1986 survey reported absence due to bronchitis, cold, or influenza, and for 51 of the 79 men in the 1975 surveys. Excluding those who, in the absence of a diagnosis, could not be classified reliably, the proportions whose positive questionnaire response was supported by sickness absence returns were 87 percent in 1986 and 85 percent in 1975.

To the question in the survey about absence due to a chest illness, 286 men answered "no" in 1986. Sickness absence returns supported the negative response to the questions in 201 (70 percent) of these men. Nevertheless, almost 30 percent of the men who in 1986 answered "no" to the question on chest illness did have certified sickness absence with a respiratory infection of at least seven days in the preceding three years. Relatively sparse data from 1975 indicate, similarly, that 30 percent of the men reporting no absence for three years due to chest illness did have a diagnosis of respiratory infection in that time; the 1975 proportion rises to 50 percent on exclusion of those whose sickness absence records were ambiguous because of missing diagnoses.

An alternative way of viewing the information in Table 4 is to consider the distribution of questionnaire responses within particular sickness absence diagnoses (the column totals). For instance, the sum of the first two columns from the 1986 survey data (84 + 21 = 105) refers to men with diagnoses that may be regarded as referring to respiratory infections; only 20 of these 105 men gave survey responses indicating that they had been absent because of bronchitis, a cold, or influenza.

It would be misleading to make a similar calculation from the 1975 data, because of the stratified sampling plan that was used. However, an approximate adjustment of the raw 1975 survey data, taking into account the sampling fractions that were imposed in the original design, gave a result of about 20 percent, consistent with the later (1986) survey.

The low (about 20 percent) "sensitivity" of the "bronchitis, cold, or influenza" response (with respect to the broad grouping of diagnoses interpreted as respiratory infections) varies, depending on the particular diagnosis recorded by the physician. For instance, the 1986 data show that 15 (62.5 percent) of 24 diagnoses of bronchitis referred to men who at survey reported a chest illness due to bronchitis, cold, or influenza, as did six (37.5 percent) of the 16 diagnoses of chest infection (Table 3). On the other hand, the corresponding figures for diagnoses of influenza were 17 (16 percent) out of 104; for colds, one out of 10; and for diagnoses of upper respiratory tract infection, eight (18 percent) out of 45. It appears, therefore, that the men's assessments in the survey of what was or was not a chest illness were related to the specific conditions as diagnosed by their physicians; references on certificates to episodes of bronchitis or chest infections were more likely to be reported later as an absence due to a "chest illness" than were certified absences due to colds or influenza.

Negative responses to the question about chest illnesses in the 1986 survey were recorded for 201 of the 210 men whose sickness absence records included no reference to a chest infection. Adjustment of the raw data obtained about the men who were surveyed in 1975 suggested similarly high specificity of the questionnaire response, with at least 80 percent of the miners whose sickness absence records included no reference to a chest infection likely to answer "no" in a survey to the question of interest.

The smoking habits and mean ages of the subgroups identified in Table 4 are recorded in Table 5. This shows, among other things, less smoking and a lower mean age for the miners seen in 1986, as compared with those surveyed in 1975. Detailed analyses of these data (Appendix D) confirmed the statistical significance of the association between the questionnaire responses and diagnosed sickness absences. The analyses showed also that the lower mean age in those seen in 1986 was significantly more pronounced among those with sickness absences that had been diagnosed due to bronchitis, cold, or influenza, and in those with undiagnosed certified sickness absences. However, among those with diagnosed sickness absences, there were no significant differences in age or smoking habits between those who reported an absence in the survey and those who did not. The low sensitivity of the questionnaire response, with respect to physicians' diagnoses of respiratory infections, is therefore not explicable in terms of confounding due to age or smoking habits. In particular, it can be verified from Table 5 that among the miners with diagnosed respiratory infections, smokers were not more liable to respond negatively in the survey than were nonsmokers.

Table 5. Smoking Habits and Mean Ages[a] of Subgroups of 471 Miners Described in Table 4

			Certified Sickness Absence Record				
Medical Survey	Questionnaire Response	Smoking Habit	Bronchitis, Cold, or Influenza	Chest/URT[b] Infection	No Absence Due to a Respiratory Infection	Certified Absence with No Diagnosis	Total
1986	Bronchitis, cold, influenza	Nonsmokers	4	1	0	0	5
		Other smokers	4	1	0	1	6
		Cigarettes	9	1	3	0	13
		Mean age (yr)	40.1	39.1	40.0	47.9	40.3
	No absence with chest illness	Nonsmokers	23	5	59	2	89
		Other smokers	9	4	60	0	73
		Cigarettes	32	8	82	2	124
		Mean age (yr)	38.3	39.2	42.0	36.0	40.9
	Other response	Nonsmokers	2	0	2	0	4
		Other smokers	1	1	4	0	6
		Cigarettes	0	0	0	0	0
		Mean age (yr)	36.8	39.7	46.5	0.0	42.9
1975	Bronchitis, cold, influenza	Nonsmokers	10	0	2	5	17
		Other smokers	13	1	3	5	22
		Cigarettes	24	3	4	9	40
		Mean age (yr)	49.2	49.6	39.2	49.6	48.2
	No absence with chest illness	Nonsmokers	1	0	3	2	6
		Other smokers	4	0	0	3	7
		Cigarettes	4	1	7	9	21
		Mean age (yr)	45.1	40.6	46.3	44.5	45.1
	Other response	Nonsmokers	0	4	2	0	6
		Other smokers	0	2	2	5	9
		Cigarettes	12	4	4	3	23
		Mean age (yr)	54.2	41.0	46.9	54.8	49.3

[a] The mean ages refer to all men in the three smoking groups.

[b] URT = upper respiratory tract.

Examinations of the chest radiographs from the miners whose questionnaire responses were compared with their sickness absence returns did not provide any useful information about the validity of the questionnaire (Appendix D).

The results may be summarized as follows:

1. References to bronchitis, to influenza, or to colds in answers to the survey question about sickness absences due to chest illnesses did, in general, reflect real spells of absence from work, lasting at least seven days, that had been diagnosed by doctors as due to one or another respiratory infection.
2. The percentage of "false positives" (the fraction of men who said that there had been an absence due to one or another of the three named conditions among those whose sickness absence records did not indicate such an occurrence) was low, probably in the order of 5 percent and certainly less than 20 percent.
3. The percentage of "false negatives" (the fraction of negative responses to the survey question among men whose sickness absence records indicated that there had been a spell of prolonged absence due to a respiratory infection) was high, on the order of at least 60 percent and possibly reaching 80 percent.
4. The low sensitivity of the group of responses that referred to spells of bronchitis, colds, or influenza was not related to the miners' ages or to their smoking habits. It was due primarily to miners' failure to volunteer positive responses when their physicians had provided certificates referring to colds, influenza, or upper respiratory tract infection. Absences certified as due specifically to bronchitis were followed more frequently by positive responses to the questionnaire, with most of them mentioning bronchitis; and bronchitis was the most frequently cited cause of sickness absence by those who replied positively to the question.

The findings suggest that the use of the triplet of questionnaire responses, referring to bronchitis, influenza, or colds as a single indicator of the likely occurrence of at least one spell of absence certified as due to a respiratory infection, may be acceptable for epidemiological purposes in this population, since this type of survey answer appeared to be fairly specific to the conditions of interest. Therefore, we adopted this approach for most of the analyses reported below, although it was recognized that the relatively low sensitivity of the index implied reduced statistical power to detect real relationships between the responses and explanatory variables. This issue, and that of possible biases arising from the convention adopted, is considered further in the Discussion section of the report.

CONCENTRATIONS OF NITROGEN OXIDES AND FORMALDEHYDE UNDERGROUND

Results from the three underground surveys of NO and NO_2 (during 1976 through 1979, 1980 through 1982, and in 1985) are summarized in Tables 6 and 7 as colliery-specific mean values associated with five types of mining activity: work on the coal face, development work, driving diesel vehicles, shot firing, and, finally, all other underground work. The higher levels of NO_x were associated, as expected, with shot firing and use of diesel engines. This affects the mean levels associated with the different collieries, since both shot-firing practice and diesel usage varied among collieries. (No diesel engines were used at four of them [Figure 1].) The statistical significance of the differences between collieries and between mining activities was confirmed by multiple regression (Appendix B). Those analyses also quantified the (significant) variations between collieries in the magnitudes of effects associated with the different mining activities.

The distributions of the individual measurements, aggregated over collieries, are shown in Figure 4 separately for the three calendar periods. The general patterns from the 1976 through 1979 and 1980 through 1982 surveys are similar: a marked positive skewness overall, with the upper 10 percent of both sets of results showing concentrations higher than 0.9 ppm NO and 0.07 ppm NO_2. Measurements in diesel cabins generated more uniform distributions over the whole range, and constituted a high proportion of the upper tails of the overall distributions. There were fewer high NO levels at the four mines sampled in 1980 through 1982, and there was an increase in average NO_2 concentrations at three of them. Tables 6 and 7 verify that reductions in levels of both gases at the later (1985) surveys reflect real changes at the two mines involved.

One-third of the 104 samples taken in 1985 for assessment of formaldehyde (HCHO) concentrations had levels below the laboratory detection limit (0.01 ppm). Nearly all (52 of 54) of the measurements at colliery Y showed concentrations of HCHO less than 0.2 ppm. At colliery Q, however, 26 of the 50 results exceeded 0.1 ppm, with 17 greater than 0.2 ppm. The highest level recorded at colliery Q was 2.9 ppm, in a sample taken near a coal-cutting machine operator at the face. The relatively high levels of HCHO at colliery Q were not connected with either shot firing or diesel usage, and there were no associations, generally, between the NO_x and HCHO measurements that were made at the two mines (Appendix E).

MINERS' EXPOSURES TO NITROGEN OXIDES AND THEIR REPORTS OF RESPIRATORY INFECTIONS

Four sets of data are described separately below, corresponding to the four groups of miners (A through D) identified in Figure 2.

Exposures and Responses in 560 Miners

Figure 5 shows the joint distributions of exposures [$E_i(t)$] to NO and to NO_2 over periods (t) averaging 2.8 years for 559 of the 560 men described by Robertson and colleagues (1984).

Table 6. Mean Concentrations of Nitric Oxide at Three Surveys[a]

Colliery	C	F	K	P	Q	V	W	X	Y
1976-1979									
Face workers	0.173	0.153	0.170	0.682	0.979	0.141	0.452	0.198	0.694
	(162)[b]	(205)	(175)	(246)	(308)	(243)	(248)	(94)	(328)
Developers	0.174	0.100	0.222	0.651	1.188	0.155	[c]	0.120	0.457
	(46)	(2)	(14)	(31)	(40)	(29)		(30)	(128)
Diesel drivers	-	-	-[d]	-	2.411	-	0.852	0.133	3.866
	-	-	-	-	(18)	-	(78)	(12)	(6)
Other underground workers	0.119	0.137	0.208[d]	0.263	0.913	0.117	0.497	0.158	0.452
	(77)	(79)	(103)	(63)	(114)	(41)	(78)	(77)	(71)
Shot firers	0.146[e]	0.140	0.252	0.958	2.053	-	0.390	0.168	-
	(129)	(5)	(23)	(12)	(19)	-	(30)	(22)	-
Total	0.155	0.148	0.191	0.614	1.073	0.139	0.529	0.169	0.641
	(414)	(291)	(315)	(352)	(499)	(313)	(434)	(235)	(533)
1980-1982									
Face workers	-	0.193	-	-	0.794	-	-	0.120	0.487
		(175)	-	-	(172)	-	-	(340)	(94)
Developers	-	0.204	-	-	0.505	-	-	0.210	0.612
		(11)	-	-	(15)	-	-	(92)	(21)
Diesel drivers	-	-	-	-	1.561	-	-	0.203	1.445
	-	-	-	-	(16)	-	-	(26)	(18)
Other underground workers	-	0.141	-	-	0.618	-	-	0.114	0.440
	-	(77)	-	-	(122)	-	-	(217)	(35)
Shot firers	-	-	-	-	0.603	-	-	0.123	-
	-	-	-	-	(12)	-	-	(65)	
Total	-	0.178	-	-	0.747	-	-	0.133	0.595
		(263)	-	-	(337)	-	-	(740)	(168)
1985									
Face workers	-	-	-	-	0.060	-	-	-	0.053
	-	-	-	-	(39)	-	-	-	(28)
Developers	-	-	-	-	0.217	-	-	-	0.070
	-	-	-	-	(3)	-	-	-	(5)
Diesel drivers	-	-	-	-	0.250	-	-	-	0.103
	-	-	-	-	(5)	-	-	-	(12)
Other underground workers	-	-	-	-	0.113	-	-	-	0.051
	-	-	-	-	(3)	-	-	-	(10)
Shot firers	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-
Total	-	-	-	-	0.091	-	-	-	0.065
	-	-	-	-	(50)	-	-	-	(55)

[a] Concentrations are given in ppm.

[b] The numbers in parentheses give the number of samples of NO taken.

[c] Development workers at colliery W were included with other underground workers since there was no reason to suppose that they would have been exposed to different levels of NO_x: the shot firing is carried out between shifts.

[d] Diesel drivers at colliery K were included with other underground workers.

[e] There was no specific occupational group for shot firers employed at colliery C during the sampling period. These 129 NO samples refer to a single occupational group that includes the jobs named "ringing, back-ripping, and repairing". The men concerned at colliery C worked underground, away from the face, and were exposed to some shot-firing fumes. Analyses of results from colliery C take account of this fact.

Table 7. Mean Concentrations of Nitrogen Dioxide at Three Surveys[a]

Colliery	C	F	K	P	Q	V	W	X	Y
1976-1979									
Face workers	0.026	0.025	0.029	0.046	0.059	0.029	0.034	0.031	0.047
	(162)[b]	(205)	(175)	(246)	(308)	(243)	(248)	(94)	(328)
Developers	0.021	0.025	0.034	0.076	0.065	0.024	[c]	0.033	0.043
	(46)	(2)	(12)	(31)	(51)	(29)		(30)	(128)
Diesel drivers	-	-	-[d]	-	0.355	-	0.118	0.021	0.837
	-	-	-	-	(18)	-	(78)	(12)	(21)
Other underground workers	0.021	0.026	0.029[d]	0.030	0.057	0.034	0.051	0.037	0.052
	(76)	(79)	(97)	(63)	(113)	(41)	(78)	(78)	(72)
Shot firers	0.023	0.012	0.028	0.046	0.096	-	0.044	0.028	-
	(128)[e]	(5)	(20)	(12)	(19)	-	(30)	(22)	-
Total	0.024	0.025	0.029	0.046	0.070	0.029	0.053	0.032	0.077
	(412)	(291)	(304)	(352)	(509)	(313)	(434)	(236)	(549)
1980-1982									
Face workers	-	0.036	-	-	0.057	-	-	0.044	0.063
	-	(176)	-	-	(172)	-	-	(340)	(94)
Developers	-	0.061	-	-	0.060	-	-	0.078	0.117
	-	(11)	-	-	(15)	-	-	(92)	(21)
Diesel drivers	-	-	-	-	0.256	-	-	0.078	0.527
	-	-	-	-	(16)	-	-	(27)	(18)
Other underground workers	-	0.047	-	-	0.077	-	-	0.050	0.096
	-	(77)	-	-	(122)	-	-	(217)	(35)
Shot firers	-	-	-	-	0.047	-	-	0.060	-
	-	-	-	-	(12)	-	-	(65)	-
Total	-	0.040	-	-	0.074	-	-	0.053	0.127
	-	(264)	-	-	(337)	-	-	(741)	(168)
1985									
Face workers	-	-	-	-	0.016	-	-	-	0.014
	-	-	-	-	(39)	-	-	-	(28)
Developers	-	-	-	-	0.020	-	-	-	0.010
	-	-	-	-	(3)	-	-	-	(5)
Diesel drivers	-	-	-	-	0.094	-	-	-	0.045
	-	-	-	-	(5)	-	-	-	(12)
Other underground workers	-	-	-	-	0.013	-	-	-	0.011
	-	-	-	-	(3)	-	-	-	(10)
Shot firers	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	-	-
Total	-	-	-	-	0.024	-	-	-	0.018
	-	-	-	-	(50)	-	-	-	(55)

[a] Concentrations are given in ppm.

[b] The numbers in parentheses give the number of samples of NO_2 taken.

[c] Development workers at colliery W were included with other underground workers since there was no reason to suppose that they would have been exposed to different levels of NO_x: the shot firing is carried out between shifts.

[d] Diesel drivers at colliery K were included with other underground workers.

[e] There was no specific occupational group for shot firers employed at colliery C during the sampling period. These 128 NO_2 samples refer to a single occupational group that includes the jobs named "ringing, back-ripping, and repairing". The men concerned at colliery C worked underground, away from the face, and were exposed to some shot-firing fumes. Analyses of results from colliery C take account of this fact.

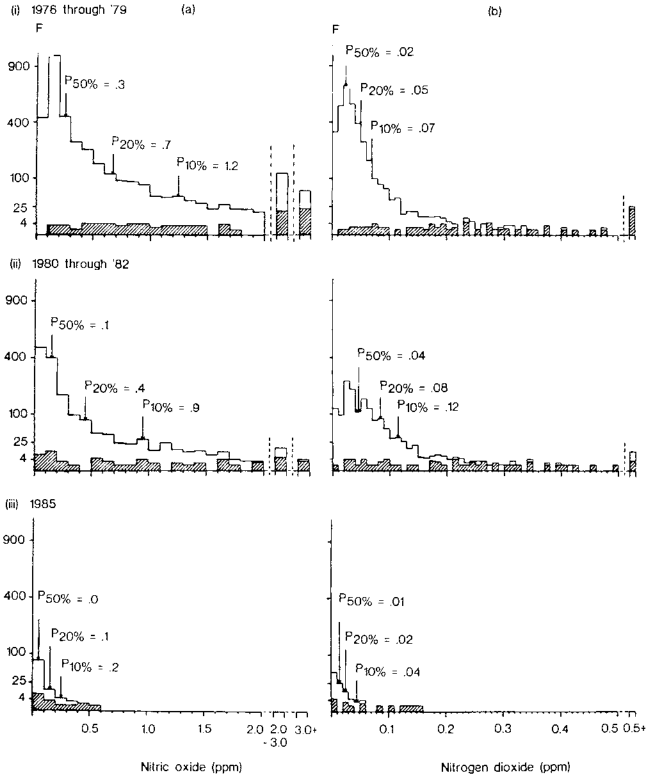

Figure 4. Distributions and selected percentiles (P) of (a) NO and (b) NO_2 concentrations: (i) at nine collieries (Figure 1), 1976 througb 1979 (n = 3,422); (ii) at collieries F, Q, X, and Y, 1980 through 1982 (n = 1,511); and (iii) at collieries Q and Y, 1985 (n = 105). Hatched areas indicate measurements in diesel cabins. Note that the ordinates of these graphs are linear with respect to the square roots of the frequencies (F).

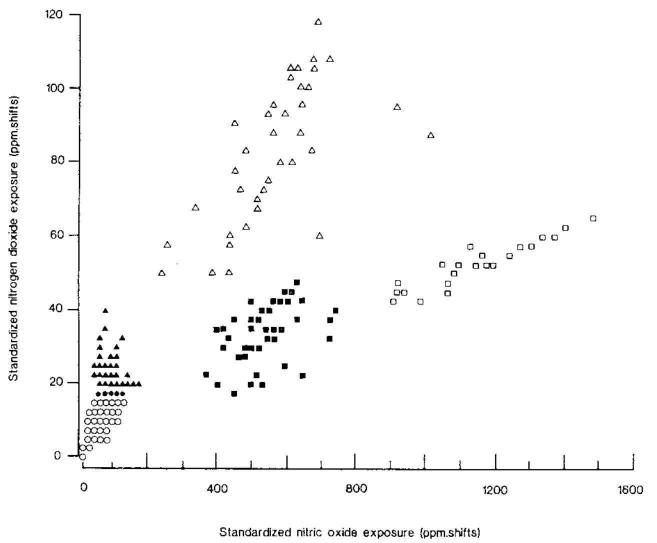

Figure 5. Joint distribution of 559 miners' exposures underground to NO and to NO_2, standardized to 2.8 years, the mean of the nine exposure periods (range: 2.1 to 3.4 years). Symbols show five subgroups, identified for later analyses; O = subgroup (i); ▲ = subgroup (ii); ■ = subgroup (iii); □ = subgroup (iv); Δ = subgroup (v); and ● = denotes coincident points.

(The work attendance records for the man not included in the analyses reported here referred to only 10 percent of the more than 70 shifts that he might have worked during the period concerned.) The corresponding average concentrations [$C_i(t)$] to which the men were exposed ranged up to 2.2 ppm NO and 0.16 ppm NO_2. The positive correlation between the men's exposures to the two gases was high but not complete. Figure 5 shows that, at various particular levels of exposure to NO, variations in the corresponding exposures to NO_2 are wide enough to permit estimates of the effects of both exposures separately. The scatter-plot suggests a clustering of the data into five areas on the graph, each representing different ranges of ratios of exposures to the two oxides of nitrogen ($NO:NO_2$). These clusters are identified (arbitrarily) in Figure 5 as subgroups (i) through (v). The corresponding five ratios of mean concentrations experienced [$C_i(t)$] are 4.9, 3.5, 15.2, 21.3, and 6.6 for subgroups (i) through (v), respectively.

The nine collieries contributed very unevenly to the five subgroups (Table 8). Two subgroups with high ($NO:NO_2$) exposure ratios are composed essentially of men who had worked at two of the mines where diesel engines were used, as was the other subgroup (v) in which exposures to NO_2 were relatively high. Note, however, that measurements of NO_x at one of the collieries where diesels were used (colliery K) were relatively low; 43 of those pairs of results are classified as group (i) in Figure 5, and 17 others as group (ii).

Table 9 records the smoking habits, mean age, and exposure to respirable dust and to NO_x of the five subgroups [(i) through (v)] in relation to selected responses to the question about sickness absence in surveys that were conducted just before or during the period when the NO_x measurements were made. This summary of the data does not suggest that relatively high exposures to NO_x were associated with more frequent reports of respiratory infections, but note the small numbers of men in subgroups (iii) through (v).

The impression of no association (Table 9) was examined rigorously in a series of logistic regression analyses. The dichotomous response variable was defined as positive if a cold, influenza, or bronchitis had been reported in the latest survey; all other responses were treated as negative. Explanatory variables, considered in sequence and in combination, included age, whether or not an individual was a smoker, colliery, cumulative exposure to respirable dust (with an allowance for possible variations between collieries in the effect of dust exposure), reports of early chronic bronchitic symptoms (that is, chronic cough and phlegm production) at the third round of surveys about 10 years earlier, level of forced expiratory volume in one second (FEV_1) also measured at the third round of surveys, exposures to NO and to NO_2 (the $E_i(t)$, standardized to t = 2.8 years), and the five distinct $NO:NO_2$ exposure ratio groups [(i) through (v)].

Table 8. Distribution of 559 Miners[a] by Collieries and Nitrogen Oxide Exposure Group

Colliery		Subgroup[b] (i)	(ii)	(iii)	(iv)	(v)	All Groups
C		126	7	0	0	0	133
F		87	3	0	0	0	90
K[c]		43	17	0	0	0	60
P		0	11	1	0	0	12
Q[c]		0	0	27	24	15	66
V		49	54	0	0	0	103
W[c]		0	0	0	0	14	14
X[c]		37	1	0	0	4	42
Y[c]		0	0	27	0	12	39
All collieries		342	93	55	24	45	559
Mean concentrations experienced (ppm)	NO	0.10	0.11	0.90	2.00	0.83	0.32
	NO_2	0.02	0.03	0.06	0.09	0.13	0.04

[a] Group A in Figure 2.

[b] Groupings based on realized exposures; see Figure 5.

[c] Diesel engines used at these collieries.

Table 9. Characteristics of the 559 Coal Miners[a]

		Means (and SDs) of Exposures					Percent Whose Survey[b] Questionnaire Responses Indicated Absence from Work Due to:			
Subgroup[c]	Number of Men	Respirable Coal Mine Dust[b] (gh/m³)	NO[d] (ppm•shift)	NO_2[d] (ppm•shift)	Mean (and SD) Age[b] (yr)	Percent Smokers[b]	Colds	Influenza	Bronchitis	Any "Chest Illness"
(i)	342	152 (112)	53.1 (23.4)	11.3 (3.8)	47.1 (8.7)	77.5	1.8	2.3	12.3	27.4
(ii)	93	136 (95)	77.1 (26.2)	22.3 (4.5)	45.7 (9.8)	77.4	1.1	0.0	10.8	18.3
(iii)	55	181 (103)	519.0 (78.7)	34.6 (7.5)	44.3 (7.9)	83.6	1.8	1.8	0.0	16.4
(iv)	24	244 (103)	1125.4 (163.1)	52.9 (6.1)	46.2 (7.9)	79.2	4.2	4.2	4.2	20.8
(v)	45	127 (72)	542.5 (140.5)	83.0 (18.3)	47.1 (8.2)	71.1	2.2	2.2	2.2	8.9

[a] Group A in Figure 2.

[b] At fifth medical surveys (1974 through 1977).

[c] Groupings based on realized exposures, as illustrated in Figure 5.

[d] During NO_x sampling surveys (1976 through 1979), standardized to 2.8 years.

These analyses provided no evidence that the standardized exposures to NO or to NO_2, or their ratios, were related to the defined measure of response. The estimated effects of exposures to nitrogen oxides were trivial and did not differ significantly from zero (Table 10).

