

**OCCUPATIONAL EXPOSURES and CHRONIC
OBSTRUCTIVE PULMONARY DISEASE: A hospital-
based case- control study**

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BY

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DECLARATION

I, Nadira Govender, declare that this Masters in Medicine (Occupational Medicine) dissertation is my own work and all primary and secondary sources have been appropriately acknowledged. This dissertation has not been submitted to any other institution as part of an academic qualification.

This Dissertation is prepared in partial fulfilment of the requirement of the Masters in Medicine (Occupational Medicine) degree at the School of Family and Public Health Medicine, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban South Africa.

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SIGNATURE

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ACRONYMS AND ABBREVIATIONS

ATS	: American Thoracic Society
BOLD	: Burden of Occupational Lung Disease
CI	: Confidence interval
COPD	: Chronic Obstructive Pulmonary Disease
CGF	: Chemicals, gas or fumes
ECRHS	: European Community Respiratory Health Survey
ERS	: European Respiratory Society
FEV1	: Forced expiratory volume in one second
FVC	: Forced vital capacity
GOLD	: Global Initiative on Obstructive Lung Disease
LFT	: Lung function test
OR	: Odds ratio
PAR	: Population Attributable Risk
PLATINO	: Latin American Project for the Investigation of Obstructive Lung Disease
PR	: Prevalence Ratio
RR	: Relative Risk
TB	: Tuberculosis
VGDF	: Vapours, gases, dusts or fumes
WHO	: World Health Organisation

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ABSTRACT

Introduction

Chronic Obstructive Pulmonary Disease is projected to rank 5th among the leading causes of disease by the year 2020. Risk factors include smoking, indoor and outdoor air pollution, previous respiratory infections, genetics, as well as occupational exposures.

Aim

The aim of this study was to determine the contribution of occupational exposures to the burden of Chronic Obstructive Pulmonary Disease (COPD) among a sample of hospital based patients.

Methods

Cases (n=110) with specialist physician diagnosed COPD from the three public sector specialist respiratory clinics in KZN and controls (n=102) from other non-respiratory chronic ailment specialist clinics at the same institutions were selected. An interviewer administered questionnaire and exposure history was obtained for each participant. In addition, a valid lung function test was obtained for each case. Data was analysed using STATA version 10. Multivariate regression models were developed to examine the relationship between COPD and occupational exposures while adjusting for age, sex, smoking and previous history of tuberculosis. The relationship of FEV1 and occupational exposures, adjusted for

age, height, previous history of tuberculosis and smoking history, was investigated among cases.

Results

Cases and controls were similar with respect to age and sex distribution. Cigarette smoking differed significantly between cases and controls with a larger proportion of cases having ceased to smoke compared to controls (72% vs 46%, $p < 0.01$). A higher proportion of controls reported employment in administrative, managerial and quality control positions (21.3% vs 12.0%, 7.7% vs 2.6% and 5.4% vs 0.3% respectively). Employment in the construction and shoe manufacturing industries was reported more frequently by cases (10.3% vs 3.2% and 10.0% vs 4.9% respectively). Cases were more likely than controls to have been exposed to dust (72% vs 28%, $p < 0.001$) or to chemicals, gas or fumes (74% vs 25.5%, $p < 0.001$) and reported exposure durations 3-4 fold higher than that of controls ($p < 0.001$). Dust and chemical, gas or fume exposure was associated with an increased odds of developing COPD. Exposure to dusts (OR 7.9, 95% CI 3.9-15.7, $p < 0.001$), chemicals, gas or fumes (OR 6.4, 95% CI 3.2-12.8, $p < 0.001$) were significantly associated with odds of developing COPD. In addition, previous history of tuberculosis, as well as smoking were associated with an increased odds of COPD (OR 5.7, 95% CI 1.2-27.4 $p < 0.001$ and OR 6.4, 95% CI 2.3-17.7, $p < 0.001$).

Discussion and Conclusion

This is one of the first hospital based case-control studies looking at occupational contribution to COPD undertaken in South Africa. In this sample of participants, strong associations were observed between self-reported occupational exposures to dust, and chemicals, gas or fumes, and physician's diagnosis of COPD. The study also demonstrated a strong association between smoking and previous

history of tuberculosis, and risk of COPD. The findings suggest that persons with known occupational exposures to respiratory irritants should be monitored to detect the onset of respiratory ill-health and that preventive strategies should reduce exposure to these agents in the workplace.

CHAPTER I

INTRODUCTION AND LITERATURE REVIEW

INTRODUCTION

According to the World Bank and the World Health Organisation (WHO), Chronic Obstructive Pulmonary Disease (COPD) is projected to rank 5th among the leading causes of disease worldwide by 2020 [1]. The WHO's Global Burden of Disease and Risk Factors project in 2001 reported that COPD is the 5th leading cause of death in developed countries and the 6th leading cause of death in developing countries [1].

As the classical mineral dust induced pneumoconiosis decreases in frequency because of the control of exposure, obstructive airways disease has emerged as the most prevalent category of occupational respiratory disorder in industrialized countries. [2]. The prevalence of COPD is increasing worldwide. Risk factors are numerous and include smoking (an important universal risk factor), previous respiratory infections, indoor and outdoor air pollution as well as occupational exposures. There is increasing evidence that environmental factors (to which men and women are exposed at work) other than cigarette smoking also play a role [3].

As COPD is a common disease in the general population, even a small increase in the prevalence due to occupational exposure would have a major public health impact and should be preventable [2]. Assessing the occupational component of

COPD can better inform prevention strategies designed to reduce the morbidity and mortality associated with COPD [2].

LITERATURE REVIEW

DEFINITION OF COPD

Measurement of COPD in epidemiological studies has not been simple as no agreement existed regarding the definition of COPD until the Global Initiative on Obstructive Lung Disease (GOLD) classification system was published in 2001. Position papers on COPD by the The American Thoracic Society (ATS) and the European Respiratory Society (ERS) were published in 1995. The ATS defined COPD as a “disease state characterised by the presence of airflow obstruction due to chronic bronchitis or emphysema.” The definition by the ERS is based on progressive and irreversible decline of maximum expiratory flow [4]. The current definition of COPD as established by GOLD states that “COPD is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterised by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases”[5]. This definition has also been adopted, in the main, by the American Thoracic Society (ATS) as well as the European Respiratory Society (ERS) [6].

Airflow limitation in COPD as measured by spirometry, is a persistently low forced expiratory volume in one second (FEV1) and FEV1/ forced vital capacity (FVC)

ratio regardless of treatment. The current definition used by the above three organisations for airflow limitation is an FEV1/ FVC ratio of < 0.7. COPD is classified into 4 stages based on the level of impairment assessed by FEV1. The GOLD stages as well as the presence of chronic respiratory symptoms have been shown to be predictors of mortality [5]. GOLD classification of COPD by severity is based on post-bronchodilator FEV1 (Table 5) [5].

Table 1. GOLD classification of COPD based on post-bronchodilator FEV1 and FEV1/FVC <0.70

GOLD stage	FEV1 as percent predicted
I: Mild COPD	≥ 80%
II: Moderate COPD	50%≤FEV1<80%
III: Severe COPD	30%≤FEV1<50%
IV: Very severe COPD	<30% or <50% and chronic respiratory failure*

(* Respiratory failure: arterial partial pressure of oxygen (Pao₂) <8.0 kPa (60mm Hg) with or without arterial partial pressure of CO₂ (PaCO₂) > 6.7 kPa (50mm Hg) while breathing air at sea level)

Historically, there have been many other components of the COPD classification. Chronic bronchitis and emphysema are two such independent components which may co-exist in one individual. Chronic bronchitis is defined as the “presence of a chronic productive cough for three months in each of two successive years, provided other causes of chronic cough have been ruled out” [6]. Emphysema, defined pathologically, is the “destruction of alveolar walls and permanent enlargement of the airspaces distal to the terminal bronchioles” [6]. As uncertainty

remains around how most clinicians diagnose COPD, the use of a standardized classification system such as that proposed by GOLD is advocated.

PATHOPHYSIOLOGY AND RADIOLOGICAL FEATURES OF COPD

Pathological changes of COPD include chronic inflammation as well as structural changes due to a repeated injury and repair process. These changes increase with disease severity. The inflammatory response in the lung, which is also exacerbated by oxidative stress, is considered to be an amplified normal response to the inhalation of noxious, chronic irritants. Chronic inflammation and structural changes leads to fibrosis and narrowing of peripheral airways, dynamic collapse of airways, as well as decreased gas transfer [5]. Radiological features if present, may include hyperinflation, bullae, as well as flattened hemidiaphragms.

PREVALENCE OF COPD

Global population estimates of COPD vary because of differences in definition, risk factors and diagnostic methodology. Although there have been several studies of chronic bronchitis in middle- and lower- income countries, the burden and determinants of COPD have not been well documented [7].

The lack of consistent methods in many countries, including South Africa, to adequately diagnose COPD has resulted in unreliable estimates of the prevalence of COPD worldwide [8]. Prior to the countrywide standardized prevalence studies, various population based studies were undertaken to assist in arriving at an estimate of COPD prevalence (Table 2). These include estimates from the United States of America (US) [6] and South Africa [7]. Limitations that were

acknowledged in the National Health Interview Survey [6], namely dependency on the proper recognition and diagnosis of COPD, as well as lack of validation of airway obstruction, were addressed, in part, by the Third National Health and Nutrition Examination Survey [6], whose population prevalence estimate (13.9%) was almost twice that of the preceding survey.

Table 2. Population based Prevalence studies of chronic bronchitis/ COPD

Country	Prevalence (%)	Year of study
US (National Health Interview Survey) [6]	5.9	2000
US (Third National Health and Nutrition Examination Survey) [6]	13.9	2003
South Africa [7]		2004
Males	2.3	
Females	2.8	
12 study sites [8]	10.1	2006

As accurate estimates of COPD prevalence and risk factors are necessary to assist governments in health care planning for services that will be required, new initiatives, namely The Burden of Obstructive Lung Disease (BOLD) Initiative, in conjunction with The Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO), developed standardized methods for estimating COPD prevalence. These methods, which can be used in countries at all stages of development, were used to measure the worldwide prevalence of COPD [8]. The PLATINO study [9] launched in 2002 reported on the prevalence of COPD in adults aged 40 years or older in 5 major Latin American cities. Crude prevalence of COPD ranged from 7.8% (95% CI 5.9-9.7) in Mexico City to 19.7% (95% CI 17.2-22.2) in Montevideo with males consistently demonstrating a higher

prevalence at each site. These estimates exceed the 4-10% prevalence reported in an international review of 32 studies, "Interpreting COPD Prevalence Estimates" by Halbert RJ et al in 2003. [10]. The multicentre BOLD study (Table 3) undertaken in 2006 with 9425 participants aged 40 years or older estimated the worldwide prevalence of COPD across the 12 study sites. There was significant variation of GOLD Stage I ($p < 0.0001$) with a higher prevalence in males compared to females (11.8% vs 8.5% respectively). The overall prevalence reported for South Africa was 22.2% (± 2.4) for males and 16.7% (± 1.7) for females. This large difference compared to the other sites could be explained by several possible factors, foremost being the high prevalence of tuberculosis in South Africa as well as by the use of biomass fuels for heating and cooking among the rural and semi-urban population. In addition, as South Africa is still a developing country, a large proportion of the population is employed in traditionally dusty trades with exposure to occupational factors which may be implicated in the causation of COPD. The prevalence of GOLD stage II or higher among participants from South Africa was higher than that among participants in other developing countries, namely China, Turkey, and the Philippines. Finally, smoking prevalence may be increasing and contributing to the increase in prevalence [8]. BOLD's reported prevalence's are similar to the PLATINO study which used similar study methods, but higher than the meta-analysis of 32 population based surveys mentioned above [10].

