



American University of Armenia

Department of Public Health

**Cement Dust and Chronic Obstructive Pulmonary Disease:
A Nested Case-Control Study among Plant Workers**

(Grant Proposal)

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Table of Contents

Abstract	2
Background information	3
Methods	7
Potential confounders	9
Sample size	9
Data Collection	9
Ethical considerations	11
Study limitations	11
Data analysis	12
Time frame for the Project	12
Budget	13
Acknowledgements	14
References	15
Appendices	17

Abstract

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. It results in a substantial and increasing economic and social burden for individuals, families, health care organizations, and society.

Cement plant workers are at increased risk for COPD. According to data obtained from the head doctor of Ararat polyclinic, the prevalence rate of COPD was 128 per 1,000 in this occupational group during 1999-2000. To assess the relationship between cement dust exposure and COPD and to conduct dose-response analysis, a nested case-control study among “Ararat cement” plant workers will be conducted. Cases are defined as cement plant employees with a clinical diagnosis of COPD who worked in the plant during 1995-2000. Controls are cement plant employees who worked in the plant during 1995-2000 and have not been diagnosed with COPD by the general practitioner. The required sample size is 78 for each group.

The selection of cases and controls will be done by simple random sampling and systematic sampling techniques using the polyclinic’s rosters of workers. Ascertainment of cases and controls will occur during face-to face interviews using a standardized questionnaire with specific questions about COPD-related symptoms (American Thoracic Society Adult Questionnaire-78). During interviews, information about potential confounders will also be gathered. Information about work history of cases and controls will be obtained from work employee records and interviews. The exposed workers will be divided according to the duration of work in an exposed job, to determine if increased duration led to increased risk of COPD (dose-response analysis). Logistic regression will be used for analysis to estimate a summary odds ratio after adjustment for confounders and to evaluate interactions between variables.

The total budget is about \$17,538.

Background information

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide and results in a substantial and increasing economic and social burden for individuals, families, health care organizations, and society.¹ There are several lung diseases collectively known as COPD, including asthmatic bronchitis, chronic bronchitis, chronic obstructive bronchitis, emphysema and asthma.² According to WHO, COPDs account each year for the deaths of almost 3 million people.³

The World Bank Global Burden of Disease Study estimated the worldwide prevalence of COPD at 9.34/1,000 in men and 7.33/1,000 in women.¹ However, this study included all ages and grossly underestimated the true prevalence of this disease in the adult population, because COPD usually becomes clinically apparent after age 40.¹

Recent estimates from surveys in European countries suggest that the prevalence of COPD may be closer to 80-100/1,000 in areas where the prevalence of smoking is very high.¹ Cross-country comparisons made by the Global Burden of Disease Study also showed that the prevalence of COPD is highest in countries where cigarette smoking is very common, while the prevalence is lowest in countries where smoking is less common.¹

According to data obtained from the Ministry of Health of Armenia more than three-fourth of adult males in Yerevan are smokers. Among other groups, the rate of smoking is as follows: about 40% of adult women, 37% of adolescents (half of whom are girls). Even though there is no reliable data regarding prevalence of COPD in Armenia, considering the high rate of smoking among Armenian population, COPD is an important Public Health problem. Moreover, morbidity data on COPD probably greatly underestimate the total burden of the disease because COPD is not usually recognized and diagnosed until it is clinically apparent and moderately

advanced. Mortality data also underestimate COPD as a cause of death because the disease is more likely to be cited as a contributory than as an underlying cause of death, or may not be cited at all.

