Received: February 24, 2025 Accepted: April 1, 2025 Acad Med J 2025;5(1):95-106 UDC: 616.24-002.2-057.75(497.711) https://www.doi.org/10.53582/AMJ255195s Original article

COPD PREVALENCE AND CHARACTERISTICS AMONG RETIRED WORKERS

Stoleski Sasho, Minov Jordan, Mijakoski Dragan, Atanasovska Aneta, Bislimovska Dragana, Panajotovic-Radevska Maja, Zdraveski David

Institute for Occupational Health of R North Macedonia, Skopje, Republic of North Macedonia; Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia *e-mail:* sstoleski@yahoo.com

Abstract

Introduction: Age and exposure to noxious particles and gases are considered as important risk factors for the development of COPD.

Aim of the study: To assess the prevalence of COPD in a sample of retired persons from the Skopje region.

Material and methods: We performed a cross-sectional study (prevalence study) in a sample of 392 randomly selected retired persons, 207 males and 185 females, aged 56 to 84 years. Study protocol included completion of a questionnaire and pre- and post-bronchodilator spirometry.

Results: The prevalence of COPD in the whole sample was 8.7% (34/392), being nonsignificantly higher in men (9.1%) than in women (8.1%). The difference in COPD prevalence between smoking and non-smoking retired persons was within the borders of statistical significance (10.7% vs. 7.5; P=0.084). The difference in COPD prevalence between retired persons exposed to vapors, gases, dusts, and fumes (VGDF) at their workplace during their active period and retired persons with no such exposure just missed statistical significance (9.5% vs. 7.4%; P=0.073). COPD prevalence in the smoking retired persons occupationally exposed to VGDF during their active period was significantly higher than its prevalence in the smoking retired persons occupationally unexposed to VGDF during their active period (12.6% vs. 8.2%; P=0.036).

Conclusion: Our results confirm the role of age and exposure to noxious particles and gases in the COPD development.

Keywords: COPD, occupational exposure, noxious particles and gases, pre- and postbronchodilator spirometry, questionnaire

Introduction

Chronic obstructive pulmonary disease (COPD) is a respiratory disease characterized by various chronic respiratory symptoms resulting from airway and lung impairments such as bronchitis and/or emphysema^[1]. It is one of the most common chronic respiratory diseases worldwide and continues to be a major cause of death and disability^[2,3]. In 2021, both World Health Organization (WHO) and International Labor Organization (ILO) reported that COPD due to occupational exposure to particulate matter, gases, and fumes had the greatest number of work-related deaths and the third-highest number of work-related disability-adjusted life years (DALYs) globally^[4]. The prevalence of COPD is higher in males than in females which may arise from under-diagnosis in females and historic differences in exposure potentially

leading to an underestimation of the current burden of disease in females^[5]. Tobacco smoking is the biggest and most important established cause of COPD^[6]. However, it is estimated that 25-45% of people with COPD never smoked, which emphasizes the importance of examining other potential risk factors, as well^[3,7]. Other possible causes include history of childhood respiratory conditions (e.g., asthma), outdoor air pollution, and finally occupational exposures (including second hand smoke)^[6,8]. Occupational exposures are an under-estimated risk factor for COPD. Based on evidence showing that occupational exposure to vapors, gases, dusts, and fumes (VGDF) significantly increases the risk of COPD^[9-11], the American Thoracic Society (ATS) and European Respiratory Society (ERS) estimated that workplace exposures contribute to 14% of all COPD cases^[8]. Increased risk of COPD has been observed among specific groups such as construction workers^[11-13], farm and wood industry workers^[14]. COPD has been also linked to a wide range of specific substances common in certain workplaces, including cotton dust, farm dust, grain dust, wood dust, welding fumes, and crystalline silica^[9]. Other exposures linked to COPD may include diesel engine exhaust^[11], pesticides^[15,16], organic dust^[14], and second-hand smoke^[11]. Workers can be exposed to multiple overlapping occupational exposures which pose a challenge in separating out individual exposures related to risk of COPD. Age and exposure to noxious particles and gases are considered as important risk factors for the development of COPD. The risk of developing COPD in predisposed nonsmoking workers from dusty occupations is high, but, as previously stated, it is even higher among smokers from those occupations. This is due to the fact that the risk of the interaction of tobacco smoke and occupational exposure at certain workplaces and job positions is not additive, but multiplicative^[11,17].