Differences between collieries in tendencies to elicit reports of respiratory infections were highly significant, associated with the geographical regions in which the mines were situated, but not with regional variations in diesel usage at the mines. Lower levels of FEV_1 at the earlier survey were also associated with significantly increased chances of a positive response ($t = 2.36$, $p < 0.02$), and there was a positive, but not significant, association between the response and earlier reports of chronic bronchitic symptoms. (The estimated relative risk was 1.7, with $p \approx 0.15$.)

Table 10. Estimates of Selected Coefficients from Two Logistic Regression Analyses of Probabilities of Reporting Colds, Influenza, or Bronchitis in Group A (Figure 2)[a]

	Variable	Coefficient	Standard Error
A	Constant	-3.01	1.18
	Age at fifth survey (yr)	0.036	0.020
	Exposure to NO (ppm•shifts)	0.0011	0.0019
	Exposure to NO_2 (ppm•shifts)	-0.0290	0.0195
B	Constant	-3.27	1.18
	Age at fifth survey (yr)	0.037	0.020
	Exposure group (ii) relative to (i)	-0.39	0.41
	Exposure group (iii) relative to (i)	-3.58	7.10
	Exposure group (iv) relative to (i)	-1.34	7.14
	Exposure group (v) relative to (i)	-3.79	6.98

[a] Also included in these analyses were eight dummy variables, representing the nine collieries involved, and a further eight colliery-specific cumulative dust-exposure variables. Differences between collieries (but not between dust exposures) were highly significant (see text).

Cumulative Exposures and Responses in 7,463 Miners

Cumulative exposures to NO_x were calculated for the 7,463 miners in group B (Figure 2), from the time that mechanization was introduced at the mine up to the latest of the medical surveys there. The median number of shifts contributing to the NO_x exposure estimates was 1,560, equivalent to approximately 6.5 years (assuming 240 shifts per working year). On the same assumption, the exposures to NO_x for 20 percent of these 7,463 men are estimated as having been accumulated over 11 years or more, and for 10 percent of them the results represent exposures during 15 years or more.

Estimates of individuals' partial lifetime occupational exposures to NO and to NO_2 were correlated positively within collieries; at two of them (collieries Q and Y), they were virtually indistinguishable statistically. At the other seven mines, the ratios of exposures to the two gases varied from about 5:1 to 16:1. Figure 6 illustrates the dispersion and the highest correlation (at colliery Y).

The sensitivity of these retrospective estimates of long-term exposures based on measurements made in the late 1970s, to fluctuations in NO_x levels during earlier years, was studied as follows. Further estimates of exposures to each of the two gases were calculated for non-coal-face workers from four mines where NO_x was sampled after 1979. The later measurements, from the 1980 through 1982 and 1985 surveys, were used to provide new estimates of the changed underlying colliery levels of concentrations of NO_x, and these figures were used to generate new cumulative exposure estimates, using the same algorithm as previously (Appendix B). The new estimates of exposures were highly correlated with the original values; the range of results is illustrated in Figure 7. (The new estimates are simple multiples of the original estimates when a miner worked in only one of the nine designated categories of mining activity. This was reflected in the large number of points that fell on distinct straight lines through the origin on various graphs similar to those illustrated in Figure 7. Men whose work histories were less homogeneous contributed data points between those straight lines.)

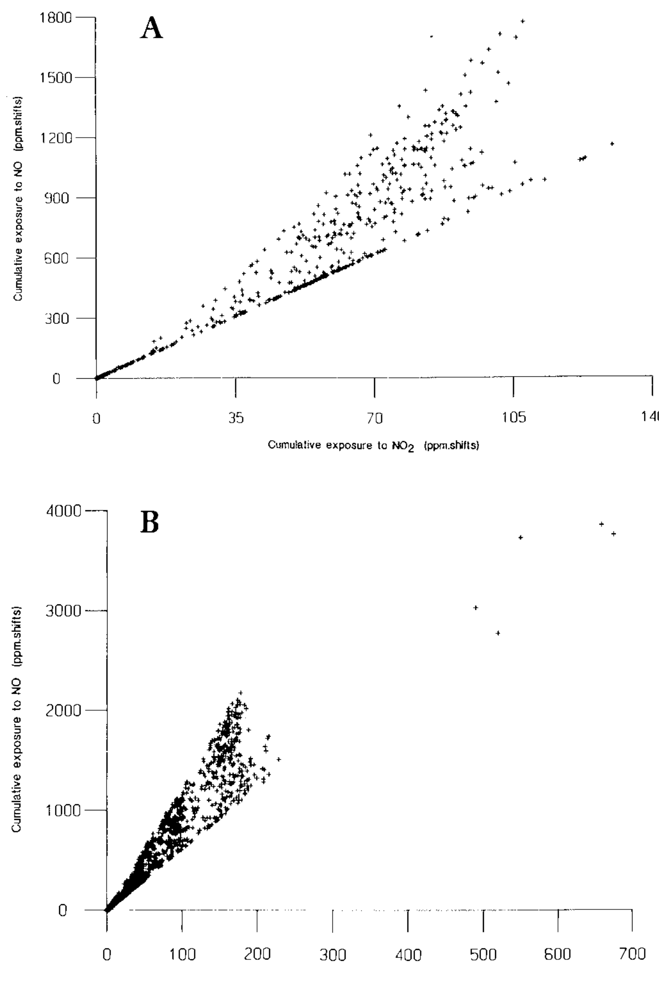

Figure 6. Joint distribution of estimated cumulative occupational exposures to NO and NO_2 at (A) colliery P, and (B) colliery Y, based on measurements of NO_x, 1976 through 1979.

Nearly a quarter of the miners in group B answered "yes" to the question about sickness absence in the latest survey, and 1,034 (14 percent of 7,463) referred to a cold, influenza, or bronchitis in their answer to the supplementary question (Table 11). On average, men in the latter subgroup worked more shifts on underground, as distinct from surface, jobs than the 5,702 miners who answered "no" to the question, but estimates of cumulative exposures to NO_x were very similar for the two groups. The results do not suggest that higher exposures to the NO_x were associated with more frequent reports of respiratory infections.

The 1,034 men who reported a cold, influenza, or bronchitis were, however, nearly six years older on average, and they included a higher proportion of smokers, than those who replied "no" to the question about chest illnesses. Inspection of colliery-specific tabulations, similar in structure to Table 11, showed that this aggregate pattern was apparent at eight of the nine collieries. Differences in mean exposures to NO_x between those who reported the infections and those who did not were small and not consistent in direction at the nine mines; and there were no consistent trends associated with average times worked in any of the nine major job categories contributing to the P_{ik}.

The aggregated results in Table 11 indicate that the mean cumulative exposure to respirable dust was lowest for those who reported no absences due to chest illnesses, 13 percent higher on average for those who reported absences due to colds, influenza, or bronchitis, and 24 percent higher for those who noted some other reason for their sickness absence. The same ordering of mean exposures to dust occurred at seven of the nine collieries, while at all nine mines the dust exposures for those who reported the infections were higher on average than for those who answered "no" to the question.

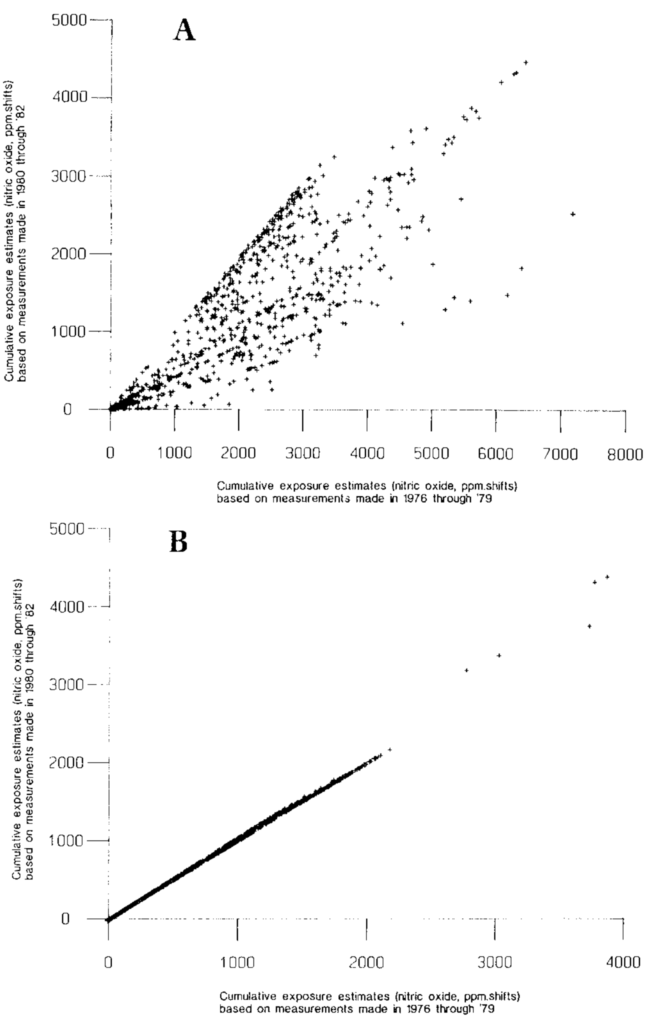

Figure 7. Joint distribution of estimated cumulative exposures to NO based on two environmental surveys at (A) colliery Q, and (B) colliery Y.

The binary response for logistic analyses of these data was defined as positive if a man referred to a cold, influenza, or bronchitis in his answer to the supplementary question, and negative if he answered "no" to the original question; other answers (the third column in Table 11) were ignored. All analyses included variables to adjust for the effects of age, of smoking habits as reported at the last survey (with allowance for an interaction between age and smoking, to reflect the cumulative effect of tobacco consumption), and of cumulative exposure to respirable coal mine dust from first to last survey. The possible additional effects of exposures to NO_x were considered using two approaches. First, variables were included to represent the number of shifts worked, from the first medical survey up to the last, in the nine different job categories that had been defined to estimate the NO_x exposures. The second approach used the cumulative exposures to NO (and in separate analyses, to NO_2) expressed as $E_i(t)$, with t referring to the time from mechanization up to the last survey. The latter analyses also included two additional explanatory variables: time worked on hand-filled faces [that is, time not contributing to the $E_i(t)$], and the total number of shifts on the surface plus those contributing to NO_x exposures (a variable likely, in general, to be correlated negatively with prolonged spells of sickness absence).

The results indicated a more than two-fold increase, with every 20 years of age, in the chance that a miner will report sickness absence due to a cold, influenza, or bronchitis. That gradient, averaged over all nine collieries, was similar for smokers and for nonsmokers (Figures 8 and 9) and was highly significant ($p < 0.001$). The average results showed, however, that at any age smokers were more likely to report those conditions than were nonsmokers. The relative risk was estimated as 1.45 (the same increase as for 10 years of age), and was also highly significant ($p < 0.001$).

Estimates of age- and smoking-adjusted relative risks that might be associated with exposures to respirable dust or to NO_x are also illustrated in Figure 9. When the results were averaged over collieries, there was no evidence that exposure to respirable dust was associated with the response. However, adjusted for age and smoking, the relative risk associated with total shifts worked at the colliery was less than unity ($p <$ 0.001), confirming the expected negative association between time worked and spells of sickness absence. Six of the nine relative risks associated with time worked in specific categories were also less than unity, but several were associated

Table 11. Characteristics of 7,463 Miners from Nine Collieries Who Attended the Latest Medical Surveys by Responses to the Questions About Sickness Absence[a]

	Response to Question About Sickness Absence Due to Chest Illnesses[b]			
		Yes		
	No	Cold, Influenza, or Bronchitis	Other Response	All Responses
Number of men	5,702	1,034	727	7,463
Mean age at survey (yr)	41.9	47.6	47.5	43.2
Smoking status distribution (%)[c]				
Cigarettes only	55.3	60.4	54.9	56.0
Other smoker	24.0	25.4	29.4	24.2
Life-long nonsmoker	20.7	14.1	15.7	19.3
Mean number of shifts worked on:				
Mechanized faces with some shot firing	657	697	834	680
Mechanized faces with no shot firing	87	88	78	86
Shot firing	100	144	125	109
Diesel driving	22	36	24	24
Development	118	121	112	118
Intakes of hand-filled faces	14	21	15	15
Other underground activities	886	952	929	899
Hand filling	109	134	145	116
Surface	607	427	482	570
Mean number of shifts contributing to NO_x exposure estimates	1,788	1,703	1,764	1,774
Mean cumulative exposures:				
To nitric oxide[d] (ppm•shifts)	539	482	505	528
To nitrogen dioxide[d] (ppm•shifts)	46	45	45	46
To respirable dust[e] (gh/m^3)	55	62	68	57

[a] The 7,463 miners are defined in Group B in Figure 2; the latest medical surveys are the fifth and sixth ones in 1975 through 1978.

[b] Question 9, Appendix 1.

[c] At time of survey; "other smoker" includes pipe smokers, cigar smokers, exsmokers, and those with mixed smoking habit; nonsmokers answered "no" to question 8.e in Appendix 1.

[d] The $E_i(t)$, averaged over the number of men indicated in the first row of the corresponding column of the table, with t varying between collieries from 4 to 16 years.

[e] From first to latest surveys; that is, periods ranging from 19 to 25 years and averaging 21 years for the nine collieries.

with wide confidence limits, reflecting substantial residual variability within collieries (Appendix F), attributable to the relative sparsity of data for these categories. Time worked on the surface was, however, significantly and negatively associated with the measure of response, and the negative associations with time in development and time elsewhere underground were close to the conventional 5-percent significance level.

On the other hand, variables reflecting exposure to NO_x showed no evidence of an association with the response. Averaged over nine collieries, the relative risks associated with exposure to 100 ppm•shifts of NO, or to 10 ppm•shifts of NO_2, were each estimated as 0.99. The associated confidence intervals were narrow (Figure 9); indeed, the average estimates were so precise that an elevated relative risk as small as 1.02 for 100 ppm•shifts of NO, or 1.03 for 10 ppm•shifts of NO_2, would have been detected as significant at the 5-percent level. This precision reflects the findings within collieries, where, almost uniformly, there was again no evidence that might be interpreted as indicating that exposures to NO or to NO_2 were associated with more frequent reports of colds, influenza, or bronchitis (Appendix F).

Exposures and Responses in 19,901 Miners

The 40,071 answers to the question about sickness absence from miners in group C (Figure 2) included 5,408 (13 percent) with references to colds, influenza, or bronchitis, and another 3,365 (8 percent) with other positive responses. Men who answered "yes" to the question were seven years older on average, were less likely to be lifelong nonsmokers, were more likely to have reported respiratory symptoms and sickness absences at earlier surveys, and were more likely to have low lung function and pneumoconiosis than were miners who answered "no" to the question (Table 12).

These differences are not easily explicable in terms of confounding between weak temporal trends in the type of

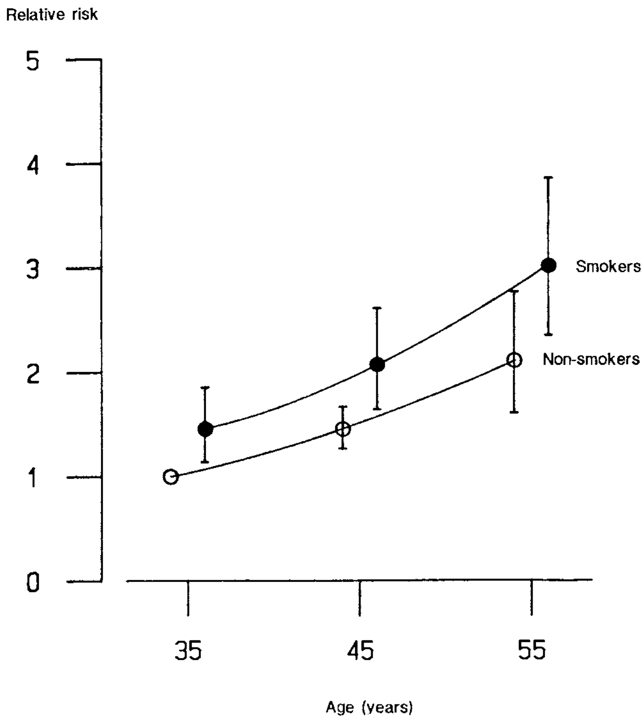

Figure 8. Estimated risks (with 95 percent confidence intervals) of reporting an infection, relative to a nonsmoking miner at age 35 years, based on data from group B.

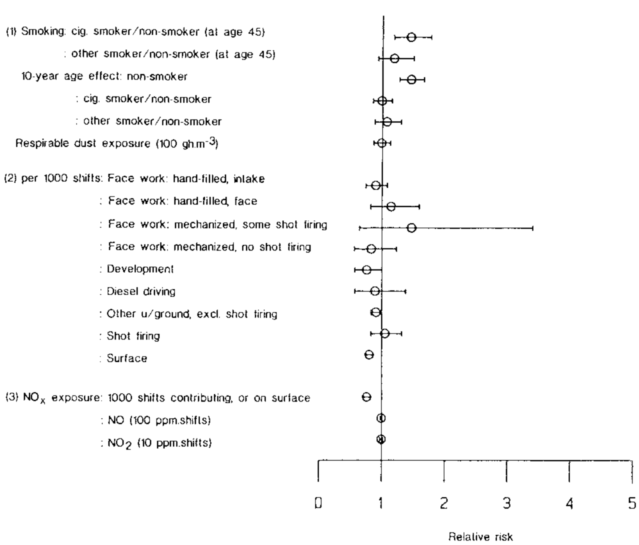

Figure 9. Relative risks (with 95 percent confidence intervals) of reporting an infection, using weighted means of estimates from nine sets of colliery-specific analyses of data from group B. Models (2) and (3) also included all terms in model (1); see text for more details.

survey answers volunteered (Figure 10) and the changing smoking habits and age distributions of the miners that were seen at the various surveys. The percentage of current cigarette smokers among those interviewed declined steadily over the years, from around 77 percent in the early 1960s to a little under 60 percent in the late 1970s (Figure 11). There was a corresponding increase in the proportion of men classified as other smokers, including exsmokers. The percentage of lifelong nonsmokers in this changing population also increased slightly, despite a small increase in the mean age of those interviewed at the separate surveys, from around 38 years at the start to 40 years on average at the last nine surveys, in the 1970s.

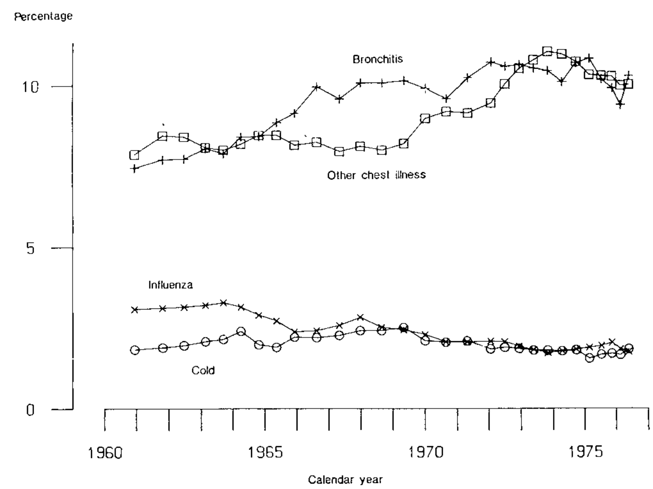

Figure 10. Percentage positive responses to question 9a, expressed as moving averages of nine consecutive surveys, by date of midsurvey.

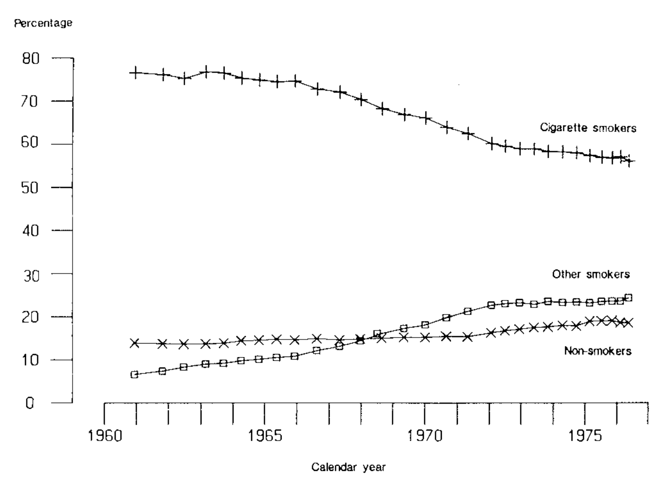

Figure 11. Percentage in smoking groups, expressed as moving averages of nine consecutive surveys, by date of midsurvey.

Table 12. Distribution of 40,071 Responses from 19,901 Miners from All Nine Collieries in Repeated Surveys to the Question About Sickness Absence[a] in Relation to Average Values of Potential Explanatory Variables

	Response to Question About Sickness Absence Due to Chest Illnesses			
		Yes		
	No	Cold, Influenza or Bronchitis	Other Response	All Responses
Number of man-surveys[b]	31,298	5,408	3,365	40,071
Mean age at survey (yr)[c]	41.4	47.8	48.8	42.9
Smoking status distribution (%)[c,d]				
Cigarettes only	68.2	70.5	68.8	68.5
Other smokers	14.8	18.0	19.0	15.6
Life-long nonsmokers	17.0	11.5	12.3	15.9
Prevalence rates (%) as determined at preceding medical surveys[e]				
Sickness absence attributed to colds, influenza, or bronchitis[a]	6.1	34.4	15.8	11.3
	(50.4)	(42.8)	(40.2)	(48.5)
Persistent cough or phlegm[f]	23.1	45.2	44.9	28.9
	(61.3)	(52.1)	(49.4)	(59.1)
Low FEV_1[g]	15.0	31.6	26.1	18.7
	(61.8)	(52.8)	(50.5)	(59.6)
Pneumoconiosis[h]	8.4	14.9	26.8	11.2
	(50.4)	(42.9)	(40.3)	(48.6)
Mean of time-weighted mean concentrations of respirable dust to which miners were exposed in the preceding (approximately five-year) intervals (mg/m^3)	2.7	2.8	2.6	2.7
Mean number[i] (and percentage of man-surveys contributing to mean) of shifts worked on:				
Mechanized faces with some shot firing	468	408	403	455
	(49.3)	(48.3)	(47.3)	(49.0)
Mechanized faces with no shot firing	213	213	193	212
	(11.7)	(13.7)	(12.4)	(12.0)
Shot firing	186	182	188	186
	(21.7)	(28.8)	(26.7)	(23.1)
Diesel driving	98	121	133	106
	(6.5)	(10.2)	(8.7)	(7.2)
Development	105	84	79	100
	(36.8)	(38.1)	(33.5)	(36.7)
Intakes of hand-filled faces	91	110	119	95
	(10.3)	(8.8)	(8.2)	(9.9)
Other underground activities	471	505	534	481
	(76.6)	(79.4)	(81.1)	(77.4)
Hand filling	296	260	263	289
	(19.0)	(16.5)	(16.4)	(18.4)
Surface	452	404	393	440
	(49.4)	(48.8)	(46.3)	(49.0)
Mean number of shifts in the preceding intervals contributing to the NO_x exposure estimates[j]	268	302	306	276
Mean exposure (ppm•shifts)				
To nitric oxide	338	293	274	325
To nitrogen dioxide	30	30	26	29
Mean of time-weighted mean concentrations of NO_x to which miners were exposed in the preceding (approximately five-year) intervals (ppm)[k]				
Nitric oxide	0.48	0.42	0.40	0.47
Nitrogen dioxide	0.048	0.042	0.040	0.047

[a] Question 9, Appendix A.

[b] The number of man-surveys in any one column provides the denominator for the corresponding average age and smoking statistics tabulated below. It includes more than one response from individuals who were interviewed on more than one occasion.

[c] As determined at the survey where the response about sickness absence was established.

[d] At time of survey; "other smoker" includes pipe smokers, cigar smokers, exsmokers, and those with mixed smoking habit; nonsmokers answered "no" to question 8.e in Appendix 1.

[e] The preceding medical surveys took place about five years before the surveys when the answers to the question about sickness absence, used to classify the response into one or other of the three mutually exclusive groups represented by the first three columns of the table, were recorded. (Not all individuals who contributed to the total man-surveys recorded in the first row of the table attended the preceding surveys or provided valid data on those occasions.) The figures in parentheses show the percentage of the total man-surveys (row 1) that contribute to the prevalence statistics immediately above.

[f] From questions 1 through 4 in Appendix A.

[g] Low FEV_1 was defined as $KI < 0.6$, where KI (Khosla's index of FEV_1) = (ml FEV_1) × (years of age)$^{1/3}$/(cm height)^2. This index of timed forced expiratory volume is approximately independent of age and height (Khosla, 1971).

[h] Combined prevalence of all categories of pneumoconiosis (that is, 1, 2, and 3 of simple pneumoconiosis and A, B, and C of progressive massive fibrosis) (International Labour Organisation, 1980).

[i] The denominators for the mean number of shifts worked refer only to man-surveys for which nonzero numbers of shifts were allocated to the job category concerned. (Each denominator, expressed as percentage of the total man-surveys in the first row of the table, is shown in parentheses.)

[j] The shifts contributing to the NO_x exposure estimates do not include those worked on hand-filled faces or on the surface.

[k] The $C_i(t)$, averaged over all relevant intersurvey intervals where exposures to NO_x were calculable.

