Evaluation of the economic and social burden of chronic obstructive pulmonary disease (COPD)

Konstantin Tachkov, Maria Kamusheva, Ventsislava Pencheva and Konstantin Mitova

ABSTRACT
The aim of this study was to calculate the economic and social burden of chronic obstructive pulmonary disease (COPD) in Bulgaria generated from the loss of productivity due to absence from work (absenteeism), due to premature retirement, due to reduced productivity (presenteeism), and the disability adjusted life years (DALY). An observational study among 426 Bulgarian COPD patients was conducted for the period 2014–2015. Human capital approach was used to calculate the productivity losses and the DALY methodology of the World Health Organization was applied. The patients with moderate (50%) and severe (48%) disease were absent from work more frequently than those with mild COPD (2%) and generated productivity losses of 521.45€ per patient per year. The average indirect costs per patient for the remaining working ages due to premature retirement account for 25,000€ (6250 per patient on average), while those due to presenteeism, for about 3750.64€ per year. Accordingly, the DALYs in the group of patients with mild severity were lowest due to the low disutility index and number of patients in this sample group. On average, a patient with mild COPD spends 0.62 years of his life in disability due to the disease, while those with moderate and severe disease spend 6.00 and 9.00 years, respectively. This amounted to the following indirect costs experienced by patients: 3596.52€; 34,204.01€; 51,332.20€, respectively. We demonstrated a significant indirect financial and societal burden of COPD in Bulgaria, which is in correlation with the severity of the disease.

Introduction
The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines chronic obstructive pulmonary disease (COPD) as ‘a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases’ [1]. It is projected that COPD will become the second largest diagnosis after diabetes by 2030 [2,3]. Globally, it is the fourth leading cause of mortality and is projected to be the third leading cause by 2020. Its definition and projections point out that COPD might cause a significant health, economic and social burden to society [4,5].

Evaluations of the clinical and economic burden of COPD are essential for patients, healthcare professionals, decision-makers and society [6]. Indirect costs, such as loss of productivity, early retirement and reduced ability to work, account for a significant proportion of total costs, with some estimates varying between 20% and 69% [7]. All these factors provide important information for the economic burden of the disease as loss of human capital [8].

Since the introduction of the disability adjusted life years (DALY) as one of the essential measures of the burdens imposed by all health issues into a single, consistent unit, it has been used by many researchers for different diseases [9]. It is the metric of choice for disease severity evaluation and is used widely by the World Health Organization (WHO) [10]. Monetizing DALYs is a way to evaluate the economic impact of health care interventions on the disability imposed by debilitating diseases such as blindness, skin diseases, respiratory diseases, etc. [11]. Therefore, DALYs in monetary units could be considered as another way of measuring the economic impact of lost productivity.

According to WHO, the net loss of productivity is estimated to be 27,700 DALYs globally [12], with the social and economic impact being particularly hard on working-age patients, where COPD is classified as the 11th worldwide burden, and is expected to become the 7th by 2030 [13]. Furthermore, COPD is often accompanied by other co-
morbidities, including cardiovascular disease, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression, anxiety and lung cancer, which can influence the mortality and hospitalizations independently [14].

Despite the abundance of epidemiological and economic data available, hardly any economic data exist for Eastern Europe and Bulgaria [15]. No official national register for the number of COPD patients exists, but according to experts from the Bulgarian Society of Pulmonary Diseases, the approximate number is about 480,000 [16]. Evaluating the burden of COPD as a disease will contribute to better understanding of COPD in the context of an Eastern-European setting.

The aim of this study was to calculate the economic and social burden of COPD in Bulgaria generated from the lost productivity due to absence from work (absenteeism), premature retirement, reduced productivity in the workplace (presenteeism), and DALY.