The aim of the present study was to determine the COPD prevalence in a sample of retired workers with or without previous job exposure to noxious particles and dusts, and to classify the disease according to the degree of its severity. Also, the aim was to determine the disease distribution among retired workers according to their exposure to occupational factors of interest and length of exposure, smoking status, family history of asthma/chronic bronchitis, and mode of household heating and cooking.

Methods

Study design and setting

A cross-sectional epidemiological study (prevalence study) was carried out at the Institute for Occupational Health of the Republic of North Macedonia, Skopje, in the period 2018-2021. The study was performed within the scientific projects of all departments of the Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, based on the Decision of the Faculty Management, and approved by the Ethics Committee of the Institute for Occupational Health of R. North Macedonia, Skopje for conducting the study and publishing the obtained results (0302-236/2018). All study subjects were informed about the study and gave their written consent.

Study population

The principal survey included a total of 2,348 subjects (active workers, retired workers and students)^[18]. The current study population included 392(16.7%) retired workers, 207 men and 185 women, aged 56-84. Of them, 368 subjects (93.8%) were old-age pension beneficiaries, while 24(6.2%) subjects received disability pension.

Regarding occupational exposure during the period of employment, 161(41.1%) of retired subjects were not exposed, and 231(58.9%) were exposed to occupational hazards. The study population also included 1,867 workers (959 males and 908 females, aged 18 to 67 years) from the Skopje region recruited during their preventive check-ups at the Institute for Occupational Health of R. North Macedonia - Skopje.

Study protocol

The study was performed following the current recommendations of European Respiratory Society (ERS) and American Thoracic Society (ATS) for epidemiological studies on COPD^[19].

The study protocol included completion of a questionnaire and spirometric measurements. An interviewer-led questionnaire was based on two standardized questionnaires, i.e., Population-based screening questionnaire for COPD and Symptom-based questionnaire for identifying COPD, and it consisted of three parts^[20,21].

The first part of the study included questions on demographics of the subjects, personal and family history of chronic bronchitis and asthma, the fuels used for heating, cooking and other household needs, as well as questions on current or/and previous occupational exposures. Occupational exposures in the working population were assessed also by the Risk assessment report of the company in which they were employed.

The second part of the study included questions on smoking status of the subjects. The smoking status (active smoker, ex-smoker, and non-smoker) was defined by the World Health Organization (WHO) criteria^[22]. The third part of the questionnaire included questions on respiratory symptoms in the last 12 months (nasal symptoms, cough, phlegm, dyspnea, wheezing, and chest tightness). In the subjects with dyspnea, its severity was assessed according to the criteria of Modified British Medical Council (mMRC)^[23].

Baseline and post-bronchodilator spirometry

Spirometric measurements included baseline (pre-bronchodilator) spirometry which was performed in all study subjects, and post-bronchodilator spirometry which was performed in subjects whose ratio between forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) was less than 0.70. The baseline spirometry, including measures of FVC, FEV1, FEV1/FVC, and maximal expiratory flow at 75%, 50%, 25%, and 25-75% of FVC (MEF75, MEF50, MEF25, and MEF25-75, respectively), was performed in all subjects using spirometer Ganshorn SanoScope LF8 (Ganshorn Medizin Electronic GmbH, Germany) with recording the best result from three measurements where the values of FEV1 were within 5% of each other.

The results of spirometry were expressed as percentages of the predicted values according to the current recommendations of ERS and ATS. The post-bronchodilator spirometry was performed according to the current recommendations, i.e., spirometric measurements were performed 20 minutes after administration of 400 μ g salbutamol by metered dose inhaler through spacer. Fixed airflow narrowing characteristic for COPD was considered if post-bronchodilator FEV1/FVC remained less than 0.70^[24-26].