Because COPD can be severely disabling, medical expenditures for treating COPD and the indirect costs of morbidity can represent a substantial economic and social burden for society¹. In 1998, the annual economic burden for COPD in the US was estimated to be \$23.9 billion, including \$14.7 billion in direct expenditures for medical care services, \$4.7 billion in indirect morbidity costs and \$4.5 billion in costs related to premature mortality.⁴ Based on a prevalence of 15.7 million cases, the estimated impact of COPD is \$1,522 per patient per year.⁴

According to the projections of the World Bank Global Burden of Disease Study, COPD will rank 5th in 2020, responsible for 4.1% of total DALYs (Disability-Adjusted Life Year) lost.¹ Only ischemic heart disease, major depression, traffic accidents, and cerebrovascular disease will cause a greater burden.¹

In Armenia, disabled individuals usually do not receive long-term supportive care services; therefore, COPD may force two individuals to leave the workplace - the affected individual and a family member who must now stay home to care for the disabled relative. Thus, in terms of productivity lost, COPD may be doubly burdensome for Armenia.

The factor common to all known environmental causes of COPD is prolonged exposure to small airborne particles, whether in cigarette smoke, ambient air, or the workplace environment.⁵ Tobacco use is a major risk factor for COPD.¹ Data from the third National Health and Nutrition Examination Survey (NHANES 3), a large national survey carried out in the US between 1988 and 1994, reinforce the view that smoking status is the most important determinant of COPD prevalence in developed countries.¹ Among white males, airflow limitation

was present in 14.2 % of current smokers, 6.9 % of ex-smokers, and 3.3 % of never smokers.¹ Among white females, the prevalence of airflow limitation was 13.6 % in smokers, 6.8 % in ex-smokers and 3.1 % in never smokers.¹

Recent studies of chronic obstructive pulmonary disease have raised interest in its relation to nutrition. Data from the Third National Health and Nutrition Examination Survey showed that higher levels of antioxidant nutrients are associated with better lung function.¹³ In particular, a diet rich in fresh fruit and fish is associated with a salutary effect on lung health. Reduced intake of fresh fruit and vegetables was linked with poorer lung function in a study of more than 9,000 adults in the United Kingdom.¹³ However, the role of deficiency of antioxidant nutrients as a risk factor for COPD is putative.^{13,14}

Until recently, virtually all population-based studies in developed countries showed a marked male preponderance of COPD prevalence and mortality.¹ A different pattern has been reported from developing countries, where a slightly higher prevalence in women than men is reported. The patterns seen in developing countries possibly reflect gender-related differences both in smoking and other COPD risk factors.¹

Other risk factors include age, heredity and socioeconomic status.¹⁴ Having alpha-1-antitrypsin (AAT) deficiency, also called familial emphysema, is a known risk factor. People with familial emphysema have a hereditary deficiency of alpha-1-protease inhibitor.^{15,16} Approximately 1% to 3% of all cases of emphysema are due to AAT deficiency.^{15,16}

In developing countries, there is evidence that risk for COPD is inversely related to socioeconomic status.¹⁴ It is not clear, however, whether this is a reflection of exposures to indoor and outdoor air pollutants, nutrition, and other factors which are related to socioeconomic status.¹⁴

Workers at increased risk for COPD include coal miners, construction workers who handle cement, metal workers who are subject to heat exposure from furnaces, transport workers, grain handlers, cotton workers, and workers in paper mills.^{6, 7} Studies of cement workers in Yugoslavia have shown a significant degree of obstructive airway diseases (decreased FEV1/FVC) compared to controls and reduced mean forced expiratory flow during the third quarter of the FVC (FEF_{50-75%}); these findings suggest the presence of small airway disease.⁸ These studies also found that the amount of reduction was proportionate to the length of cement factory employment.⁸ Several studies in countries of the former Soviet Union and Taiwan also found an increased rate of bronchitis among cement workers.^{9,10} However, a number of these studies did not “control” for the effect of smoking.