Table 3. Estimated population prevalence of COPD according to GOLD stage

	Guangzhou, China	Adana, Turkey	Salzburg, Austria	Cape Town, South Africa	Reykjavik, Iceland	Hannover, Germany	Krakow, Poland	Bergen, Norway	Vancouver, Canada	Lexington, USA	Manila, Philippines	Sydney, Australia
Men												
n	236	389	685	315	402	349	266	324	344	206	378	265
No airflow obstruction	84.7% (2.3)	71.5% (2.0)	73.4% (1.7)	71.3% (2.7)	81.8% (2.0)	81.9% (2.2)	72.3% (2.4)	77.4% (2.3)	78.0% (2.4)	81.9% (2.7)	80.4% (1.7)	81.1% (2.4)
Stage I	5.9% (1.5)	13.1% (1.7)	16.3% (1.4)	6.5% (1.5)	9.7% (1.5)	9.4% (1.7)	14.4% (2.1)	11.6% (1.7)	12.7% (1.9)	5.4% (1.6)	0.9% (0.4)	9.6% (1.8)
Stage II	7.6% (1.7)	13.1% (1.5)	9.3% (1.1)	14.2% (2.1)	6.7% (1.3)	7.5% (1.5)	10.3% (1.7)	9.4% (1.6)	9.3% (1.7)	7.1% (1.6)	11.3% (1.4)	7.2% (1.6)
Stage III-IV	1.7% (0.8)	2.3% (0.9)	1.0% (0.4)	8.0% (1.6)	1.9% (0.7)	1.1% (0.6)	3.0% (1.0)	1.6% (0.6)	0	5.6% (1.7)	7.4% (1.2)	2.1% (0.9)
Women												
n	237	417	573	532	353	334	260	334	483	302	515	276
No airflow obstruction	92.4% (1.7)	89.7% (1.9)	74.3% (2.0)	80.0% (1.9)	82.5% (2.1)	90.7% (1.6)	83.4% (2.2)	84.6% (1.9)	83.2% (1.8)	79.2% (2.7)	91.4% (1.4)	80.5% (2.5)
Stage I	2.5% (1.0)	4.3% (1.1)	14.7% (1.6)	3.3% (1.0)	8.1% (1.5)	5.6% (1.3)	8.1% (1.7)	9.5% (1.6)	9.5% (1.4)	5.2% (1.5)	1.8% (0.9)	7.3% (1.6)
Stage II	3.4% (1.2)	5.3% (1.1)	9.2% (1.4)	11.0% (1.4)	7.4% (1.4)	3.1% (1.0)	7.8% (1.7)	5.0% (1.1)	5.5% (1.1)	12.6% (2.2)	4.0% (0.8)	11.4% (2.0)
Stage III-IV	1.7% (0.8)	0.7% (0.4)	1.8% (0.7)	5.7% (1.1)	2.0% (0.7)	0.6% (0.5)	0.8% (0.6)	0.9% (0.5)	1.8% (0.6)	3.0% (1.0)	2.8% (0.8)	0.8% (0.6)
Overall												
n	473	806	1258	847	755	683	526	658	827	508	893	541
No airflow obstruction	88.6% (1.5)	80.9% (1.5)	73.9% (1.3)	76.2% (1.6)	82.1% (1.4)	86.7% (1.3)	77.9% (1.6)	81.2% (1.5)	80.7% (1.5)	80.4% (1.9)	86.2% (1.1)	80.8% (1.7)
Stage I	4.2% (0.9)	8.6% (1.0)	15.5% (1.1)	4.7% (0.9)	8.9% (1.1)	7.3% (1.0)	11.2% (2.3)	10.5% (1.2)	11.1% (1.2)	5.3% (1.1)	1.4% (0.6)	8.4% (1.2)
Stage II	5.5% (1.0)	9.1% (0.9)	9.2% (0.9)	12.4% (1.1)	7.0% (0.9)	5.1% (0.9)	9.0% (1.2)	7.1% (1.0)	7.3% (1.0)	10.1% (1.4)	7.5% (0.8)	9.4% (1.2)
Stage III-IV	1.7% (0.6)	1.5% (0.4)	1.4% (0.4)	6.7% (0.9)	1.9% (0.5)	0.8% (0.8)	1.9% (0.6)	1.2% (0.4)	0.9% (0.3)	4.2% (1.0)	5.0% (0.7)	1.4% (0.5)

Data are % (SE).

Source: Buist A S , McBurnie M A, Vollmer W M, Gillespie S, Burney P, Mannino D M, et al. International variation in the prevalence of COPD (The BOLD Study): a population-based prevalence study .Lancet. 2007; 370:741-50.

In view of the diagnostic or reporting biases that may occur with the different methodologies used in the estimation of COPD prevalence, the “best” method of determining population prevalence is in all probability by the ascertainment of lung function parameters. Spirometry, if performed appropriately, is minimally influenced by diagnostic methods and can produce a valid result. In addition, lung function is a rational, objective predictor of functional limitations and mortality.

OCCUPATION AS A RISK FACTOR FOR COPD

The significance of occupational exposures as a risk factor for COPD was observed as far back as the 1950s by Fletcher and other researchers. Fletcher, in 1958 stated that “men who work in dusty trades, especially coal miners, have a higher prevalence of symptoms and chronic bronchitis and emphysema” [11]. Until

the early 1980's, the contributory role of only one aetiological agent, tobacco smoke, in the causation of COPD had been established beyond doubt [13]. Nonetheless, since 1984, a large body of evidence from worker cohort and community studies has supported occupational exposures as risk factors for the development of COPD [2, 4, 12, 13]. Furthermore, in less developed countries where occupational exposures could be greater due to less rigorous legislation and poor control measures, the contribution of work may be even more significant than in developed countries.

There are inherent difficulties in establishing relationships between work-exposures and COPD. They include the multifactorial aetiology of COPD with important host and non-occupational environmental determinants of risk. In addition, unlike other occupational dust related diseases eg the pneumoconiosis, patients with COPD secondary to occupational causes cannot be distinguished from individuals with COPD from another cause. Third, there is often dual exposure to cigarette smoke and workplace irritants. Fourthly, epidemiological studies are subject to the healthy worker effect and are often limited to the surviving "healthy" workforce thereby underestimating the effects of occupational exposures. Despite this, a notable body of evidence demonstrating that COPD is linked to specific occupational exposures has accumulated in the past two decades [2, 3, 11, 13-15]. Occupational exposures may affect the course of COPD in one or more different ways. They may cause COPD; modify the effect of tobacco smoke in causing COPD; produce greater disability by adding work related impairment to that caused by smoking; and may also accelerate the rate of lung function decline in persons with recognized COPD [16].

Reviews of COPD and occupation

Becklake conducted two landmark reviews which examined the role of occupation in the causation of chronic airflow limitation [3, 13]. The earlier review conducted in 1985 looked at the relationship of chronic airflow limitation to work in dusty occupations. Selected longitudinal as well as cross-sectional studies published after 1973 comparing either dust-exposed with non-exposed workers, or lightly and heavily exposed workers were included in the review.

In the 12 cross-sectional mining studies reviewed by Becklake, exposure assessments were done from job classification in all, and environmental measurements in 11 of the 12 studies. Personal exposure measurements were available for only 2 studies. Most of the cross-sectional studies revealed higher prevalence (46.3% and 71.7% for active and retired coal workers respectively) of bronchitis, defined as cough and sputum production for at least 3 months for two consecutive years [17], or cough and phlegm for at least 3 consecutive months of the year [18], and significant lower average ventilatory function in exposed workers compared to non-exposed or less exposed workers. A similar effect was also seen in smokers compared to non-smokers in most of the studies; however, 2 studies [19, 20] assessing the independent contribution of both smoking and dust exposure confirmed the independent effect of dust on COPD by comparing the data obtained from smoking and non-smoking matched pairs of dust exposed and non dust exposed workers within the cohort

Evidence for the contribution of occupational exposures to chronic airflow limitation was strengthened by results of several longitudinal studies published after 1973. These studies were undertaken in foundries, fertilizer factories, in construction, metallurgy, chemistry, flour milling, coal mining as well as in hard rock mining and had follow-up periods ranging from 5 to 12 years. All of the reviewed studies [21-24], except one [25], showed significant annual generally equivalent smoking and occupational exposure related decline in ventilatory function. FEV1 declines ranged from 37 to 54 ml per year among non-smokers and from 48 to 56 ml per year among smokers. Among exposed and non or least exposed workers, FEV1 declined between 50 to 54 ml and 42 to 53 ml per year respectively. In addition, one of the follow-up studies [21] performed among 556 Parisian workers in metallurgy, chemistry and flour milling, demonstrated that reducing occupational exposure resulted in reduced risk and a lesser lung function decline over time. The annual rate of decline of FEV1 during 12 years was estimated for each participant from lung function measurements in 1960 and 1972 using a specific formula. Heavily exposed workers, who during the 12 year follow-up period (1960-1972) changed their jobs for non-medically related reasons had a diminished decline of FEV1 compared to other heavily exposed workers whose exposure remained unchanged; 42 ml/year versus 56 ml/year decline respectively. This increased rate of lung function decline with change in occupation supports the causal role of these occupational exposures.

A consistent feature of these studies, as pointed out by Becklake, was a comparable magnitude of effect for occupational exposures and moderate smoking. The excess annual loss of FEV1 ranged from 7-8 ml/year for dust after

accounting for age and smoking. The range for annual loss of FEV₁ for smoking after accounting for age and dust exposure was similar at between 9-11 ml/ year. In this review, the criteria of consistency, strength, coherence and dose-response relationship required by Bradford-Hill to differentiate between association and causation have been met for coal mining as well as certain industrial exposures namely a variety of mineral dusts (silica, abrasives, iron), grain dusts, various gases as well as heat in the decline of lung function over time [3]. Apart from the mining and quarrying industries, the 1985 review also implicated fiberglass, saw dust, freon, auto exhaust, solvents as well as the tunneling and agricultural industries in the genesis of COPD [3].

The benchmark review evaluating the role of occupational factors in relation to COPD is the 2003 ATS statement, "Occupational Contribution to the Burden of Airway Disease" [2]. In the main, the ATS statement provides a comprehensive review and analysis of appropriate population- based studies spanning several occupations and industries up until 1999 [11]. In addition, numerous reviews on COPD have followed the ATS statement that support the conclusions of the earlier reviews [26-29].

Occupational exposures and decline in lung function

In addition to numerous studies [18, 19, 21, 23, 24, 30-38] in cohorts of industrial workers, and a limited number of case-control studies [39-41], several population or community based studies have demonstrated the effects of occupational exposures on respiratory symptoms and annual lung function decline. One of the major advantages of conducting community based studies is avoidance of the

healthy worker effect. Numerous community based studies [42-46] from Europe, China, New Zealand and the United States have demonstrated increased relative risks for respiratory symptoms, decline in lung function consistent with COPD, and excess annual declines in FEV1 due to work related exposures. In addition, the most current ATS review suggests that occupational exposures contribute an extra mean decline of 7-8ml/ year in FEV1 [2] in contrast to normal aging where the mean decline in FEV1 averages between 30-35 ml/year as demonstrated by cross-sectional studies. Over a 40 year work life, this seemingly low mean loss of 7-8ml/ year would result in approximately 320ml loss in FEV1, with some individuals experiencing either greater or lesser declines than estimated. Considering the mean 30-35ml/ year loss due to aging, the loss of 320ml contributed to by occupational exposures amounts to a 10 year decline in FEV1 over the lifetime of an individual.

Krzyzanowski et al [45] observed an accelerated decline in FEV1 in men with self-reported occupational exposure to dusts in a 13 year population-based prospective study in Cracow. The observed mean annual rate of FEV1 decline among men exposed to dust or chemicals at work was 61.1ml/year and 61.3ml/year respectively after adjustment for age and height. In a 25 year follow-up study [44] among 1591 Norwegian men, significant adjusted declines in FEV1(mean \pm standard error) was noted for those exposed to metal fumes (56.8 \pm 1.9ml/ year) and sulphur dioxide (58.7 \pm 2.7 ml/year). In addition, subjects exposed to increasing numbers of workplace agents showed a progressive increase in the mean annual decline of FEV1 adjusted for age, height and smoking status. The decline ranged from 52 ml/ year in subjects with no known

exposure to 61 ml/year in those individuals exposed to six or more occupational agents. In the Chinese study [42], FEV1 and F₂₅₋₇₅ were significantly lower in those occupationally exposed compared to subjects without occupational exposure (among participants reporting not using coal stove heating). In individuals with early COPD, persistent work-related fume exposure as well as smoking, were reported to be significant independent predictors of post-bronchodilator decrements in FEV1 in men [16]. Ongoing occupational fume exposure resulted in an adjusted 10ml/ year loss in FEV1.

In contrast, a large population based study conducted on 13 253 participants aged 20-44 years in 14 industrialised countries was unable to detect an association between occupational exposures and lung function decline. Probable explanations for this effect is a sample composed of young participants with limited duration of exposure among whom a decline in lung function was not evident at the time of the study, the healthy worker effect or newer, cleaner working environments [47].

Respiratory symptoms and occupational exposures

Significant associations between respiratory symptoms and occupational exposures were reported in population based studies [42, 43, 46]. Occupational exposure to biological dusts was associated with an increased risk (RR 1.9; 95% CI 1.0-3.7) of chronic cough as well as chronic phlegm (RR 2.0; 95% CI 1.1-3.8) [46].

Industries, agents and job descriptions associated with an increased risk of COPD

Recent reviews have identified specific jobs [48], occupational agents [14, 48] and industries [49, 50] as having an increased risk for the development of COPD. .

Occupational exposures that have been studied include grain dust, wood dust, isocyanates, cadmium, coal and other mineral dusts, adhesives and welding fumes [13, 15, 20, 21, 24, 47, 51, 52]. Industries having a high risk for COPD include mining, construction and quarrying, textile, paper, agriculture, and foundries [3, 15, 17, 18, 30, 43, 44].

Among textile, wood and food processing workers, an increased prevalence ratio (PR) of 2.2 (95% CI 0.5-9.2), 1.6 (95% CI 0.4-7.0) and 3.4 (95% CI 1.3-8.6) respectively for ex-smokers and 2.5 (95% CI 1.3-4.6), 2.1 (95% CI 1.1-4.1) and 2.0 (95% CI 1.3-3.1) respectively for current smokers [47]. In another population based study, occupational exposure to biological dusts was reported to be associated with an increased odds (OR 2.7; 95% CI 1.4-5.2) of developing COPD [15] after adjustment for age, sex, smoking status and pack years.

COPD in silica exposed workers

Numerous epidemiological [18, 19, 31-33, 53] as well as pathological studies [54-56] suggest that even in the absence of radiological signs of silicosis, silica dust exposure can lead to COPD. In most developed countries worldwide, the reduction in silica dust levels has resulted in a decline in morbidity and mortality from silicosis as well as silica dust associated tuberculosis. However, in both

developed as well as less developed countries, COPD remains a health concern for exposed workers [13, 30, 44].