Definition and classification of COPD

The existence of COPD is determined according to the presence of symptoms in subjects in whom a persistent decrease in air flow through the airways has been proven by spirometry, i.e. a post-bronchodilator value of the FEV1/FVC ratio lower than 0.7. According to the degree of severity of the spirometric impairment, subjects with COPD are classified into four groups: mild COPD or GOLD 1 (FEV1 value equal to or higher than 80% of the predicted value), moderate COPD or GOLD 2 (FEV1 value from 50 to 80% of predicted value), severe COPD or GOLD 3 (FEV1 value from 30 to 50% of the predicted value) and very severe COPD or GOLD 4 (FEV1 value lower than 30% of the predicted value)^[1,19].

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences

(SPSS), version 11.0 for Windows. Continuous variables were expressed as mean values with standard deviation (SD), and the nominal variables as numbers and percentages. In line with the aim of the study, univariate statistical models for testing the differences in prevalence and comparison of the means were used for data analyses. Chi-square test (or Fisher's exact test where appropriate) was used for testing difference in the prevalence. Comparison of spirometric measurements was performed by independent-samples T-test. A P-value less than 0.05 was considered as statistically significant.

Results

Demographics of the study subjects

The study population included 392(16.7%) retired workers, 207 men and 185 women, aged 56-84. Of them 368 subjects (93.8%) were old-age pension beneficiaries, while 24 subjects (6.2%) received disability pension. Regarding the occupational exposure during the period of employment, 161(41.1%) of retired subjects were not exposed, and 231(58.9%) were exposed to occupational hazards. The working population included 1,867 workers (959 males and 908 females, aged 18 to 67 years) from the Skopje region recruited during their preventive check-ups at the Institute for Occupational Health of R. North Macedonia - Skopje.

Prevalence and characteristics of COPD among the examined subjects

Respiratory symptoms in the last 12 months were registered in 40.3% of retired workers. The most common individual respiratory symptoms in the last 12 months among retired workers were cough (24.7%) and cough with phlegm (13.2%) (Figure 1). The frequency of respiratory symptoms in the last 12 months of interest in retired workers was higher than their frequency among working population subjects, but the difference in frequency was not statistically significant for any of them.

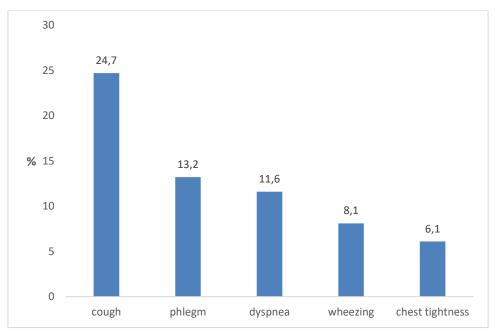


Fig. 1. Respiratory symptoms in the last 12 months among retired workers

The frequency of COPD among retired workers was 8.7% (Figure 2), and the difference in its frequency among males and females was not statistically significant (9.1% among men and 8.1% among women).

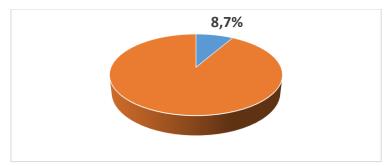


Fig. 2. Frequency of COPD in retired workers

The frequency of COPD among retired workers was significantly higher than its frequency among all study subjects (4.6%) (P=0.0008) and subjects among the working population (3.9%) (P=0.0001) (Figure 3).

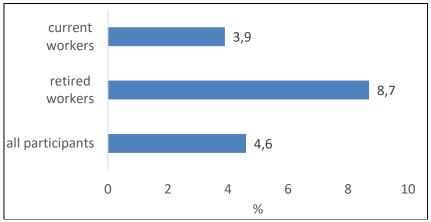


Fig. 3. COPD frequency among all study subjects, working population subjects and retired workers

The most common respiratory symptoms among retired workers with COPD were cough with phlegm (85.3%) and dyspnea (76.4%) (Figure 4). The frequency of respiratory symptoms in the last 12 months in retired subjects with COPD was higher in relation to their frequency in subjects with COPD from the working population, but significant difference was not registered for any of them.