Materials and methods

Type of study, sample size and inclusion criteria
An observational study among 426 Bulgarian COPD patients was conducted for the period 2014–2015. The cohort size included in the study was representative and all participants signed an informed consent form. The patients’ selection was based on specific inclusion criteria: age over 40 years, COPD diagnosis confirmed by spirometer test more than 1 year ago and prescribed pharmacotherapy in the last year. A total of 426 patients from five main regions of Bulgaria, chosen on a random principle participated in the study [17]. They were then divided into three main categories defined by stage of COPD: mild, moderate and severe.

Health economics data
The indirect costs were calculated using the human capital approach [18]. The gross domestic product per capita was considered in calculations of the absenteeism (lost productivity due to sick leave) and presenteeism (lost productivity due to reduced working capacity) corrected with an incapacity coefficient [19]. Minimal pension in case of disability (early retirement or permanent reduced working capacity) was also taken into account.

The lost productivity was calculated on the basis of the following formula:

\[
\text{Lost productivity} = \frac{\text{Number of days out of work} \times \text{(yearly GDP per capita)}}{\text{number of working days in one year}}.
\]

GDP per capita in 2015 was equal to 5700€ and the number of working days in 2015 were 252 [20].

The reduced productivity for a year per patient was calculated by multiplying the yearly GDP per capita by the percent disability for every patient.

The lifetime losses due to premature retirement were calculated in terms of assumptions for the age of normal retirement. The retirement age in Bulgaria varies in women and men and for 2015 it was determined to be 60 years and 8 months and 63 years and 8 months, respectively. Pensionable service should be taken into account as well [21]. We assumed that the average retirement age is 61 and 64 for women and men, respectively, and we did not include the pensionable service for both genders.

\[
\text{Lifetime losses for women} = \left(\frac{61\text{ – actual age of retirement}}{\text{yearly GDP per capita}}\right)
\]

\[
\text{Lifetime losses for men} = \left(\frac{64\text{ – actual age of retirement}}{\text{yearly GDP per capita}}\right).
\]

Pension paid due to disability was calculated using data about the minimal pension per month:

\[
\text{Pension paid due to disability} = \text{minimal pension} \times 12\text{months} \times \text{remaining years of life}.
\]

According to officially published data in Bulgaria, the amount of money paid due to disability should not be lower than the determined degree of permanent reduced working capacity values: over 90% rate of disability – 115% of the minimal pension, equal to 94.89€; 71%–90% disability – 105% of the minimal pension, equal to 86.64€; 50%–70.99% rate of disability – 85%, equal to 70.13€.

Disability-adjusted life years (DALYs) calculations
DALYs were estimated as per the WHO methodology [22,23]. In our cohort, no patients died during the study period; that is why a value of 0 was assumed for years of life lost (YLL). The disability weight (DW) for COPD value was obtained from the study of Haagsma et al. [24] due to the fact that the study contained data from Eastern Europe. Although the average life expectancy for Bulgaria is 72 years for men and 79 years for women [25], all subgroups in our sample contained patients above the age of 80. Therefore, in our calculations, we assumed the average life expectancy to be 88 years, as per WHO methodology. The monetarized
value was obtained through the multiplication of DALY by the GDP/capita.

\[ \text{DALY} = \text{YLL} + \text{YLD}, \]

where

\[ \text{Years of life lost (YLL)} = 0. \]
\[ \text{Years of life in disability (YLD)} = \text{DW} \times I_{(c \text{ and } a)} \times L, \]

where \( \text{DW} \) is the disability weights for mild, moderate and severe COPD; \( I \) is the number of cases for \( a \) (age) and \( c \) (severity of COPD) and \( L \) is the average duration of case until remission or death (years).

### Statistical analysis

Descriptive statistics were applied for the purposes of reporting the patients’ characteristics (age, gender), the days out of work, reduced productivity, the age of retirement as well as the severity of COPD. The non-parametric Kruskal–Wallis method was applied to compare the medians of the indirect costs for different groups of patients according to COPD severity.