The differing patterns of age and of smoking status among the men who answered differently to the question about sickness absence were also not due to confounding by collieries, or with diesel usage at some of them (Figures 12a and 12b). However, miners' reports of absence due to colds, influenza, or bronchitis followed fairly closely the general sickness absence patterns in the coal fields where the mines were located (Figure 12c).

The overall mean levels of the variables likely to be associated with occupational exposures to oxides of nitrogen during the five-year periods preceding the medical surveys showed no clear or consistent pattern to suggest a relationship between the exposures and responses. Average time worked on diesel engines was 23 percent and 36 percent higher, respectively, for those who reported colds, influenza, or bronchitis, and for those who offered other positive responses, compared with men who gave negative responses (Table 12). But the mean number of shifts spent on shot firing was very similar in these subgroups. The estimates of exposures to NO_x, expressed as mean $E_i(t)$, and the means of the corresponding individually experienced average concentrations at the workplace [the $C_i(t)$, in ppm] were lower, rather than higher, among those who replied positively to the question as compared with those who answered "no" (Table 12).

Colliery-specific results, aggregated over all relevant surveys (Table 13), showed no consistent pattern within collieries of mean exposures to NO_x and the type of response to the survey question, with one exception. At only one of the nine mines (K) was the mean exposure to NO for men who mentioned bronchitis more than that for men who answered "no" to the question. This draws attention to the possibility that the analysis of the combined index of positive response (bronchitis, colds, or influenza) might mask a real relationship between exposures to NO_x and either colds or influenza, if such relationships exist.

In general, however, the differences in average exposures between collieries (the last column in Table 13) were substantially greater than the differences within collieries. As expected, exposures to NO_x at the five mines where diesels were used were, on the whole, higher than at the other mines. But there was no obvious correlation between the nine colliery mean measures of exposure and the corresponding patterns of responses to the question about sickness absences.

Mean exposures to NO_x were examined further in some subgroups (Table 14) identified (from Table 12) as more likely to report prolonged sickness absences due to chest illnesses. There are no conspicuous differences in the ordering of mean exposures within the various rows of Table 14 and that recorded in the bottom row, which refers to all the available exposure data. In particular, the mean exposures among those whose earlier medical examinations indicated the presence of chronic obstructive lung disease (reports of persistent cough and sputum production, low FEV_1) do not suggest a positive relationship between the exposures and the chance of reporting sickness absences due to either bronchitis, or influenza, or colds in these conceivably more susceptible subgroups.

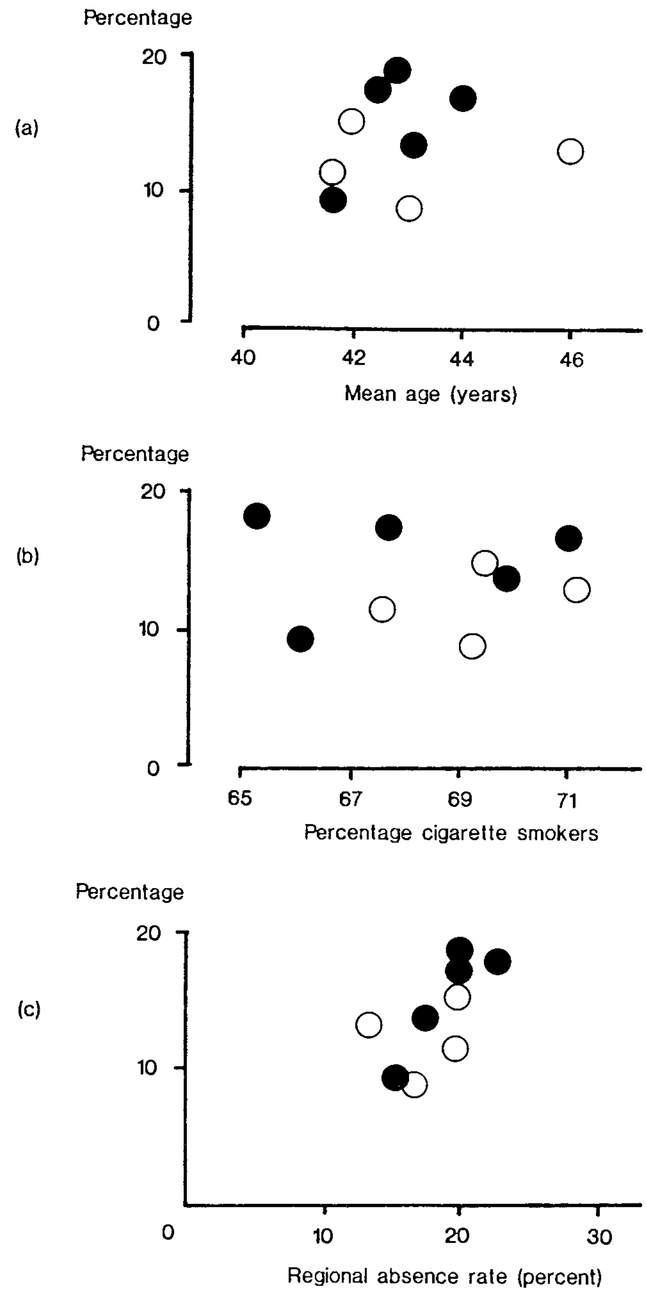

Figure 12. Colliery-specific percentages (aggregated over surveys) of men reporting absence due to infections in relation to age, smoking habit, and regional absence rates for 1971 through 1972 (National Coal Board, 1973). ● = mines with diesel usage; ○ = mines with no diesel usage.

Table 13. Mean Exposures to Nitric Oxide and Nitrogen Dioxide at Nine Collieries and the Numbers of Man-Surveys on Which They Are Based, for Different Responses to the Question About Sickness Absence

		Response to Question About Sickness Absence Due to Chest Illnesses[a]					
			Yes				
Colliery		No	Bronchitis	Influenza	Cold	Other Response	All Responses
With diesels							
K	MS[b]	1,079	225	32	35	145	1,516
	E(NO)[c]	124	133	93	119	118	124
	$E(NO_2)$[d]	15	16	11	15	14	15
Q	MS	1,715	146	36	38	151	2,086
	E(NO)	1,014	932	830	1,304	1,021	1,011
	$E(NO_2)$	49	46	39	58	47	48
W	MS	200	28	8	9	29	274
	E(NO)	380	317	443	448	338	373
	$E(NO_2)$	30	26	33	38	26	30
X	MS	2,009	430	52	71	299	2,861
	E(NO)	212	205	253	198	211	211
	$E(NO_2)$	26	25	32	24	26	26
Y	MS	2,831	367	140	75	264	3,677
	E(NO)	381	370	444	359	337	379
	$E(NO_2)$	44	48	57	40	42	45
Without diesels							
C	MS	798	84	13	13	77	985
	E(NO)	82	82	87	94	83	82
	$E(NO_2)$	11	11	12	12	11	11
F	MS	913	170	25	20	223	1,351
	E(NO)	93	85	88	121	104	94
	$E(NO_2)$	14	14	12	17	16	14
P	MS	1,101	82	19	14	129	1,345
	E(NO)	287	261	302	301	258	283
	$E(NO_2)$	25	23	28	26	23	25
V	MS	1,265	157	35	16	189	1,662
	E(NO)	82	72	82	87	88	82
	$E(NO_2)$	16	16	17	18	19	17

[a] Question 9, Appendix A.
[b] MS = man-surveys.
[c] E(NO) = mean exposure to nitric oxide (ppm•shifts).
[d] $E(NO_2)$ = mean exposure to nitrogen dioxide (ppm•shifts).

The tendency for men who mentioned bronchitis in their answers to the survey question to have had lower mean exposures to NO_x than men who answered "no" is evident again in Table 14, but note that separate horizontal sections of that table do not refer to mutually exclusive sets of men or man-surveys.

The response variable for the first set of logistic analyses of individual data summarized in Table 12 was again defined as positive if a miner mentioned bronchitis, influenza, or a cold in his answer to the question, and negative if he answered "no". The models that were postulated also followed closely those investigated in the analyses of long-term cumulative exposures in group B, above. However, all measures of time worked and exposure referred only to the five-year periods immediately preceding the surveys; time worked in various categories was expressed as a proportion of total shifts worked (the P_{ik}), and exposures to NO_x were expressed in terms of the time-weighted average concentrations experienced [the $C_i(t)$, in ppm] rather than the $E_i(t)$. (The former indices are less sensitive than the latter to possible large fluctuations in

Table 14. Mean Exposures to Nitric Oxide and Nitrogen Dioxide in Selected Subsets of Man-Surveys

		Response to Question About Sickness Absence Due to Chest Illnesses[a]					
			Yes				
Subset		No	Bronchitis	Influenza	Cold	Other Response	All Responses
Cigarette smokers	MS[b]	6,956	1,060	215	172	893	9,296
	E(NO)[c]	333	262	384	354	275	321
	$E(NO_2)$[d]	30	28	43	31	27	29
Other smokers	MS	2,661	442	88	65	400	3,656
	E(NO)	381	282	298	451	287	358
	$E(NO_2)$	32	27	29	31	26	30
Lifelong nonsmokers	MS	2,293	187	57	54	213	2,804
	E(NO)	301	273	263	330	247	295
	$E(NO_2)$	27	30	26	30	25	27
Low FEV_1	MS	1,034	433	32	29	243	1,771
	E(NO)	335	267	207	288	254	304
	$E(NO_2)$	29	26	25	27	25	28
Persistent cough & phlegm	MS	1,684	607	57	50	452	2,850
	E(NO)	352	235	358	361	251	311
	$E(NO_2)$	30	24	30	30	25	28
Positive response at previous survey to question about sickness absence							
Bronchitis	MS	270	497	15	16	110	908
	E(NO)	271	264	357	314	287	271
	$E(NO_2)$	25	30	37	28	26	28
Influenza	MS	173	46	42	12	45	318
	E(NO)	357	309	262	499	338	340
	$E(NO_2)$	35	33	32	34	36	34
Cold	MS	134	36	8	17	35	230
	E(NO)	343	315	301	344	328	335
	$E(NO_2)$	31	29	36	30	28	30
Other	MS	371	138	23	23	255	810
	E(NO)	357	227	521	479	239	306
	$E(NO_2)$	33	25	82	42	25	31
Pneumoconiosis (all categories)	MS	704	183	50	32	288	1,257
	E(NO)	391	270	345	354	281	346
	$E(NO_2)$	40	33	42	41	31	37
All[e]	MS	11,911	1,689	360	291	1,506	15,757
	E(NO)	338	268	344	371	274	325
	$E(NO_2)$	30	28	37	31	26	29

[a] Question 9, Appendix A.

[b] MS = man-surveys.

[c] E(NO) = mean exposure to nitric oxide (ppm•shifts).

[d] $E(NO_2)$ = mean exposure to nitrogen dioxide (ppm•shifts).

[e] All man-surveys contributing to the mean exposures in Tables 12 and 13.

exposures experienced during the relatively short, five-year intervals considered now, simply because of prolonged absences from work.) Exposure to respirable dust was also expressed as a time-weighted average concentration, with either time contributing to this exposure, or total shifts worked at the colliery, also included in the analyses. Responses recorded at any one survey at each colliery were analyzed separately.

Estimates of effects associated with age and smoking (Figure 13) were broadly similar to those observed in group B. There

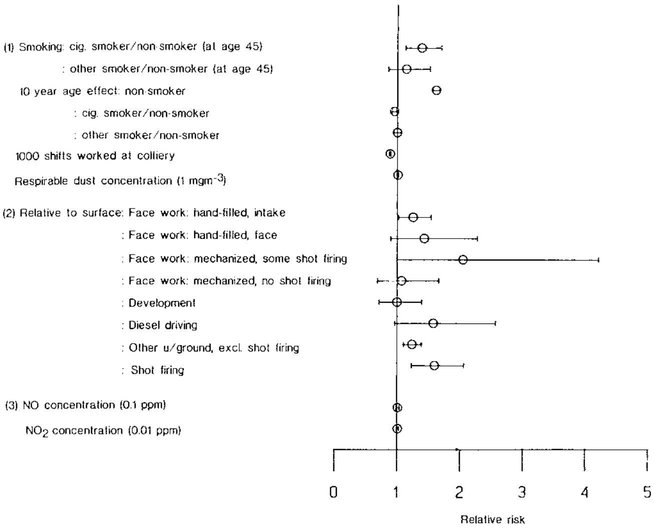

Figure 13. Relative risks (with 95 percent confidence intervals) of reporting an infection, using weighted means of estimates from 37 sets of colliery- and survey-specific analyses (18 sets for NO_x concentrations) of data from group C. Models (2) and (3) also included all terms in model (1), but with small changes to the time variable; see text for more details.

was, again, a highly significant age effect, estimated as a 2.5-fold increase with 20 years of age in nonsmokers; the increase with age in smokers was a little less. However, at age 45 the chances of reporting an infection were 1.4 times higher in smokers than in nonsmokers ($p < 0.001$). After adjustment for age and smoking, there was, again, highly significant evidence that reported absences were negatively associated with time worked at the colliery in the presurvey interval. Results averaged over all intervals and all collieries showed no evidence that exposure to higher concentrations of respirable dust increased the risk of response (Figure 13), while the narrow confidence interval shows that even a small average effect would have been detected. There was, however, some evidence of difference in dust effects between collieries and surveys, or both: the dust coefficient from six of the 37 separate analyses was significant; in three analyses a positive and in three a negative dust effect was suggested (Appendix F).

Relative risk associated with proportion of time spent in specific categories of work underground, relative to surface work, varied considerably between collieries, and often between surveys at a given colliery. The data were often sparse, with several of the 37 analyses yielding no information on particular categories, or giving estimates with very high standard errors (Appendix F); confidence intervals in Figure 13 are correspondingly large. Nevertheless, some patterns emerged clearly from the average results. In general, the estimated relative risks were high (relative to surface work), significantly so for shot firing ($p < 0.001$), less markedly, but also significantly ($p < 0.05$), for time in mechanized faces with some firing, and for work elsewhere underground. The higher relative risks were due mainly to results recorded at earlier medical surveys, in the 1960s, and there was also a downward trend, with time, in relative risk associated with work on hand-filled faces and in development.

Separate estimates (adjusted for concomitant variables) of relative risk associated with 0.1-ppm increments in concentrations of NO, and 0.01-ppm increments in concentrations of NO_2, varied between 0.38 and 1.70, with most values close to unity, and no tendency for the risk to increase or decrease over the years (Figures 14 and 15). On average, the estimated relative risks at these concentrations were again very close to unity (Figure 13), while the small confidence intervals again show the power of the study to detect even small increases in relative risk.

Further sets of logistic analyses were made with redefined binary response variables, as follows: (1) positive if a man mentioned influenza or cold, negative if he mentioned bronchitis; (2) positive if he mentioned influenza, negative if he answered "no" to the question; and (3) positive if he mentioned a cold, negative if he answered "no". The sets of explanatory variables were unchanged. The results, with respect to the effects of exposure to NO_x, were broadly consistent with those described above for the combined positive response (bronchitis, or influenza, or colds): no systematic or consistent pattern was found to indicate a significant increase in relative risk of any of the three named infections with increasing exposures to NO or to NO_2. For example, under (1) above, 17 combinations of colliery and survey were informative about NO_x; of these, relative risks greater than unity were estimated in eight analyses for increase in NO, and in seven for increase in NO_2 concentrations. None of the 34 coefficients was significant. Weighted averages overall suggested relative risks lower than unity, but not significantly so. However, a clear age effect was apparent, with older men at higher risk of bronchitis than of colds or influenza; there was no clear effect of smoking; and there was a significant positive association between response and number of shifts worked at the colliery (Appendix F).

Pairs of Responses in Consecutive Surveys and Intervening Exposures

Participation in at least two consecutive surveys by 11,039 miners in group D (Figure 2) generated 19,515 man-intervals, with records of responses to the question about sickness absence due to chest illnesses available at the start and end of the intervals. Positive responses referring to conditions other than bronchitis, influenza, or colds on either occasion, and intervening periods where records of attendance at work were not classifiable securely into the nine job categories, involved 2,835 man-intervals that are not considered further here.

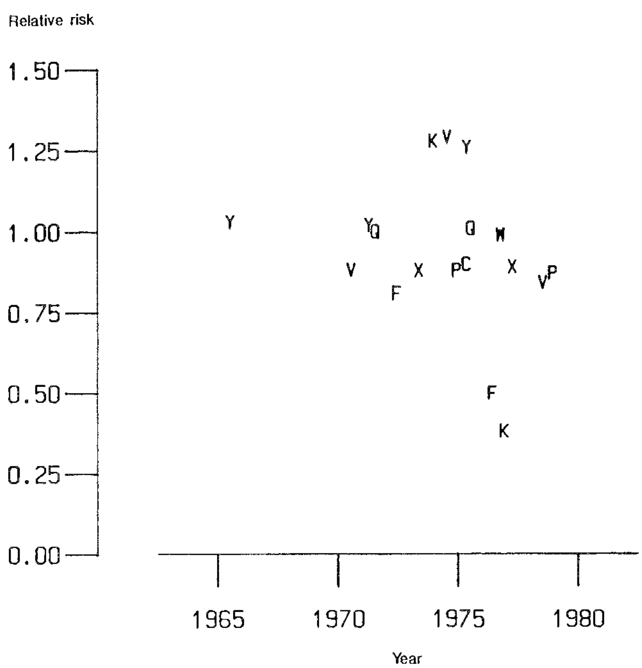

Figure 14. Estimated relative risks associated with 0.1 ppm NO during five-year periods prior to survey, from 18 colliery- and survey-specific analyses of group C, using model (3). Letters indicate colliery.

The remaining 16,680 man-intervals included 14,675 with negative and 2,005 with positive answers at the start. References to bronchitis or influenza or colds at the end of the intervals, about five years later, occurred nearly nine times more frequently in those who replied "yes" than in those who replied "no" initially (Table 15). The difference was clearly positively associated with age and with smoking, and was negatively associated with the mean number of shifts that had been worked during the interval. The proportion of time worked in different job categories, and the mean concentration of NO and NO_2 experienced by men who had worked during intervals for which NO_x exposures were calculable, were not obviously related to the responses.

Logistic regression analyses were made separately on two sets of pairs of consecutive answers, based on initial response to the question: those where the initial response was "no" and those where it was "yes" with reference to bronchitis, influenza, or colds. In both cases, the binary response variable was defined as positive if the second answer in the pair mentioned one or another of the three conditions. Analyses involving the proportions of time worked in different job categories [the $P_{jk}(t)$] used all man-intervals contributing to Table 15; those that included the exposures to NO_x, expressed as mean concentrations experienced during the intervals [$C_i(t)$], were based on the subset of intervals shown in the bottom row of Table 15. The regression models considered were identical with those for group C, except that time at the colliery, rather than time contributing to dust exposure (which includes exposure at other pits), was used in all the analyses. Data from the various collieries were analyzed separately. An age effect was shown clearly in both sets of analyses; the estimated relative risk among nonsmokers was a little less than two for an age increase of 20 years. Where the initial response was "no", cigarette smokers were estimated as having a slight excess risk of 1.17 at age 45, almost significant at the 5-percent level, with less difference in older men (Figure 16a). When the initial response was "yes", however, the estimated effect of smoking was 1.46 at age 45 ($p < 0.05$), and possibly increasing with age (Figure 16b). Neither set of analyses suggested an effect of dust concentration.

Overall time worked at the colliery was negatively associated with response in both analyses, and especially so where the initial response had also been "yes". In general, however, time spent in various job categories underground did not lead to risk estimates significantly different from those associated with surface work (Figure 16).

Figure 16 shows, further, that once again the risks associated with higher concentrations of NO_x were not significantly different from unity, whether the initial response had been "no" or "yes". And again, given the data, these analyses were powerful enough to detect a real effect. For example, the less powerful analyses, where the initial response was "yes", would

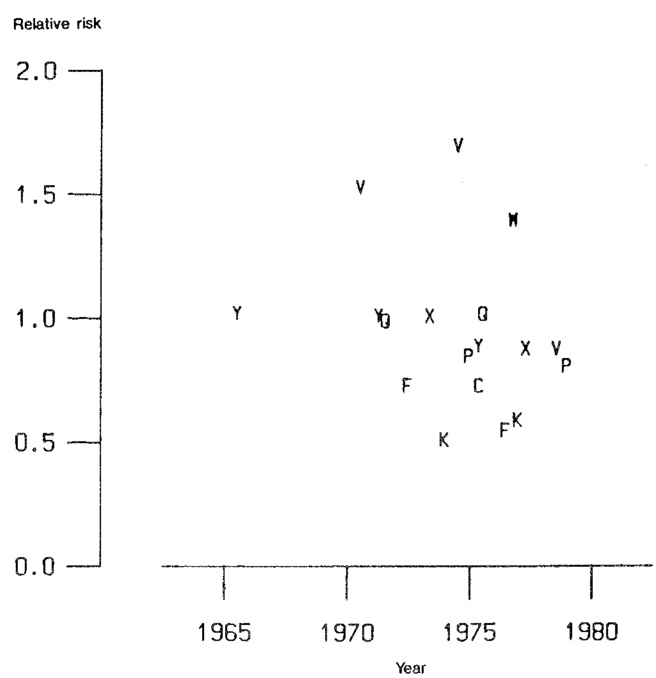

Figure 15. Estimated relative risks associated with 0.01 ppm NO_2 during five-year periods prior to survey, from 18 colliery- and survey-specific analyses of group C, using model (3). Letters indicate colliery.

nevertheless have detected as significant a relative risk of even 1.07 for each 0.1 ppm NO. Colliery-specific results where the initial response was "no" showed no clear or systematic trends in relative risk of NO or of NO_2 (Appendix F). Where the initial response was "yes", the risk estimates from most collieries were greater than unity. The weighted averages were, however, close to unity because, in absolute terms, the estimates of less than unity were evidently more precise and so were given greater weight.

DISCUSSION

The reliability and relevance of the results are discussed below under four broad headings: the indices of response, the measures of exposure, the search for a relationship between exposure and response, and the men that were studied.

RESPONSES

Integrity of the Questionnaire

The data that were used to test the reliability of the miners' answers to the question about sickness absence did not conform to the stratified sample (from collieries and types of answer) that was sought originally; data were returned from two collieries only. Nevertheless, it was possible to examine physicians' diagnoses on sickness absence certificates from more than 400 miners, including 123 who had named various conditions as the causes of the sickness absences that they reported. There was a clear and substantial degree of correspondence between what these miners recollected about prolonged sickness absences in the three years preceding the surveys and the facts as recorded in colliery medical records. We note, moreover, that this association was present in two separately acquired sets of data. The finding is not trivial.

Table 15. Distribution of 16,680 Pairs of Responses at Consecutive, Approximately Quinquennial, Surveys and Potential Explanatory Variables

	Response[a] to Question About Sickness Absence			
At start of interval	No		Yes	
At end of interval	No	Yes[a]	No	Yes[a]
Number of man-intervals	13,023	1,652	941	1,064
Mean age (yr)[b]	39.9	43.1	43.5	46.4
Smoking status distribution (%)[b]				
Cigarettes only	69.9	74.3	70.8	73.5
Other smokers	13.1	11.7	13.9	15.4
Lifelong nonsmokers	16.9	14.0	15.3	11.1
Mean concentration of respirable dust experienced in the interval (mg/m^3)	2.6	2.7	2.5	2.5
Proportion of time worked on				
Mechanized faces with some shot firing	0.28	0.26	0.22	0.22
Mechanized faces with no shot firing	0.03	0.03	0.04	0.03
Shot firing	0.04	0.05	0.06	0.06
Diesel driving	0.01	0.01	0.01	0.02
Development	0.05	0.04	0.04	0.03
Intakes of hand-filled faces	0.00	0.00	0.00	0.00
Other underground activities	0.36	0.40	0.39	0.45
Hand filling	0.02	0.02	0.02	0.01
Surface	0.20	0.19	0.22	0.17
Mean number of shifts worked in the interval	1,162	1,109	1,059	965
Mean of time-weighted mean concentrations experienced in the intervals				
Nitric oxide (ppm)	0.43	0.39	0.37	0.34
Nitrogen dioxide (ppm)	0.038	0.038	0.035	0.036
Number of man-intervals contributing to the mean NO_x exposure calculations	7,289	875	577	689

[a] Responses to questions 9 and 9a of Appendix A. "Yes" refers only to mention of bronchitis, influenza, or colds; other positive responses are not included in this table.
[b] At start of interval.

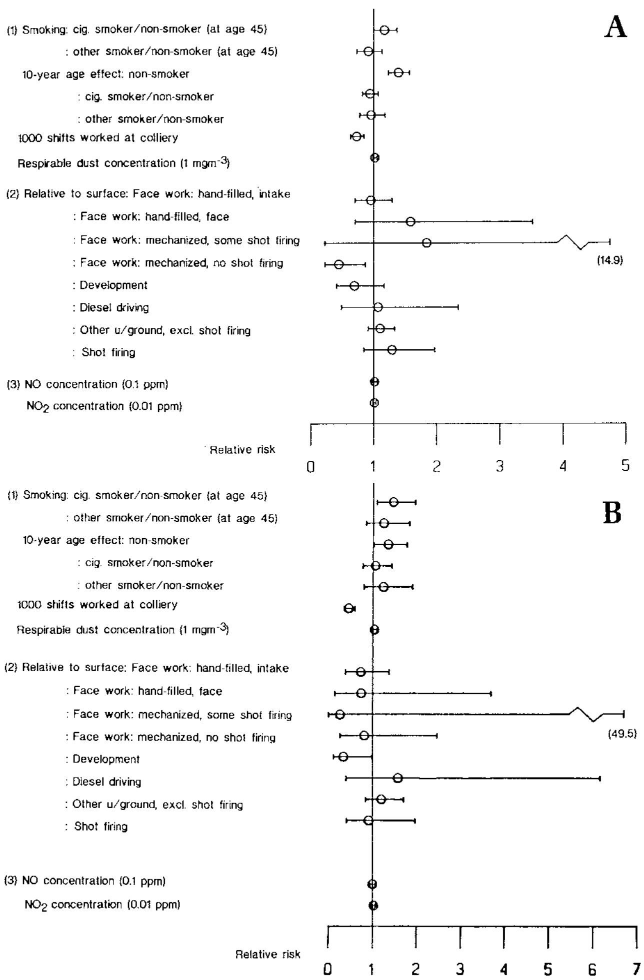

Figure 16. Relative risks (with 95 percent confidence intervals) of reporting an infection, using weighted means of estimates from nine sets of colliery- and survey-specific analyses of data from group D, where response at initial survey was (A) "no", and (B) "yes". Models (2) and (3) also included all terms in model (1); see text for more details.