A 2002 review [4] of studies (where radiological signs of silicosis were found or where results for radiological silicosis were not reported) looking at the association between silica dust exposure and COPD, reported a decrease in FEV1 and FEV1/ FVC with escalating respirable dust exposure. This decrement was observed in both smokers and non-smokers. The study populations in these studies included white South African (SA) gold miners, black gold miners from South African mines, Canadian hard rock miners as well as American molybdenum miners.

A landmark study [33] examined the effects of silicosis and dust exposure on a working population of black miners on South African gold mines. FEV1 decreased by 200mls ($p=0.006$) and FEV1/FVC% by 3.6% ($p= 0.0001$) after 25 years of dust exposure, equating to an annual average loss of 8 mls FEV1. This was equivalent to the annual reduction of 6.9mls due to similar duration of smoking, adjusted for silicosis and dust exposure. Furthermore, silicosis was associated with a reduction of all measured lung function parameters and association persisted after adjustment for smoking, duration and intensity of underground exposure. Men with profusion 2/2 had a significant reduction of FEV1 of 320 mls compared to men with profusion 0/0 ($p= 0.0001$).

In a five year follow up study [32] of 2209 white South African gold miners, exposure, in a 50 year old male, to an average cumulative dust exposure of

14.4mg/m³, was associated with a loss of 236 ml of FEV1 (95% CI 135-338 ml) and 217 ml of FVC (95% CI 110-324 ml). As the average duration of underground dust exposure was 24 years, the loss equates to an adjusted mean decrement of 9.8 ml/yr of FEV1 and 9.0 ml/yr of FVC due to dust exposure. In addition, the five year follow up revealed that miners had a steeper decline in FEV1 compared to similar aged non-miners in the general population.

Norwegian tunnel workers were observed to have an increased adjusted OR of 2.5 (95% CI 1.31-4.96) for development of COPD. In addition, for each year of exposure, the observed adjusted effect on FEV1 showed a statistically significant decline of 17 ml/ year in tunnel workers compared to 0.5 ml/year in outdoor construction workers [30]. A follow up study of 45 granite workers between 1976 and 1988 reported a significant decline of 4.6% in FEV1, 5.4% in FEV1/FVC, and 13.7% in FEF₅₀ compared to the change in the population controls. These changes were larger in the retired granite workers compared to the younger active workers. A possible reason for this finding would be the relatively longer duration of exposure as well as the larger cumulative exposure of the retired workers. Furthermore, deposited dust in lung tissue would continue to effect changes in airway patency long after the worker is removed from exposure.

ATTRIBUTABLE RISK DUE TO OCCUPATION

ATS concluded in 2003 that the attributable fraction of COPD due to occupational exposures was 15-20% [2].

A study by Hnizdo et al, 2002, investigated the association between COPD and employment by industry and occupation in the US population. The overall

projected PAR was 19% among smokers, and 31% among never smokers [57]. An additional US population based study reported the adjusted PAR for similarly exposed workers as in the Hnidzo study to be 20%. [58]. Excluding chronic bronchitis from the COPD definition increased the PAR to 31%.

A recent review lends support to the 2003 ATS Statement on the association between occupation and COPD [11]. For chronic bronchitis (defined by standard questionnaire criteria), the PAR (adjusted for smoking) ranged from 0-34% with a median value of 15%, similar to the ATS estimate. Individual studies provided COPD PAR estimates of 20% [58], 11% [51], 27% [15], and 15% [57]. Additional estimates for the PAR for occupational exposures among non-smokers ranged from 26% for COPD [57] to 53% for COPD mortality [51].

ADDITIONAL RISK FACTORS FOR COPD

Although cigarette smoking and occupational exposures account for the major proportion of cases, other factors have been implicated in the development of COPD. They include genetic factors [12], indoor and outdoor air pollution [7, 29], previous respiratory infections including tuberculosis [4, 7, 59-62], age [29], sex [29], and reactive airways [4, 13].

Smoking

Among the environmental factors concerned in the genesis of COPD, tobacco smoking is the most important [3]. Estimates from the WHO are that 73% of COPD in developed countries and 40% of COPD in less developed countries is related to smoking [29]. Not all smokers develop COPD. However in those that do, inter-

individual variation exists, in respect to the severity of COPD as well as to reaction to interventions.

A South African based study showed an increasing association of chronic bronchitis with increasing daily smoking among men with odds ratios of 1.5 (95% CI 0.8-3.0) and 2.5 (95% CI 1.2-5.3) among light daily (1-14 per day) and heavy daily (15+ per day) smokers respectively. However, among women, the odds of developing chronic bronchitis were higher if you were a light daily smoker as compared to a heavy daily smoker; odds ratio of 2.3 (95% CI 1.4-3.8) versus 1.8 (95% CI 0.6-5.8) [7]. A partial explanation for the lack of an exposure-response trend among women is the relatively low prevalence of smoking among women, especially heavy smoking [7].

A synergistic effect of silica dust and tobacco smoke on COPD mortality was reported in a South African study.[63]. Within the total sample, the odds of dying ranged from 1.0 (for the lowest dust level) to 5.3 (95% CI 1.8-15.9) for the highest level of dust exposure. The odds of COPD mortality ranged from 1.0 (for lowest smoking level) to 32.3 (95% CI 4.2-248.2) for the highest smoking level. The odds of dying for the highest smoking and dust exposure categories, was 21.0, much higher than that expected (8.8) if an additive effect was postulated.

A recent case-control study [64] reported that exposure to cigarette smoking was associated with a seven-fold increase in the odds for developing COPD (OR 6.7; 95% CI 4.6-9.8) and occupational exposure to VGDF was responsible for a doubling of risk over baseline (OR 1.9; 95% CI 1.3-3.1). However, combined exposure to cigarettes and occupation was associated with a significantly

increased risk (OR 14.1; 95% CI 9.3-21.2). The excess probability analyses reported an additive effect for joint risk of both the exposures when COPD was defined as GOLD stage II or higher. Data from a more recent population-based study also reported that the risk estimate for chronic bronchitis in occupationally exposed smokers was greater than the sum of the OR of the individual exposures (3.9 versus 1.6 and 1.3) [65]

Respiratory infections and tuberculosis

Respiratory infections, including tuberculosis (TB), play an important role in both the development as well as progression of COPD. Even among individuals who successfully complete anti-tuberculosis treatment, permanent damage to the lungs is frequently observed with airways obstruction as a long-term complication of tuberculosis. Several studies [59, 61, 62, 66] have shown that silicosis, as well as exposure to silica dust, are risk factors for tuberculosis. Tuberculosis was found to be a strong predictor of chronic bronchitis in multivariate analysis in both males and females among 13 061 participants in a population based study. Among males the odds ratio was 4.9 (95% confidence interval of 2.6-9.1) and among females, 6.6, with a 95% confidence interval of 3.7-11.7 [7].

In a recent population based study [67] looking at the association between TB and COPD using post-bronchodilator spirometry, among those participants with a history of TB, prevalence of airways obstruction was 30.7% compared with 13.7% among subjects without a history of TB. For the entire sample, the adjusted OR (95% CI) for airways obstruction in those with TB was 2.3 (1.5-3.6). Following stratification by sex, and after adjustment for confounders, males and females with a history of TB were 3.9 (95% CI 1.9-8.3) and 1.7 (95% CI 0.95-3.1) times more

likely respectively, to present with airways obstruction than individuals without a history of TB.

Genetic factors, indoor and outdoor air pollutants, age, gender and reactive airways

Serine protease Alpha 1- antitrypsin (protease inhibitor phenotype Z [PI*Z]) deficiency is at present, the only genetic factor undoubtedly associated with COPD in humans. This phenotype affects only a small percentage of the general population and as such, is responsible for only a small proportion of the COPD cases. It is found in 1-3% of individuals with COPD [29]. Individuals with this deficiency have been shown to be at increased risk of chronic cough, lower FEV1 as well as lower FEV1/FVC with exposure to gases, dusts, fumes and smoke, independent of personal cigarette smoking [12].

Exposure to biomass fuels is an important global risk factor for the development of COPD. In less developed countries, the WHO estimates that as much as 35% of COPD cases can be attributable to exposure to indoor smoke from biomass fuels. A report on risk factors for COPD in females in China showed that never- smoking women in rural areas exposed to biomass fuel smoke had a two to three fold higher prevalence of COPD when compared to women from urban areas not exposed to biomass fuels [29]. A similar effect was shown by Ehrlich et al in 2004 who reported an increased risk of developing chronic bronchitis among women with domestic exposure to smoky fuels. The authors reported an odds ratio of 2.0 (95% CI 1.1-3.4) and this finding of increased risk was limited to female participants only [7]. Outdoor air pollutants contribute only a very small risk

towards the development of COPD. The WHO estimates are 1% and 2% cases of COPD in developed and less developed countries respectively [29].

COPD prevalence increases with age, with concomitant decline in lung function after the fourth decade of life. On account of the changing demographics of the world's population due to improved nutrition and a decrease in infectious diseases and other causes of death in young individuals, a larger percentage of the world's population is living longer with an increased risk of developing chronic diseases such as COPD [29]. Older workers with longer duration of exposure to agents recognized in COPD causation may be at greater risk for developing COPD.

The role of gender in the pathogenesis of COPD remains controversial.

Historically, men smoked more than women, and together with occupational exposures exhibited a greater prevalence of COPD. However, evidence has shown that the proportion of women who smoke is increasing worldwide [29] and the question of whether women, given similar environmental and or occupational exposures are at higher risk of developing COPD compared to men remains unresolved.

Although occupational exposures are increasingly implicated in the causation of COPD, not all individuals similarly exposed are affected. Two studies conducted in 1978 and 1984 showed that among workers with similar demographic, smoking and occupational reports, those with positive metacholine challenge tests demonstrated a greater loss of lung function than those with a negative challenge test [13]. Atopy and non-specific bronchial hyper responsiveness have been

recognized as risk factors for COPD. Furthermore, although there has been a suggestion that atopy and non-specific bronchial hyper responsiveness can modify the effect of smoking on COPD, current evidence does not support this theory for the effect of silica dust on lung function loss [4].

In summary, studies internationally have indicated that occupational exposures may account for 15% of COPD, with a synergistic effect with smoking, and the implication of a range of exposures in the causation of COPD. The majority of these studies have been undertaken in developed countries with established laws and regulations governing occupational exposures, and so the presumption is that a greater burden of disease may be prevalent in less developed countries due to unregulated or poorly regulated working conditions. As there is a scarcity of research into COPD and occupational exposures in developing countries, South Africa included, this study intends to determine if similar exposure-response associations are valid for occupationally exposed workers in developing countries.

PURPOSE OF THE RESEARCH

To determine the role of occupational exposures as a risk factor for chronic obstructive pulmonary disease (COPD) among physician-diagnosed COPD patients attending three hospitals in Kwazulu-Natal.

SPECIFIC OBJECTIVES

1. To describe the demographics, lung function and severity of disease in patients with a confirmed diagnosis of COPD from three hospitals.

2. To describe the occupational exposure history among cases of COPD and controls from three hospitals.
3. To describe the respiratory symptoms of participants
4. To determine the association between occupational exposure history and COPD

CHAPTER II

METHODS

OVERVIEW

110 cases with a physician's diagnosis of COPD and 102 controls with non-respiratory related diagnoses were recruited from three public sector hospitals in KwaZulu-Natal. All participants completed an interviewer administered questionnaire which assessed past medical history, smoking and occupational history. Cases provided a copy of a lung function test performed on the day of the interview. Analysis was done using STATA version 10. Multivariate logistic models were developed to evaluate the effect of occupational exposures on COPD whilst controlling for other co-variates. Ethical approval for the study was obtained from the relevant institutions and voluntary informed consent was sought from each participant.

STUDY DESIGN AND STUDY POPULATION

This was a hospital based case-control epidemiological study. Participants were recruited from three public sector respiratory clinics in KwaZulu-Natal between December 2008 and May 2009. These clinics are located at Inkosi Albert Luthuli Central Hospital, Grey's Hospital and RK Khan Hospital. Although these hospitals

offer three different levels of care, the respiratory clinics are specialist level clinics. The diagnosis of COPD by a respiratory physician formed the basis of the case definition in this study. Cases of COPD were known and newly diagnosed cases (n=110), as diagnosed by a respiratory physician and supported by spirometry. All outpatients with a confirmed diagnosis of COPD attending the respiratory clinics were eligible for inclusion in the study. These patients are referred to these specialist centers either for improved control of symptoms, correction of inhaler technique, or confirmation of diagnosis.

Controls (n=102) were recruited from non-respiratory chronic illness clinics, namely cardiovascular, diabetic and renal clinics (Table 6) at the same hospitals. The diagnoses among the controls included diabetes, ischaemic heart disease, hypertension and renal disease. Potential controls were excluded if they had ever had a diagnosis of a respiratory or COPD related disease or if they had used any COPD respiratory medication including inhalers within the past 12 months. Controls and cases were group frequency matched for sex and age.