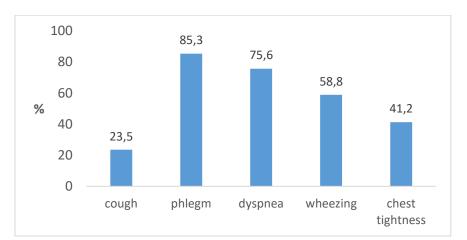


Fig. 4. Respiratory symptoms in the last 12 months among retired workers with COPD

The mean post-bronchodilator values of the basic spirometric parameters in retired workers with COPD were significantly lower than their mean values in the working population subjects with COPD (Table 1).

Spirometric parameter	Retired workers with COPD (N = 74)	Subjects from the working population with COPD (N = 34)	P-value*
FVC	75.3 ± 10.2	80.8 ± 14.1	0.000
FEV1	53.1 ± 6.1	59.2 ± 9.1	0.000
FEV1/ FVC	0.63 ± 0.01	0.66 ± 0.02	0.000

Table 1. Mean post-bronchodilator values of basic spirometric parameters in retired workers and subjects from the working population with COPD

According to disease severity, the frequency of subjects with mild and moderate COPD was higher in retired workers than in subjects from the working population. On the other hand, severe and very severe COPD was more frequent in working population subjects, being significant for very severe disease (P=0.001) (Table 2).

Table 2. Frequency of COPD subjects with different degrees of disease severity in retired workers and working population subjects

GOLD stadium	Retired workers (N = 74)	Subjects from the working population (N = 34)	<i>P</i> -value*
GOLD1	35(47.2%)	11(32.3%)	P = 0.211
GOLD2	29(39.2%)	8(23.5%)	P = 0.169
GOLD3	9(12.2%)	8(23.5%)	P = 0.221
GOLD4	1(1.6%)	7(20.5%)	P = 0.001

The frequency of COPD among retired workers who were exposed to the occupational hazards of interest during the working period (9.5%) was higher than its frequency among those who were not exposed to these hazards (7.4%), and the difference just missed the statistical significance (P = 0.073) (Figure 5).



Fig. 5. Frequency of COPD among retired workers who were or were not exposed to the occupational hazards of interest during their working period

The COPD frequency among retired workers who were smokers (10.7%) was higher than in non-smokers (7.5%), and the difference just missed the statistical significance (P=0.084) (Figure 6).

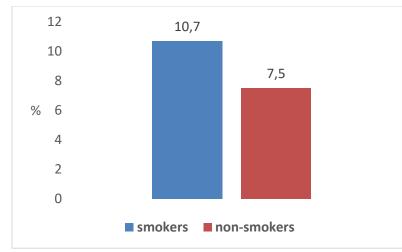


Fig. 6. Frequency of COPD among retired smokers and non-smokers

The frequency of COPD among retired smokers who had been exposed at work (12.6%) was higher than its prevalence among retired smokers who had not been exposed (8.2%), but the difference was not statistically significant (Figure 7).

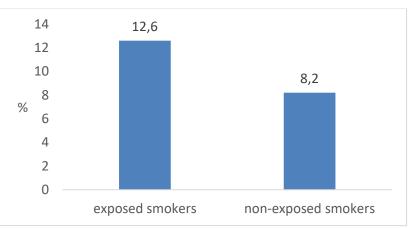


Fig. 7. Frequency of COPD among retired smokers who were or were not exposed at work

The frequency of COPD among non-smokers who had been exposed at work (8.1%) was higher than its frequency among non-smoking retired workers who had not been exposed (6.4%), and the difference was still without statistical significance (P=0.059) (Figure 8).