### Results and discussion

The total number of participants in the study was 426. More than half of the patients were retirees (65.5%) and the rest of them (34.5%) were in active working age. The men prevailed over the women regarding their absence from work due to COPD (77% vs. 33%) (Table 1). The number of patients with mild COPD was the lowest, which might be interpreted as late diagnosis of the disease. No statistically significant difference was observed in the average age of the patients, which leads us to believe that 65.63 years is the average age when symptoms are evident and patients actively seek help. The patients with moderate and severe COPD did not differ significantly according to their age and number.

The distribution of patients according to age group and severity of COPD was observed to follow similar patterns in all three stages (Figure 1). The peak was shown to be around 60 years of age for the moderate and severe form and to slowly decrease until 79 years, which is the average life expectancy for women in the Bulgarian population [25]. In the mild form of COPD, the peak of patients was around 56 years of age pointing at a shift of the disease towards a younger age.

The patients with moderate (50%) and severe (48%) disease were absent from work more frequently than those with mild COPD (2%). The average annual indirect costs per patient generated as a result of lost productivity were calculated to amount to 521.45€ (Table 2).

### Table 1. Distribution of patients according to the severity of COPD.

| Severity   | Number of patients | Average age (SD) | \( p \) (95% CI) |
|------------|--------------------|------------------|-----------------|
| Mild       | 30                 | 63.1 (9.2)       |                 |
| Moderate   | 211                | 67.1 (7.4)       | 0.042           |
| Severe     | 185                | 66.7 (7.1)       | 0.0565          |

SD, standard deviation; CI, confidence interval.

### Table 2. Patients’ indirect costs due to sick leave (€).

| Gender  | Number (average) | Age | Mild  | Moderate  | Severe  | Average IC_LP per patient per year (SD) |
|---------|------------------|-----|-------|-----------|---------|----------------------------------------|
| Men     | 56               | 60  | 0     | 28        | 28      | 596.98 (381.46)                        |
| Women   | 28               | 59.8| 2     | 14        | 12      | 445.92 (378.84)                        |

IC_LP, indirect costs as a result of loss of productivity.

Figure 1. Distribution of patients according to age group and COPD severity.
Prematurely retired COPD patients constituted only 13% of the total number of patients included in the cohort and their average age was 58 years. Their distribution in groups according to disease severity was as follows: 4 patients with mild COPD, 24 ones with moderate and 28 ones with severe COPD. The average indirect costs per patient for the remaining working ages due to premature retirement among the population observed were significant: about 25,000€ (6250 per patient on average) (Table 3).

The average percent of patients’ disability was approximately 66% and the average indirect costs per patient generated due to reduced productivity was around 3750.64€ per year. The highest number of patients was that of disabled patients with severe COPD, 51.51% (Table 4).

About 23% of all patients from the sample received pensions incurred because of disability related to COPD. More than half of them (62%) were with severe form of the disease with average lifetime indirect costs of about 10,000€ per patient. The costs for men were 4836€ per patient because they only had two working years left until the normal retirement age (Table 5).

The disease severity affected significantly the productivity at work. Statistical differences were detected among different groups of patients on the basis of COPD severity. The work productivity of patients with mild COPD was less affected than the work productivity of the groups of patients with moderate and severe disease. Overall, the percentage of reduced productivity for patients with severe COPD was shown to be higher than that for patients with moderate COPD, approximately 70% vs. 62%. For those men who were retired prematurely and were with severe or moderate COPD, the average indirect costs per patient were estimated to be approximately 24,000 and 36,000 €, respectively. These costs were lower for women, which could be explained with their earlier age of regular retirement. The higher the severity of disease, the lower the indirect costs incurred due to premature retirement, which could be explained with the lower life expectancy for older patients with more severe COPD. Premature retirement and reduced productivity account for higher cost burden (Figure 2). Kruskal–Wallis analysis showed that the indirect costs are higher in the patients with more severe disease, which is statistically significant ($p = 0.0425$ for reduced productivity, $p = 0.000051$ for lost productivity and $p = 0.04267$ for premature retirement).