COLLECTION OF INTERVIEW DATA

Each participant (case and control) was subject to an interviewer administered questionnaire. The questionnaire (Appendix D) was developed using a previously validated questionnaire (extensively field validated in other South African settings) [68] based on the ATS, National Institute of Occupational Health and Safety (NIOSH), and ECRHS. Questionnaires were prepared in two official South African languages namely English and isiZulu and the latter was verified by back translation into English. The questionnaire was administered to the participants in the language of their choice by trained interviewers during the participants' routine

follow-up visits to the respiratory clinics. The questionnaire contained predominantly closed questions with a few open ended questions. The questionnaire included questions on demographics, medical and occupational history, respiratory symptoms, smoking habits, family history, as well as domestic and environmental exposures. Tobacco smoking questions included age of starting and stopping smoking, duration and intensity of smoking.

COLLECTION OF EXPOSURE DATA

Several questions concerning occupation were incorporated in the questionnaire. These included: employment status, current and all previous jobs held (job description, industry, duration of employment), and self-reported occupational exposures. Information on all self reported exposures was collected for each participant for all jobs (up to 10) performed up until retirement or retrenchment. Every exposure was given a specific numerical code and up to 5 exposures were entered for each job performed by the participant. The total number of years with exposure to jobs involving exposure to dust and or chemicals, gas or fumes was summed up for each participant. If they were employed in the same industry but in different occupational categories, they were treated as different jobs.

In addition, questions relating to employment in industries with exposures associated with the development of COPD, including duration of exposure, were also included to ensure that as complete an exposure history as possible was collected. These included questions on whether or not they had ever worked in a foundry, with asbestos, in pottery, with diesel or diesel fumes, in a flax, cotton or

hemp mill, in tunnelling, in drilling, in sandblasting, in a quarry, and with any other dusty occupations or with chemicals. Gases and fumes were also asked about.

SPIROMETRY

A copy of an acceptable and reproducible lung function test (LFT) was obtained for all but two of the participants with a physician confirmed diagnosis of COPD. The lung function tests were performed on the day of the interview. The tests were performed by each of the three hospitals own inhouse respiratory technician. All the technicians followed the procedures stipulated in the South African Thoracic Society and the ATS guidelines [69, 70]. LFTs were assessed for acceptability and reproducibility using the ATS criteria and those LFTs that met the criteria were accepted. Acceptability criteria that were considered included a “crisp” unhesitating start, peak expiratory flow of the flow-volume curve achieved within the first 25% of the volume expired from maximum inspiration, a continuous smooth exhalation, and a complete exhalation [69]. The measurements that were considered for the purposes of this study were forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and FEV1/FVC ratio.

Failure to meet reproducibility criteria was not a basis for exclusion of the subject from the data analysis, as prior studies indicate that this can introduce a substantial selection bias. Those with chronic disease are less likely to provide repeatable results and “test failure” may be an indication of ill-health [71]. Those LFTs not meeting the ATS criteria were reviewed in terms of the latter statement as a substantial percentage of the participants had moderate to severe COPD.

The lung function test equipment used was volume calibrated every four hours on the days of testing with a 3 litre calibrated syringe. Systems were checked for leaks as well. A minimum of 3 acceptable forced vital capacity (FVC) manoeuvres were performed up to a maximum of 8 if reproducibility criteria were not met. The largest FVC and FEV₁ obtained from any acceptable curves were used for recording purposes. Reproducibility criteria were a less than 5% variation or 0.1L difference of the largest FVC and FEV₁ and the next largest of these parameters among all acceptable curves. Internal standardisation of spirometry was done using regression equations for height, age and cumulative exposure. As there is substantial variation in lung function values between populations and the absence of an appropriate set of reference values for the population under study, external standardisation was only done to determine levels of disability for the purposes of identifying those workers who were eligible for workers' compensation [72]. Reference values of the European Community for Coal and Steel [73] were used for the latter purpose. The Global Initiative for Obstructive Lung Disease (GOLD) classification system was used to classify severity of lung function impairment.

STATISTICAL ANALYSIS

Data was captured on an excel spreadsheet and analysed using STATA version 10. Data was double entered to ensure accuracy. The database was structured such that ranges were examined for impermissible values, logic checks for ensuring answer validity and consistency and automated skip patterns were incorporated.

The data analysis examined the relationship between COPD and occupational exposures. The main health outcome variable (dichotomous) for this study was the presence or absence of COPD. Other symptom-related outcome variables included respiratory symptoms of shortness of breath, sputum production, cough and wheeze (all dichotomous variables). Exposure variables assessed were exposure to two composite variables (dust and chemicals, gas or fumes (CGF)), duration of exposure to each, as well as specific exposures such as to asbestos, diesel and diesel fumes, sandblasting and tunnelling. Duration of exposure for asbestos, sanding etcetera was included in the composite variable "dust". Participants were categorised as having exposure "yes" for the variable CGF if they reported having exposure to one or more of the three exposures. The potential confounding risk factors for COPD included age, sex, smoking status, and history of previous personal respiratory illness such as tuberculosis and asthma. Univariate analyses described the characteristics of the study population as well as the frequencies of independent and dependant variables. Bivariate analyses described the crude associations between the variables of interest. For bivariate analysis we used the independent samples t test to determine the significance of differences between the cases and controls with respect to continuous variables (age, years of exposure to dust, years of exposure to chemicals, gas or fumes) and the chi-square test for categorical variables sex, smoking history, history of tuberculosis, dust exposure, chemical, gas or fume exposure, respiratory symptoms.

Linear and logistic regression analyses using 3 models were performed. Logistic regression analysis was used to describe the association between COPD and

occupational exposure to dust and chemicals, while controlling for age (analysed in 10 year age increments), sex, past history of tuberculosis and smoking history. Three dummy variables for smoking (never, ex and current smoking) were created to evaluate the effect of each level of smoking on risk of COPD. For the multivariate logistic regression models, odds ratios and 95% confidence intervals (CI) are presented. For FEV1 outcome, the linear regression models were adjusted for age, height, smoking history and past history of tuberculosis. The accepted level of significance for bivariate and multivariate analyses was set at 0.05.

ETHICS

Ethical approval for the study was obtained from the Biomedical Research Ethics Committee of the University of Kwa-Zulu Natal (Reference Number: BF 123/08) (Appendix A). Institutional permission was obtained from each of the three participating hospitals as well as from the Health Research and Knowledge Management sub-component department of the Provincial Department of Health (Appendix B). Informed consent was obtained from each study participant for questionnaire administration and from each case for a copy of their lung function test. Hard copies of the questionnaires were kept in a locked filing cabinet in the Department of Occupational and Environmental Health. The electronic copy was stored on the laptop of the investigator to which only the primary investigator and co-investigator had access. In the event of publication, data will be presented as grouped data without any individual identifiers. Feedback on study findings will be provided to the Department of Health, the relevant hospital managers, as well as to the individual participants on completion of the study. In the event that any

participant is identified as being eligible for compensation, necessary steps will be undertaken to facilitate that process with his/ her consent.

CHAPTER III

RESULTS

DEMOGRAPHIC CHARACTERISTICS AND SMOKING

112 patients with COPD assessed at the clinics during the study period were invited to participate. With the exception of two cases, (one male and one female) all agreed to participate. Of those patients (103) invited to join the study as a control, one declined to participate citing unwillingness to lose his position in the consultation booking system.

The sample comprised a total of 110 cases with a physician-confirmed diagnosis of COPD and 102 controls (Table 4). In total, there were 25 (11.8%) females and 187 (88.2%) males. In both the groups, males constituted just fewer than 90% of participants. There was no significant difference between cases and controls with respect to sex distribution or age. The mean age among the cases was 61.5 years (sd: 8.9) and among the controls was 62.1 years (sd: 8.9). Cigarette smoking across the various smoking categories differed significantly ($p=0.000$) between cases and controls (93% vs 74% ever smokers) (Tables 4 and 5)

Controls reported hypertension, cardiac disease as well as other chronic illnesses (Table 6). A large proportion of the control patients reported a combination of medical conditions. Forty three (42%) of the controls were diagnosed with hypertension as well as cardiac disease; 42 (41%) with hypertension and other chronic illness, and 25 (24.5%) with both cardiac and other chronic illness (data not shown). Among the cases, 47 (42.7%), 26 (23.6%) and 16 (14.5%) reported

hypertension, cardiac disease, and both hypertension and cardiac disease respectively.

Table 4. Demographic and smoking characteristics of cases and controls

<i>Characteristic</i>	<i>Cases (n=110)</i>	<i>Controls (n=102)</i>
Age (mean) (range)		
Male	61.4 (41-86)	62.6 (40-87)
Female	62.5 (43-80)	58.5 (41-77)
Sex, n (%)		
Male	96 (87.3)	91 (89.2)
Female	14 (12.7)	11 (10.8)
Smoking status, n (%)		
Non-smokers	8 (7.3)	27 (26.5)*
Ex-smokers	79 (71.8)	47 (46.0)*
Current smokers	23 (20.9)	28 (27.5)

*p<0.01

Table 5. Smoking history by sex within each group of smokers

	Never smokers, n (%)		Ex-smokers, n (%)		Current smokers, n (%)	
	Cases	controls	Cases	Controls	Cases	Controls
Males**	5 (5.0)	19 (21.0)	70 (73.0)	45 (49.0)	21 (22.0)	27 (30.0)
Females*	3 (21.0)	8 (73.0)	9 (64.0)	2 (18.0)	2 (15.0)	1 (9.0)

*p<0.05

**p<0.01

Table 6. Reported medical conditions of controls

<i>Diagnosis</i>	<i>Number (%)</i>
Hypertension	74 (72.5)
Cardiac disease	58 (56.9)
Other chronic illness (diabetes, renal)	54 (52.9)

OCCUPATIONAL HISTORY AND EXPOSURES

The 110 cases self-reported a total of 340 job descriptions among themselves, averaging 3 different jobs over their working lifetime (Table 7). Controls reported 221 job descriptions, an average of 2 jobs per control. A larger proportion of the controls reported employment in administrative (21.3% vs 12.0%), managerial (7.7% vs 2.6%) and quality control (5.4% vs 0.3%) positions compared to cases. With the exception of employment in the construction and shoe manufacturing industries, reported percentage of employment of cases and controls in other industries was similar (Table 8). Job descriptions and employing industries that were less frequently reported are not shown in these tables.

Table 7. Frequent job descriptions reported by cases and controls

<i>Job description*</i>	<i>Cases.n</i> <i>(%)</i>	<i>Controls n</i> <i>(%)</i>
Administrative	41 (12.0)	47 (21.3)
Machinist (textile and shoe)	30 (8.8)	13 (5.9)
Builder	27 (8.0)	6 (2.7)
Driver	19 (5.6)	22 (10.0)
Fitter and turner	19 (5.6)	4 (1.8)
Operator	18 (5.3)	17 (7.7)
Painter	16 (4.7)	0
Supervisor	14 (4.1)	8 (3.6)
Welder	12 (3.5)	2 (1.0)
Maintenance	10 (3.0)	0
Manager	9 (2.6)	17 (7.7)
Mechanic	6 (1.8)	5 (2.2)
QC	1 (0.3)	12 (5.4)

*There were a total of 340 different job descriptions among cases, and 221 among Controls

Table 8. Cases and controls employment by industry

<i>Industry</i>	<i>Cases n</i> <i>(%)</i>	<i>Controls.n</i> <i>(%)</i>
Construction	35 (10.3)	7 (3.2)
Shoe manufacturing	34 (10.0)	11 (4.9)
Food industry	31 (9.1)	21 (9.5)
Textile and clothing	30 (8.8)	33 (14.9)
Transportation	23 (6.8)	14 (6.3)
Retail	18 (5.3)	17 (7.7)
Motor industry	15 (4.4)	14 (6.3)
Paper/ packaging/printing	13 (3.8)	12 (5.4)
Engineering	13 (3.8)	5 (2.2)
Furniture manufacturing	12 (3.5)	8 (3.6)
Metal and steel industry	12 (3.5)	3 (1.4)
Petroleum industry	9 (2.6)	2 (1.0)
Shipping	8 (2.4)	4 (1.8)
Health care	7 (2.0)	7 (3.2)
Mining	6 (1.8)	0 (0.0)
Chemical	5 (1.5)	0 (0.0)
Plastic	4 (1.2)	5 (2.2)
Finance	3 (0.8)	5 (2.2)

Self-reported occupational exposures were more common among the cases than controls. Among the cases, 72% reported exposure to dust, 74.5% reported exposure to CGF and 76.9% reported exposure to dust as well as CGF. The proportion of controls exposed to dust, to CGF and to both dust, and CGF was 28%, 25.5% and 23.1% respectively. The proportion of cases with occupational exposures was significantly higher when compared to controls ($p < 0.001$) (Table 9). Stratification by sex revealed that a significantly higher proportion of both male

and female cases reported occupational exposures compared to controls (Table 10).

Employment status (“ever being employed”) did not differ significantly between cases and controls. However, cases were more likely to be currently unemployed due to poor health than controls (54% vs.18%, $p= 0.02$) (not shown).