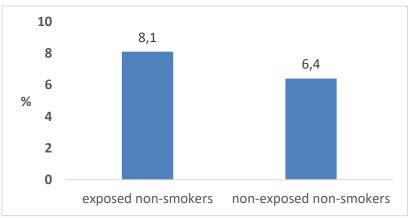
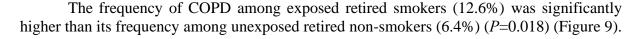


Fig. 8. Frequency of COPD among non-smoking retired workers who had or had not been exposed at work



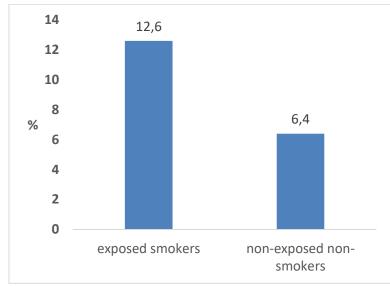


Fig. 9. Frequency of COPD among exposed retired smokers and retired non-smokers

No significant difference was registered in the frequency of COPD between retired workers who had a positive family history of asthma/chronic bronchitis (9.6%) and those with a negative family history of these diseases (7.7%).

The difference among retired workers with COPD in terms of the use of solid and liquid biofossil fuels at home (9.8%) and central heating/electricity heating (8.3%) was not significant.

Discussion

COPD has become one of the leading causes of morbidity, mortality and disability in both developed and developing countries in the last decades, and continues to grow and generate huge costs. Although cigarette smoking is the major and well-studied causative factor for COPD, there is consistent evidence that a substantial proportion of COPD cases cannot be explained by smoking alone. Other noxious particles and gases, such as workplace dusts, vapors, fumes or gases, indoor air pollution from burning biomass fuels from cooking and heating and urban outdoor air pollution are important risk factors of COPD. According to current knowledge, 15-20% of COPD cases are likely caused or made worse by workplace exposures. Around 4,000 COPD deaths every year are related to workplace exposures and 40% of COPD patients are below retirement age, and a quarter of those below retirement age are unable to work at all ^[27,28].

It is assumed that there are about 100,000 people with COPD in the Republic of North Macedonia, but until now, as in many other countries, no epidemiological research has been performed at the level of a working population (population-based study). In the last decade, several studies have been carried out in our country in which workers from certain workplaces were included (workplace-based study) and in which the frequency of the disease in workers with occupational exposure, which is considered a risk factor for the occurrence and progression of COPD, was compared with its frequency among workers who are not exposed to those occupational hazards^[29,30].

In this population study, the first of its kind in our country, 392 retired workers and 1867 active workers were included. The research methodology followed the recommendations for performing this type of study on COPD, that is, it consisted of filling out a questionnaire

(interviewer-led questionnaire) and spirometry for all subjects with a bronchodilator test for subjects with reduced lung function (spirometrically defined COPD). The study included retired workers, and depending on the exposure to the occupational hazards of interest (dust, gases, vapors and fumes, physical exertion and low temperatures), it consisted of retired subjects who were exposed and retired subjects who were not exposed.

The study revealed that smokers were more frequent among retired workers compared to non-smokers, but without statistical significance. Regarding the frequency of respiratory symptoms in the last 12 months, the highest frequency was registered for cough, and the frequency of COPD among retired workers was 8.7%, which was significantly higher than its frequency among the working population subjects (3.9%) (P=0.0001). The obtained results are similar to the results registered in our previous research, as well as in the research in this area performed in other countries^[31]. Regarding the distribution of the disease according to the degree of its severity, the largest number of retired workers with COPD fall into the categories of mild and moderately severe disease.

Tobacco smoke, i.e. active smoking, is the most important and until now the best studied risk factor for the occurrence and progression of COPD with a proven dose-response relationship. It is considered that exposure to tobacco smoke is responsible for the occurrence of about two-thirds of all cases of COPD (tobacco-induced COPD), both in active and passive smoking^[27]. The results of the current research indicated that the COPD prevalence in retired smoking subjects was higher compared to non-smokers. A significant percentage of all COPD cases also occur in people who have never smoked, indicating both the effects and other factors in the disease development. The results of several studies carried out in the last two decades indicated the importance of occupational exposure to dusts, gases, vapors and fumes in the occurrence and progression of COPD^[32].