Although the epidemiological validity of the miners' answers to questions about respiratory symptoms and smoking habits, using the same questionnaire, is well established (Rae et al. 1971; Robertson et al. 1984; Marine et al. 1988), the integrity of the answers to the question about sickness absences had not been documented previously.

The conclusion that the miners' answers about sickness absences are not simply random or capricious statements is consistent with results from the main study. Those who said that they had been absent due to a chest illness during the preceding three years included a disproportionately high number with chronic ill health, as determined from their responses to earlier questions about cough and phlegm, their levels of lung function, and the appearance of their chest radiographs. This finding contrasts with observations in studies of other industries, in which sickness absences have not been closely related to physiologically defined chronic ill health (Hinkle et al. 1961; Taylor 1968a,b). Taylor (1979) noted, however, that sickness absences were more likely to occur in workers with a history of such absences. Our results also demonstrate this serial correlation.

Only two of the nine collieries provided data for the comparison of miners' answers to the question with physician-certified sickness absence, and the main analyses showed that there were substantial differences between collieries in the way that miners answered the question. But there is no reason to believe that there are systematic differences between collieries in the degree to which miners' responses were accurate reflections of reality. Conclusions on that issue are not necessarily biased. We think that the results provide a useful, though not optimal, basis for quantitative statements about the epidemiological validity of answers to the question about sickness absences due to chest illnesses.

Validity of the Responses

References to bronchitis, influenza, or colds in the answer to the supplementary question following positive responses were, as a group, acceptably specific to absences certified as due to some form of respiratory or chest infection, with certainly less than 20 percent and probably only about 5 percent "false positives". But the epidemiological sensitivity of the combined index was low. A large proportion (up to 80 percent) of men with absences that had been diagnosed as due to a respiratory or chest infection did not acknowledge them in the surveys as an absence due to "a chest illness". This will have impaired power to detect relationships between respiratory infections, as diagnosed by physicians, and potential explanatory variables.

Low sensitivity did not, however, necessarily lead to biases in the main results. It is unlikely, for example, that it influenced the estimated relationships of survey response with men's ages and smoking habits, because the incomplete reporting was not associated with these characteristics. However, false negative responses were associated with absences that had been diagnosed as due to influenza or colds, rather than bronchitis. We examined, therefore, whether possible associations between episodes of influenza or colds and exposures to NO_x might have been distorted or obscured by considering only a combined index of positive response that included references to bronchitis. Our limited investigation of this question did not indicate any systematic differences between the relationship of NO_x exposure and the three individual infections considered separately. Combining the three types of answer as a single index of positive response is unlikely, therefore, to have biased the results, unless the under-reporting of episodes of influenza and colds was itself associated with exposures to NO_x. We can think of no plausible mechanism that might have generated such an association.

Relevance of Physicians' Diagnoses

The relevance of the chosen measure of response to the occurrence of respiratory infections depends, finally, on the degree to which physicians' diagnoses of these conditions, in the context of a busy general practice, correspond to real respiratory infections. Certainly there will have been some erroneous diagnoses. In the context of conditions that resulted in absences from work for at least seven days, it seems more likely that such errors would tend to be in the direction of doctors referring loosely to some ill-defined malaise as "influenza" or "cold", rather than misdiagnoses of acute respiratory conditions. If this speculation is sound, then it may be that the effect of the resulting bias, in over-diagnosing what we have regarded as respiratory infections, will have been reduced to some extent by the miners' tendencies, noted above, to underreport absences certified as due to influenza or colds.

In general practice, most respiratory infections are diagnosed on the basis of symptoms reported by the patient and clinical signs observed by the doctor; confirmatory laboratory tests on sputum samples are sought only rarely. We suggest, therefore, that if the aim is to assess the impact of motor vehicle exhaust emissions on public health generally, then physicians' diagnoses of respiratory infections must be considered an important part of the relevant evidence.

EXPOSURES

Reliability of Occupational Exposure Estimates

Estimates of concentrations of NO_x were based primarily on a series of systematic environmental surveys that provided 3,422 pairs of full-shift samples in 459 OGs during 1976 through 1979. Regression methods were used to estimate the mean concentrations experienced in OGs for earlier periods. The OG system had been designed to estimate dust concentrations; it was, therefore, not optimal for the estimation of levels of NO_x. Nevertheless, the regression models of OG mean concentration found in 1976 through 1979 accounted for very high percentages of the variation in the observed NO_x levels.

Implicit in the use of the 1976 through 1979 results to estimate miners' exposures to the gases in earlier years was the assumption that the relationship between mean concentrations and other characteristics of the OGs had remained stable over time. The validity of this assumption is not directly verifiable, but the sensitivity of the exposure estimates to temporal changes in mean levels of NO_x underground was examined in a limited way. The exposures were recalculated for some of the men, using results from post-1979 measurements of NO_x concentrations at four of the mines where there had been some real changes in mining practices (and NO_x levels) in the later years. The two sets of retrospective exposure estimates were highly correlated, suggesting that *relative* magnitudes of individuals' estimated exposures were not disturbed seriously by any changes underground that were not reflected in the multiple regression models.

Nevertheless, it is possible that the results from the surveys in 1976 through 1979 may have differed systematically from earlier (postmechanization) levels at some of the collieries. If so, then we think it likely that the earlier concentrations were underestimated, rather than overestimated. That suggestion is based primarily on what we know about how mining methods changed at the collieries over the years, and it is supported circumstantially by the data themselves. Time spent on jobs involving shot firing was associated with a highly significant increase in the probability of recording a positive response, and this result was due largely to high relative risks at some mines in the earlier period of research. Similar suggestions of downward temporal trends in relative risks were evident in some of the results for work on mechanized faces involved in shot firing, for work on hand-filled faces, and in development work. These activities are most likely to have been affected by any temporal reductions in levels of NO_x that may have taken place. In particular, concentrations of NO_x on hand-filled faces and in development work may have been reduced in the 1960s; some explosives in use during the early period of the research were known to be associated with levels of fumes sufficient to cause acute respiratory problems (Kennedy 1972, 1974), and they were, therefore, withdrawn from use during that period. (Note that time spent on hand-filled faces did not contribute to the estimates of miners' occupational exposures to NO_x.)

The higher relative risks associated with work involving shot firing in the earlier years of the study period may thus reflect, in part, an effect attributable to the (unmeasured) higher levels of shot firing fumes that we think are likely to have occurred then. If that conjecture is correct then this would strengthen, in two ways, our main conclusion: that exposure to the more recent, measured, concentrations of NO_x does not have detectable effects on the rate of occurrence of respiratory infections. In the first place, our interpretation of the downward temporal trend in relative risks would imply that the chosen index of response is sensitive enough to detect a real effect associated with relatively high exposure to fumes. Second, if the regression estimates of NO_x concentration for some unsampled OGs were indeed underestimated, as suggested, then any positive relationship between the response and the supposed exposure (based on measurements made in the late 1970s) will have been over- (rather than under-) stated.

Data on times worked in OGs were based on continuous monitoring, from the mid-1950s onward, of the men's workplaces, with a view to estimating their exposures to respirable dust. The estimated exposures are therefore based on much more detailed information than is generally available for epidemiological studies. We think they are acceptable estimates of the men's true exposures to NO_x underground at the nine collieries for the time periods to which they apply.

Importance of Nonoccupational Factors

Implicit in our efforts to quantify a possible gradient in responses related to occupational exposures was the idea that such an effect, if it exists, would be a guide to the kind of additional effect that might be expected from urban pollution, since the range of concentrations of NO_x that we found underground was similar to that recorded in some cities.

However, the occupational exposures that were estimated are only fractions, in many cases probably small fractions, of individuals' total exposures to NO_x. Total exposures would include those from domestic and outdoor sources, as well as smokers' self-imposed additional exposures. We consider two implications.

Suppose, first, that real effects due to nonoccupational NO_x exposures were substantial. In an extreme situation, the responses that were recorded might then correspond to those that would be expected in the upper (flatter) part of a true exposure-response curve, where small increments due to the relatively low occupational exposures would not be detectable. Limited analyses of data from smokers and nonsmokers support our view that such a situation is implausible. No separate regression analyses were made of data from smokers and nonsmokers, but the pattern of mean exposures for subgroups of lifelong nonsmokers, with different responses to the questionnaire, was similar to those found among cigarette smokers and other smokers. It seems unlikely, therefore, that the absence of a relationship between the occupational exposures and the responses of smokers and nonsmokers combined is due to the effect's having been overwhelmed by smoking-related responses among the smokers. We assume, therefore, that the potential response to NO_x of the men studied was not already exhausted by their nonoccupational exposures.

The relevance of the finding that there were no detectable effects of the occupational exposures depends, then, to a large extent, on how well the analyses of the data were able to take account both of the miners' unmeasured exposures to NO_x, and of other risk factors that might have confounding effects on the estimated risk associated with occupational exposures.

The inclusion of age, smoking habits, and exposures to respirable dust as concomitant variables in all the analyses that were undertaken was designed to make them more sensitive to effects that might be associated with the range of occupational exposures to NO_x that were experienced. Age and smoking were related to the occurrence of respiratory infections. After allowing for these factors, exposure to respirable dust was not related directly to the response, although the known consequences of high exposures to coal mine dust (pneumoconiosis, chronic obstructive lung disease) were associated with more frequent reports of respiratory infections. Both nitric oxide and nitrogen dioxide adsorb readily onto airborne coal mine dusts, but this does not enhance the cytotoxicity of those dusts or their main mineral components (Robertson et al. 1982). The absence of a demonstrable effect attributable to respirable coal mine dust exposure per se, in the analyses reported here, is consistent with the negative findings from the in vitro studies.

Unmeasured occupational exposures to NO_x, and ambient surface exposures, were also allowed for, very approximately, by including variables related to the time spent in these circumstances. Almost certainly, such representations do not reliably reflect the real complexity of factors that influence miners' reports of infections. However, inadequacies in the models would lead to a bias in the main results only if the poorly measured factors were both influential and correlated with the NO_x exposures as estimated, and there are no general considerations that lead us to think that any such correlations may have been important. The effect of physical work load underground, not included in the analyses, is a relevant example. It is known that associations between occupation and sickness absence may reflect the demands of physical work load rather than occupational exposure (Cornwall and Raffle 1961). And different types of mining work (for example, face work, other underground work, surface work) differ considerably in the physical demands that they make on the workers. This general finding was substantiated with respect to British coal miners by Buzzard and Liddell (1963). They concluded that the physical environment and the "effort of work" influenced both attendance at work and the age of retirement from work at the coal face. In practice, however, the environmental factors that they identified as important (air temperature, velocity, and the frequency of belt stoppages) were not important elements in the construction of our NO_x exposure indices. Buzzard and Liddell (1963) found no relationship between sickness absence and working height, dust or fume levels, or assessments of comfort. We think it unlikely, therefore, that omission of physical work load as an explanatory variable has distorted the results.

POWER OF THE STUDY

Types of Analyses

Various complementary approaches were used to analyze the data from four distinct (but overlapping) groups of miners. The small and highly selected group of men (A), studied previously by Robertson and associates (1984), was known to include, by design, extremes of exposures during relatively short three- to four-year periods. Those exposure estimates are likely to have been among the most reliable of all considered (they required no estimation of concentrations in OGs that were not in existence at the times concerned), and they referred to periods close in time to the medical surveys when the responses were obtained.

The study of single responses from the larger and less restricted group B, at the latest medical surveys, was intended to examine the idea that the effects being considered might be related to longer-term, cumulative occupational exposures to NO_x.

Consideration of multiple responses from group C, in relation to exposures in the corresponding approximately five-year periods preceding the medical surveys, was an attempt to systematically explore as much as possible of the potentially useful data. This, it was thought, would reduce possible biases due to over-restrictive population selection criteria.

Regression analyses that were made on subsets of the latter material referred to data from the 37 colliery-specific surveys at which the responses were recorded, and generalizations in terms of (weighted) average effects were made only when justified by the separate results. But the regression models that were used for the analyses of responses from group C did not incorporate an allowance for serial correlations between individuals' responses at successive surveys, although the tabular summaries of the raw data indicated that such correlations were positive and substantial. The analyses of pairs of serial responses from individuals, in group D, verified that this simplification had not obscured a relationship between the chosen measure of response and the five-year exposures to NO_x. The results, with respect to the exposures, from the subset of man-intervals that began with positive responses were consistent with those that began with negative responses, and the latter were, in turn, consistent with those found for groups C, B, and A.

Statistical Power

No formal assessments have been made of the statistical power of the analyses reported. However, there is indirect evidence of power. Statistically significant effects associated with cigarette smoking over the range of ages represented were detected, even though no estimates of amount smoked were made, and the estimate of relative risk for a 20-year increase in age among the nonsmokers was in the order of two in analyses of most groups, and very highly significant statistically. The results also provide direct evidence: given the data, even a small excess in relative risk (varying from 1.02 for 100 ppm•shifts of NO in group B, to 1.07 for 0.1 ppm NO in group D when the initial response was "yes") would have been detectable as significant at the 5-percent level. We think, therefore, that it is highly unlikely that failure to find a convincing relationship between the men's occupational exposures to NO_x and their reports of prolonged sickness absences due to respiratory infections was due to inadequate statistical power.

THE MINERS STUDIED

All the responses considered in this study were from working coal miners: men who were fit enough at the time of the surveys to cope with a physically demanding job. More than half of the data analyzed referred to men who had worked at the collieries for at least 10 years. None of the data were from men who had left the pits, possibly because of ill health, and there is no information from this study on how women, infants, or elderly people may react to the range of NO_x exposures that were considered. These caveats are important when considering the extent to which the findings may be extrapolated, because standards to control environmental pollution generally, and motor vehicle exhaust emissions in particular, must take into consideration possible effects on the health of especially vulnerable groups.

But the miners studied did include subgroups with clearly established chronic obstructive lung disease and with pneumoconiosis. The broad patterns of response to the estimates of exposure to NO_x in these possibly more susceptible groups, and in smokers, did not differ strongly from those observed generally, although the frequency of respiratory infections was substantially higher in these groups than in the other miners. Moreover, miners who had prolonged absences from work due to respiratory infections during any one three-year period were more susceptible than others to further such illnesses in a later period. Yet, the evidently more susceptible group showed no more convincing relationship between NO_x exposure and survey response than did the apparently less susceptible miners. It appears, therefore, that susceptibility to respiratory infections, as defined by our measures of response, was neither generated, nor increased, by the exposures to NO_x that were studied.

CONCLUSIONS

This work was stimulated by the Health Effects Institute's request for new information about the possible effects in humans of long-term exposures to NO_x (Health Effects Institute 1983). In particular, there was the question of the relationship between levels of NO_x, of the kind that might be found in urban environments that are polluted by motor vehicle exhaust emissions, and susceptibility to respiratory infections in individuals exposed. It was known that levels of these gases at some British coal mines had covered a range that included the kind of concentrations that might be found in some American cities (Robertson et al. 1984). The collieries concerned had been involved since the 1950s in a large-scale epidemiological study of coal miners' health, and all the accumulated data were available for further analysis. The plan was to combine the information about the occupational histories and concentrations of NO_x underground with the existing data about the respiratory health, smoking habits, working conditions, and exposures to respirable dust of the men who had worked in the mines. The central objective was to establish whether the miners' occupational exposures to NO_x had been associated with increased susceptibility to respiratory infections, as indicated by the men's responses in medical surveys to standardized questions about chest illnesses.

Positive responses were associated significantly with more time spent underground on work involving shot firing, and, to a lesser extent, with diesel driving, as compared with time spent at work above-ground. On their own, these observations do not convincingly implicate the NO_x-containing fumes that are associated with those activities, because positive responses were generally more frequent among men who had spent more time on underground (as distinct from surface) work, irrespective of whether or not that work was likely to be associated with relatively high levels of NO_x. Analyses that used quantitative estimates of individual miners' occupational exposures to NO and to NO_2, based on measurements made at the collieries in the late 1970s, showed that these exposures do not detectably increase the chances that miners will absent themselves from work because of chest infections. This conclusion supplements our previous results (Robertson et al. 1984), based on a more limited set of data, which did not show any adverse effect of the same range of concentrations of NO_x on the incidence of chronic bronchitis symptoms or the miners' respiratory functions. However, the results are consistent with the idea that exposure to concentrations of NO_x higher than those found at the mines in the 1970s may be associated with increased incidence of respiratory infections.

The absence of a detectable relationship between exposure to the concentrations of NO_x that were measured in the mines during the 1970s and what we think are useful indices of respiratory infection suggests that most working men are unlikely to develop these complaints as a result of exposure to similar concentrations of NO_x in urban environments. This study provides no information on how infants, children, women, or elderly people are likely to react to the same concentrations of pollutants.

ACKNOWLEDGMENTS

All the medical and exposure data used in this study are from the files of the Pneumoconiosis Field Research, which was funded, since its inception in 1953, by the British Coal Corporation. The surveys of NO_x underground from 1976 through 1982 were supported, in part, by a research grant from the Commission of the European Communities (Contract No. 7256-33/028/08). The Health Effects Institute commissioned the additional underground surveys at two mines in 1985 and all the statistical analyses reported here. We gratefully acknowledge the indispensable cooperation from various mine managers, and from colliery medical officers and many of our colleagues at this institute. In particular, we wish to thank Drs. Raymond Agius and Colin Soutar for film reading and medical advice; Dr. Sara Randall, for a comprehensive and critical review of the literature on industrial sickness absence data; Mr. Brian Miller, for the analysis of the results from the study of the reliability of the questionnaire responses; and Mr. Patrick Brown, for a major contribution to programming the computing of exposures to NO_x.

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APPENDIX A. The Respiratory Symptoms Questionnaire Used in the Pneumoconiosis Field Research

The facsimile reproduced here includes the instructions to the interviewer, and the format and numbering of questions, used in the research from 1970 onward. This version of the questionnaire differs in some details from that first described by Rogan and colleagues (1961) and Holland and coworkers (1966). (The latter paper provides a useful comparison with the 1960 version of the BMRC questionnaire.) However, the wording of the question about sickness absence due to chest illnesses (Question 9 on the version reproduced here) has remained unchanged throughout the research period.

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'

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

APPENDIX B. Estimates of Concentrations of Nitrogen Oxides in Unsampled Occupational Groups

Linear regression analyses of NO_x levels measured during 1976 through 1979 were used to estimate shift average concentrations of NO and NO_2 in most of the occupational groups that had not been sampled.

First, each occupational group was allocated to one of six broad categories of coal mining work (Figure B.1). The 1976 through 1979 data were uninformative about surface work and face work on nonmechanized coal faces; levels for these groups were not estimated, though concentrations of NO_x for hand-filled face work were likely to have been high. Then, colliery-specific estimates were made of base-line levels of NO_x in the five remaining types of activity (A through E in Figure B.1), with adjustments at five collieries for travel in diesel trains. Estimates were made by regressing the 1976 through 1979 NO_x data simultaneously on colliery-specific indicator variables for each activity A through E; on five variables giving distance traveled in diesels, where known, at collieries K, Q, W, X, Y; and on one indicator variable (common to all five collieries) for unknown distances traveled in diesels.

The estimated base-line levels (rows A through E of Tables B.1 and B.2) are simply the mean concentrations of all samples taken at that activity at that colliery, unless diesels had been in use. The effect of unknown traveling distance in diesels, estimated as 0.166 ppm for NO and 0.0216 ppm for NO_2, formed part of the adjustment for travel in diesels at the five collieries concerned (row K of the tables).

Estimates for face work on mechanized faces were refined further. Shift-specific records of mining practices were used to enumerate the number of locations where shot firing occurred routinely, upwind of the site of work of the specified occupational group. In most cases, a measure of the rate at which explosives were used in these locations[1] was also obtainable from coal output statistics and from the recorded dimensions of the coal face. Ventilation flow rates were also known for most coal faces.

Boxes F, G, H, and J (Figure B.1) symbolize the further adjustments for face work on mechanized faces, according to availability of coal output and ventilation data. The corresponding coefficients (not colliery-specific) are given in rows F through J of Tables B.1 and B.2. They were estimated by least-squares methods, as before, using regression models that included additional variables based on the number of shot firing locations upwind, the estimated rate of advance of the face, and the ventilation flow rate.

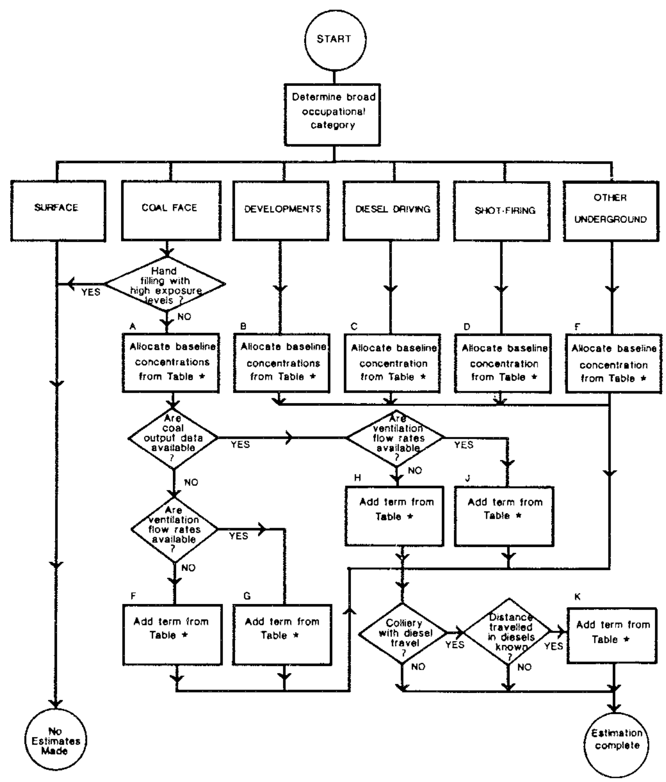

Figure B.1. The algorithm used to estimate concentrations of NO_x. The table referred to is B.1 or B.2.

[1] The word "locations" here refers to the sites indicated with the numbers 1 through 7 in the plan of a coal face (see Figure C.1). The amount of explosive used at any one location was assumed to be roughly proportional to the rate of advance of the coal face, which, in turn, is proportional to the volume of coal extracted and inversely proportional to the cross-sectional area of the coal face.

Table B.1. Coefficients Used to Estimate Colliery- and Activity-Specific Concentrations of Nitric Oxide[a]

	Colliery								
	C	F	K	P	Q	V	W	X	Y
Base-Line Concentrations									
A[b]	0.092	0.131	0.118	0.425	0.565	0.092	0.293	0.293	0.546
B	0.174	0.100	0.221	0.651	1.188	0.155	0.293	0.277	0.425
C	—	—	0.349[c]	—	2.411	—	0.852	0.349	4.520
D	0.146	0.122	0.252	0.958	2.053	0.003	0.390	0.293	0.546
E	0.119	0.125	0.218	0.263	0.908	0.120	0.497	0.374	0.452
Add for Coal-Face Workers (All Pits)[d]									
F	0.156 S								
G	0.313 S – 0.023 wS								
H	0.240 SA								
J	0.052 + 0.240 SA – 0.0198 wSA								
Add for Diesel Travel Where Known									
K	—	—	– 0.166 + 0.0144d[e]	—	– 0.166 + 0.0593d	—	– 0.166 + 0.0428d	– 0.166 + 0.0290d	– 0.166 + 0.0144d

[a] NO concentrations given in ppm.

[b] Letters refer to adjustment points in Figure B.1.

[c] No concentration measurements for diesel drivers were made at pit K. The figure quoted corresponds to that for pit X, at which conditions were most similar to those at pit K.

[d] S is the number of locations on the intake side of the place of work where shot firing occurs; w is the ventilation flow rate in m^3/sec; A is the rate of advance of the face; that is, output per shift (in tons) divided by the cross-sectional area of the face (in m^2).

[e] d is the distance traveled in diesel trains (km per shift).