Table 9. Occupational exposure profile of cases and controls

	Cases, n (%)	Controls, n (%)
Dust	80 (72.0)	31 (28.0)*
Chemicals, gas or fumes	76 (74.5)	26 (25.5)*
Dust and chemicals, gas or Fumes	60 (76.9)	18 (23.1)*

* $p<0.001$; χ^2 test

Table 10. Occupational exposure by sex

	Cases, n (%)	Controls, n (%)
Female, n, (%)		
Dust	8 (57.1)	0 (0)**
Chemicals, gas or fumes	8 (57.1)	1 (9.1)*
Dust and chemicals, gas or fumes	4 (28.8)	0 (0)
Males, n, (%)		
Dust	72 (75)	31 (34.1)***
Chemicals, gas or fumes	68 (70.8)	25 (27.5)***
Dust and chemicals, gas or fumes	56 (58.3)	18 (19.8)***

* $p<0.05$; ** $p<0.01$; *** $p<0.001$; χ^2 test

As indicated in Table 11, duration of exposure to self reported occupational exposures differed significantly between cases and controls ($p < 0.001$). Among the cases the mean number of years for exposure to dust and CGF was 15.7 years and 14.0 years respectively. The corresponding mean duration of exposure for controls was approximately 3-4 times lower than those for the cases.

Table 11. Occupational exposures and duration among cases and controls

Exposure	Cases	Controls
	<i>Mean (SD)</i> <i>(Range)</i>	<i>Mean (SD)</i> <i>(Range)</i>
Total dust years	15.7 (14.7) (0-62)	4.67 (9.2)* (0-35)
Total chemical, Gas or fume years	14.0 (14.1) (0-49)	3.48 (8.9)* (0-35)

* $p < 0.001$

RESPIRATORY SYMPTOMS AND DISEASE DIAGNOSIS REPORTED BY PARTICIPANTS

As expected, respiratory symptoms of cough, phlegm, breathlessness, and wheeze were reported by 66%, 69%, 85% and 89% of the cases respectively. Of note however, is the reporting of breathlessness by approximately 53% of the controls, with wheeze reported by 22%.

Disease diagnoses of asthma (68%) and pneumonia (35%) were the most common respiratory diseases reported by cases. A history of tuberculosis was reported by 15.5% of the cases and 2.0% of controls. Fewer than 10% of controls

reported the presence of any other respiratory diseases (data not shown). Of the 110 cases, 59 (54%), reported ever experiencing symptoms of tight chest or wheeze at work compared to 11(11%) of the controls. In addition, 39 (35.5%) of those with COPD left work because of respiratory complaints compared with 4 (3.9%) of the controls ($p<0.001$).

MULTIVARIABLE LOGISTIC REGRESSION ANALYSES

The association between self-reported exposure to dust and chemical, gas or fumes and COPD is summarized in Table 12.

After adjustment for co-variables including smoking, exposure to dust, and exposure to CGF was associated with an increased odds of developing COPD. The odds ratio for exposure to dust was 7.9 (95% CI 3.9-15.7; $p<0.001$). For exposure to chemicals, gas or fumes, the odds ratio was 6.4 (95% CI 3.2-12.8; $p<0.001$). For participants exposed to dusts as well as chemicals, gas or fumes, the odds ratio was also significantly elevated at 5.8 (95% CI 2.9-11.7; $p<0.001$).

A history of tuberculosis was strongly associated with an increased odds of being a case especially in the two models incorporating dust exposure ($p< 0.05$ for both). Although tuberculosis was associated with COPD in the 2nd model, the association was not significant ($p=0.13$). Smoking history showed a strong association with COPD. The odds ratio for ex smokers were markedly higher than for current smokers and were significant across all three models. Current smoking was associated with COPD only in the models that included dust exposure.

Male sex was protective against having COPD and the association was significant in the models that included exposure to dust. The OR for COPD for 10 year increments in age was not significant in any exposure group.

Table 12. Adjusted odds ratios for COPD

	Model 1 [#]	Model 2 ^{##}	Model 3 ^{###}
	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Age ^{***}	1.01 (0.98-1.06)	1.02 (0.98-1.06)	1.02 (0.98-1.05)
Sex [^]	0.2 (0.07-0.7)*	0.3 (0.1-1.0)	0.3 (0.1-0.8)*
Tuberculosis	8.1 (1.6-40.4)*	3.5 (0.7-16.9)	5.7 (1.2-27.4)*
Ex-smoker	7.9 (2.8-22.2)**	5.4 (2.1-16.5)*	6.4 (2.3-17.7)**
Current smoker	4.6 (1.4-14.3)*	2.7 (0.9-8.4)	3.5 (1.1-10.9) *
Dust exposure	7.9 (3.9-15.7)**	-----	-----
Chemical, gas or fume exposure	-----	6.4 (3.2-12.8)**	-----
Dust and chemical, gas or fume exposure	-----	-----	5.8 (2.9-11.7)**

* $p < 0.05$

** $p < 0.001$

OR= odds ratio

CI= confidence interval

*** based on 10 year increments in age

Model 1: Dust exposed

Model 2: Chemical, gas or fume exposed

Model 3: Dust and chemical, gas or fume exposed

^ Comparing male with female

LUNG FUNCTION AMONG CASES

Acceptable and reproducible lung function test results were available for 98% of cases (no lung function tests were obtained for any of the controls, and hence no comparative analysis has been done). Approximately 97% of subjects with COPD had GOLD stage II or greater disease severity with just about 70% having stage III or higher disease severity (Table 13).

Table 13. Lung function classification of cases as per the GOLD Staging system

GOLD Stage	n (%)
GOLD Stage II	30 (27.8)
GOLD Stage III	44 (40.7)
GOLD State IV	31 (28.7)

Table 14 presents the results of the unadjusted lung function parameters. The analyses of the effect of self-reported dust and chemical, gas or fume exposure on FEV₁ is summarised in Table 15. Models adjusting for age, sex, height, smoking status and history of tuberculosis did not indicate any significant association between FEV₁ and occupational exposures.

Table 14. Unadjusted lung function parameters

<i>Lung function parameter (litres)</i>	<i>Cases</i>
	<i>Mean (SD)</i>
<i>Dust exposed</i>	
FEV1	1.06 (0.48)
FVC	2.14 (0.76)
<i>Chemicals, gas or fume exposed</i>	
FEV1	1.06 (0.54)
FVC	2.12 (0.77)

Table 15. Adjusted effect of explanatory variables on FEV1 from different linear regression models

Co-variates	Model 1#	Model 2##	Model 3###
	Co-efficient (95% CI)	Co-efficient (95% CI)	Co-efficient (95% CI)
Age	-0.0 (-0.01 - 0.01)	0.0 (-0.01 - 0.01)	0.0 (-0.01 - 0.01)
Tuberculosis	-0.18 (-0.4 - 0.1)	-0.2 (-0.4 - 0.1)	-0.8 (-0.4 - 0.1)
Height	0.02 (0.0 - 0.03)*	0.02 (0.0 - 0.03)*	0.02 (0.0 - 0.03)*
Ex-smoker	-0.4 (-0.8 - 0.03)*	-0.4 (-0.8 - -0.01)*	-0.4 (-0.7 - -0.0)*
Current smoker	-0.4 (-0.8 - 0.05)	-0.3 (-0.7 - 0.1)	-0.3 (-0.7 - 0.1)
Sex	0.2 (-0.1 - 0.5)	0.2 (-0.2 - 0.5)	0.2 (-0.2 - 0.5)
Dust exposure	-0.07 (-0.3 - 0.2)	-	-
Chemical, gas or fume exposure	-	0.02 (-0.2 - 0.2)	-
Dust and chemical, gas or fume exposure	-	-	0.03 (-0.2 - 0.2)

*p<0.05

Model 1: Dust exposed

Model 2: Chemical, gas or fume exposed

Model 3: Dust and chemical, gas or fume exposed

CHAPTER IV

DISCUSSION

This, the first hospital based case-control study of COPD undertaken in South Africa, indicated that occupational exposures are associated with a substantially increased odds for the development of COPD. For those exposed to occupational dusts there was an almost 8 fold increased odds, while those exposed to chemicals, gases or fumes had a 6.4 fold increased odds for having COPD. The exposure-related odds estimates (OR 7.9; 6.4 for dust and CGF exposure respectively) were higher than that for current smokers (OR 4.6; 2.7), and similar to that of ex-smokers (OR 7.9; 5.4).

The findings of this study are consistent with those described in several other studies internationally [4, 7, 11,13-16, 27,41,64]. Occupational exposures, namely organic and inorganic dusts, as well as vapours, gases and fumes have been identified as important predictors of COPD in numerous epidemiological studies. In two recently published case control studies, exposure to vapours, gases, dust and fumes was associated with a two-fold increase in the risk of COPD [41, 64]. The odd ratios described in other studies range from 1.6 through to 2.7 [16,27,7]. In this study however, we observed considerably higher odds estimates for COPD. There are several possible explanations for this finding. A substantial proportion of cases in this study reported employment in the textile and shoe manufacturing industries. Previous studies reporting an increased risk of COPD were conducted mainly in the construction, agricultural, food

processing, mining, quarrying, and wood industries as well as foundries [3, 15, 17, 18, 30, 43, 53]. Mastrangelo et al [39] observed a limited distribution of participants within the textile and shoe industries. It is possible that a greater proportion of cases in this study, employed in the textile and shoe manufacturing industries were occupationally exposed to dust and to chemicals, gas or fumes. An additional hypothesis is that participants in this study had higher levels of exposure to risk factors. However, we have no reason to believe that the problem is greater in this industry without gaining more objective data.

From a public health point of view, the current study provides several important findings. A past history of tuberculosis was strongly and significantly associated with the presence of COPD – odds ratios ranging from 3.5 to 8.1, depending on the exposure variable. A similar finding was demonstrated in a South African population based study in 2004 [7] in which the strongest predictor of chronic bronchitis was a past history of tuberculosis (males, OR 4.9, 95% CI 2.6-9.2; females, OR 6.6, 95% CI 3.7-11.9). In a more recent population-based study, tuberculosis was also associated with airways obstruction, with the authors reporting an adjusted OR of 2.33 (95% CI 1.5-3.6) [67]. This has important implications for tuberculosis detection and cure rates as single as well as repeated episodes of tuberculosis have been associated with chronic airflow limitation [60]. Although not explicitly investigated in this study, it is possible that lung function loss from tuberculosis could be modified by occupational exposures in the workplace. It is thus in the interests of public health to

ensure that the tuberculosis control programme meets its targets for detection and cure rates, to assist in diminishing the burden of COPD in addition to the obvious objectives of reduced mortality and spread of the disease. However, more if not just as important, would be the development of TB programmes in dusty workplaces which would identify workers with TB early in the course of disease. Early identification and appropriate treatment could reduce the potential for developing COPD.

The positive association between smoking and COPD in our study was similar to that for occupational exposures among ex-smokers, and is very similar to the risk reported by other researchers (61). The similarity in risk estimates for smoking and occupational exposures provides a considerable argument for the focusing of similar attention and resources to the control of workplace exposures as to anti-smoking campaigns nationally and internationally.

Given that the estimated worldwide population attributable fraction (PAF) for COPD due to occupational exposures is 15-20% [2], better characterisation of specific occupational exposures has important public health policy implications. The findings from this study suggest that persons with known occupational exposures to respiratory irritants should be monitored to detect the onset of respiratory ill-health and that preventive strategies should reduce exposure to these agents in the workplace. A study [16] among 5724 participants with early COPD investigating the effect of occupational exposures on decline of lung function in early COPD,

provided clear evidence for secondary screening and secondary prevention in persons with early COPD exposed to fumes. Individuals with early COPD should avoid, or at least limit ongoing occupational fume exposures, as evidence indicates that regular exposure to fume after COPD onset has an adverse impact on lung function [16]. In particular, because individuals with COPD already have existing impaired lung function, and in comparison to normal people, have an accelerated loss of lung function capacity, any further functional loss due to workplace exposures may be very significant. This view is supported by the 1985 review of MR Becklake which identified certain exposures for which there is evidence of a causal relationship in the development of chronic airflow limitation [3]

Cases and controls exhibited large differences in self reported symptoms and disease, with the reported prevalence of breathlessness and wheeze surprisingly high in the controls (53% and 22%). A possible explanation lies in the source clinics from which the controls were recruited, All of the controls were recruited from either the cardiac, hypertensive, diabetic or renal clinics with the majority reporting a hypertensive or other cardiac related diagnosis and this could account for the increased prevalence of the respiratory symptoms. An additional interesting finding is the large number of cases (68%) who reported having asthma. In the authors opinion, it is likely that individuals who develop wheeze and breathlessness assume that they have asthma and that this misconception is rarely corrected by the treating doctor.

Although this study has found strong associations between occupational exposures and risk of COPD, several limitations were identified that may have biased the estimate away from the null. Cases (both prevalent and incident) were identified and selected from the specialist respiratory clinics of three public sector hospitals and disease status and severity confirmed by spirometry. This study found that approximately 70 % of cases had stage 3 to 4 disease as per the GOLD classification system. Individuals with less severe stages of disease were under-represented in the study. A likely explanation would be that only patients with moderate to severe disease are usually referred to these specialist respiratory clinics while those with less severe disease are managed at peripheral hospitals and clinics. Furthermore, inclusion of cases from the more severe end of the spectrum could have biased the estimate away from the null.