Portland cement (commonly known as cement) is a fine grayish-green powder that is produced by heating ground cement rock or other limestone- bearing materials into a fused clinker, which is then ground into a fine powder.¹⁰ The US Environment Protection Agency estimates total particle emissions of 180 kg per ton of cement produced, the majority being from the cement kiln.¹¹ Other sources of dust from cement production are the handling of raw materials, grinding cement clinker, and packaging or loading finished cement, which is ground to an extremely fine powder.¹²

The Ararat Cement plant is continuously operating throughout the economic hardship in Armenia. There are about 1,000 employees in the plant, which consists of two parts (old section and new section). Due to economic difficulties, the sections function intermittently. After the collapse of USSR, routine monitoring by the Ararat Center of Hygienic-Antiepidemic Control, which is responsible for occupational hygiene of the workplace environment, is poorly managed. All employees of the Ararat Cement plant undergo free annual medical examinations in the

Ararat polyclinic. According to data obtained from the head doctor of Ararat polyclinic, during 1999-2000 there were 128 employees with COPD. This means that the prevalence rate of COPD was approximately 128 per 1,000 in this occupational group.

Methods

Taking into account the importance of cement dust exposure as a major risk factor for COPD and the fact that no epidemiological studies in this regard have been done in Armenia, a nested case-control study among Ararat Cement plant workers will be conducted. The study is aimed to assess the relationship between cement dust exposure and COPD and to conduct dose-response analysis among Ararat Cement plant workers. The data can be used to develop industrial health programs in this sphere.

The most feasible method for this study, within the constraints of the time and money of the investigators, is a case-control study. It should be mentioned that COPD is a common disease and reliable estimates of the relative risk cannot be derived from the odds ratio obtained from this case-control study. Nevertheless, the case-control method is appropriate for the research question of this study. In addition, medical records and information regarding exposure used for the case-control method are easily accessible from Ararat polyclinic and plant documentation. The research question for the study is to reveal the strength of association between exposure to cement dust and COPD among workers of Ararat Cement plant. The null hypothesis: there is no association between cement dust exposure and COPD; the alternative hypothesis: there is association between cement dust exposure and COPD. The dependent variable is COPD, the independent variable is cement dust exposure. It should be emphasized that the results of this study will be applicable only to the employees of the cement plant.

Cases are defined as cement plant employees with a clinical diagnosis of COPD who worked in the plant during 1995-2000. Controls are cement plant employees who worked in the plant during 1995-2000 and had not been diagnosed with COPD by the general practitioner.

Taking into account the fact that physicians may not capture people with mild to moderate disease which leads to underdiagnosis of COPD among plant workers, the ascertainment of cases and controls will be done using a standardized questionnaire with specified questions about COPD-related symptoms. The respiratory part of the questionnaire is derived from the American Thoracic Society Adult Questionnaire (ATS DLD -78) and used for epidemiologic research.¹⁷ Although the authors did not provide a scoring manual for this questionnaire, scoring can be performed using articles on similar epidemiologic studies which used the same questionnaire.^{18,19} The questionnaire will include additional questions regarding work history, smoking status, and presence of comorbidities. The parts related to occupational history and smoking habits are derived from the standardized Questionnaire on Disease and Waste Dust Exposure.²⁰

There are 21 departments in the Ararat Cement plant. To estimate the degree of exposure, it is necessary to investigate each of them separately and to conduct measurements of cement dust. However, the filters used for this purpose cannot provide the estimation of particle size distribution. The size of particles is very important, because the small particles are most hazardous to health, as they can be inhaled deep into the lungs.¹⁰ Considering this fact, it is not useful to perform measurements by these filters. Exposure to cement dust in each department will be based on evaluation made by the industrial hygienist of the plant. In 12 departments where the handling of raw materials, grinding cement clinker, and packaging and loading of finished cement are done, workers are exposed to cement dust. In another 9 departments

including offices for administration, engineers, security, accountants, communication service, personnel department, fire station, kindergarten, and health center, employees are not exposed to cement dust.

Potential confounders

Age, gender, smoking status, place of residence, work history, and presence of comorbidities (including chest illnesses, chest operations, chest injuries, heart troubles) are factors that may confound the relationships between cement dust exposure and COPD. Frequency matching will be used to deal with confounding by age and sex. Because all cases and controls live in the same residential district, place of residence cannot be a confounder in this study. In general, plant workers do not differ significantly by their socio-economic class and this factor is not considered as a potential confounder also.