The results of the current study confirmed the association of COPD with the previous occupational exposure among subjects. Namely, the frequency of COPD in retired subjects who were exposed to dust, gases, vapors and fumes was higher than in unexposed retired subjects. Similar results were obtained in our previous workplace-based studies, as well as in population and workplace-based surveys conducted in other countries^[11,28-30].

The results of the current research indicated that the frequency of COPD in exposed retired workers was higher than in exposed workers who did not smoke but still without statistical significance (P=0.059). Furthermore, the frequency of COPD among exposed retired smokers was significantly higher than its frequency among unexposed retired non-smokers (P=0.018) The combined effect of tobacco smoke and occupational exposure to dusts, gases, vapors and fumes in the development of COPD is not additive, but multiplicative. The results of longitudinal research indicate that the risk of COPD among workers in dusty occupations is about twice as high as the risk of the disease among workers from other ("non-dusty") occupations; the risk of COPD among workers-smokers who are not occupationally exposed to dusts, gases, vapors and fumes is about seven times higher than the risk of non-exposed nonsmoking workers, while the risk of COPD in smoking workers from dusty occupations is about 14 times higher than the risk in unexposed non-smoking workers^[33]. Gender, genetic factors and exposure to harmful agents and gases from the environment, primarily indoor air pollutants released during the combustion of solid and liquid biofuels, are considered risk factors for the development of COPD^[1,9]. According to the results of our study, the frequency of the disease was higher in men than in women, but the difference was not statistically significant. Also, no statistically significant difference was registered between subjects with a positive family history of asthma/chronic bronchitis and those with a negative family history of these diseases, nor between subjects who used solid and liquid biofuels for heating and cooking at home and those who used other sources for these purposes.

Despite consistent evidence of their role in the development and progression of the disease, occupational exposures are still under-appreciated risk factor of COPD. According to the Official American Thoracic Society (ATS) and European Respiratory Society (ERS) Statement for the occupational burden of nonmalignant respiratory diseases from 2019, the estimated contribution of workplace exposures to the burden of COPD was 14%^[8]. Summarizing results from several Macedonian studies on COPD prevalence in workers from varying occupations, the authors found significantly higher prevalence of the disease in the dusty occupation groups as compared to its prevalence in the groups of matched administrative workers, varying from 10.7% in dairy farmers, 10.8% in grain workers, 11.4% in cotton workers, 14.9% in bricklayers to 15.2% in welders^[29,34]. The occupational contribution to COPD is high among nonsmokers. On the other side, the highest risk of COPD is found in smokers from 'dusty' occupations as the joint effect of certain occupational exposures and tobacco smoke is estimated to be greater than additive. In the study carried out in 2009, Blanc et al. found that subjects occupationally exposed to dusts, gases, vapors, and fumes had a double risk of COPD compared to those with neither occupational exposure nor smoking risk. Additionally, smoking alone was associated with a 7-fold increased risk of COPD, whereas those with combined exposure had a 14-fold increased risk of COPD^[9,11].

The results obtained in the present study should be interpreted keeping in mind its limitations and strengths. The distribution of subjects that previously worked in certain job positions, was not even, which may have influenced the obtained results. Furthermore, the results about the registered frequency of COPD in previously exposed subjects may be lower due to the so-called "healthy workers' effect", meaning that workers with respiratory symptoms often leave these hazardous workplaces. The data on the previous exposure among retired workers and current occupational exposure among the working population were based mainly on the questionnaire and without qualitative and quantitative assessment. Finally, the study was also affected by the restrictive measures adopted due to the Covid-19 pandemic. However, an advantage of the current study is that, as a part of a broader population study on COPD in our country, the study sample is large enough to obtain relevant results. In addition, another advantage is the fact that the study was performed according to the latest recommendations for studies on COPD prevalence (questionnaire with pre- and postbronchodilator spirometry). Our findings confirmed the role of past and current occupational exposures in COPD development indicating a need of more effective preventive activities in order to reduce the overall disease burden.

Conflict of interest statement. None declared.