Table B.2. Coefficients Used to Estimate Colliery- and Activity-Specific Concentrations of Nitrogen Dioxide[a]

	Colliery								
	C	F	K	P	Q	V	W	X	Y
Base-Line Concentrations									
A[b]	0.0221	0.0248	0.0276	0.0403	0.0732	0.0277	0.0515	0.0488	0.0628
B	0.0210	0.0250	0.0342	0.0760	0.0870	0.0240	0.0515	0.0506	0.0632
C	—	—	0.0425[c]	—	0.3767	—	0.1398	0.0425	0.8922
D	0.0230	0.0120	0.0276	0.0460	0.1175	0.0277	0.0660	0.0494	0.0628
E	0.0210	0.0260	0.0239	0.0300	0.0785	0.0214	0.0725	0.0589	0.0734
Add for Coal-Face Workers[d]									
F	0.0055 S								
G	0.0107 S – 0.000761 wS								
H	0.0071 SA								
J	–0.0001 + 0.0071 SA – 0.00046 wSA								
Add for Diesel Travel Where Known									
E	0.0210	0.0260	0.0239	0.0300	0.0785	0.0214	0.0725	0.0589	0.0734
K	—	—	– 0.0216 + 0.0038d[e]	—	– 0.0216 + 0.0056d	—	– 0.0216 + 0.0145d	– 0.0216 + 0.0169d	– 0.0216 + 0.0038d

[a] NO_2 concentrations given in ppm.

[b] Letters refer to adjustment points in Figure B.1.

[c] No concentration measurements for diesel drivers were made at pit K. The figure quoted corresponds to that for pit X, at which conditions were most similar to those at pit K.

[d] S is the number of locations on the intake side of the place of work where shot firing occurs; w is the ventilation flow rate in m^3/sec; A is the rate of advance of the face; that is, output per shift (in tons) divided by the cross-sectional area of the face (in m^2).

[e] d is the distance traveled in diesel trains (km per shift).

APPENDIX C. Sources of Nitrogen Oxides at Nine British Coal Mines

INTRODUCTION

This appendix outlines the developments in mining methods during the past three decades that are likely to have influenced NO_x levels underground, that is, from shot firing and from diesel engines. It is based on unpublished records of environmental conditions in the nine collieries and of the occupations of the work force, from 1954 to 1980 through 1982.

MINING METHODS AFFECTING NITROGEN OXIDES LEVELS

Coal-Face Technology

Almost all the coal extracted at the mines was from advancing long-wall faces (Figure C.1). Two parallel tunnels delimit the ends of the coal to be extracted. As the coal is removed, these tunnels are advanced together with the face. The roof behind the advancing face is allowed to collapse.

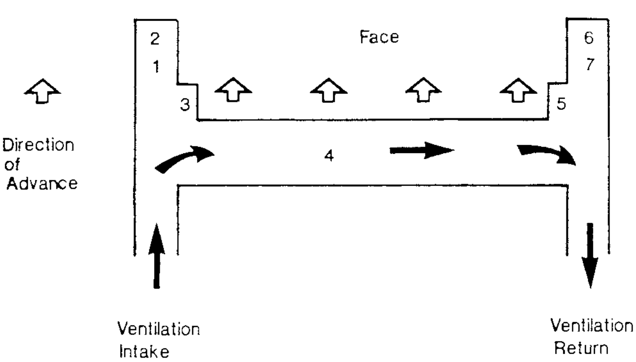

Figure C.1. Plan of an advancing long-wall coal face. 1 = intake ripping; 2 = intake advance heading; 3 = intake stable; 4 = face; 5 = return stable; 6 = return advance heading; 7 = return ripping.

At the start of the study period, coal was usually broken up with explosives and then loaded onto the conveyor by hand (hand filling). Tunnels (roadways) in other parts of the mines were also excavated with explosives. Men working on the face in the period just after the blasting had occurred, or when blasting was occurring on the intake side of their place of work, were thus exposed to high levels of fumes from explosives, but we have no measurements of corresponding NO_x levels.

By the late 1950s, machines that loaded the coal automatically (cutter loaders) were widely used in Britain. Normally electrically operated, some were driven by compressed air; several different models were used at the nine collieries. Considerable supplementary use of explosives was required initially, but not now. During the 1960s and 1970s (including 1976 through 1979, when NO_x levels were measured), explosives were generally used at the face ends (stables) to allow the machines to move forward, and to extend the tunnels at the end of the faces (ripping; see Figure C.1). These tasks have now been mechanized. Also, large mechanical heading machines capable of cutting hard rock have now almost entirely replaced shot firing in the development of new roadways, with the consequent decline in development workers' exposures to NO_x since the early 1970s.

Blasting Technology

Present-day explosives are designed to give minimum NO_x emissions, but in the 1960s at least one explosive (probably little used at the nine collieries) was known to give excessive fume (Kennedy 1972). Blasting technology also improved throughout the period, generally with less fume emissions and probably lower NO_x levels. However, some blasting techniques in the 1950s and 1960s used compressed air or carbon dioxide, giving rise to no fumes at all.

Ventilation

Ventilation rates in coal mines have gradually increased, mainly to reduce explosion hazards. This increase in ventilation has reduced dust levels and has led to more rapid dilution and dispersion of shot-firing fume. Detailed records of ventilation rates are available for many coal faces.

Use of Diesels

Diesel engines were used for hauling men and materials at five of the nine collieries. The same engines were operated in these mines for long periods.

OCCUPATIONAL GROUPS AND JOB CATEGORIES

Occupational groups were classified, separately at each colliery, into nine broad job categories:

- work on hand-filled faces;
- work at the ventilation intake of hand-filled faces;
- work on the surface;
- work on mechanized faces involving some shot firing;
- work on mechanized faces with no shot firing;
- development work;
- driving diesels;
- work involving shot firing;
- other underground work.

The classification was approximate, in that OGs did not fit exactly into only one job category. For instance, it was necessary to include some other haulage workers in the job category of diesel drivers, whenever the diesel drivers had not been identified in a separate OG. Sometimes shot firers were distinguished as a separate OG; sometimes they were included in OGs identified as "deputies" or "officials". Problems arose also where shot-firing practices on hand-filled faces were atypical. Moreover, it was not always possible to ascertain the dates when shot firing ceased in developments. Specific instances of this are discussed below.

The occupational classifications at the different mines are not exactly equivalent, and so the proportions of the work force in each category may differ among collieries, in ways other than reflecting real differences in the division of labor.

Few men were employed driving diesels or at the ventilation intake of hand-filled faces. The percentages of the study population working in each of the other seven categories during each intersurvey period at each colliery are shown in Figures C.2 through C.10.[1] The numbers of men employed per year for the same time period are also indicated, together with the dates of the medical surveys and the starting date adopted for estimating NO_x exposures $[E_i(t)]$ at the colliery concerned.

Temporal trends within collieries in Figures C.2 through C.10 reflect some of the changes in mining methods, and are discussed below, starting with colliery K, which may be taken as representative of the industry in this regard.

Colliery K

In about 1960, most face workers at colliery K (Figure C.2) worked on hand-filled faces with high NO_x levels from shot firing, but work on hand-filled faces ceased about 1970, long before NO_x sampling started in 1976.

With face mechanization, the total work force was reduced. Mechanized faces with some shot firing predominated from 1965 through 1975, though a change to mechanization without explosives, from about 1970, eventually led to most face workers being employed at faces without use of explosives. The proportion of miners involved in shot firing on mechanized faces, therefore, declined rapidly during the 1970s.

The proportions of times worked underground, other than on the face, increased throughout. The introduction of mechanization coincided with a gradual increase in the proportion of total time worked above-ground; development work accounted for a more or less constant proportion throughout that period.

Colliery C

The broad pattern in colliery C (Figure C.3) is similar to that in colliery K. However, prior to mechanization, a unique "lift" system of working the coal was used, with considerable use of explosives on all shifts, but it is unclear how consequent NO_x exposure compared with hand-filling work at other collieries. Also, problems with ventilation were noted at this mine. Compressed-air- or carbon-dioxide-based systems were used, but not to the exclusion of explosives; it seems likely that most face workers were exposed to NO_x before mechanization.

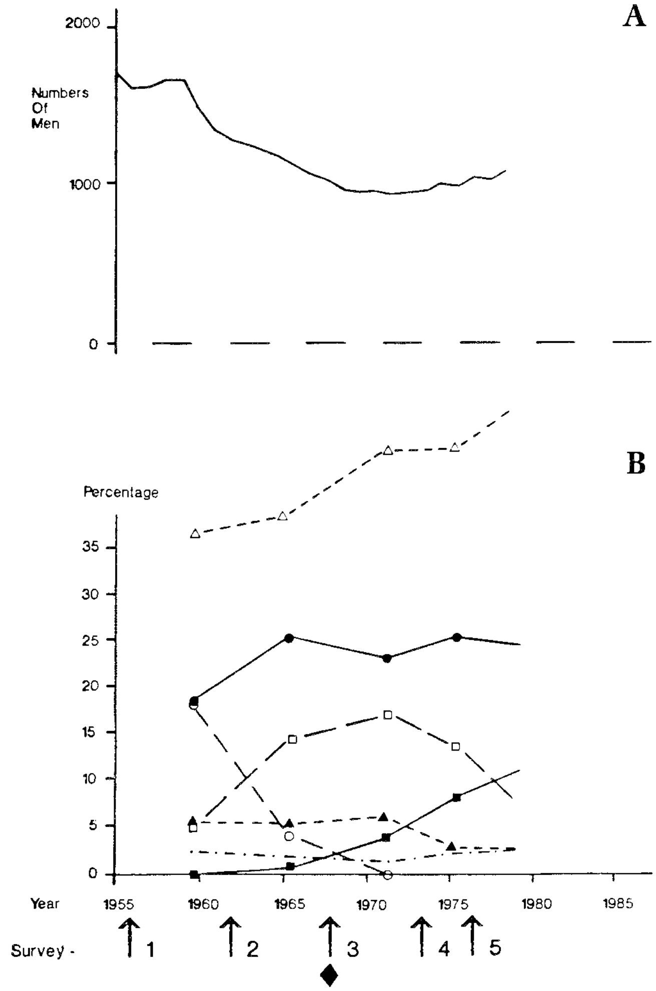

Figure C.2. Summary of the history of work at colliery K. A: Numbers of miners employed by year. B: Proportion of total number of shifts worked by miners in the study, classified by job category. ● = surface work; ○ = face work (hand-filled faces); □ = face work (mechanized faces, some shot firing); ■ = face work (mechanized faces, no shot firing), -•- = development; ▲ = shot firing; and Δ = other underground work. The two job categories of diesel driving and work at the intake of hand-filled faces are not included, as the proportions of time allocated to these categories were zero or very small. ↑ = the date of a medical survey; and ♦ = exposures to NO_x were estimated from this survey onwards.

[1] Figures C.2 through C.10 show the distribution of occupations among all 21,490 men who participated in the surveys. Following the last medical survey, data for new recruits are not included, so the occupational information then relates disproportionately to older, senior workers, who are least likely to have been working on coal faces.

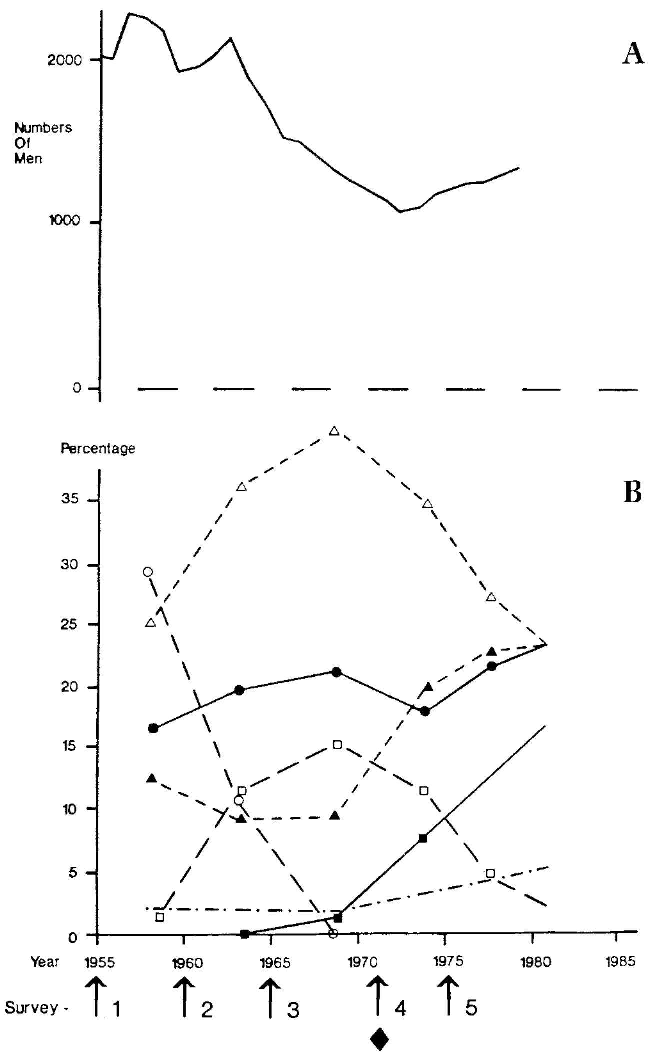

Figure C.3. Summary of the history of work at colliery C. Key as for Figure C.2.

From about 1970, shot firers were no longer identified in a separate OG. This obliged us to adopt a wider definition of "shot firing" for subsequent years, resulting in an artifactual increase in the proportion of shifts thus categorized in Figure C.3.

Colliery F

Pneumatic picks were used in colliery F (Figure C.4), instead of explosives, on most of the hand-filled faces. Compressed carbon dioxide was also used. However, shot firing in stone was still carried out in the rippings and developments, comparable to mechanized faces subsequently.

More conventional hand-filling, with more explosives, was used briefly in the 1960s. Face machinery, with the use of high-speed explosives, was also introduced then. The effect on

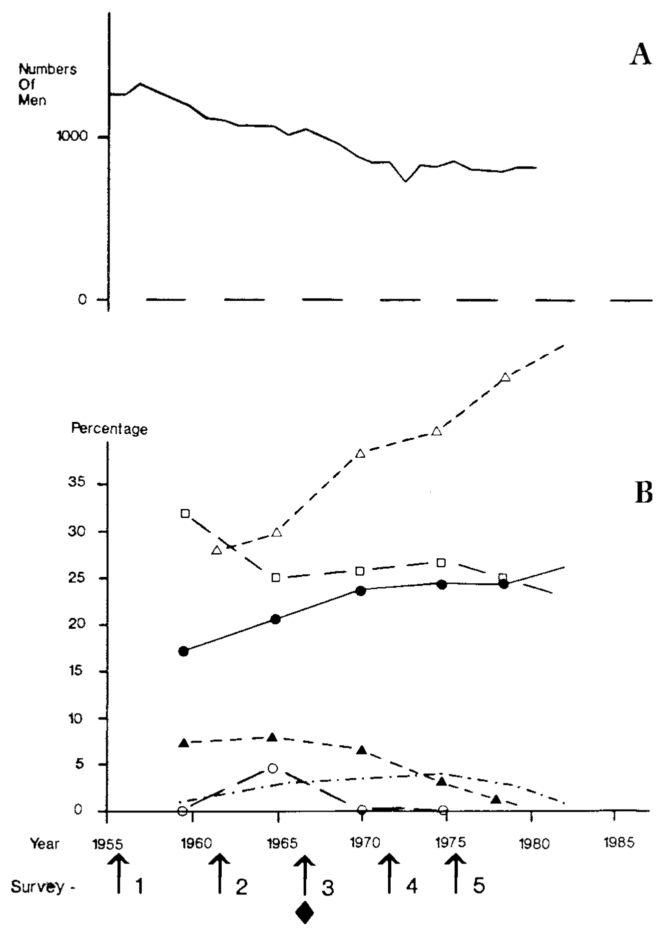

Figure C.4. Summary of the history of work at colliery F. Key as for Figure C.2.

NO_x levels is unclear: NO_x was first sampled in 1976, when levels were probably representative of conditions from the late 1960s onward, and we cannot reliably estimate NO_x concentrations before then.

Colliery P

Again, colliery P (Figure C.5) is similar to colliery K except that most mechanized faces continued to use explosives at the face ends; consequently, sampled levels of NO_x from 1976 through 1979 were high. The work force, declining throughout, had a stable composition from about 1968 onwards.

Colliery Q

Hand-filling ended at colliery Q (Figure C.6) quite early. Thereafter, work force numbers and composition were relatively stable, the apparent increase in shot firers again being artifactual. It appears that conditions changed little for almost 20 years, between 1962 and 1982. These conditions included

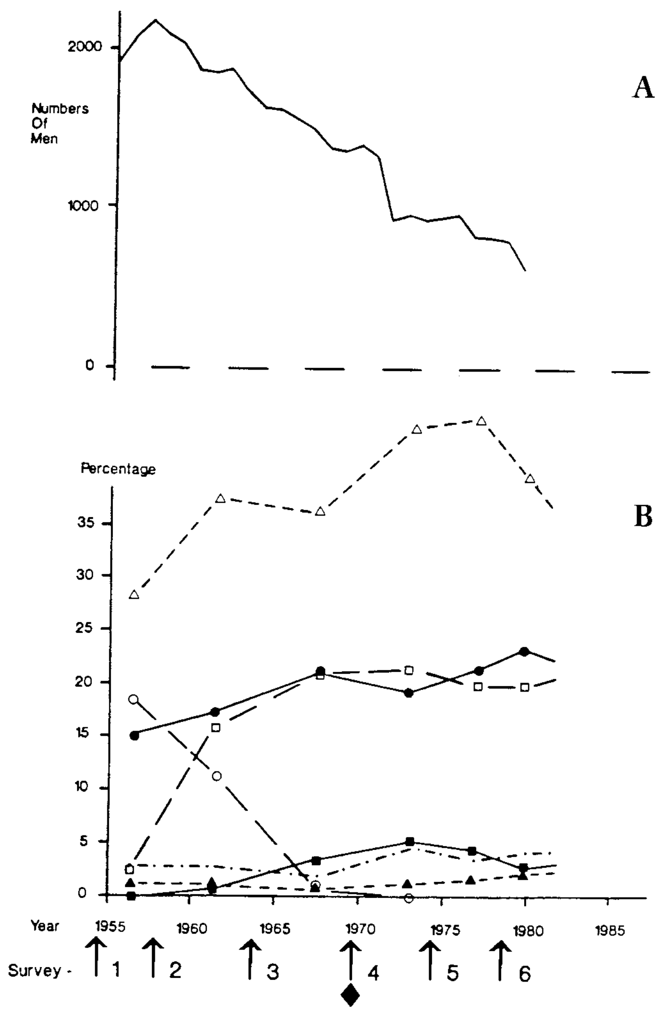

Figure C.5. Summary of the history of work at colliery P. Key as for Figure C.2.

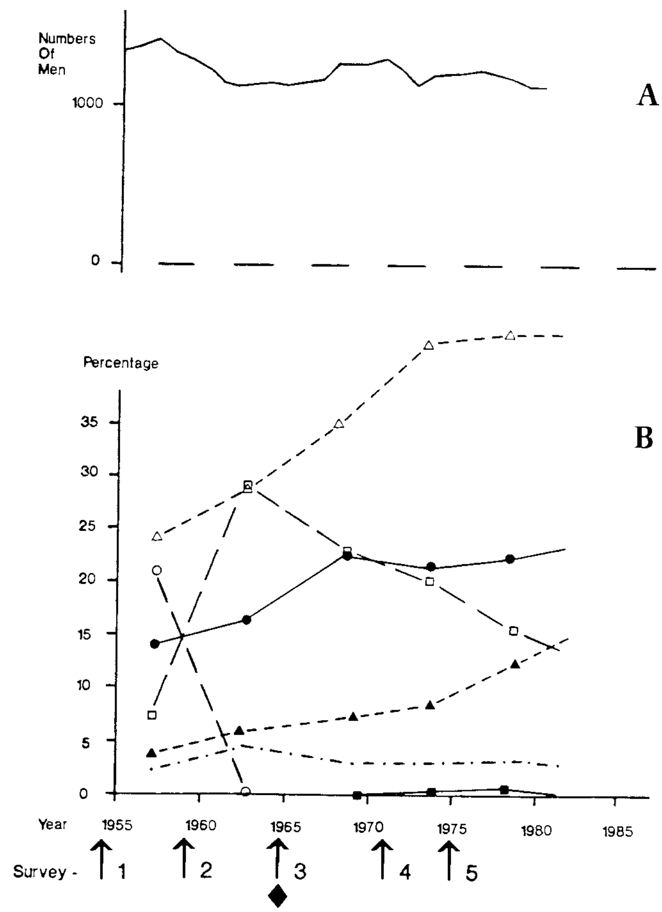

Figure C.6. Summary of the history of work at colliery Q. Key as for Figure C.2.

relatively high levels of NO_x from 1976 through 1979 and 1980 through 1982, largely, it was thought, because of diesel fumes, but also because explosives were still used at the face ends. Between 1982 and 1985, reorganization of haulage led to a considerable reduction in diesel travel.

Colliery V

On hand-filled faces at colliery V (Figure C.7), compressed carbon dioxide was used extensively to break up the coal, so exposures to NO_x were low. Face machinery and high-speed explosives were introduced simultaneously (and the work force reduced), and we do not know if mechanization led to a general decrease in NO_x levels (as it undoubtedly did at colliery K, for example). No distinction was made, when classifying OGs, between work on the mechanized faces and work on nonmechanized faces; both involved some exposure to shot-firing fumes.

Colliery W

In 1972, colliery W (Figure C.8) was linked underground with a neighboring mine. Prior to the merger, it was worked entirely by hand-filling; diesels, used extensively in the amalgamated mine, were not used.

Shot firing at both collieries is generally carried out between shifts, when only the shot firers and borers are in the colliery, because of the danger of gas outbursts. Sampling of nitrogen oxides from 1976 through 1979, after the merger, showed no noticeable gradient in NO_x concentrations across faces, suggesting that NO_x exposure was primarily due to diesels, and not to between-shift shot firing. Thus, no attempt was made to divide face workers by type of face; and though prior to the merger all faces were fired, with considerable release of NO_x between shifts, there may have been very little exposure of the work force.

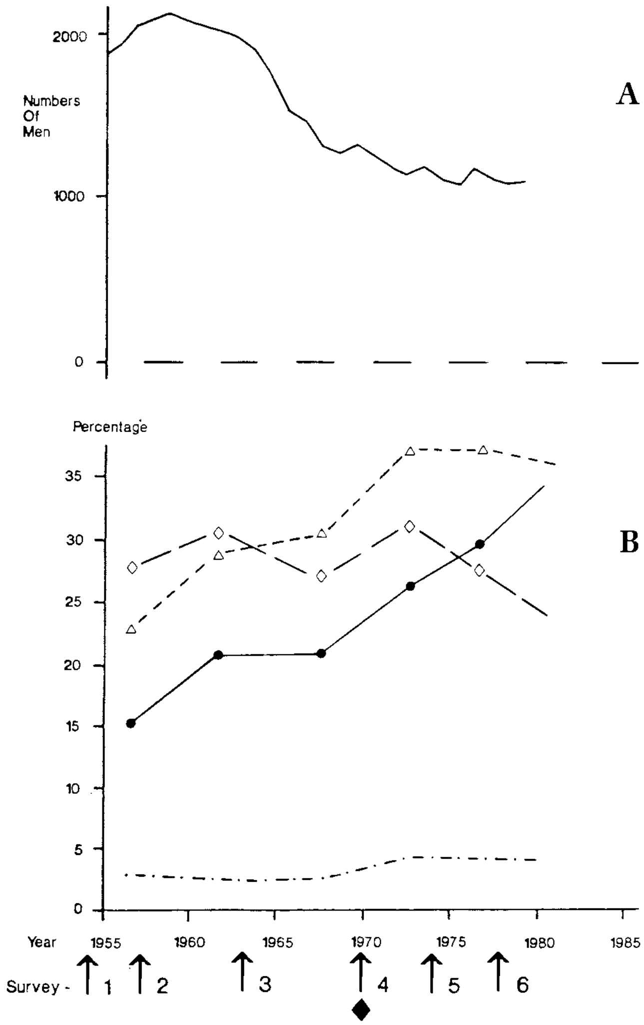

Figure C.7. Summary of the history of work at colliery V. A: Numbers of miners employed by year. B: Proportion of total number of shifts worked by miners in the study, classified by job category. ● = surface work; ◇ = face work (all faces); -•- = development; Δ = other underground work. See legend to Figure C.2 for further details.

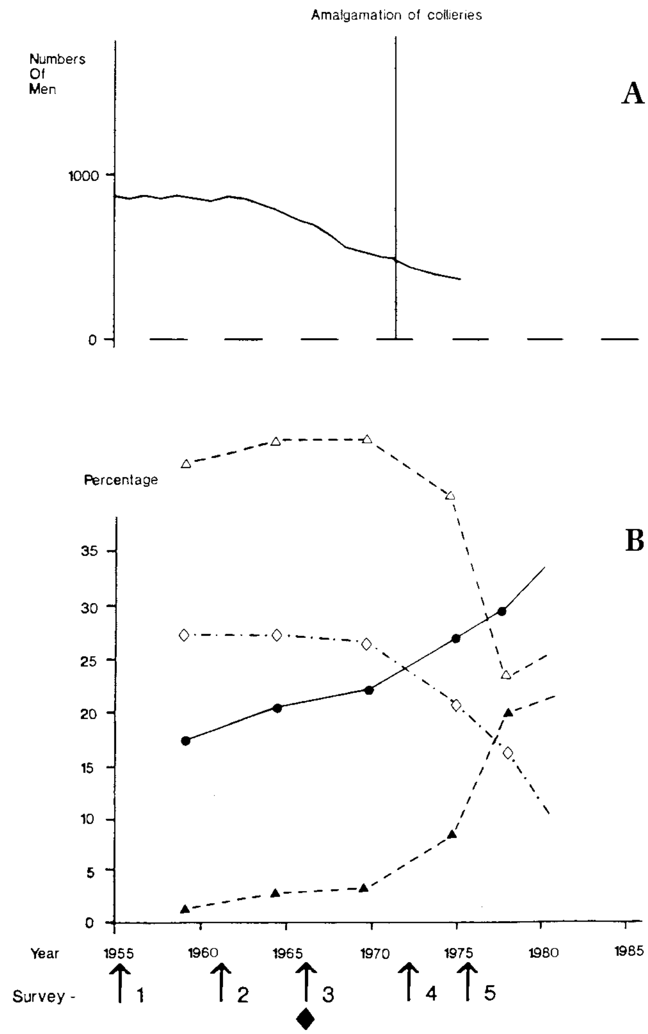

Figure C.8. Summary of the history of work at colliery W. A: Numbers of miners employed by year. B: Proportion of total number of shifts worked by miners in the study, classified by job category. ● = surface work; ◇ = face work (all faces) and development; ▲ = shot firing; and Δ = other underground work. See legend to Figure C.2 for further details.