Misclassification of controls as non COPD could have occurred as they were not systematically and objectively screened via spirometry to exclude obstructive lung disease. For controls, disease misclassification was limited by enquiring about and subsequently excluding, those individuals who provided an affirmative response to questions relating to ever having had a diagnosis of a COPD related disease or ever having used any COPD related medication including inhalers within 12 months of the interview. For all cases, except two, medical records as well as availability of lung function testing enabled verification of reported physician's diagnosis of COPD. The availability of objective measures of lung function allowed the researcher to

reduce clinical diagnostic error, to validate airway obstruction, as well as to ascertain objectively the stage of disease.

As the majority of the participants were currently not employed, self reported information on occupational exposures was collected retrospectively with the potential for recall bias. Considering the range of ages and the fact that just over 60% of our participants were older than 60 years, many of them would have left their last job many years prior to this study. In addition, many of their exposures would have occurred decades earlier, making recall difficult. Exposure classification could be affected either by differential or non-differential misclassification. Differential misclassification could have occurred if COPD cases reported a more complete history of employment and exposures than did controls. However, the information on occupation was collected twice on the questionnaire and in almost all instances; the participants provided similar accounts of occupations and exposures. Without objective quantifiable evidence of workplace exposures, it is possible that many cases of COPD may have overestimated their exposures and this could be biasing the results towards an inflated OR. Other objective measures of exposure eg job exposure matrices would probably better identify cases that are exposed as opposed to self reports of exposure. If cases were more likely to recall their past exposures than controls, this is likely to have biased the odds ratio estimate away from the null. Furthermore, misclassification of COPD patients as controls would have biased the estimate towards the null. An additional

limitation is the lack of analysis of the broad classes of occupations and industries.

An additional limitation is the bias introduced by the selection of controls from specialist clinics. Controls who attend these clinics may be similar to cases with regard to health service location; however, they do not necessarily represent the general working population with regards to exposures, namely smoking and occupational exposures. Controls with longstanding diagnoses of eg cardiovascular disease or diabetes may have a different smoking pattern than the general population. It is also possible that their choice of occupation may have been influenced by their chronic illnesses in that they may have selected less exposed occupations.

Due to difficulty in apportioning the relative contributions of different exposures to the development of COPD, there may be an adversarial approach to compensation of COPD as an occupational disease. No guidelines exist to assist in attributing risk among multiple exposures. In South Africa, COPD is recognised as a compensable occupational lung disease only among miners with more than 10 years history of exposure. In addition, in less developed countries where the prevalence of cigarette smoking is typically lower, the relative contribution of exposures other than smoking may be more significant [7]. Furthermore, in South Africa, the control of occupational exposures suffers from inadequate enforcement of the good enabling legislation that does exist [7] .

The question “should a person with COPD remain in his or her job if it involves exposure to gases, dusts or fumes?” begs an answer. Although studies [16, 52] have reported that ongoing exposure increased lung function impairment removal of individuals from their jobs without suitable alternatives for employment can result in severe consequences. The better option would be to protect workers’ health by reducing workplace exposures to ensure the health and safety of all employees.

In conclusion, these findings lend further support to the body of evidence causally linking occupational exposures to the development of COPD. This recognition is important for the public health sector in its attempts to address the morbidity and mortality associated with COPD by focussing on smoking cessation as well as reduction of causal occupational exposures. Control of occupational exposures could have a profound impact on COPD by reducing prevalence by at least 15% [2]. Furthermore, renewed efforts to improve tuberculosis detection and cure rates, in addition to reducing morbidity and spread of disease, will also assist in diminishing the burden of COPD. Clinicians involved in the management of patients with COPD, or patients employed in jobs with potential for occupational exposure to causal agents, need to identify the disease at its early stages and appropriately advise reduction of exposures to prevent initiation and or progression of COPD. Regulatory agencies and decision makers responsible for compensation of occupationally acquired diseases, specifically in the non-mining sector in South Africa, need to take cognisance of these findings and to provide for COPD as an occupational disease.

REFERENCES

- [1] Lopez A D, Mathers C D, Ezzati M, Jamison D T, Murray C J L. Global Burden of Disease and Risk Factors. Washington DC: The World Bank, 2006.
- [2] Balmes J, Becklake M, Blanc P, Henneberger P, Kreiss K, Mapp C, et al. American Thoracic Society Statement: Occupational contribution to the burden of airway disease. *Am J Respir Crit Care Med*. 2003;167(5):787-97.
- [3] Becklake M. Chronic airflow limitation: its relationship to work in dusty occupations. *Chest*. 1985;88(4):608-17.
- [4] Hnidzo E, Vallyathan V. Chronic obstructive pulmonary disease due to occupational exposure to silica dust: a review of epidemiological and pathological evidence. *Occup Environ Med*. 2003;60:237-43.
- [5] Rabe K F, Hurd S, Anzueto A, Barnes P J, Buist S A, Calverley P, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med*. 2007;176:pp 532–55.
- [6] Mannino DM, Holguin F. Epidemiology and global impact of chronic obstructive pulmonary disease. *Respiratory Medicine: COPD Update* (2006). 2006;1:114-20.
- [7] Ehrlich R I, White N, Norman R, Laubscher R, Steyn K, Lombard C, et al. Predictors of chronic bronchitis in South African adults. *Int J Tuberc Lung Dis* 2004; 8(3):369-76.
- [8] Buist A S , McBurnie M A, Vollmer W M, Gillespie S, Burney P, Mannino D M, et al. International variation in the prevalence of COPD (The BOLD Study): a population-based prevalence study *Lancet*. 2007; 370(9589):741-50.
- [9] Menezes AMB, Perez-Padilla R, Jardim JRB, Muino A, Lopez MV, Valdivia G, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. *Lancet*. 2005;366:1875-81.
- [10] Halbert R J, Isonaka S, George D, Iqbal A. Interpreting COPD Prevalence Estimates. *Chest*. 2003;123:1684-92.
- [11] Blanc P D, Toren K. Occupation in Chronic obstructive pulmonary disease and chronic bronchitis: an update. *Int J Tuberc Lung Dis* 2007;11(3):251-7.
- [12] Balmes J R. Occupational Contribution to the Burden of Chronic Obstructive Pulmonary Disease. *J Occup Environ Med* 2005;47(2):154-60.

- [13] Becklake M. Occupational exposures: evidence for a causal association with chronic obstructive pulmonary disease
Am Rev Respir Dis 1989;140:S85-91.
- [14] Viegi G, Pede CD. Chronic obstructive lung diseases and occupational exposure. J Allergy Clin Immunol. 2002;2:115-21.
- [15] Matheson MC, Benke G, Raven J, Sim MR, Kromhout H, Vermeulen R, et al. Biological dust exposure in the workplace is a risk factor for chronic obstructive pulmonary disease Thorax. 2005;60:645-51.
- [16] Harber P, Tashkin DP, Simmons M, Crawford L, Hnidzo E, J C. Effect of Occupational Exposures on Decline of Lung Function in Early Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2007;179:994-1000.
- [17] Rom WN, Kanner RE, Renzetti AD, Shigeoka JW, Barkman HW, Nichols M, et al. Respiratory Disease in Utah Coal Miners. Am Rev Resp Dis. 1981;123:372-7.
- [18] Manfreda J, Sidwall G, Maini K, West P, Cherniack RM. Respiratory Abnormalities in Employees of the Hard Rock Mining Industry. Am Rev Resp Dis. 1982;126:629-34.
- [19] Irwig LM, Rocks P. Lung Function and Respiratory Symptoms in Silicotic and Nonsilicotic Gold Miners. Am Rev Resp Dis. 1978;117:429-35.
- [20] Schmidt U. Dust exposure, chronic bronchitis and emphysema. Eur J Respir Dis. 1982;63 (suppl 118):59-67.
- [21] Kauffman F, Drouet D, Lellouch J, Brille D. Occupational exposure and 12 year spirometric changes among Paris area workers. Br J Ind Med. 1982;39:221-32.
- [22] Jedrychowski W. A consideration of risk factors and development of chronic bronchitis in a five year followup study of an industrial population. J Epi Comm Health. 1979;33:210-4.
- [23] Pham QT, Mastrangelo B, Chau N, Haluska J. Five year longitudinal comparison of respiratory symptoms and function in steel workers and unexposed workers. Bull Europ Physiopath respir. 1979;15:469-80.
- [24] Love RG, Miller BG. Longitudinal study of lung function in coal miners. Thorax. 1982;37:193-7.
- [25] Brinkman GL, Block DL, Cress C. Effects of bronchitis and occupation on pulmonary ventilation over an 11 year period. J Occ Med. 1972;14:615-20.
- [26] Boschetto P, Quintavalle S, Miotto D, Lo Cascio N, Elena Zeni E, Mapp CE. Chronic obstructive pulmonary disease (COPD) and occupational exposures. Journal of Occupational Medicine and Toxicology. 2006;1(11).

- [27] Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist A, Mannino DM. Global burden on COPD: systematic review and meta-analysis. *Eur Respir J* 2006;28:523-32.
- [28] Lopez A D, Shibuya K, Rao c, Mathers C D, Hansell AL, Held LS, et al. Chronic Obstructive Pulmonary disease: current burden and future projections. *Eur Respir J.* 2006;27:397-412.
- [29] Mannino D M, Buist A S. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet.* 2007;370:765-73.
- [30] Ulvestad B, Bakke B, Melbostad E, Fuglerud P, Kongerud J, Lund MB. Increased risk of pulmonary disease in tunnel workers. *Thorax.* 2000;55:277-82.
- [31] Malmberg P, Hedenstrom H, Sundblad B-M. Changes in lung function of granite crushers exposed to moderately high silica concentrations: a 12 year follow up. *Br J Ind Med.* 1993;50:726-31.
- [32] Hnizdo E. Loss of lung function associated with exposure to silica dust and with smoking and its relation to disability and mortality in South African gold miners. *Br J Ind Med.* 1992;49:472-9.
- [33] Cowie RL, Mabena SK. Silicosis, Chronic Airflow Limitation, and Chronic Bronchitis in South African Gold Miners. *Am Rev Resp Dis.* 1991;143:80-4.
- [34] Meijers JM, Swaen GM, Slangen JJ. Mortality of Dutch coal miners in relation to pneumoconiosis, chronic obstructive pulmonary disease, and lung function. *Occup Environ Med.* 1997;54:708-13.
- [35] Meijers JM, Swaen GM, Slangen JJ, van Vliet K, F S. Long-term mortality in miners with coal workers' pneumoconiosis in the Netherlands. *Am J Ind Med.* 1991;19:43-50.
- [36] Romundstad P, Andersen A, Haldorsen T. Non- malignant mortality among Norwegian silicon carbide smelter workers. *Occup Environ Med.* 2002;59:345-7.
- [37] Soutar CA, Hurley JF. Relation between dust exposure and lung function in miners and ex-miners. *Br J Ind Med.* 1986;43:307-20.
- [38] Harber P, Muranko H, Solis S, Torossian A, Merz B. Effect of carbon black exposure on respiratory function and symptoms. *J Occup Environ Med.* 2003;45:144-55.
- [39] Mastrangelo G, Tartari M, Fedeli U, Fadda E, Saia B. Ascertaining the risk of chronic obstructive pulmonary disease in relation to occupation using a case-control design. *Occ Med.* 2003;53:165-72.
- [40] Weinmann S, Vollmer WM, Breen V, Heumann M, Hnizdo E, Villnave J, et al. COPD and occupational exposures: a case-control study. *J Occup Environ Med.* 2008;50(5):561-9.
- [41] Blanc PD, Eisner MD, Earnest G, Trupin L, Balmes JR, Yelin EH, et al. Further Exploration of the Links Between Occupational

Exposures and Chronic Obstructive Pulmonary Disease. *J Occup Environ Med.* 2009;51:804-10.

[42] Xu X, Christiani DC, Dockery DW, Wang L. Exposure-response relationships between occupational exposures and chronic respiratory illness: a community based study. *Am Rev Resp Dis.* 1992;146:413-8.

[43] Fishwick D, Bradshaw LM, D'Souza W, Town I, Armstrong R, Pearce N, et al. Chronic Bronchitis, Shortness of Breath, and Airway Obstruction in New Zealand. *Am J Respir Crit Care Med.* 1997;156:1440-6.

[44] Hummerfelt S, Gulsvik A, Skjaerven R. Decline in FEV1 and airflow limitation related to occupational exposures in men of an urban community. *Eur Respir J.* 1993;6:1095-103.

[45] Krzyanowski M, Jedrychowski W, Wysocki M. Factors associated with the change in ventilatory function and the development of chronic obstructive pulmonary disease in a 13 year follow-up of the Cracow study. *Am Rev Resp Dis.* 1986;134:1011-9.

[46] Sunyer J, Kogevinas M, Kromhout H, Anto JM, Roca J, Tobias A, et al. Pulmonary Ventilatory Defects and Occupational Exposures in a Population- based Study in Spain. *Am J Respir Crit Care Med.* 1998;157:512-7.

[47] Zock JP, Sunyer J, Kogevinas M, Kromhout H, Burney P, Antó JM. Occupation, chronic bronchitis, and lung function in young adults. An international study. *Am J Respir Crit Care Med.* 2001 163((7)):1572-7.

[48] Viegi G, Scognamiglio A, Baldacci S, Pistelli F, L C. Epidemiology of Chronic Obstructive Pulmonary Disease (COPD). *Respiration* 2001;68(1):4-19.

[49] Piera Boschetto P, Quintavalle S, Miotto D, Lo Cascio N, Elena Zeni E, Mapp CE. Chronic obstructive pulmonary disease (COPD) and occupational exposures. *J Occup Med Toxicol.* 2006;1(11).