Accordingly, the DALYs in the group of patients with mild severity are lowest due to the low disutility index and number of patients in this sample group. On average, a patient with mild COPD spends 0.62 years of their life in disability due to the disease, whereas those with moderate and severe COPD spend 6.00 and 9.00 years, respectively. Assuming that annual working income is lost by patients for the DALY period, the costs of lost productivity could be obtained by multiplying the average DALYs by the GDP per capita, thus expressing the

**Table 3. Patients’ indirect costs due to premature retirement (€).**

| Gender | Number | Age (average) | Number of patients according to COPD severity | Average IC_PR per patient per year (SD) |
|--------|--------|--------------|---------------------------------------------|---------------------------------------|
| Men    | 39     | 58.7         | Mild 2 Moderate 16 Severe 21                  | 30,253.85 (23,616.16)                 |
| Women  | 17     | 57.4         | 2 8 7                                        | 20,452.94 (16,254.85)                 |

IC_PR, indirect costs as a result of premature retirement.

**Table 4. Patients’ indirect costs due to reduced productivity (€).**

| Gender | Number | Age (average) | Number of patients according to COPD severity | Average IC_RP per patient per year (SD) | Average % disability |
|--------|--------|--------------|---------------------------------------------|---------------------------------------|---------------------|
| Men    | 44     | 58.5         | Mild 0 Moderate 15 Severe 29                 | 3870.82 (863.84)                      | 67.40%              |
| Women  | 22     | 58.5         | 0 8                                          | 3630.46 (844.38)                      | 63.70%              |

IC_RP, indirect costs as a result of reduced productivity.

**Table 5. Patients’ lifetime indirect costs due to paid disability pensions (€).**

| Gender | Number | Age (average) | Number of patients according to COPD severity | Average lifetime IC_PD per patient (SD) |
|--------|--------|--------------|---------------------------------------------|---------------------------------------|
| Men    | 56     | 61           | Mild 0 Moderate 20 Severe 36                 | 9652.13 (5513.18)                     |
| Women  | 41     | 65           | 1 15 25                                      | 11,804.4 (5524.63)                    |

IC_PD, indirect costs as a result of pension paid due to disability.

![Figure 2. Distribution of indirect costs in euro due to productivity losses.](image-url)
resources ‘lost’ per patient throughout their life (Table 6). Although the calculations do not account for premature retirement, these costs provide a higher estimate of the productivity losses in comparison to the human capital approach data presented in Tables 2–4.

This is the first Bulgarian study evaluating the economic and social burden of COPD and the first one that applies DALYs for COPD in Bulgaria. To the best of our knowledge, it is also the first one that monetizes the values for DALYs.

Although the estimates of the productivity losses associated with COPD varied, it is clear that COPD has a significant impact on individuals and employers in terms of work loss, disability, activity limitation, earlier retirement, DALYs, and this impact results in a substantial indirect cost burden. Among the productivity losses, premature retirement is the main cost driver. The present study gives a clear picture of indirect costs generated by COPD patients and the number of DALYs associated with the disease. Therefore, it could be used as evidence for defining the financial indirect burden of COPD on the Bulgarian society, as well as to initiate discussion to reduce this burden.

The average annual indirect costs per patient in terms of absenteeism and presenteeism were calculated to be between 520 and 3700€, which is approximately two times less than the GDP/capita/year in Bulgaria (approximately 6000€). The lifetime indirect costs per patient due to premature retirement and pension paid by the government were estimated to be much higher: between 11,000 and 25,000€ per patient. The indirect costs due to premature retirement were not as high as they were expected to be (between two and four times GDP/capita) because the average lost working years were between 3 and 5 years only. In our cohort, the number of patients who were absent from work for a particular period of time and who were with reduced productivity was relatively low, approximately 20% and 15%, respectively. This could be explained with the fact that information about sick leaves was collected mainly on the basis of hospitalization days due to COPD. Only 12 patients reported any additional days out of work outside of hospital stay. Only 13% of all patients were prematurely retired, 52% of whom were with severe and very severe form of the disease. Some of the patients with COPD continue to work despite their diagnosis probably because of the decreased income and possible financial problems in the period of retirement for the prevailing part of retirees in Bulgaria. This result is in accordance with a study by Fletcher et al. [26], where some respondents reported continuing to work despite their disease because of concerns about their future incomes. Patients reported delaying their age of retirement, but the uncovered average was lower than that in our study: 54 years vs. 59 years, respectively [26].