Developers, probably not exposed to atypical levels of NOx, were included with other underground workers. Changes in work force composition in the late 1970s (probably reflecting effects of the merger) are irrelevant because they post-date the last medical survey.

Colliery X

The population at colliery X (Figure C.9) peaked in 1968, following the closing of a neighboring mine. The increasing proportion of surface and other underground workers is a typical pattern. Other haulage workers were included in the "diesel driver" category because the OG structure did not separate the two groups. Diesel trains, used on some seams, are likely to have caused some NO_x exposure, although the levels measured from 1976 through 1979 were relatively low.

Colliery Y

From 1960 onward at colliery Y (Figure C.10), diesel trains were used for travel and coal haulage on some seams; their use has declined following recent reorganization. Shot firing around coal faces is also less frequent now, and heading machines are used in the developments. The extent of explosive use early in the research period is unclear, because of experiments in mining methods then.

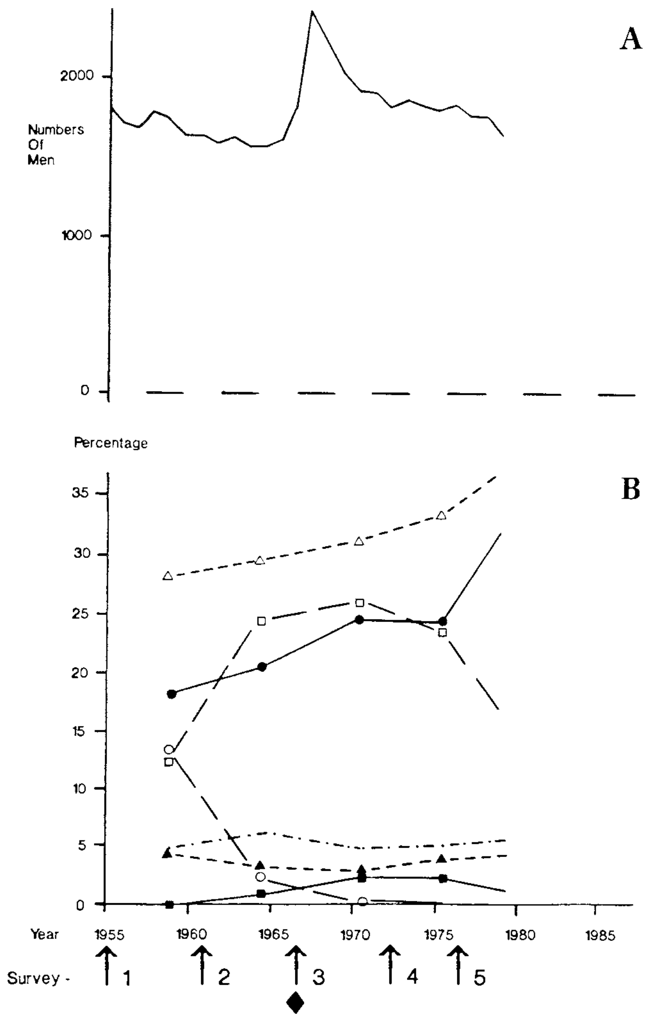

Figure C.9. Summary of the history of work at colliery X. Key as for Figure C.2.

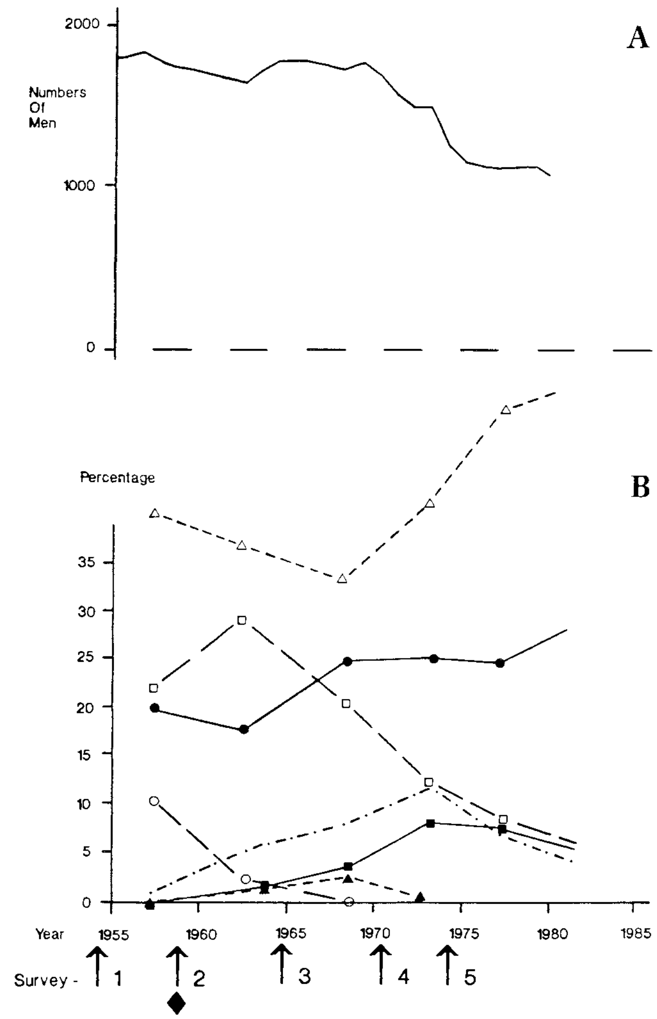

Figure C.10. Summary of the history of work at colliery Y. Key as for Figure C.2.

APPENDIX D. Supplementary Results from the Investigation of the Reliability of the Questionnaire Responses About Sickness Absence Due to Chest Illnesses

INTRODUCTION

This appendix describes the analyses directed to determining whether variations in the association between miners' survey responses to the question about sickness absences and physicians' certified diagnoses were influenced by the men's ages or smoking habits. Study design, data collection, and classification of responses are described in the main report; Table 5 there summarizes the data used for the analyses.

Also presented in this appendix are details of how chest radiographs from the men concerned were examined, and what was found.

AGE-RELATED DIFFERENCES

Age, a quantitative variable, was considered in an unbalanced analysis of variance (ANOVA) with three factors, namely, study period (1986 or 1975), questionnaire response, and sickness absence diagnosis. Computations used the linear regression facilities of the GENSTAT statistical package (Alvey et al. 1977).

Results from the ANOVA are summarized in Table D.1; because the data are unbalanced, the order in which the terms were fitted is relevant.

The men surveyed at the later period were, on average, younger. This may be partly due to the different sampling strategies, but age did not differ significantly over questionnaire responses, so the explanation may simply be that the distribution of age in the mining work force had changed between the surveys. The interaction between sickness absence and period was statistically significant. There was no significant interaction in the age variable between questionnaire response and sickness absence, whether or not the periods were separated. We interpret this finding as lack of evidence for any association between age and failure to report sickness absences due to chest illness.

SMOKING-RELATED DIFFERENCES

The data are frequencies classified by four factors: study period (1975 or 1986); questionnaire response; sickness absence diagnosis; and smoking habit (Table 5). They were analyzed, first, by assuming a log-linear model structure and Poisson error variation, using the generalized linear model facilities of GENSTAT (Alvey et al. 1977). The contributions of various factors to the fit of the models are quantified by changes in the deviance (McCullagh and Nelder 1983), which is analogous to a weighted sum of squares. As in unbalanced ANOVAs (Table D.1), the change due to a term's inclusion can depend on the order of fitting other terms.

In the present analyses, terms were fitted initially for the differences in frequencies between periods, for the three grouped questionnaire responses, and for their interaction (because the questionnaire distributions from the two surveys were known to be from different sampling strategies). Terms for differences in the frequencies of the sickness absence diagnoses and interactions with the first two factors were then introduced, before terms for smoking habit and its interactions with the other three factors.

Table D.1. Analysis of Variance for Age at Survey by Other Factors

Term Added[b]	Change[a] DF	Change[a] SS	Mean Change	Variance Ratio
Period	1	4,786.91	4,786.91	51.49[c]
Response	7	1,078.32	154.05	1.66
Diagnosis	3	672.66	224.22	2.41
Response × period	5	805.02	161.00	1.73
Diagnosis × period	3	1,362.22	454.07	4.88[d]
Response × diagnosis	14	1,537.56	109.83	1.18
Response × diagnosis × period	6	358.27	59.71	0.64
Residual	431	40,067.64	92.96	

[a] DF = degress of freedom; SS = sum of squares.

[b] Period = study period (1986 or 1975); response = questionnaire response; diagnosis = sickness absence diagnosis.

[c] Formal significance level for variance ratios, tested as F-statistics: $p < 0.001$.

[d] Formal significance level for variance ratios, tested as F-statistics: $p < 0.01$.

Also by analogy with ANOVA (Table D.1), results from the analyses of counts in Table 5 are summarized in an analysis-of-deviance table (Table D.2). The residual deviance of 16.97, considered as chi-square with 12 degrees of freedom, is just significant at around the 15-percent level. This may indicate some over-dispersion relative to the Poisson distribution, a possibility allowed for by using the mean residual deviance of 1.414 as the denominator when calculating mean deviance ratios in Table D.2. In general, and again by analogy with ANOVA, each mean deviance ratio is distributed under an appropriate null hypothesis as an F-statistic with the stated degrees of freedom. The first three terms in Table D.2 do not, however, correspond to valid tests of null hypotheses. Instead, the significant differences they show reflect the intentional differences in sampling strategies employed in 1975 and 1986.

Of the remaining terms, the interaction between questionnaire response and sickness absence record, significant at less than 1 percent, is notable; it confirms that the association between these variables was highly unlikely to be due to chance. The significant smoking effect reflects the fact that, in general, cigarette smokers were more prevalent than other smokers, or nonsmokers (Table 5). However, none of the interactions of smoking with any of the other three factors reached statistical significance at the 5 percent level, indicating that the distribution of men to smoking categories was not detectably associated with survey period, questionnaire response, or sickness absence record.

In particular, there was no suggestion that the three-way interaction of smoking, response, and sickness absence was significant. We interpret this as lack of evidence for any association between smoking habits and failure to report sickness absences due to chest illness.

QUESTIONNAIRE RESPONSES AND CHEST RADIOGRAPHS

Most infections do not cause radiographic abnormalities. However, persistent changes, in particular obliteration of the costophrenic angles, might be observed as a result of respiratory infections. Acute transient changes would be unlikely.

Full-size posterior-anterior chest radiographs had been obtained, primarily to be examined for evidence of pneumoconiotic changes. Two readers were invited to examine each of the available films as if in a clinical situation, and to record, on a standard form, first, whether either or both costophrenic angles were obliterated, using the definition in the International Labour Organisation (1980) classification; and second, whether there was any other radiographic evidence consistent with the occurrence of a respiratory infection. Both readers completed their examinations of all the films for 361 men from the 1986 survey. The 152 earlier films were read by only one reader.

Table D.3 gives the numbers of films for which the assessments were positive for either costophrenic angle obliteration,

Table D.2. Analysis of Deviance for Smoking Distribution by Other Factors

	Change			
Term Added[a]	DF[b]	Deviance	Mean Change	Mean Deviance Ratio
Period	1	62.012	62.012	43.85[c]
Response	2	255.131	127.566	90.21[c]
Period × response	2	213.265	106.632	75.41[c]
Diagnosis	3	237.382	79.127	55.96[c]
Period × diagnosis	3	133.273	44.424	31.42[c]
Response × diagnosis	6	54.205	9.034	6.39[d]
Period × response × diagnosis	6	6.035	1.006	0.71[d]
Smoking	2	37.225	18.612	13.16[c]
Period × smoking	2	8.840	4.420	3.13
Smoking × response	4	2.231	0.558	0.39
Period × smoking × response	4	13.186	3.297	2.33
Smoking × diagnosis	6	5.780	0.963	0.68
Period × smoking × diagnosis	6	6.106	1.018	0.72
Smoking × response × diagnosis	12	23.738	1.978	1.40
Residual	12	16.969	1.414	

[a] Period = study period (1986 or 1975); response = questionnaire response; diagnosis = sickness absence diagnosis; smoking = smoking habit.
[b] DF = degrees of freedom.
[c] Formal significance level for mean deviance ratios, tested as F-statistics: $p < 0.001$.
[d] Formal significance level for mean deviance ratios, tested as F-statistics: $p < 0.01$.

or other evidence of respiratory infection, or both. The number of positive assessments was low in the earlier films, and almost negligible in those from the later survey. It was concluded that the films showed no evidence of an association between any radiographic indication of respiratory infection and the likelihood that a man would report absence due to bronchitis, cold, or influenza, and that, overall, the examination of the radiographs had failed to produce any useful information about the validity of the questionnaire responses as indicators of respiratory infection.

Table D.3. Number of Films for Which Costophrenic Angle Obliteration (CPAO) or Other Evidence[a] of Respiratory Infection Were Recorded by Two Readers, Grouped by Survey Questionnaire Response

			Reader 1			Reader 2		
Period	Questionnaire Response	No. of Men	CPAO Only	Other Signs[a] Only	CPAO and Other Signs[a]	CPAO Only	Other Signs[a] Only	CPAO and Other Signs[a]
1986 Survey	Bronchitis	13	0	0	0	0	0	0
	Influenza	6	0	0	0	0	0	0
	Cold	5	0	0	0	0	0	0
	Bronchitis and asthma	1	0	0	0	0	1	0
	Asthma	0	0	0	0	0	0	0
	Other chest	5	0	0	0	0	0	0
	Not chest	4	0	0	0	0	0	0
	Not absent	286	2	4	1	6	7	2
	Total	320	2	4	1	6	8	2
1975 Surveys	Bronchitis	32				5	3	0
	Influenza	22				1	0	1
	Cold	25				4	1	1
	Bronchitis and asthma	1				0	0	0
	Asthma	1		Not assessed		1	0	0
	Other chest	36				4	7	2
	Not chest	0				0	0	0
	Not absent	34				3	4	3
	Total	151				18	15	7

[a] Other signs recorded as "Y" (present) or "P" (possibly present).

APPENDIX E. The Relationship Between Formaldehyde and Nitrogen Oxides Concentrations Underground at Two Collieries in 1985

The measurements of formaldehyde (HCHO) levels at collieries Q and Y were made, in 1985, in an effort to determine whether, and to what extent, the earlier (1976 through 1979) measurements of NO_x might be correlated with HCHO levels. Diesel engines were used at both collieries.

Figure E.1 shows the distribution of HCHO levels described in the Results section of the report. Figure E.2 verifies that there were no correlations, generally, between the simultaneous NO_x and HCHO measurements that were made at the two mines. This observation is consistent with results from other British collieries (Robertson et al. 1983).

Nevertheless, Figures E.2c and E.2d suggest that there is a weak association between HCHO and NO_x levels as measured in diesel cabins. It seems unlikely that this will have introduced any serious confounding in the statistical analyses reported here, based on all NO_x measurements underground at the nine collieries.

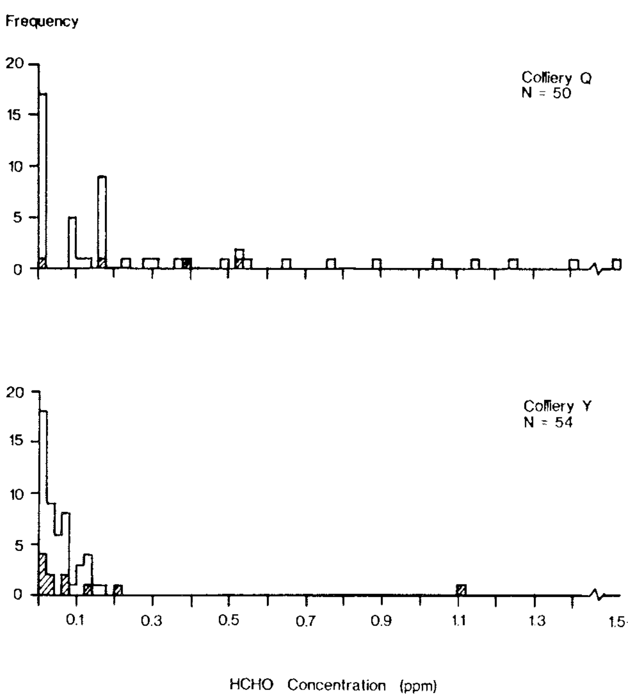

Figure E.1. Distributions of formaldehyde concentrations at collieries Q and Y in 1985. Hatched areas indicate measurements in diesel cabins.

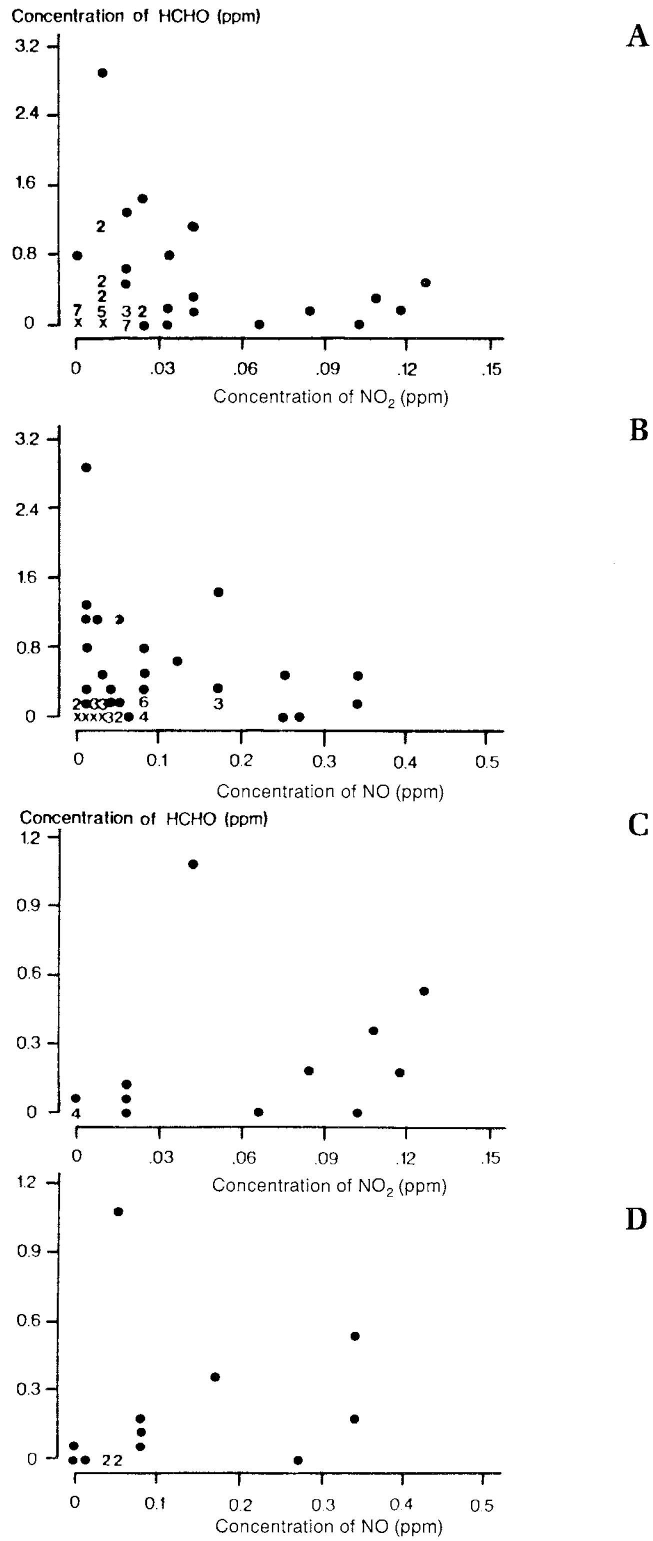

Figure E.2. Scatter of measured shift-average concentrations of A: HCHO vs. NO_2 (all 1985 measurements); B: HCHO vs. NO (all 1985 measurements); C: HCHO vs. NO_2 (diesel cabins only); D: HCHO vs. NO (diesel cabins only). x = multiple points.

APPENDIX F. Logistic Regression Analyses: Notes and Further Results

STATISTICAL SIGNIFICANCE

Differences between smoking groups, and an age-smoking interaction, were included in all analyses irrespective of their statistical significance. We have reported the associated degrees of freedom as contrasts between, respectively, the risks for cigarette smokers relative to nonsmokers, and for other smokers relative to nonsmokers. These are meaningful but not independent contrasts. In particular, the significance of the individual terms may not be a good guide to the overall significance of differences between smoking groups, or of the age-smoking interaction.

Similarly, in analyses of groups C and D, the risks of time worked in various categories underground are presented relative to risks for surface workers. Again, these contrasts are meaningful; but while the significance of individual terms may also be of interest, they are again not a good guide to the significance of overall differences between the nine types of activity. In addition, the problem of multiple comparisons arises: When so many terms are examined, it is likely that some will appear as significant simply by chance. The extent of this effect is particularly difficult to assess when, as here, the contrasts are, by definition, correlated.

FURTHER RESULTS

Detailed results from the colliery-specific (and, for group C, survey-specific) analyses are presented in Tables F.1 through F.5 and Figures F.1 through F.3. The regression strategy (see, for example, page 7 or 17) was based on three sets of models. The first set considered age, smoking habit, and dust exposure. The second set examined time worked in various activities in addition to the variables in the first set. In the third set, most time variables were replaced by estimates of NO or NO_2 exposures or concentrations. Corresponding models are described as (1), (2), or (3) in the figures throughout this report, and as A, C, and B, respectively, in the tables of this appendix. As noted above, markers of statistical significance are inexact and indicative only. Note that some extremely high (or extremely low) relative risks were not significant, indicating that these estimates were based on sparse data. Because of the large associated standard errors, such extreme values had little influence on the weighted overall relative risks displayed graphically in the report.

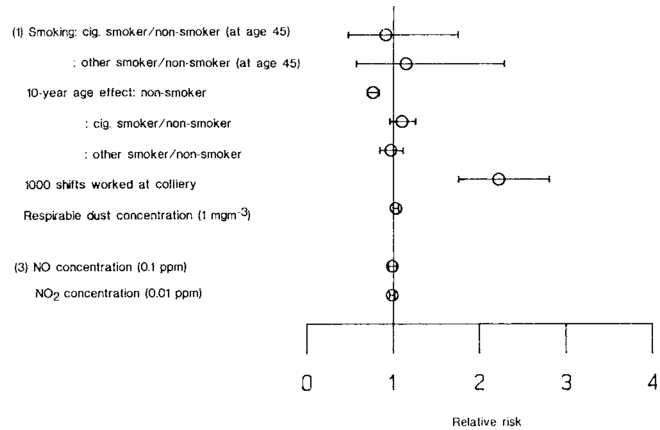

Figure F.1. Relative risk (with 95 percent confidence intervals) of reporting colds or influenza rather than bronchitis, using weighted means of estimates from 37 sets of colliery- and survey-specific analyses (18 sets for NO_x concentrations) of man-intervals where an infection was reported by miners in group C. Model (3) also included all terms in model (1); see main text.

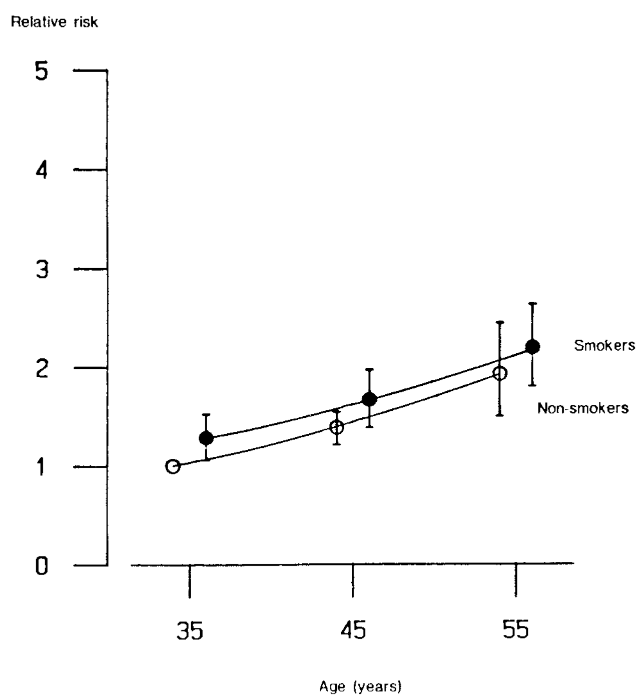

Figure F.2. Estimated risk (with 95 percent confidence intervals) of reporting an infection, relative to a nonsmoking miner at age 35 years, based on data from group D where response at initial survey was "no".