[50] Jaen A, Zock JP, Kogevinas M, Ferrer A, Marin A. Occupation, smoking, and chronic obstructive respiratory disorders: a cross sectional study in an industrial area of Catalonia, Spain. *Environmental Health: A Global Access Science Source* 2006. 2006;5(2).

[51] Bergdahl IA, Toren K, Eriksson K, Hedlund U, Nilsson T, Flodin R, et al. Increased mortality in COPD among construction workers exposed to inorganic dust. *Eur Respir J.* 2004;23:402-6.

[52] Blanc P D, Eisner M D, Trupin L, Yelin E H, Katz P P, Balmes J R The association between occupational factors and adverse health outcomes in chronic obstructive pulmonary disease. *Occup. Environ Med* 2004;61:661-7.

- [53] Hummerfelt S, Eide GE, Gulsvik A. Association of years of occupational quartz exposure with spirometric airflow limitation in Norwegian men aged 30-46 years. *Thorax*. 1998;53:649-55.
- [54] Becklake MR, Irwig LM, Kielkowski D, Webster I, De Beer M, Landau S. The Predictors of Emphysema in South African Gold Miners. *Am Rev Resp Dis*. 1987;1234-41.
- [55] Hnidzo E, Sluis-Cremer GK, Abramowitz JA. Emphysema Type in Relation to Silica Dust Exposure in South African Gold Miners. *Am Rev Resp Dis*. 1991;143:1241-7.
- [56] Naidoo RN, Robins TG, Murray J. Respiratory outcomes among South African coal miners at autopsy. *Am J Ind Med*. 2005;48:217-24.
- [57] Hnidzo E, Sullivan PA, Bang KM, Wagner G. Association between chronic obstructive pulmonary disease and employment by industry and occupation in the US population: a study from the third national health and nutrition examination survey. *Am J Epidemiol*. 2002;156:738-46.
- [58] Trupin L, Earnest G, San Pedro M, Balmes J R, Eisner M D, Yelin E, et al. The occupational burden of chronic obstructive pulmonary disease *Eur Respir J* 2003;22:462-9.
- [59] Hnidzo E, Murray J. Risk of pulmonary tuberculosis relative to silicosis and exposure to silica dust in South African gold miners. *Occup Environ Med*. 1998;55:496-502.
- [60] Hnidzo E, Singh T, Churchyard GJ. Chronic pulmonary function impairment caused by initial and recurrent pulmonary tuberculosis following treatment. *Thorax*. 2000;55:32-8.
- [61] Corbett EL, Churchyard GJ, Clayton T, Herselman P, Williams B, Hayes R, et al. Risk Factors for Pulmonary Mycobacterial disease in South African Gold Miners. *Am J Respir Crit Care Med*. 1999;159:94-9.
- [62] teWaterNaude JM, Ehrlich RI, Churchyard GJ, Pemba L, Dekker K, Vermeis M, et al. Tuberculosis and silica exposure in South African gold miners. *Occup Environ Med*. 2004;63:187-92.
- [63] Hnidzo E. Combined effect of silica dust and tobacco smoking on mortality from chronic obstructive lung disease in gold miners. *Br J Ind Med*. 1990;47:656-64.
- [64] Blanc P D, Iribarren C, Trupin L, Earnest G, Katz P P, Balmes J, et al. Chronic Obstructive Pulmonary Disease. Occupational exposures and the risk of COPD: dusty trades revisited. *Thorax*. 2009;64:6-12.
- [65] De Meer G, Kerkhof M, Kromhout H, Schouten JP, Heederik D. Interaction of atopy and smoking on respiratory effects of occupational dust exposure: a general population-based study. *Environmental Health: A Global Access Science Source* 2006. 2004;3.

- [66] Girdler-Brown BV, White NW, Ehrlich RI, Churchyard GJ. The Burden of Silicosis, Pulmonary Tuberculosis and COPD Among Former Basotho Goldminers. *Am J Ind Med.* 2008.
- [67] Menezes AMB, Hallal PC, Perez-Padilla R, Jardim JRB, Muino A, Lopez A D, et al. Tuberculosis and airflow obstruction: evidence from the PLATINO study in Latin America. *Eur J Respir Dis.* 2007;30:1180-5.
- [68] Naidoo R, Robins TG, Seixas N, Laloo UG, Becklake M. Respirable coal dust exposure and respiratory symptoms in South African coal miners: A comparison of current and ex-miners. *J Occup Environ Med.* 2006;48(6): 581-590.
- [69] South African Thoracic Society. Guideline for Office Spirometry in Adults, 2004. *S Afr Med J.* 2004; 94(7): 576-587
- [70] American Thoracic Society. Standardisation of spirometry. *Eur Respir J.* 2005; 26: 319-338
- [71] Eisen EA, Robins JM. Estimation of Ventilatory Capacity in Subjects with Unacceptable Lung Function Tests. *Int J Epidemiol.* 1988. 15(3):337-42.
- [72] Becklake MR, White NW. Sources of variation in spirometric measurements. Identifying the signal and dealing with noise. *Occup Med.* 1993;8(2):241-64.
- [73] Quanjer PH, Tammeling GJ, Cotes JE, Pederson OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests. European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl.* 1993;16:5-40.

APPENDICES

APPENDIX A

ETHICS CLEARANCE CERTIFICATE



UNIVERSITY OF
KWAZULU-NATAL

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
Private Bag X 54001
Durban
4000

KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2904788 - Fax: 27 31 2804800
Email: BRE@ukzn.ac.za

Website: <http://research.ukzn.ac.za/ResearchEthics1141E.9608>

01 December 2008

Dr N Govender
Department of Occupational and Environmental Health
Nelson R. School of Medicine
University of KwaZulu-Natal

PROTOCOL: Occupational exposure and chronic obstructive pulmonary disease. Dr N Govender, Department of Occupational and Environmental Health. Ref No: BF123/08

Dear Dr Govender

The Biomedical Research Ethics Committee considered the abovementioned application and the protocol was approved by a **full sitting of the committee** at a meeting held on **09 September 2008** pending appropriate responses to queries raised. Your responses dated **28 November 2008** to queries raised on **17 November 2008** have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given full ethics approval and may begin as at today's date; **01 December 2008**

The Information/Consent Documents as submitted with your application has also been approved.

This approval is valid for one year from (**01 December 2008**). To ensure continuous approval, an application for recertification should be submitted a couple of months before the expiry date. In addition, when consent is a requirement, the consent process will need to be repeated annually.

I take this opportunity to wish you everything of the best with your study. Please send the Biomedical Research Ethics Committee a copy of your report once completed.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'D. Wassenaar', written over a horizontal line.

PROFESSOR D WASSENAAR
Chair: Biomedical Research Ethics Committee

APPENDIX B

LETTER OF PERMISSION FROM DEPARTMENT OF HEALTH

DEC 17 21:06 04:27 03353189



HEALTH
KwaZulu Natal

HEALTH SERVICE DELIVERY #5765 21006 1006
Health Research & Knowledge Management sub component
1C – 103 Natalia Building, 330 Langolhele Street
Private Bag X9051
Pietermaritzburg
3200
Tel: 033 – 3953 189
Fax: 033 – 364 3762
Email: hrkm@kznhealth.gov.za
www.kznhealth.gov.za

Reference : HRKM030/08
Enquiries : Mrs G Khumalo
Telephone : 033 - 3953189

08 December 2008

Dear Dr Govender

Subject: Approval of a Research Proposal

1. The research proposal titled '**Occupational Exposures and Chronic Obstructive Pulmonary Disease**' was reviewed by the KwaZulu-Natal Department of Health. The proposal is hereby **approved** for research to be undertaken at RK Khan, Crays and Inkosi Albert Luthuli Central Hospitals.
2. You are requested to undertake the following:
 - a. Make the necessary arrangement with identified facility before commencing with your research project.
 - b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.
3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mrs G Khumalo on 033-3953189.

Yours Sincerely


Dr. S.S.S. Bulhoek
Chairperson: Provincial Health Research Committee
KwaZulu-Natal Department of Health

uMnyango Wezempilo - Departament van Gesondheid

Fighting Disease, Fighting Poverty, Giving Hope

APPENDIX C

CONSENT TO PARTICIPATE IN A STUDY OF OCCUPATIONAL EXPOSURES AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE

1. Title of research project

Occupational Exposures and Chronic Obstructive Pulmonary Disease

2. Introduction

My name is Dr N Govender and I am from the Department of Occupational and Environmental Health at the Nelson R Mandela School of Medicine. I am conducting research about a lung disease called Chronic Obstructive Pulmonary disease and would like a few minutes of your time to determine if you would be interested in being part of the study. I have selected you because you have the disease that I am interested in. The number of people with Chronic Obstructive Pulmonary Disease is increasing worldwide. As a result there are more patients with this disease being seen at health care facilities. We know that cigarette smoking is the commonest cause of this disease. However, there is a lot of research that shows that hazards to which people are exposed to at work may also be causing or contributing to this illness. These hazards/ exposures may include certain types of dusts and chemicals that workers inhale and we believe that workers exposure to these hazards is increasing and as a result more workers are developing COPD. However there is very little information on this in our local setting in KwaZulu-Natal.

3. Names of the researchers

Dr. Rajen Naidoo, MB.ChB, PhD	Department of Occupational and Environmental Health, University of KwaZulu-Natal, South Africa Telephone: 031-260 4385; Fax: 031-260 4663
Dr. Nadira Govender, MB. ChB, DOH	Department of Occupational and Environmental Health, University of KwaZulu-Natal, South Africa Telephone: 031-260 4385/ 4676; Fax: 031-260 4663

4. Purpose of the research

We wish to ask you to participate in an investigation, called " Occupational Exposures And Chronic Obstructive Pulmonary Disease". The purpose of this study is to determine the role of occupational exposures as a risk factor for chronic obstructive pulmonary disease. Identifying the possible contributing causes of COPD among workers will assist us in identifying the types of work and industries that may be responsible for contributing to this increased burden of COPD. This will assist in contributing to the development of policy relating to work-related COPD.

5. Description of the research project

If you agree to participate in the study, you will be asked to complete the following at one of your clinic visits to this hospital:

a). Complete a questionnaire. A member of our research team will administer a questionnaire to you in one of the following languages of your choice: English or isiZulu. Should these not be a language of your choice, please advise the interviewer, who will inform the Principal Investigator of the study. You will be asked questions about yourself, about your health and any chest symptoms that you may have or had in the past, past chest illnesses, your smoking history, history of your job including previous jobs and your family history. Based on our previous experience in the administering of similar questionnaires, this interview will take about 45 minutes to complete. You may be asked to complete the questionnaire for a second time. This is a check to determine if the information is being collected and entered correctly. The re-interview will take place at your next clinic visit and will thus not require a special visit to the clinic.

We will also obtain the following information from your hospital records:

a). Lung function test: This is a test of how well your lungs work, and you will have had this done at one of your visits to this clinic over the last year. Should this test not be of appropriate quality, then we will request that another test be done at the date of your interview, as part of your normal clinical assessment. You will be asked to blow into a machine. The results of this test will tell us whether your lungs work normally or whether there are problems present.

Risks and discomforts of the research and measures taken to reduce this

- a). From the interview. During the interview, you will be asked personal questions. This may cause you to feel uncomfortable. If you are unhappy to answer any question, please inform the interviewer. You will not be forced to answer any question.
- b). From lung function tests.** Should a new lung function test be required, this will be done by trained technicians. There are no side effects of this test, but if you do suffer from wheezing or asthma, the deep blow that you give into the machine may cause your chest to become a little tight for a short while. This can always be quickly treated by asthma treatment. You should inform the technician and doctor before you do the test, that you do have this problem. Should your chest become tight after the test, inform the technician immediately, who will inform the doctor to supervise your medication.

6. Expected benefits to you and to others

You will be given a written copy of all your test results along with an interpretation of their meaning. Should any of our results find that you have a disease as a result of the work that you do, and should this be compensable under the law, then we will refer you to an appropriate centre for further assessment and intervention. On completion of the study, a report highlighting the main study conclusions will be forwarded to you

7. Costs to you resulting from participation in the study

The study is offered at no cost to you. In the event a compensable disease is identified and you need to be referred to a specialist unit, we can recommend to you who to see. However, any additional costs of such medical visits or treatments will not be the responsibility of the study team. The interviews and any other tests that may be necessary will be done during your normal clinic visit, while you wait to be assessed by the respiratory consultants. We do not anticipate taking up any additional time. However, should unexpected delays occur, and you incur additional costs related to the research, this will be covered by the research team.

9. Confidentiality of information collected

Your name will not appear in any reports on this study. The records of questionnaires and other tests will be kept completely confidential and will be seen only by members of the study team.

10. Voluntary nature of participation

Your participation in this project is entirely voluntary. Even after you give your consent, you may refuse to participate in or withdraw from the study at any time without penalty or loss of benefits.

11. Documentation of the consent

One copy of this document will be kept together with our research records on this study. A second copy will be given to you to keep.