A lot of studies regarding the financial burden of COPD are officially published, but unlike our study, they present both indirect and direct costs as a percent of the total costs. Patel et al. [27] summarized the available literature about the indirect costs of COPD in the United States and concluded that the disease is associated with significant indirect burden in terms of lost and reduced productivity between $893 and $2234/person. Similar results were demonstrated for absenteeism in our study: approximately between 520 and 3700€/patient. The trend observed in our study about a positive correlation between the amount of indirect costs and severity of COPD is in agreement with that reported by Wacker et al. [28] ranging from 8621 to 27,658€ according to severity [26,28]. A study performed from the perspective of the employers in Canada presents a significant percent of indirect costs (51%) and shows that the higher the severity, the higher the indirect costs per patient: $1079 (mild), $1554 (moderate) and $2198 (severe and very severe) [29], which was supported by our observations.

The results from our study are similar to those reported in another study from Greece focused on the magnitude of direct and indirect costs of COPD of patients living in a rural area. The indirect costs in terms of lost productivity due to absence from work were higher for men than for women in both studies: 315€ vs. 156€ in the Greek study [30] and 597€ vs. 446€ in our study.

Taking into account the lost productivity due to DALYs, it is noteworthy that, as the disease progresses, the burden on the patients and on the society increases. Patients in moderate and severe stages experience a far greater loss of productivity than those in the mild stage. The costs rank as the highest, assuming that all annual income is lost for all years lost due to disability. As mentioned previously, the low number of patients in the

### Table 6. DALYs per severity stage

| Severity | Number of people | Utilities [24] | Number of DALYs | Average DALY per patient | Lost productivity per patient (€) |
|----------|------------------|----------------|-----------------|--------------------------|----------------------------------|
| Mild     | 30               | 0.025 (0.019–0.031) | 18.56 (14.10–23.01) | 0.619 | 3596.52 |
| Moderate | 211              | 0.284 (0.242–0.329) | 1260.15 (1073.19–1459.82) | 6.00  | 34,204.01 |
| Severe   | 185              | 0.418 (0.367–0.464) | 1639.03 (1439.05–1819.40) | 9.00  | 51,332.20 |
mild COPD group could be attributed to the fact that many patients are only diagnosed once they have already entered the moderate stage. Improving diagnosis of COPD at earlier stages would dramatically decrease the indirect costs associated with years spent in disability. These findings are consistent by the results reported by Jansson et al. [31], where the indirect costs in the severe group were three times higher than those in the mild group.

Our results confirm the findings of other authors that COPD imputes a high burden to the society by decreasing the productivity and adding disabilities [32]. We could not rank the social burden of COPD in comparison with other diseases in Bulgaria but the number of DALYs is comparable with that reported by Murray and Lopez [32] for the United States, Lopez et al. [33] for the European region and Feenstra et al. [34] for the Netherlands, considering the differences in the population.

A limitation of our study is the short follow-up period (1 year). Under these circumstances, a static population was assumed, where no patients progressed. Another limitation is the use of GDP per capita, due to the fact that individual data for each patient’s income could not be obtained. An issue with DALY calculations could be that the YLL was assumed to be 0, due to the fact that no patients died for the duration of the study period. This tied the DALY directly to the years spent in disability.