References

- 1. Global Initiative for Chronic Obstructive Lung Disease. 2025 Report. Available at: https://goldcopd.org/2025-gold-report/ (Assessed 28.03.2025).
- Najafzadeh M, Marra CA, Lynd LD, Sadatsafavi M, FitzGerald JM, McManus B, et al. Future Impact of Various Interventions on the Burden of COPD in Canada: A Dynamic Population Model. PLoS ONE. 2012;7(10):e46746. https://doi.org/10.1371/journal.pone. 0046746
- 3. Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. Lancet 2009; 374(9691): 733-743. doi: 10.1016/S0140-6736(09)61303-9.
- 4. World Health Organization and International Labor Organization (WHO/ILO). Global Monitoring Report: WHO/ILO Joint Estimates of the Work-Related Burden of Disease and Injury, 2000-2016; 2021. https://www.who.int/publications/i/item/9789240034945.

- 5. Varkey AB. Chronic obstructive pulmonary disease in women: Exploring gender differences. *Curr Opin Pulm Med* 2004; 10(2): 98-103. doi: 10.1097/00063198-200403000-00003.
- 6. World Health Organization. Chronic obstructive pulmonary disease. Available at: https://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd).
- 7. Lopez-Campos JL, Tan W, Soriano JB. Global burden of COPD. *Respirology* 2016; 21(1): 14-23. doi: 10.1111/resp.12660.
- Blanc PD, Annesi-Maesano I, Balmes JR, Cummings KJ, Fishwick D, Miedinger D, *et al.* The occupational burden of nonmalignant respiratory diseases. An official American Thoracic Society and European Respiratory Society statement. *Am J Respir Crit Care Med* 2019; 199(11): 1312-1334. doi: 10.1164/rccm.201904-0717ST.
- 9. Omland Ø, Würtz ET, Aasen TB, Blanc P, Brisman JB, Miller MR, *et al.* Occupational chronic obstructive pulmonary disease: a systematic literature review. *Scand J Work Environ Health* 2014; 40(1): 19-35. doi: 10.5271/sjweh.3400.
- 10. Ryu JY, Sunwoo YE, Lee SY, Lee CK, Kim JH, Lee JT, Kim DH. Chronic Obstructive Pulmonary Disease (COPD) and Vapors, Gases, Dusts, or Fumes (VGDF): A Metaanalysis. *COPD* 2015; 12(4): 374-380. doi: 10.3109/15412555.2014.949000.
- 11. Blanc PD, Iribarren C, Trupin L, Earnest G, Katz PP, Balmes J, *et al.* Occupational exposures and the risk of COPD: dusty trades revisited. *Thorax* 2009; 64(1): 6-12. doi: 10.1136/thx.2008.099390.
- 12. Dement JM, Cloeren M, Ringen K, Quinn P, Chen A, Cranford K, *et al.* COPD risk among older construction workers-Updated analyses 2020. *Am J Ind Med* 2021; 64(6): 462-475. doi: 10.1002/ajim.23244.
- 13. Bergdahl IA, Torén 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(3): 402-406. doi: 10.1183/09031936.04.00034304.
- Vested A, Basinas I, Burdorf A, Elholm G, Heederik DJJ, Jacobsen GH, *et al.* A nationwide follow-up study of occupational organic dust exposure and risk of chronic obstructive pulmonary disease (COPD). *Occup Environ Med* 2019; 76(2): 105-113. doi: 10.1136/oemed-2018-105323.
- 15. Alif SM, Dharmage SC, Benke G, Dennekamp M, Burgess JA, Perret JL, *et al.* Occupational exposure to pesticides is associated with fixed airflow obstruction in middle-age. *Thorax* 2017; 72(11): 990-997. doi: 10.1136/thoraxjnl-2016-209665.
- 16. Pourhassan B, Meysamie A, Alizadeh S, Habibian A, Beigzadeh Z. Risk of obstructive pulmonary diseases and occupational exposure to pesticides: A systematic review and meta-analysis. *Public Health* 2019; 174: 31-41. doi: 10.1016/j.puhe.2019.05.024.
- 17. Minov J. COPD and the workplace. New York: Nova Science Publishers, Inc.; 2016.
- Minov J, Stoleski S, Stikova E, Mijakoski D, Atanasovska A, Bislimovska Karadzinska Jovanka. COPD in a sample of general ault population from the Skopje Region. *Acad Med J* 2022; 2(1): 47-58. doi: 10.53582/AMJ2221047m.
- 19. Bakke PS, Rönmark E, Eagan T, Pistelli F, Annesi-Maesano I, Maly M, *et al.* Recommendations for epidemiological studies on COPD. *Eur Respir J* 2011; 38(6): 1261-1277. doi: 10.1183/09031936.00193809.
- Calverley PM, Nordyke RJ, Halbert RJ, Isonaka S, Nonikov D. Development of a population-based screening questionnaire for COPD. COPD 2005; 2(2): 225-232. PMID: 17136949.
- 21. Price DB, Tinkelman DG, Halbert RJ, Nordyke RJ, Isonaka S, Nonikov D, *et al.* Symptom-based questionnaire for identifying COPD in smokers. *Respiration* 2006; 73(3): 285-295. doi: 10.1159/000090142.