Sample size

Sample size has been calculated by STATA version 6, assuming equal number of cases and controls for an unmatched study. The value for α was set at 0.05 (two-sided), 0.2 for β . The proportion exposed in controls was determined from the roster and equalled 63 %. The smallest detectable odds ratio was set at 3. The calculations result in n of 78 for each group.

Data collection

Systematic random sampling will be used to select cases, from the lists of workers diagnosed with COPD. The selection of controls will be done by simple random sampling using polyclinic rosters of workers who are not diagnosed with COPD

Data collection will be done by face-to-face interviews using the questionnaire. [Appendix B]. Information about the work history of cases and controls will be obtained from two sources: employee work records and information obtained during interviews. Each person will be assigned to exposure of the occupation in which he had worked the longest. The exposed workers will be divided according to the duration of work in an exposed job, to determine if increased duration led to increased risk of COPD (dose-response analysis).

Considering the fact that medical records and questionnaire will be used for ascertainment of cases and controls there is a possibility of discrepancies between these two sources. For example, a person who was diagnosed with COPD by a doctor may give negative answers to questions about COPD related symptoms. In this case, the subjects will be assigned to the cases, but during the analysis these data will be analyzed separately. This decision is based on the fact the diagnosis made by physicians is more comprehensive since they use several diagnostic tools (particularly x-ray). A person who was not diagnosed with COPD by a doctor may report having COPD related symptoms (estimated by scoring of the questionnaire). The subjects who were not known to the general practitioner as having COPD are most likely to be mild cases. Thus, they should be excluded and replaced by another randomly selected control.

Ethical considerations

This proposal was submitted to the Institutional Review Board/Committee on Human Research of the American University of Armenia. It received approval from the Institutional Review Board.

The study possesses minimal risk. Consent will be provided prior to the interview, so that participants will have opportunity to ask questions, get answers, and to think about whether they want to be involved in the research. [Appendix A]

Giving a unique identifier to each interview will ensure confidentiality of participants. Only the study investigators will have access to the names and identification numbers of participants.

Study limitations

The most important limitation is the absence of environmental data indicating historical levels of exposure to cement dust among the study population. Another potential problem in this study is recall bias. In this respect, information regarding work history obtained during the interviews will be compared with documentation of the plant. However, information about smoking history can be obtained only from the interviews. In addition, it is possible that instrumental bias may be created by the questionnaire.

Data analysis

The statistical analysis of the data will be carried out using the STATA computer program. Statistical analysis will consist of the use of chi-square tests, where odds ratio with 95% confidence interval will be determined.

Logistic regression will be used to estimate a summary odds ratio after adjustment for confounders. The dependent variable is COPD and the independent variables are smoking, work history, presence of comorbidities (including chest illnesses, chest operations, chest injuries, and heart troubles). Logistic regression also permits the evaluation of interactions between variables.

Time Frame for the Project

At the beginning of the study the personnel conducting the study will be hired. In total, 156 interviews will be conducted. The time spent for each interview is about 30 minutes. Thus an interviewer will be able to conduct about 10 interviews per day. Considering the fact that plant documentation about each study subject should be obtained by interviewer as well, data collection will be completed in a period of one month. Coding and data entry will begin after completion of the interviews and will last two months. Then, analysis of the study will be done. The overall duration of the study is seven months. [Appendix C]

Budget

The estimated expenditures for implementing the proposed study are presented in the budget. [Appendix D]. The total budget is approximately \$17,538. The direct costs comprise \$12,236. Five percent of the direct costs is provided for unexpected needs. Administrative fee includes \$4,690.

Personnel Responsibilities

The program Coordinator is responsible for administration and management of the study. He/she will perform data analysis and submit the final report.

The Project Assistant is responsible for administration and monitoring of interviewer's activities, interviewer's training, and data entry into computer program. The interviewer will complete questionnaires and will obtain plant documentation for study subjects. He/she should have MD degree (preferably live in Ararat).

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