Despite these limitations, however, our study presents an up-to-date calculation of indirect costs on the basis of real-life data. Therefore, the study gives relatively comprehensive knowledge about the indirect burden of COPD in Bulgaria. Further investigations could be performed so that the influence of COPD progression on the amount of indirect costs can be revealed.

Conclusions

In this study, we demonstrated a significant indirect financial and societal burden of COPD in Bulgaria, which is proportional to the severity of the disease. Improvement of the time of diagnosis and of the treatment could reduce the burden on patients in regards to disability-adjusted life years. Adoption of educational and prophylaxis programmes, such as vaccination among COPD patients, for the purposes of limiting and prevention of exacerbation episodes could decrease the indirect costs as a result of lost or reduced productivity. Further studies about the influence of such programmes on the indirect costs of COPD could provide data for comparison and analysis and for drawing valuable conclusions about the development of the Bulgarian healthcare policy in the area of chronic non-communicable diseases.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This study was partly supported by the Bulgarian National Science Fund [grant number B 02-12/12.12.2014].

ORCID

Maria Kamusheva http://orcid.org/0000-0002-4379-5283

References

[1] Agusti A, Decramer M, Baltolome R et al., Global initiative for chronic obstructive lung disease. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease [Internet]. 2017; [cited 2017 Mar 3]. Available from: http://goldcopd.org/

[2] Hubbard R. The burden of lung disease. Thorax. 2006;61(7):557–558.

[3] Buist AS, McBurnie MA, Vollmer WM, et al. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet. 2007;370(9589):741–750.

[4] Buist AS, Vollmer WM, Sullivan SD, et al. The Burden of Obstructive Lung Disease Initiative (BOLD): rationale and design. COPD. 2005;2(2):277–283.

[5] Trupin L, Earnest G, San Pedro M, et al. The occupational burden of chronic obstructive pulmonary disease. Eur Respir J. 2003;22(3):462–469.

[6] Tinkelman D, Nordyke RJ, Isonaka S, et al. The impact of chronic obstructive pulmonary disease on long-term disability costs. J Manag Care Pharm. 2005;11(1):25–32.

[7] Jeetvan GP, Saurabh PN, Dalal AA. Indirect costs in chronic obstructive pulmonary disease: a review of the economic burden on employers and individuals in the United States. Int J Chron Obstruct Pulmon Dis. 2014;9:289–300.

[8] Erdal M, Johanssena A, Askildsen JE, et al. Productivity losses in chronic obstructive pulmonary disease: a population-based survey. BMJ Open Respir Res. 2014;1(1):e000049.

[9] Murray CJ. Quantifying the burden of disease: the technical basis for disability adjusted life years. Bull World Health Org. 1994;72(3):429–445.

[10] Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. Lancet. 1997;349(9064):1498–1504.

[11] Murray CJ, Asharya AK. Understanding DALYs (Disability Adjusted Life Years). J Health Econ. 1997;16(6):703–730.

[12] WHO. WHO methods and data sources for global burden of disease estimates 2000–2011. Geneva: World Health Organization. (Global Health Estimates Technical Paper WHO/HIS/HSI/GHE/2013.4).

[13] WHO. Measurement of healthy life expectancy and well-being: report of a technical meeting, Geneva 10–11 December 2012. Geneva: World Health Organization. Available from: http://www.who.int/healthinfo/sage/meet ing_reports/en/
[14] Dalal AA, Shah M, Lunacsek O, et al. Clinical and economic burden of patients diagnosed with COPD with comorbid cardiovascular disease. Respir Med. 2011;105(10):1516–1522.

[15] Chen JC, Mannino DM. Worldwide epidemiology of chronic obstructive pulmonary disease. Curr Opin Pulm Med. 1999;5:93–99.

[16] Pavlov P, Glogovska P, Ivanov Y, et al. Epidemiology of chronic respiratory symptoms in patients with COPD and in common population. Thorac Med. 2013;5(1):37–42.

[17] Kamusheva M, Dimitrova M, van de Boven J, et al. Clinical characteristics, treatment patterns, and socio-economic burden of COPD in Bulgaria. J Med Econ. 2017;20(5):503–509.