- 22. World Health Organization. (1998). Guidelines for controlling and monitoring the tobacco epidemic. World Health Organization. https://iris.who.int/handle/10665/42049
- 23. Standardized Questionaries on Respiratory Symptoms. Br Med J. 1960 Dec 3;2(5213):1665. PMCID: PMC2098438.
- 24. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, *et al.* Standardisation of spirometry. *Eur Respir J* 2005; 26(2): 319-38. doi: 10.1183/ 09031936.05.00034805.
- 25. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, *et al.* Interpretative strategies for lung function tests. *Eur Respir J* 2005; 26(5): 948-968. doi: 10.1183/09031936.05.00035205.
- 26. Culver BH, Graham BL, Coates AL, Wanger J, Berry CE, Clarke PK, et al. Recommendations for a Standardized Pulmonary Function Report. An Official American Thoracic Society Technical Statement. Am J Respir Crit Care Med 2017; 196(11): 1463-1472. doi: 10.1164/rccm.201710-1981ST.
- 27. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, *et al.* Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. *J Glob Health* 2015; 5(2): 020415. doi: 10.7189/jogh.05.020415.
- Sadhra S, Kurmi OP, Sadhra SS, Lam KB, Ayres JG. Occupational COPD and job exposure matrices: a systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis. 2017;12:725-734. doi: 10.2147/COPD.S125980. PMID: 28260879; PMCID: PMC5327910.
- 29. Minov J, Karadzinska-Bislimovska J, Vasilevska K, Stoleski S, Mijakoski D. Chronic obstructive pulmonary disease and occupational exposures: epidemiological evidence from R. Macedonia. *Arch Pulmonol Respir Care* 2016; 2(1): 032-036. doi: 10.17352/aprc.000014.
- 30. Minov J, Stoleski S. Chronic obstructive airways diseases: Where are we now? *Open Respir Med J* 2015; 9(Supp; 1): 37-38. doi: 10.2174/1874306401509010037.
- 31. Stoleski S, Minov J, Karadzinska-Bislimovska J, Mijakoski D. Chronic obstructive pulmonary disease in never-smoking dairy farmers. *Open Respir Med J* 2015; 9(1): 59-66. doi: 10.2174/1874306401509010059.
- 32. Syamlal S, Doney B, Mazurek JM. Chronic obstructive pulmonary disease prevalence among adults who have never smoked, by industry and occupation. *MMWR Morb Mortal Wkly Rep* 2019; 68(13): 303-307. doi: 10.15585/mmwr.mm6813a2.
- 33. Najdoo RN. Occupational exposures and chronic obstructive pulmonary disease: incontrovertible evidence for causality. *Am J Respir Crit Care Med* 2012; 185: 1252-1254. doi: 10.1164/rccm.201204-0604ED.
- Minov J. Occupational chronic obstructive pulmonary disorder: prevalence and prevention. Expert Rev Respir Med. 2022;16(4):429-436. doi: 10.1080/17476348.2021.2011722. Epub 2021 Dec 6. PMID: 34822743.