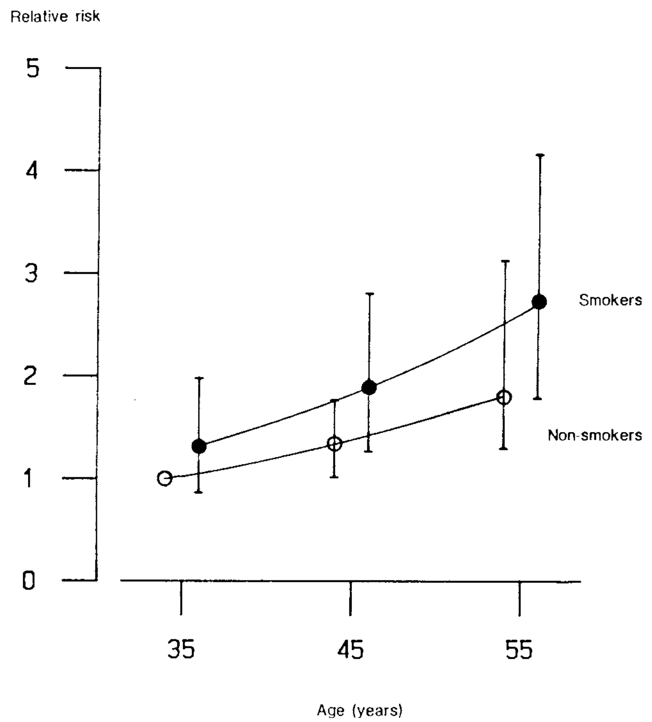

Figure F.3. Estimated risk (with 95 percent confidence intervals) of reporting an infection, relative to a nonsmoking miner at age 35 years, based on data from group D where response at initial survey was "yes".

Table F.1. Relative Risks Estimated from Colliery-Specific Logistic Regression Analyses of Reports of Bronchitis, Cold, and Influenza Relative to No Chest Illness in Group B

	Model A[a]						Model B[b]		
	Smoking[c]		Ten-Year Age Effect					NO_x Exposures[d,e]	
Pit	Cigarette	Other	Non-smoker	Cigarette[f]	Other[f]	Respirable Dust Exposure[d] (100 gh/m^3)	Time[d,g]	NO	NO_2
C	1.94	1.07	1.43	1.10	1.65	0.80	0.69[h]	0.74	0.68
F	2.24[i]	1.96	1.83[i]	0.75	1.24	1.35[i]	0.75[i]	1.06	0.99
K	1.39	1.12	1.63[h]	0.90	0.89	1.07	0.86	0.98	0.99
P	3.06	2.53	1.21	1.36	1.92	0.52	0.74	0.95	0.95
Q	0.99	1.21	1.91[i]	0.67	0.79	1.04	0.75[i]	0.99	1.00
V	1.10	0.73	1.62[i]	1.11	1.46	0.66[i]	0.82[h]	0.85	0.95
W	1.36	1.09	1.95	0.73	0.67	0.94	0.74	0.94	0.93
X	1.93[h]	1.27	1.25	1.14	0.99	0.89	0.58[j]	0.95	0.96
Y	0.99	1.04	1.20	1.03	1.06	0.93	0.78[i]	1.04	1.01

	Model C[d,k]								
	Face								
	Hand-Filled		Mechanized				Other Underground		
Pit	Intake	Face	Some Shot Firing	No Shot Firing	Develop-ment	Diesel Driving	No Shot Firing	Some Shot Firing	Surface
C	1.29	1.34	0.00	2.37	1.24	—	1.04	0.96	0.77[i]
F	0.79	0.31	1.61	—	1.14	—	0.82	1.67[i]	0.76[i]
K	1.07	1.33	0.95	2.13	0.37	0.00	0.99	1.30	0.90
P	0.48[i]	0.62	1.39	0.56	0.60	—	0.85	0.16	0.75
Q	0.84	1.20	1.89	0.00	0.88	1.20	0.78[i]	0.87	0.81[i]
V	1.16	—	—	> 30.00[i]	1.06	—	1.09	—	0.89
W	—	—	—	0.63	—	> 30.00	0.98	0.61	0.80
X	0.53[i]	1.31	1.85	0.34	0.59	0.71	0.65[h]	0.79	0.67[j]
Y	1.11	1.06	0.15	1.23	0.75	3.94	0.90	1.28	0.80[i]

[a] Model A includes only terms shown and intercept.

[b] Model B includes terms shown, all terms in model A, and time in hand-filled faces.

[c] Relative to nonsmoker at age 45 years.

[d] Refers to cumulative (lifetime) experience up to latest (fifth or sixth) survey.

[e] NO: 100 ppm•shifts; NO_2: 10 ppm•shifts.

[f] Relative to nonsmoker.

[g] Toward NO_x exposure and on surface; 1,000 shifts.

[h] Approximate statistical significance: $p < 0.01$.

[i] Approximate statistical significance: $p < 0.05$.

[j] Approximate statistical significance: $p < 0.001$.

[k] Model C includes all terms shown, and all terms in model A. Figures are per 1,000 shifts worked.

Table F.2. Relative Risks Estimated from Colliery- and Survey-Specific Logistic Regression Analyses of Reports of Bronchitis, Cold, or Influenza Relative to No Chest Illness in Group C

	Model A[a]						Model B[b]		
	Smoking[c]		Ten-Year Age Effect					NO_x Concentrations[d]	
Pit and Survey	Cigarette	Other	Non-smoker	Cigarette[e]	Other[e]	Respirable Dust Concentration[d] (1 mg/m^{-3})	Time[d,f]	NO (0.1 ppm)	NO_2 (0.01 ppm)
C2	1.85	1.70	1.77[g]	0.93	0.91	0.92	0.82[g]	—	—
C3	1.87	1.13	1.92[g]	0.93	—	0.95	0.78[g]	—	—
C4	0.66	5.62[h]	1.65[g]	1.11	0.72[h]	0.94	0.85[g]	—	—
C5	2.08	0.27	1.84[g]	0.92	1.29	1.14	0.88[h]	0.90	0.73
F2	1.01	4.85	1.45[h]	1.00	0.71	1.02	0.99	—	—
F3	0.86	2.82	1.80[g]	1.01	0.81	1.01	0.82[g]	—	—
F4	9.58[i]	0.09	2.11[g]	0.62[i]	1.57	0.87[h]	0.88[h]	0.81	0.73
F5	4.33[h]	0.39	2.13[g]	0.76[h]	1.29	1.28[i]	0.88	0.50[h]	0.55[h]
K2	4.26	0.37	2.17[g]	0.80	1.18	0.96	0.88[g]	—	—
K3	1.11	0.41	1.51[g]	1.01	1.27	0.99	0.92[h]	—	—
K4	2.05	1.88	1.58[g]	0.90	0.92	1.09	0.86[g]	1.28	0.51
K5	1.19	1.96	1.65[g]	0.99	0.87	0.99	0.71[g]	0.38	0.59
P3	2.20	0.05	2.08[g]	0.90	2.00[h]	1.09	0.91[i]	—	—
P4	0.40	2.41	1.30[h]	1.17	0.87	0.93	0.96	—	—
P5	3.40	0.17	1.85[g]	0.78	1.49	1.15	0.77[i]	0.88	0.85
P6	1.16	0.18	1.53	1.03	1.54	0.77	0.67[g]	0.87	0.81
Q2	5.06	0.04	1.30[i]	1.30	0.64	1.02	0.86[i]	—	—
Q3	7.84[h]	1.11	2.61[g]	0.68[h]	0.97	1.00	0.91[h]	—	—
Q4	1.27	0.85	1.37[i]	0.98	1.10	1.09	0.92[h]	1.00	0.99
Q5	1.94	1.25	1.77[g]	0.84	0.99	1.14[h]	0.80[g]	1.01	1.02
V2	3.79	0.14	1.94[g]	0.79	1.47	1.01	0.99	—	—
V3	0.68	2.26	1.72[g]	1.08	0.88	0.96	0.91[g]	—	—
V4	0.83	1.87	1.62[g]	1.01	0.88	0.89[h]	0.92[i]	0.88	1.53
V5	1.07	2.20	1.85[g]	0.96	0.91	0.87	0.71[g]	1.29	1.70
V6	1.44	0.32	1.76[g]	0.95	1.23	0.91	0.83[i]	0.84	0.88
W2	1.92	0.26	1.89[g]	0.85	1.44	1.09	0.94	—	—
W3	2.57	0.03	1.42	0.91	2.26[h]	1.02	0.81[i]	—	—
W4	0.70	5.67	1.20	1.14	0.71	0.87	0.90	—	—
W5	1.10	3.00	1.61[h]	0.98	0.79	1.05	0.67[i]	0.99	1.40
X2	0.68	1.25	1.47[g]	1.15	0.98	0.98	0.92[h]	—	—
X3	1.04	2.71	1.60[g]	0.99	0.86	1.10	0.94	—	—
X4	1.94	1.67	1.75[g]	0.90	0.92	1.08[h]	0.82[g]	0.88	1.01
X5	1.06	1.08	1.45[g]	1.07	0.98	1.08	0.73[g]	0.89	0.88
Y2	3.33	0.08	1.92[i]	0.78	1.56	0.99	1.00	—	—
Y3	1.17	0.43	1.65[g]	0.96	1.15	0.72[g]	0.82[g]	1.03	1.02
Y4	2.28[h]	0.52	1.42[g]	0.85	1.22	0.97	0.98	1.02	1.01
Y5	0.91	1.33	1.30[i]	1.01	0.96	0.99	0.75[g]	1.26[h]	0.89

[a] Model A includes only terms shown and intercept.
[b] Model B includes terms shown, all terms in model A, and proportion of time on hand-filled faces.
[c] Relative to nonsmoker at age 45 years.
[d] Refers to five-year period preceding survey analyzed.
[e] Relative to nonsmoker.
[f] Toward dust exposure; 1,000 shifts.
[g] Approximate statistical significance: $p < 0.001$.
[h] Approximate statistical significance: $p < 0.05$.
[i] Approximate statistical significance: $p < 0.01$.

Table F.3. Further Relative Risks Estimated from Colliery- and Survey-Specific Logistic Regression Analyses of Reports of Bronchitis, Cold, or Influenza Relative to No Chest Illness in Group C[a]

Pit and Survey	Face						Other Underground	
	Hand-Filled		Mechanized					
	Intake	Face	Some Shot Firing	No Shot Firing	Development	Diesel Driving	No Shot Firing	Some Shot Firing
C2	—	1.61	6.12	—	1.89	—	1.96[b]	1.92
C3	2.58	0.71	0.00	—	1.03	—	2.30[b]	1.07
C4	17.33[c]	0.00	—	—	1.74	—	4.51[d]	3.19
C5	0.42	—	—	0.60	0.04[b]	—	0.35	0.17[b]
F2	1.39	—	—	—	0.90	—	1.37	2.31
F3	1.71	0.83	0.22	—	2.44	—	1.35	1.01
F4	1.70	0.00	—	—	1.48	—	1.82	2.78
F5	0.73	—	—	—	1.79	—	0.80	3.51
K2	0.82	0.85	3.11	—	1.97	10.71[b]	1.46	0.88
K3	3.58	2.60	0.00	—	0.63	0.82	1.23	1.81
K4	0.34	0.00	>30.00	0.09[b]	0.01	5.06	0.64	0.22[b]
K5	1.15	—	—	3.32	0.00	—	1.02	2.47
P3	0.98	1.87	0.58	—	0.05	—	0.77	0.36
P4	0.58	2.19	—	0.85	0.14	—	1.05	5.37
P5	2.80	—	—	2.90	1.30	—	3.45[b]	0.00
P6	0.80	—	—	5.94	0.93	—	1.68	7.86
Q2	3.17	2.47	11.21[b]	—	1.44	3.22	2.07	2.68
Q3	1.56	0.15	2.23	—	0.44	0.36	1.54	1.25
Q4	0.58	—	—	0.00	0.25	0.64	0.91	0.88
Q5	0.93	—	—	1.80	1.23	0.96	0.60	1.18
V2	1.50	—	—	—	1.26	—	1.12	—
V3	1.06	—	—	0.40	1.72	—	1.22	—
V4	1.71	—	—	0.00	1.11	—	1.56	—
V5	2.44	—	—	—	0.65	—	1.56	—
V6	1.10	—	—	—	1.46	—	1.03	—
W2	—	—	—	1.55	—	—	1.37	1.83
W3	—	—	—	0.72	—	—	0.97	4.89
W4	—	—	—	0.17	—	—	0.98	0.17
W5	—	—	—	0.48	—	>30.00	1.30	0.16
X2	3.30	6.43[b]	4.48	—	11.12[c]	—	2.64[b]	5.19
X3	1.74	0.35	2.17	—	1.41	5.99	1.11	3.15
X4	0.73	0.00	0.00	0.50	0.35	0.80	0.90	2.84
X5	0.89	—	>30.00	0.69	1.01	1.01	1.05	1.24
Y2	0.43	0.52	0.37	—	0.00	13.52[b]	0.83	—
Y3	0.93	0.57	0.09	>30.00	0.50	4.14	0.99	>30.00
Y4	1.87	0.96	—	0.77	1.44	1.79	1.20	2.48
Y5	1.67	—	—	2.28	0.95	0.00	1.06	—

[a] Relative risks refer to full-time work in the named activity, relative to full-time work on the surface. Models include terms for proportions of time spent in various activities over five-year periods preceding the surveys analyzed, as well as all terms in model A of Table F.2 (with a slightly different time variable).

[b] Approximate statistical significance: $p < 0.05$.

[c] Approximate statistical significance: $p < 0.01$.

[d] Approximate statistical significance: $p < 0.001$.

Table F.4. Relative Risks Estimated from Colliery-Specific Logistic Regression Analyses of Reports of Bronchitis, Cold, or Influenza Relative to No Chest Illness in Group D Men Responding "No" at Previous Survey

	Model A[a]						Model B[b]		
	Smoking[c]		Ten-Year Age Effect					NO_x Concentrations[d]	
Pit	Cigarette	Other	Non-smoker	Cigarette[e]	Other[e]	Respirable Dust Concentration[d] (1 mg/m^3)	Time[d,f]	NO (0.1 ppm)	NO_2 (0.01 ppm)
C	1.03	0.49	1.21	1.19	1.84	1.01	0.44[g]	1.15	1.06
F	1.48	1.42	1.82[h]	0.74	0.70	1.00	0.22[g]	0.31[h]	0.63
K	1.54	1.55	1.14	0.95	1.31	1.02	0.90	0.52	0.27
P	1.18	1.85	1.25	0.94	1.13	1.08	0.74	0.81	0.72
Q	0.86	0.84	1.82[h]	0.64	0.74	1.05	0.64	1.03	1.04
V	1.02	0.76	1.60[i]	0.93	0.61[h]	0.99	0.81	1.12	0.79
W	1.61	1.52	1.31	0.81	0.93	1.00	0.34[i]	1.47[h]	5.10[i]
X	1.27	0.67	1.57[i]	0.93	1.09	1.18[g]	1.01	0.77	1.07
Y	1.13	1.04	1.26	1.07	1.04	0.89[h]	0.87	1.01	1.01

	Model C[d,k]								
	Face								
	Hand-Filled		Mechanized				Other Underground		
Pit	Intake	Face	Some Shot Firing	No Shot Firing	Develop-ment	Diesel Driving	No Shot Firing	Some Shot Firing	Surface
C	3.38[h]	2.05	0.00	0.44	1.07	—	1.98[h]	1.11	
F	1.83	4.76	0.03	—	6.41	—	1.66	1.92	
K	0.75	0.84	>30.00	1.75	0.61	0.18	0.96	0.91	
P	0.42	0.01	—	0.23	0.26	—	1.06	0.09	
Q	0.51	0.01	0.01	0.00	0.28	1.06	0.60	0.87	
V	1.05	—	—	0.00	0.62	—	1.19	—	
W	—	—	—	0.42	—	—	1.09	2.34	
X	0.60	2.31	7.45	0.12[h]	0.88	1.01	0.99	2.16	
Y	0.72	0.37	0.17	0.22	0.58	2.08	0.92	1.74	

[a] Model A includes only terms shown and intercept.

[b] Model B includes terms shown, all those in Model A, and proportion of time on hand-filled faces.

[c] Relative to nonsmoker at age 45 years.

[d] Refers to five-year period preceding survey analyzed.

[e] Relative to nonsmoker.

[f] In colliery; 1,000 shifts.

[g] Approximate statistical significance: $p < 0.001$.

[h] Approximate statistical significance: $p < 0.05$.

[i] Approximate statistical significance: $p < 0.01$.

[j] Full-time work in named activity relative to full-time work on surface. Model C includes terms shown and all those in model A.

Table F.5. Relative Risks Estimated from Colliery-Specific Logistic Regression Analyses of Reports of Bronchitis, Cold, or Influenza Relative to No Chest Illness in Group D Men Responding "Yes" at Previous Survey

	Model A[a]						Model B[b]		
	Smoking[c]		Ten-Year Age Effect					NO_x Concentrations[d]	
Pit	Cigarette	Other	Non-smoker	Cigarette[e]	Other[e]	Respirable Dust Concentration[d] (1 mg/m^3)	Time[d,f]	NO (0.1 ppm)	NO_2 (0.01 ppm)
C	4.48	10.22[g]	2.93	0.46	0.31	0.84	0.72	1.03	0.57
F	0.76	0.74	1.19	1.34	0.70	0.86	0.16[h]	1.07	0.38
K	1.34	0.87	1.46	0.92	2.20	1.13	0.27[g]	2.16	0.83
P	11.54	3.06	0.87	3.22	25.59	0.79	0.32	1.21	1.14
Q	1.18	1.07	2.09	0.63	0.56	1.28[h]	0.51	0.92	1.04
V	1.96[h]	1.25	1.49	0.99	1.54	1.10	0.63	1.07	4.41
W	0.81	0.48	0.76	1.79	2.70	0.95	0.06[i]	> 30.00	> 30.00
X	1.24	0.98	0.98	1.37	1.13	1.08	0.39[g]	1.26	1.12
Y	1.49	1.97	1.16	1.24	1.24	1.11	0.78	1.05	1.02

	Model C[d,j]								
	Face								
	Hand-Filled		Mechanized				Other Underground		
Pit	Intake	Face	Some Shot Firing	No Shot Firing	Develop-ment	Diesel Driving	No Shot Firing	Some Shot Firing	Surface
C	7.80	1.45	0.23	23.08	3.64	—	5.24[g]	2.78	
F	0.84	0.06	>30.00	—	>30.00	—	1.92	9.62	
K	0.82	0.56	0.00	1.07	0.00[g]	22.83	0.74	1.15	
P	27.37	>30.00	—	>30.00[h]	2.17	—	7.33[h]	2.47	
Q	0.88	>30.00	>30.00	0.49	0.51	3.64	1.34	0.27	
V	0.35	—	—	0.00	0.64	—	0.97	—	
W	—	—	—	0.30	—	>30.00	1.56	0.29	
X	0.22[h]	0.00[h]	0.03	0.12	0.09[h]	0.83	0.44	0.23	
Y	2.02	0.33	0.07	0.70	0.46	7.17	1.27	1.93	

[a] Model A includes only terms shown and intercept.

[b] Model B includes terms shown, all those in model A, and proportion of time on hand-filled faces.

[c] Relative to nonsmoker at age 45 years.

[d] Refers to five-year period preceding survey analyzed.

[e] Relative to nonsmoker.

[f] In colliery; 1,000 shifts.

[g] Approximate statistical significance: $p < 0.01$.

[h] Approximate statistical significance: $p < 0.05$.

[i] Approximate statistical significance: $p < 0.001$.

[j] Full-time work in named activity relative to full-time work on surface. Model C includes terms shown and all those in model A.

ABOUT THE AUTHORS

J. Fintan Hurley was born near Cork in Ireland, and graduated with a B.A. (mathematics, statistics, and economics) from the National University of Ireland (NUI) in 1970. Following an M.A. (NUI, 1971) and the award of a Traveling Studentship Prize in mathematics, he studied statistics at the University of Edinburgh. In 1975 he joined the Institute of Occupational Medicine, where he is now Head of the Statistics Group. His primary research activity has been in epidemiological studies of exposure to dust and respiratory ill health in coal miners. His current interests are in continuing research in a wide range of epidemiological studies of occupational health, in developing methods for teaching epidemiology through practical examples, and in communicating research results to nonscientific audiences.

Michael Jacobsen is Deputy Director of the Institute of Occupational Medicine, and an Honorary Senior Lecturer at the University of Edinburgh's Department of Community Medicine. His apprenticeship in science was at the laboratory bench in the chemical industry. A B.Sc. degree from the University of London in 1962 led to work in applied statistics for the pharmaceutical industry on clinical trials and efficiency studies of biochemical plant processes. Since 1968, his interests have centered on occupational health epidemiology at the Edinburgh Institute, where he has been active in studies of workers in the coal, coking, steel, asbestos, and chemical industries. His work on exposure-response relationships in coal miners' lung diseases has been used to help formulate occupational hygiene standards for coal mines in the United Kingdom, the United States, and elsewhere. He was awarded a Ph.D. degree by the University of Edinburgh in 1976. Dr. Jacobsen's publications reflect his continuing strong interest in the methodology and philosophy of epidemiological research and in practical applications of results.

Alastair Robertson obtained his B.Sc. (Hons.) in chemistry from Edinburgh University in 1971. He carried out research in inorganic chemistry at the same university and was awarded a Ph.D. in 1976. He joined the Institute of Occupational Medicine in 1974 to research oxides of nitrogen in coal mines. Dr. Robertson's interests have widened into a number of areas of analytical chemistry and occupational hygiene and he has led several research projects in these fields. Presently, he is Head of the Analytical Group and is a full member of the Council of the British Occupational Hygiene Society.

Ralph Roscrow was awarded a B.Sc. degree in computer science by the University of Edinburgh in 1983. He has concentrated since then on the design and interactive exploitation of data-base systems, initially for botanical data at the University of Glasgow, and subsequently for epidemiological data at the Edinburgh Institute of Occupational Medicine. Mr. Roscrow is currently designing data-base systems for large-scale commercial applications in England.

Tom A. Smith graduated with an M.A. in natural sciences from Caius College, Cambridge, in 1979. He was awarded a Ph.D. by the University of Edinburgh in 1983 for his work in the Department of Pathology on the genetics of teratocarcinoma cells in mice, and he obtained an M.Sc. in medical statistics at the University of Newcastle on Tyne in 1984. His enthusiasm for applying quantitative methods in biological research has led him to analyses of laboratory and epidemiological data from diverse studies in occupational health in the United Kingdom, and to studies of health statistics in the developing world. Dr. Smith's current appointment is in statistics with the Papua, New Guinea, Institute of Medical Research.

INTRODUCTION

In the summer of 1983, the Health Effects Institute (HEI) issued a Request for Applications (RFA 83-4) that solicited proposals for "Epidemiological Investigations of Effects of Automotive Emissions." In the fall of 1983, Dr. Michael Jacobsen, of the Institute of Occupational Medicine, Edinburgh, Scotland, proposed a project entitled "Respiratory Infections in Coal Miners Exposed to Nitrogen Oxides." The HEI asked Dr. Jacobsen to modify his proposal, and, in the spring of 1984, approved the two-year project and authorized total expenditures of $165,400. The project began in October, 1984, and the final report was accepted by the Health Review Committee in October, 1987. The Health Review Committee report is intended to place the investigators' final report in perspective as an aid to the sponsors of the HEI and to the public.

THE CLEAN AIR ACT

The Environmental Protection Agency (EPA) sets standards for motor vehicle emissions of oxides of nitrogen (and other pollutants) under Section 202 of the Clean Air Act, as amended in 1977. Section 202(a)(1) directs the Administrator of the EPA to "prescribe (and from time to time revise) . . . standards applicable to the emission of any air pollutant from any class or classes of new motor vehicles or new motor vehicle engines, which in his judgment cause, or contribute to, air pollution which may reasonably be anticipated to endanger public health or welfare." Sections 202(a)(3) and 202(b)(1) impose specific requirements for reductions in motor vehicle emissions of oxides of nitrogen (and other pollutants), and provide the EPA with limited discretion to modify those requirements.

The determination of the appropriate standards for emissions of oxides of nitrogen depends in part on an assessment of the risks to health they present. An epidemiological study to determine if occupational exposures to oxides of nitrogen are associated with increased susceptibility to respiratory infection can contribute knowledge useful in making the evaluations of health effects in humans that are an important part of informed regulatory decision-making under Section 202.

In addition, Section 109 of the Clean Air Act provides for the establishment of national ambient air quality standards. The current standards include primary and secondary standards for nitrogen dioxide, which were last reviewed in 1985. Also, under Section 166 of the Act, in February, 1988, the EPA published proposed regulations to prevent significant deterioration of air quality due to emissions of oxides of nitrogen. Research of the type described in the investigators' report can contribute to any assessment of the appropriateness of the existing standards and to ongoing and future regulatory initiatives.

BACKGROUND

Energy use in both mobile and stationary sources produces most of the nitrogen oxides found in urban environments. Nitrogen dioxide is the most important among the oxides of nitrogen in terms of human health effects. Adverse health effects have resulted from acute exposure to nitrogen dioxide (for review, see U.S. Environmental Protection Agency 1981, 1985); however, our understanding of the long-term effects of nitrogen dioxide exposure at concentrations at or near ambient levels is very limited. The current one-hour National Air Ambient Quality Standard for nitrogen dioxide is 0.053 parts per million (ppm) averaged over one year. Although the nitrogen dioxide standard is being met generally, typical long-term ambient concentrations of nitrogen dioxide range from 0.001 ppm in isolated rural areas to hourly peaks in urban areas that can exceed 0.3 ppm (U.S. Environmental Protection Agency, 1985).