[18] Herse F, Kiljander T, Lehtimäki L. Annual costs of chronic obstructive pulmonary disease in Finland during 1996–2006 and a prediction model for 2007–2030. Primary Care Resp Med. 2015;25:15015.

[19] Di Bonaventura Md, Paulose-Ram R, Su J, et al. The impact of COPD on quality of life, productivity loss, and resource use among the elderly United States workforce. COPD. 2012;9(1):46–57.

[20] National Statistical Institute [Internet]. [Key indicators for Bulgaria]. Sofia: NSI; [cited 2017 Mar 3.]. Available from: http://nsi.bg/sites/default/files/files/pressreleases/KeyInd2016-12_JGFNODY.pdf. Bulgarian.

[21] National Statistical Institute [Internet]. [Pensioners and their incomes]. Sofia: NSI; [cited 2017 Mar 3]. Available from: http://nsi.bg/bg/content/4070/%D0%BC%D0%B5%D1%82%D0%B0%D0%B4%D0%BD%D0%B8% D0%BF%D0%B5%D0%BD%D1%81%D0%B8% D0%88. Bulgarian.

[22] Shibya K, Mathers CD, Lopez AD. Chronic Obstructive Pulmonary Disease (COPD): consistent estimates of incidence, prevalence, and mortality by WHO region. Global Programme on Evidence for Health Policy. Geneva: World Health Organization; 2001.

[23] Stouthard MA, Essink ML, Bonsel GJ, et al. Disability weights for diseases: a modified protocol and results for a Western European region. Eur J Public Health. 2000;10(1):24–30.

[24] Haagsm A, de Noordhout CM, Poliner S, et al. Assessing disability weights based on the responses of 30,660 people from four European countries. Population Health Metrics. 2015;13:10.

[25] National Statistical Institute. Population, demography and prognosis. Sofia: NSI. Available from: http://nsi.bg/bg/content/2920

[26] Fletcher MJ, Upton J, Taylor-Fishwick J. COPD uncovered: an international survey on the impact of chronic obstructive pulmonary disease [COPD] on a working age population. BMC Public Health. 2011;11:612.

[27] Patel JG, Nagar SP, Dalal AA. Indirect costs in chronic obstructive pulmonary disease: a review of the economic burden on employers and individuals in the United States. Int J Chron Obstruct Pulmon Dis. 2014;9:289–300.

[28] Wacker ME, Jöres RA, Schul H, et al. Direct and indirect costs of COPD and its comorbidities: results from the German COSYCONET study. Respir Med. 2016;111:39–46.

[29] Ng C, Risebrough N, Jayasundara K, et al. Estimation of direct and indirect costs associated with asthma and COPD: a Canadian employers perspective. ISPOR 21st Annual International Meeting; 2016 May 21–25; Washington, DC, USA. Available from: https://www.ispor.org/research_pdfs/52/pdfs/PRS30.pdf

[30] Boikos S, Bounialetos E, Daniellides S, et al. Direct and indirect cost of COPD in Lasithi area, Crete, Greece. Conference: Wonca 2004; Orlando, USA. Available from: http://www.woncaeurope.org/content/4064-direct-and-indirect-cost-copd-lasithi-area-crete-greece

[31] Jansson SA, Andersson F, Bixten B, et al. Costs in COPD in Sweden according to disease severity. Chest. 2002;122(6):1994–2002.

[32] Murray CJL, Lopez AD. Measuring the global burden of disease. N Engl J Med. 2013;369:448–457.

[33] Lopez AD, Shibuya K, Rao C, et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J. 2006;27:397–412.

[34] Feenstra TL, van Genugten ML, Hoogvenen RT, et al. The impact of aging and smoking on the future burden of chronic obstructive pulmonary disease: A model analysis in the Netherlands. Am J Respir Crit Care Med. 2001;164 (4):590–596.