12. Contact person. This study has received ethics approval from the Biomedical Research Ethics Committee, University of Kwazulu- Natal. In addition, permission to conduct the study has also been received from the medical manager of this hospital. If you require further explanation regarding the study or if you have any concerns, or answers to further questions about the research, your rights, or any problem you may feel is related to the study please contact Dr. Nadira Govender at the following telephone numbers: Tel: (031) 2604471/4676 Cell: 0837171878

If you need to obtain additional information about this study, the contact details of the Biomedical Research Ethics Committee, University of Kwazulu-Natal are as follows:

Research Office – tel: (031) 260 4769, fax: (031) 260 4609; e-mail:

BREC@ukzn.ac.za

Consent of the participant

I have read [or been informed] of the information given above. I understand the meaning of this information. Dr./Mr./Ms. _____ has offered to answer any questions I may have concerning the study. I hereby consent to participate in the study.

I _____ (First name & Surname) consent to answering a questionnaire and to having a copy of my lung function test done either today or one done in the past 12 months used in this study.

Printed name of participant

Participant signature

Witness (Print)

Witness signature

DATE:

Consent of the participant

I have read [or been informed] of the information given above. I understand the meaning of this information. Dr./Mr./Ms. _____ has offered to answer any questions I may have concerning the study. I hereby consent to participate in the study.

I _____ (First name & Surname) consent to answering a questionnaire and to having a copy of my lung function test done either today or one done in the past 12 months used in this study.

Printed name of participant

Participant signature

Witness (Print)

Witness signature

DATE:

(investigators copy)

APPENDIX D

**QUESTIONNAIRE: Occupational exposures and Chronic
Obstructive Pulmonary Disease**

STUDY ID _____

DATE: ___/___/___

INSTITUTION: _____

A.IDENTIFICATION

1. CURRENT ADDRESS:

STREET _____

SUBURB/AREA: _____

CODE _____

CITY _____ PROVINCE _____

2. PHONE NUMBER: (_____) _____

3. IDENTITY NUMBER: _____

4. BIRTHDATE: ___/___/___

5. AGE LAST BIRTHDAY _____ (dd/mm/yy)

6. SEX

M	F
---	---

7. MARITAL STATUS:

- 1. MARRIED ___
- 2. WIDOWED ___
- 3. DIVORCED ___
- 4. SEPARATED ___
- 5. NEVER MARRIED ___

QUESTIONNAIRE: Occupational exposures and Chronic Obstructive Pulmonary Disease

STUDY ID _____

DATE: ___/___/___

INSTITUTION: _____

B. SYMPTOMS

I am going to ask you some questions, mainly about your chest. I would like you to answer "YES" or "NO" whenever possible.

* for night shift workers

8. COUGH

Do you usually have a cough?

Y 1	N 0
--------	--------

9. Do you usually cough first thing in the morning (on getting up*)
in the winter?

Y 1	N 0
--------	--------

If YES to 8 or 9:

a. Do you usually cough at all during the rest of the day or at night*?

Y 1	N 0
--------	--------

b. Do you cough like this on most days (or nights*) for as much
as three months each year?

Y 1	N 0
--------	--------

c. For how many years have you had this cough?
Number years

SPUTUM

10. Do you usually bring up any phlegm/sputum/mucus from your chest first thing in the morning (on getting up*) in the winter?

Y	N
1	0

11. Do you usually bring up any phlegm/sputum/mucus from your chest during the day (or at night*) in the winter?

Y	N
1	0

IF YES TO 10 OR 11:

a. Do you bring up phlegm like this on most days (or nights*) for as much as three months each year?

Y	N
1	0

b. Do you usually bring up phlegm at all on getting up or first thing in the morning?

Y	N
1	0

c. For how many years have you had trouble with phlegm?
years

EISODES OF COUGH AND PHLEGM

12. Have you had periods or episodes of (increased**) cough and phelgm lasting for 3 weeks or more each year?

Y	N
1	0

BREATHLESSNESS

13. Are you troubled by shortness of breath when hurrying on level ground?

Y	N
1	0

14. Do you get short of breath walking with other people of your own age on level ground?

Y	N
	0

15. Do you have to stop for breath when walking at your own pace on level ground?

Y	N
1	0

16. Are you too breathless to leave the house or breathless on dressing or undressing?

Y	N
1	0

WHEEZING

17. Does your chest ever sound wheezy or whistling:

Y	N
1	0

IF YES TO 17:

a. When you have a cold?

Y	N
1	0

b. Occasionally apart from colds?

Y	N
1	0

c. Most days or nights?

Y	N
1	0

d. For how many years has this been present?
years

18. Have you ever had an ATTACK of wheezing that has made you feel short of breath?

Y	N
1	0

IF YES TO 18:

a. How old were you when you had your first such attack?
Age in years

b. Have you ever required medicine or treatment for these attack(s)?

Y	N
1	0

c. Is/Was your breathing absolutely normal between attacks?

Y	N
1	0

CHEST ILLNESSES

19. Have you ever had pneumonia?

Y	N
1	0

IF YES TO 19:

a. Was it confirmed by a doctor?

Y	N
1	0

b. At what age did you first have it?
Age in years

20. Have you ever had Hayfever?

Y	N
1	0

IF YES TO 20:

a. Was it confirmed by a doctor?

Y	N
1	0

b. At what age did it start?
Age in years

21. Have you ever had chronic bronchitis?

Y	N
1	0

IF YES TO 21:

a. Do you still have it?

Y	N
1	0

b. Was it confirmed by a doctor?

Y	N
1	0

c. At what age did it start?

_____ Age in years

22. Have you ever had emphysema?

Y	N
1	0

IF YES TO 22:

a. Do you still have it?

Y	N
1	0

b. Was it confirmed by a doctor?

Y	N
1	0

c. At what age did it start?

_____ Age in years

23. Have you ever had asthma?

Y	N
1	0

IF YES TO 23:

a. Do you still have it?

Y	N
1	0

b. Was it confirmed by a doctor?

Y	N
1	0

c. At what age did it start?

_____ Age in years

d. If you no longer have it, at what age did it stop?

_____ Age stopped

24. Have you had chest tuberculosis?

Y	N
1	0

IF YES TO 24:

a. Do you still have it?

Y	N
1	0

b. Was it confirmed by a doctor?

Y	N
1	0

c. When did this happen?

_____ Year

d. How long did you receive treatment for this

____ months

e. Did you have a second episode of TB?

Y	N
1	0

f. When did this happen?

_____ Year

g. How long did you receive treatment for this?

_____ months

25. Have you ever been told by a doctor that you have COPD?

Y	N
1	0

IF YES,

a) When (Year)

26. Have you ever had:

a. Any other chest illnesses as mentioned by a doctor?

Y	N
1	0

If yes, please specify _____

b. Any chest operations?

Y	N
1	0

If yes, please specify _____

c. Any chest injuries?

Y	N
1	0

If yes, please specify _____

27. Have you ever had treatment for heart trouble in the past 10 years?

Y	N
1	0

28. Have you had any treatment for high blood pressure (hypertension) in the past 10 years?

Y	N
1	0

29. Have you used any medication to help your breathing at any time in the last 12 months?

Y	N
1	0

IF YES,

30. What medications do you use regularly for your lung disease?
Interviewer to record drugs as stated by the participant.

.....
.....
.....
.....
.....
.....
.....
.....
.....

(A list of drugs will be available for coding purposes)

C: OCCUPATIONAL HISTORY

I would now like to ask you some questions on the types of jobs you have done.

READ ALL OPTIONS AND TICK ONE BOX ONLY

31. Are you currently:

Employed	1
Self employed	2
Unemployed, looking for work	3
Not working because of poor health	4
Full time house person	5
Full time student	6
Retired	7
Other	8

31b. Please specify response for "Other"

32. If you had more than one job in the same company, or if you were doing more than one job at the same time, we would like to talk about them separately. Please start with your current or last job.

JOB NUMBER	JOB DESCRIPTION/TITLE	What was the name of the firm, company or organization? NAME	What did the firm, company or organization do, or what services did it provide? INDUSTRY	For each of these job titles, could you list the different types of substances that you were exposed to? EXPOSURES	In what month and year did you start working in this specific job title?		In what month and year did you stop working in this specific job title?		Duration of employment (years) in this specific job title?
					Month	Year	Month	Year	
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									

33. Do you have any records in your possession or at home that could verify the above details?

Y	N
1	0

IF YES,

a. Would you mind if we contacted you again to obtain this information?

Y	N
1	0

34. Have any of these jobs ever made your chest tight or wheezy?

Y	N
1	0

35. If yes, please tick against the appropriate job number (job number to correspond with Q 32)

(Tick implies YES)

Job number
1
2
3
4
5
6
7
8
9
10

36. Have you had to leave any of these jobs because they affected your breathing?

YES	NO
1	0

37. If yes, please tick against the appropriate job number (job number to correspond with Q 32)

(Tick implies YES)

Job number
1
2
3
4
5
6
7
8
9
10

Record on lines the number of years in which the subject has worked in any of the below listed industries.

Have you ever worked:

38. In a quarry?

Y	N
1	0

No. years

39. In a foundry?

Y	N
1	0

No. years.....

40. In a pottery?

Y	N
1	0

No. years.....

41. In a cotton, flax, or hemp mill?

Y	N
1	0

No. years.....

42. With asbestos?

Y	N
1	0

No. years.....

43. With diesel or diesel exhaust?

Y	N
1	0

No. years.....

44. In sandblasting?

Y	N
1	0

No. years.....

45. In tunneling?

Y	N
1	0

No. years.....

46. In drilling?

Y	N
1	0

No. years.....

47. In any other dusty jobs?

Y	N
1	0

48a. Specify _____

No. years.....

48b. Total number of year's _____

49. Have you ever been exposed to gas or chemical fumes in your work?

Y	N
1	0

50. Specify job/industry: _____ Total years worked ____

51. Was chemical/gas exposure 1. Mild ____ 2. Moderate ____ 3. Severe ____ ?

52. Have you been involved in an accident at home, work or elsewhere that exposed you to high levels of vapours, gas, dust or fumes?

YES	NO
1	0

IF YES,

53. Did you experience respiratory symptoms immediately following this exposure?

YES	NO
1	0

IF YES

a. Could you describe to me what it was?

D: SMOKING

I am now going to ask you some questions about your smoking habits, if any.

54. Have you ever smoked for as long as a year?
(Yes means at least 20 packs of cigarettes or 350gm of tobacco in a lifetime, or at least one cigarette per day or one cigar per week for one year)

YES	NO
1	0

If YES:

55. How old were you when you started smoking?

Years

--	--

56. Do you now smoke, as of one month ago?

YES 1	NO 0
----------	---------

If YES:

57. How much do you now smoke on average?

	Number	
No of cigarettes per day		
No of cigars per week		
Pipe tobacco in grams per week		

58. Have you stopped smoking?

YES 1	NO 0
----------	---------

If YES: Go to Q 60

59. Have you cut down smoking?

YES 1	NO 0
----------	---------

If YES: Go to Q 60

60. How old were you when you stopped or cut down smoking?

Years

--	--

61. On average, of the entire time you smoked, before you stopped or cut down, how much did you smoke?

	Number	
No of cigarettes per day		
No of cigars per week		
Pipe tobacco in grams per week		

E: FAMILY HISTORY

I am now going to ask you some questions about your family

62. Were either of your natural parents ever told by a doctor that they had a chronic lung condition such as:

		FATHER			MOTHER		
		Yes 1	No 0	Don't Know 2	Yes 1	No 0	Don't Know 2
	1 Chronic Bronchitis						
	2 Emphysema						
	3 Asthma						
	4 Lung Cancer						
	5 Other Chest conditions						

62a. If OTHER, please specify: (FATHER): _____

(MOTHER): _____

F: OTHER

I am now going to ask you some questions about your home environment

63. How many years have you lived in your current house? ----- yrs

64. Does your home have any of the following?

	Y 1	N 0
1 central heating		
2 ducted air heating (forced air heating)		
3 air conditioning		

65. Which of the following appliances do you or did you mostly use for heating or for hot water?

TICK ONE BOX ONLY

open coal, coke or wood fire	1
open gas fire	2
electric heater	3
paraffin heater	4
gas-fired boiler	5
oil-fired boiler	6
portable gas heater	7
Other	8

66. What kind of stove do you/ did you mostly use for cooking?

TICK ONE BOX ONLY

coal, coke or wood (solid fuel)	1
gas (gas from the mains)	2
electric	3
paraffin (kerosene)	4
microwave	5
gas (gas from bottles or other non-mains source) ⁶	6
other	7

67. What type of stove do you/ did you mostly use in your house?

TICK ONE BOX ONLY

Electric	1
Gas	2
Paraffin	3
wood	4
Other- specify	5

68. How often do cars pass your house?

TICK ONE BOX ONLY

never	0
seldom	1
frequently	2
constantly	3

--	--

69. How often do heavy vehicles (e.g. trucks/buses) pass your house?

TICK ONE BOX ONLY

never	0
seldom	1
frequently	2
constantly	3

70. How long have you been attending this clinic? ----- months

Thank you for your time for these questions.

We may need to contact you again to obtain additional information. Please give me the name, address and telephone number of two relatives or friends who would know where you could be reached in case we have difficulty in contacting you.

Name of first contact person:

Telephone number of first contact person: _____

Relationship of contact person to you: _____

Name of second contact person:

Telephone number of second contact person: _____

Relationship of contact person to you: _____

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE!

END: Thank you for helping us!

Interview completed at:

Time: __:__ am / pm