Animal studies have demonstrated that exposure to nitrogen dioxide also increases susceptibility to respiratory infection (Pennington 1988). One approach in animal models is to expose animals to nitrogen dioxide and then infect them with highly virulent bacterial or viral strains. The effects of nitrogen dioxide exposure on infection are assessed by comparing mortality rates in infected animals that have breathed either air or nitrogen dioxide.

A second approach, in vitro studies, focuses on specific lung defense components. After whole-animal or in vitro exposure to nitrogen dioxide, macrophages are recovered from bronchoalveolar lavage or tracheal epithelium explants and are functionally evaluated. After in vitro exposure, macrophages show reduced bactericidal capacity after exposure to nitrogen dioxide levels as low as 0.1 ppm (Voison et al. 1977). Recent studies have been more inconclusive. Mochitate and colleagues (1986) noted metabolic enhancement via enzyme assays and increased macrophage numbers when rats were exposed to 4 ppm nitrogen dioxide for 10 days. However, Lefkowitz and coworkers (1984) found no significant changes in the interferon levels (a measure of immune system responsiveness) of mice after exposure to 5 ppm nitrogen dioxide for seven days.

The relationship between nitrogen dioxide exposure and susceptibility to respiratory infections has also been the focus of numerous epidemiological studies. Specific groups have been identified as exposed to especially high concentrations of nitrogen dioxide, such as residents of homes with gas-fueled stoves or unvented gas or kerosene heaters, urban traffic police or toll collectors, and children in areas of high ambient concentrations of nitrogen dioxide.

Monitoring of nitrogen dioxide levels in homes has shown that residents who use gas cooking stoves are subject to higher average nitrogen dioxide exposures than those who use electric stoves. Most of these studies involved school children for whom symptoms were ascertained and exposure histories were compiled from parent-completed questionnaires. In 1977, Melia and collaborators published one of the first reports of adverse health effects associated with the use of gas cooking stoves (Melia et al. 1977). They surveyed the respiratory symptoms and illnesses of 5,758 school children in England and Scotland. Using an outcome variable composed of diverse symptoms and diseases, Melia and associates found significantly higher prevalences of bronchitis, cough, and chest colds for children living in homes with gas stoves than for those living in homes with electric stoves. Because the analysis did not control for the potentially important confounding effect of parental smoking, the results are not readily interpretable. In a later study, Melia and coworkers measured nitrogen dioxide levels in 183 homes each week (Melia et al. 1982). After analyses that controlled for age, sex, social class, and parental smoking, no statistically significant associations were found between the nitrogen dioxide levels and the prevalence of the composite respiratory illness variable.

Ogston and coworkers (1985) studied indoor nitrogen dioxide levels and respiratory illness during the first year of life of 1,565 infants born in Dundee, Scotland. The incidence of respiratory illness was found to be greater for infants from homes with gas, rather than electric, stoves, but the difference was not statistically significant. In a large retrospective study of children aged six to 10, Speizer and his coworkers at Harvard (1980a,b) found a small, but statistically significant, association between respiratory illness before the age of two and stove type. Upon reanalysis of the data from this study, Ware and colleagues (1984) determined that the estimated odds ratio for respiratory illness of 1.23 ($p < 0.01$) was reduced to 1.12 ($p = 0.07$) when the data were adjusted for socioeconomic status. These studies have been further criticized for the authors' reliance on current cooking fuel alone to represent exposure, rather than using historical information or measurements. Keller and associates (1979) followed the incidence of respiratory illness in 441 upper-middle-class families in Ohio. They monitored respiratory illness incidence through twice-weekly telephone calls and random sampling of nitrogen dioxide levels of homes. No statistically significant association between respiratory illness and gas stove use was found.

Only a few studies have looked at the association between gas stove use and respiratory infection in adults. In a significant survey of residents of Washington County, Maryland, Comstock and associates (1981) found an increased prevalence of respiratory symptoms in nonsmoking men who use gas stoves. In another study, Jones and coworkers (1983) conducted a case-control study of women in the Tecumseh Community Health Study. They detected a nonsignificant association between cooking stove type and lung function level.

Studies of other nitrogen-dioxide-exposed groups have not clarified the link between nitrogen dioxide levels and respiratory infections. In a comparison of urban police, who are exposed to high concentrations of nitrogen dioxide from automobile exhaust, with suburban traffic police, Speizer and Ferris (1973a,b) found no differences in the amount or types of respiratory symptoms of the two groups. A study of school children who lived in areas with low and high levels of nitrogen dioxide was undertaken in Chattanooga, Tennessee (Shy et al. 1970a,b). Postcard health surveys and parentally tested lung volumes initially revealed more respiratory symptoms and influenza in the children who lived in the high nitrogen dioxide area. Later, independent review revealed serious shortcomings in the study design and the nitrogen dioxide measurements in these studies (Ferris 1978).

In evaluating whether or not nitrogen dioxide exposure increases susceptibility to respiratory infection, both exposure and outcome variables must be assessed accurately. Precise measurement of nitrogen oxide exposure can best be accomplished by determining the personal exposure to the gas. While the ambient levels of nitrogen dioxide can be determined readily, difficulties are encountered when estimating daily personal activity patterns, individual uptake and dose, and, most of all, past exposure history. Thus, detection of both the acute effects of short-term exposure and the chronic effects of long-term exposure requires accurate measurements of exposure, which may not always be available.

Evaluating symptoms of respiratory infection and events also presents several problems. Physical examination and microbiological testing would seem the most appropriate method of diagnosing infections, but these are extremely time-consuming and expensive. Often, differentiation between types of symptoms, as in asthmatic or infectious cough, is unclear and imprecise at best. To assess past events, or to do large-scale surveys, questionnaires are often the most practical means of acquiring the needed information. However, questionnaires are susceptible to recall bias and imprecise interpretation of medical terminology. It is difficult to determine the severity, or even the duration, of respiratory infections through such questionnaires. Confounding factors, such as age, smoking, socioeconomic status, day-care use, family size and composition, and exposure to other air pollutants, may obscure the true association between measured nitrogen dioxide concentrations and incidence of respiratory infections. In addition, susceptibility to respiratory infections is influenced by the presence of concurrent respiratory and other diseases.

Overall, the results of the epidemiological studies are inconclusive as to whether or not increased nitrogen dioxide exposure is associated with increased susceptibility to respiratory illness. On the whole, the studies have focused on short-term effects, without reliable information on nitrogen dioxide exposure or the health outcome. The current national ambient standard of 0.053 ppm nitrogen dioxide (averaged annually) is based on the Chattanooga study (Shy et al. 1970a,b), which, as mentioned earlier, has serious flaws. Identifying an appropriate population that is exposed to measurable amounts of nitrogen dioxide could help clarify some of these issues.

Coal miners in Britain may occasionally be exposed to relatively high concentrations of nitrogen oxides, formed during diesel combustion in mine trains and during shot firing. To date, any association between respiratory infections and exposure to nitrogen dioxide in such populations has not been examined. A few occupational studies have been undertaken to determine the acute respiratory effects of nitrogen dioxide in miners (Ames et al. 1982; Lapp et al. 1972). These authors tested miners' lung function and capacity before and after a work shift. No attempt was made to determine if there was a relationship between respiratory infections and the levels of nitrogen dioxide to which the miners were exposed.

In 1953, a long-term epidemiological study of British coal miners (Fay 1957; Fay and Rae 1959) was begun to assess the health of the workers at 24 coal mines. Comprehensive medical surveys were undertaken, at approximately five-year intervals, at many of the mines. Dr. Jacobsen has used the information available from this population regarding the concentrations of nitrogen dioxide, nitric oxide, and dust, as well as the types of work and mining conditions, and the miners' detailed attendance records to estimate the miners' exposure to nitrogen dioxide. Respiratory symptoms and reports of chest illness, known through the periodic health surveys, were then correlated to estimates of individual exposures to determine whether or not a relationship exists between nitrogen oxides exposure and respiratory health within this population.

GOALS AND OBJECTIVES

The objectives of Dr. Jacobsen's study were to determine whether occupational exposures to nitrogen oxides were associated with increased susceptibility to respiratory infections in British coal miners, and to estimate the relative risks for such infections at different levels of exposure.

STUDY DESIGN

This study used data acquired in a long-term epidemiological project about British coal miners, the Pneumoconiosis Field Research Study. Information was available from 1953 through 1978 for coal miners working in nine British coal mines. The information consisted of records of work attendance, occupational history, mining practices, and underground conditions at the mines. In addition, information on dust levels and some information on nitrogen oxides levels were also available. Health information was obtained from repeated medical surveys.

The investigators also performed a supplementary study to measure shift-average concentrations of nitric oxide and nitrogen dioxide at some of the collieries. These results were used to estimate errors in the retrospective assessment of nitric oxide and nitrogen dioxide exposures, which were determined by a linear regression model. In another supplementary study, the reliability of miners' responses about illness was assessed by a comparison of questionnaire responses with colliery sickness absence records.

SUMMARY OF INVESTIGATORS' CONCLUSIONS

The investigators conclude that there were no consistent associations between estimated occupational exposures to nitric oxide or nitrogen dioxide and reported respiratory illnesses, either in the total group of coal miners or in the three population subsamples that were studied. In addition, there was no evidence of consistent association between nitrogen oxides exposure and chest illness in smokers, nonsmokers, or other susceptible subgroups. Rates of reported respiratory illness increased with increasing age, and were higher among men with chronic bronchitis, low levels of lung function, pneumoconiosis, and past histories of respiratory illness. More respiratory illnesses were reported by cigarette smokers and by men who worked for longer periods underground, especially in work involving shot firing or diesel driving, as opposed to on the surface. The investigators conclude that long-term occupational exposures to low levels of nitric oxide or nitrogen dioxide (median levels were 0.2 ppm nitric oxide and 0.03 ppm nitrogen dioxide) are not associated with increased reporting of respiratory illnesses by British coal miners.

TECHNICAL EVALUATION

ASSESSMENT OF METHODS AND STUDY DESIGN

This is a complex and comprehensive investigation that consists of two methodological studies and four substantive analyses that involve overlapping subsets of the entire population (21,490 men who attended at least one medical survey and had records of cumulative exposure to dust).

The methodological studies were performed to develop a linear regression model to estimate the shift-average concentrations of nitrogen dioxide for various occupational groups, and to assess the reliability of the miners' responses. The substantive studies are investigations of the relationships between exposure to nitrogen oxides and reports of respiratory infections in the extensive data set available to the investigators. The entire population, as well as three subsets of the population, were considered in these studies. In general, estimated exposures to nitrogen oxides were compared among men who were classified according to their questionnaire responses about respiratory illnesses at a designated survey. The miners' responses were grouped as having no sickness absence because of chest illness, an absence attributed to a cold, influenza, or bronchitis, or an absence attributed to some other chest illness. The authors used regression models and relative risk measures to detect any association between the miners' respiratory health status and their nitrogen oxides exposure levels. They are to be commended for their exhaustive and thorough analysis of the extensive data set.

Measurements and Estimates of Exposure

The first of the methodological studies involved an evaluation of the reliability of the estimated nitric oxide and nitrogen dioxide levels. The levels of nitric oxide and nitrogen dioxide had been measured directly only from 1976 through 1979 and from 1980 through 1982. In 1985, additional measurements were undertaken in conjunction with the present study. Nine coal mines were included in the first survey, four in the second, and two in the third.

Extensive information about occupations, specific work locations, mining procedures, and conditions underground were incorporated into a linear regression model to estimate exposure to nitrogen oxides in earlier years for various occupational groups of miners. The authors state that 68 percent and 86 percent of the variations in measured nitric oxide and nitrogen dioxide could be explained by their regression models, which incorporate these measures of exposure.

However, these estimated exposures for occupational groups are likely to be underestimates. The regression model developed by the investigators did not include information on surface occupations or on conditions associated with hand-filled coal extraction, prevalent before the 1960s, that are believed to have resulted in higher levels of exposure to nitric oxide and nitrogen dioxide, particularly among workers exposed to shot-firing fumes. As mining practices improved during the last three decades, and mining operations became more mechanized, the workers' exposure to gaseous pollutants in the mines decreased. Indeed, in the two mines surveyed in 1985, the levels of both nitric oxide and nitrogen dioxide were lower in comparison to the 1980 through 1982 and the 1976 through 1979 levels. Thus some occupational exposures in the past, especially before mechanization, are not incorporated in the estimates of workers' exposure. Emissions of nitrogen dioxide from nonoccupational sources (for example, gas stoves or heaters at home) are an additional source of underestimation of the true exposure. Nevertheless, the investigators' development of a model to estimate the nitrogen oxides exposure levels for the occupational groups in their cohort was a reasonable approach given the retrospective nature of this investigation.

Reports of Chest Illnesses and Sickness Absence Records

The second methodologic study was an assessment of the validity of the miners' responses in the health surveys that were conducted every five years. The principal outcome variable is the response to the question, "In the last three years, have you had a chest illness that has kept you off work for more than one week?" Positive responses were coded according to the miners' recall of the name given to the condition by their physicians (asthma, bronchitis, cold, bronchitis and asthma, influenza, or other).

This study was undertaken because of concerns about the reliability of the miners' recall of both an illness episode and the physician's diagnosis of the illness. For this purpose, the responses of 151 men surveyed in 1975 and 320 men surveyed in 1986 were compared with the actual sickness absence records at two coal mines. There were some discrepancies, as might be expected considering the lengthy (three-year) period of recall and the fact that colds, influenza, and other upper respiratory infections do not always result in "chest illness." In fact, only about 20 percent of men with a sickness absence record for "bronchitis, cold, and influenza" reported the absence as due to the chest illness. Agreement between questionnaire responses and sickness absence records was better for bronchitis than for colds or influenza. Overall, about 85 percent of positive questionnaire responses were confirmed by sickness absence records.

Sickness absence records were lacking, appropriately, for about 70 percent of the miners who gave negative responses. However, illness may have been under-reported; about 30 percent of the men who denied a chest illness had a sickness absence certificate mentioning a respiratory illness. Verification for all of the miners, through their physicians' records, could not be attempted for practical reasons.

This methodologic investigation suggests that the use of existing information from the health surveys was an adequate approach to ascertain the respiratory health of the population, and the authors are to be commended for making an attempt to examine the reliability and quality of their data. The requirement in the original questionnaire, that illnesses reported were those that had kept the men off work for at least a week, was adopted in order to exclude minor illnesses and situations in which medical leave may have been used for other purposes. Nevertheless, this exigent requirement also had the effect of failing to ascertain many chest illnesses and respiratory infections that could have been severe but that did not keep the men off work for a week. (In fact, it was not possible to assess duration or severity of the illnesses that were documented.) This factor, as well as the long recall period, is likely to have led to an underestimation of the prevalence of respiratory illness in the study population.

DISCUSSION OF INVESTIGATORS' FINDINGS

Individual Population Results

The association between exposure to nitrogen oxides and chest illness was investigated in the entire population of coal miners with valid questionnaire responses (19,901 men), and in three subcohorts of the miners (see Figure 2 in the investigators' report).

1. The relationship between nitrogen oxides exposure and questionnaire responses was explored for 19,901 men (group C, Figure 2) for whom information was available from at least one set of valid questionnaire responses. On 40,071 completed questionnaires, 5,408 episodes of colds, influenza, or bronchitis were reported. Men who reported colds, influenza, or bronchitis were older and were more often smokers than those who denied having these illnesses. In addition, a higher percentage had reported respiratory symptoms and sickness absences at earlier surveys; their mean levels of lung function were lower, and the prevalence of pneumoconiosis was higher in these men. There were no consistent patterns to suggest a relationship between exposure to oxides of nitrogen and reports of chest illness. Relative risks associated with nitric oxide and nitrogen dioxide varied between 0.38 and 1.70 among collieries, but on the average were very close to 1. Workers who were exposed to diesel emissions, and who were involved in shot firing, reported more chest illness than other workers; however, a relationship between illness among such workers and nitrogen oxides levels could not be demonstrated. Workers who spent time underground reported more illnesses than did those who had surface jobs.

2. A subgroup of 11,039 men (group D, Figure 2), who had at least one pair of reponses about chest illness from two consecutive surveys, was studied. These men were classified according to whether or not they reported a chest illness at the first survey; their responses at the follow-up survey were then related to the presence or absence of illness at the first survey, as well as to the estimates of exposure during the interval. At the end of the interval, reports of bronchitis, influenza, or colds were nearly nine times more frequent in those who had reported one of these illnesses at the start of the interval. Positive responses were related to age and to smoking habits, but were not related to time spent working in different job categories or to mean concentrations of nitric oxide or nitrogen dioxide exposure.

3. The effect of long-term exposure to nitrogen oxides was investigated in the group of 7,463 miners (group B, Figure 2) who had attended the most recent health survey (fifth or sixth). The cumulative exposure to nitrogen oxides was calculated from the time mechanization began at the colliery to the time of the last survey. The median number of shifts contributing to nitrogen oxides exposure that these men had worked was equivalent to 6.5 years; 20 percent of the men had been exposed for the equivalent of at least 11 years. A higher proportion of men reporting a cold, influenza or bronchitis were smokers, they were six years older on the average, and their exposure to respirable dust was greater. In multiple logistic analyses adjusting for the effects of age, smoking habits, and exposure to dust, rates of reporting the combined illnesses increased with age, and were greater for smokers than for nonsmokers when other variables were controlled. Time worked underground was also positively related to reports of chest illness. Men who reported a cold, influenza, or bronchitis worked more shifts in shot firing and diesel driving than did men who denied chest illness, but their estimated cumulative exposures to nitric oxide and nitrogen dioxide were very similar.

4. In contrast to the preceding analyses, in which estimated levels of nitrogen oxides exposure were used, accurate measurements of exposures were available for a group of 560 miners. These men had all participated in the third, fourth, and fifth surveys and were the subjects of an earlier investigation by the authors' institution (Robertson et al. 1984). Of these men, 126 were exposed to relatively high levels of nitrogen oxides, whereas 434 were exposed to very low levels. For some of these analyses, miners were also classified into one of five subgroups, according to their exposure to nitric oxide and nitrogen dioxide and the ratio of the two. Mean nitrogen dioxide exposures ranged from 53 ppm•shift to 1,125 ppm•shift. This analysis did not reveal an association between exposure and reports of cold, influenza, bronchitis, or any other chest illness; however, the number of miners with relatively high exposures was small. Logistic regression analyses were used

to identify variables associated with a report of cold, influenza, or bronchitis lumped together. Exposure to nitrogen oxides was not related to the report of respiratory illness. However, the colliery at which a man worked and low forced expiratory volume in one second were associated with chest illness.

Interpretation of Data

There were no significant associations between reports of respiratory illness and exposure to nitrogen oxides in the present study. The investigators used the information accumulated on British coal miners since 1953 as part of the Pneumoconiosis Field Research Study, and skillfully manipulated and analyzed the extensive data set. Neither the four substantive analyses nor the numerous secondary analyses convincingly negated the null hypothesis.

The investigators examined the relationship between exposure to nitrogen oxides and chest illness in smokers and nonsmokers separately, and in men with and without evidence of chronic respiratory symptoms, reduced pulmonary function, or pneumoconiosis. Although they did not analyze the data to determine the relationships between these characteristics and chest illnesses, confounding was controlled by stratification on these variables. The inclusion of these separate variables did not uncover associations between exposure to nitrogen oxides at work and respiratory illness in men with or without histories of smoking or chronic obstructive pulmonary disease. However, these susceptible groups of miners were at increased risk of chest illness. These analyses do demonstrate the power of the study to detect relationships between chest illnesses and age, smoking habits, and respiratory impairments.

There was suggestive evidence that underground work was associated with more reports of chest illness than was surface work. Also, diesel engine drivers and shot firers appeared to be at greater risk of chest illness than miners in other job categories. However, a relationship between estimated or measured nitrogen oxides levels and chest illness could not be demonstrated in any of these cases. It is possible that the job categories, which are based in part on time worked before mechanization when concentrations were highest, are indicators of exposure that is relevant to chest illness; the postmechanization estimates of nitrogen oxides exposures predicted by the regression model exclude these earlier exposures. Alternatively, the greater morbidity may be associated with other factors or pollutants. Bias may have occurred because of loss to follow-up. If some men left their jobs because of respiratory symptoms, the results may reflect a "healthy worker" effect and so may underestimate the degree of association. However, it is also possible that death or injury, unrelated to exposure to nitrogen oxides, caused the men to leave the mines; such losses from the cohort would not bias the results.

Although the use of information from the health surveys was appropriate, it may have introduced some errors. As discussed above, the exigent requirement of one week's absence, and the lengthy period of recall, may have led to underestimation of chest illness. In addition, bronchitis, influenza, and colds were lumped together in most analyses. The authors felt that the use of this grouping was acceptable because none of these illnesses was associated with nitrogen oxides exposures when considered separately. However, chest illness is not synonymous with respiratory infection, and lumping other chest illnesses with upper respiratory infections may have weakened the opportunity to detect associations with more serious illnesses, if any existed. As discussed above, one of the unresolved questions about the effect of nitrogen dioxide exposure on respiratory illness is whether nitrogen dioxide affects the frequency of infection, or the severity or duration of illness. The illnesses reported on the questionnaire were severe enough to keep the men off work for a week or more. However, adequate information was not collected to assess the severity of infection or the duration of illness.

It should also be noted that the outcome measure is only a crude indicator of the *frequency* of infection. The miners were asked whether or not they had an episode of chest illness during the *last three* years; the yes or no response to this question provides information as to whether or not the miner was ill, but does not provide information on *how many times* he was ill. If the miners do not get ill very often, then the outcome measure is an indicator of frequency of illness. On the other hand, one could envision two circumstances in which this would not be the case. If miners in the entire population were often sick, or if there were a sensitive subpopulation of miners that was frequently ill, then the answer to "were you ill in the last three years" would not measure frequency adequately. The information from subgroup D showed that the rates of illness were higher in men who had reported chest illness on previous surveys, which would suggest that the outcome variable, as measured by the response to this question, is a poor indicator of frequency.

Information was not available about nitrogen oxides exposure off the job; however, other important confounding factors, such as dust, were controlled. As with the smoking and chronic obstructive pulmonary disease variables, the authors stratified the data on the dust level variable rather than analyzing the data with both oxides and dust exposures considered separately and combined.

These data appear to be a resource with potential for providing insights into the association, if any, between respiratory illness and long-term exposure to low levels of nitrogen oxides in an occupational setting in a group of relatively healthy men. Known associations between chest illness and age, smoking habits, respiratory symptoms, low forced expiratory volume, and past reports of similar illness were detected in these analyses, and the study probably has sufficient statistical power to detect the effects of exposure to nitrogen oxides, if any exist. However, the authors do not present formal power calculations. Smoking was found to increase the relative risk of respiratory illness by 50 percent over that in nonsmokers, but it may be difficult in these data to detect a smaller increase in risk with the nitrogen oxide concentrations found here. Errors in exposure estimation, misclassification of illnesses, use of inadequate measures of illness, and absence of information on duration and severity of infection are likely to reduce the power of this study.

The investigators have concluded that chest illnesses in working British coal miners are unrelated to exposure to nitrogen oxides at the low levels existing in nine mines. However, as discussed above, misclassification of exposure and outcome is clearly a problem in this study; such problems are not uncommon when existing data are used for purposes that were not foreseen when they were collected. Because of these and other problems (recall bias, confounding exposures), it would have been appropriate to have concluded that no association between nitrogen oxides exposure and chest illness could be demonstrated in this study, and that the negative results reported here must be interpreted cautiously. The authors have done an excellent job manipulating and analyzing this extensive data set, and have most likely uncovered any relationship between respiratory health and nitrogen oxides exposure that the data hold.

REMAINING UNCERTAINTIES AND DIRECTIONS FOR FUTURE RESEARCH

An epidemiological study of the association between nitrogen dioxide exposure and respiratory illness, conducted in Chattanooga, is the basis of the current nitrogen dioxide standard. However, the results of subsequent epidemiological investigations have been inconsistent and inconclusive. The study reported here relied on a very substantial body of information collected on British coal miners. The authors have done a commendable job of analyzing the data, interpreting their results, and cross-checking their interpretation. Nevertheless, the results of the study are not conclusive.

We are not aware of any other large body of data that would provide an opportunity to explore the association between nitrogen dioxide and respiratory infection. If such a data base exists, the Jacobsen study is perhaps exemplary in suggesting how an analysis of the data might be approached. However, because of the problems usually encountered in retrospective environmental epidemiologic studies, and because the effects of nitrogen dioxide are likely to be small in comparison with other possible confounding variables, it is not likely that such studies would provide a clear conclusion.

Future epidemiological studies should be performed with a prospective design and should involve careful measurement of exposure to nitrogen oxides, ranging from high levels to low levels. The design of such studies should carefully characterize illness, including measures of frequency and severity. Confounding factors and exposure to other pollutants should also be controlled or measured.

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Special Reports

Title	Publication Date
Gasoline Vapor Exposure and Human Cancer: Evaluation of Existing Scientific Information and Recommendations for Future Research	September 1985
Automotive Methanol Vapors and Human Health: An Evaluation of Existing Scientific Information and Issues for Future Research	May 1987
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Research Reports

Report No.	Title	Principal Investigator	Publication Date
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Research Report Number 18

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