



ORIGINAL
RESEARCH

Direct medical costs of COPD diagnosis and treatment, Eastern vs Western European country – examples of Serbia and Belgium

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ABSTRACT

OBJECTIVE: Comparison of COPD financial burden and underlying factors, between Eastern upper middle income and a Western European high income, healthcare settings.

METHODS: The patient sample was 433 in Belgium and 322 in Serbia, age ≥ 40 , with spirometry and clinically confirmed COPD diagnosis. Belgian trial followed patients prospectively during 2006, using structured survey of clinicians in charge. Serbian trial conducted in 2008, retrieved data from clinical invoice database. Time horizon was one year and perspective of third party payers was taken into account for both studies. Clinical outcomes of interest were disease exacerbation, hospital admission and death. Economic inputs referred to COPD-attributable medical services consumption value during observed period of time.

RESULTS: Average annual cost was 1,812.84 € for the Serbian patients and 1,738.13 €/year for the Belgian patients (not including the value of laboratory diagnostics or imaging techniques). Severity grade and duration of hospital admissions significantly directly correlated with overall cost in both populations. Pattern of diagnostic procedures requested and ATC classes of drug consumed to treat COPD remains similar and comparable in both countries. GDP per capita ratio in respective years (10.4: 37.4), exhibits the paradox of patient being much less affordable to treat in a less developed society.

CONCLUSIONS: Burden of COPD in Europe is huge and, due to contemporary life style expected to grow further. We compared cost of illness structures between two societies with different macroeconomic past in healthcare financing and management. According to our findings, direct medical costs were driven by exacerbations and hospital admissions. Significantly cheaper human labor caused higher relative relevance of drug acquisition expenses in the East and higher portion of hospital admission costs in the West. More in-depth research of indirect COPD attributable costs (e.g. lost productivity, absenteeism, premature death etc) will be needed in future. It implies serious health policy necessities to provide accessibility of care.

Keywords

COPD; Direct costs; GPD

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is severely disabling and irreversible condition with lasting impact on quality of life and working ability of an individual. Its huge impact on the health budgets worldwide puts it among five most expensive chronic disorders [1]. Few data are available about COPD costs in lower and middle income world regions [2]. It is known that lifestyle, tobacco consumption and professional risk exposure play great role in COPD pathogenesis [3]. Once diagnosed, COPD shall last, through unpredictable cycles of

remissions and exacerbations, until the end of life. Typical patient suffers from significant comorbidities which arise from bronchial obstruction. These include progressive right-sided heart failure and cardiomyopathy which cause enormous medical spending on severe disease forms [4]. This was often main selection bias in other similar studies – how to be sure that incurred cost in particular patient could be COPD attributed and not to associated conditions? From our point of view, frankly it isn't always clear whether these associated conditions precede or follow COPD, thus we didn't include cardio-

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Disclosure

BASILEUS program
and Ministry of Science
and Technological
Development of The
Republic of Serbia partially
supported this research

vascular diseases related consumption in the overall picture.

Systematic review findings show that prevalence above the age of 40 could be even as high as 9% in Western European countries [5]. Different COPD financial burden of disease estimates in high income countries, show that average patient spends 900-1,500 €/year from societal perspective [1]. We can easily calculate enormous economic and health care resources consumption imposed on a health budget by this single chronic illness. It should be mentioned that, in most countries, it has been classified among top ten causes of mortality [6,7].

This paper presents one of the first health economic efforts worldwide of comparing two different microeconomic settings in health care. Aim of the trial was to measure and explain possible differences in cost structure between two countries with different health care systems representing two main economic models inherited from recent past: Serbia and Belgium. In these two national health systems within countries with comparable size and demographic structure (Caucasian population, 10.4 vs. 7.4 million inhabitants, low fertility rate, average age 41+) we can observe very different economic milieu. Serbia, as a middle income country, had estimated annual GDP per capita 3.6 times lower than Belgian ones in 2009 (10.400\$ and 37.400\$, respectively) [8]. According to official WHO statistics, total health expenditure expressed as percentage of gross domestic product was 8% in Serbia and 9.6% in Belgium [9]. As a transitional eastern European economy, in the recent past it had only mandatory general health insurance for employed and their families and provided almost equal access to available health care (mostly state owned sector) to all citizens irrespective to their income level. However in the past decade expanded voluntary health insurance package was introduced and also major changes were made in sense of shifting outpatient and less expensive inpatient services towards privately owned health care sector. Health economic assessment based on decision making is actually still taking roots with local policy makers in governmental sector, although it is very important for countries with lower health budget. It still has to prepare its way as a useful tool for assignment of resources which are significantly poorer than OECD average [10].

On the other side Belgian national health care system provides several types of health insurance. Financing of public medical needs comes from both one large national and several smaller private insurance funds. Access

to health care is guaranteed to the almost all layers of population (regardless of income level). Health economic evaluation reports as a way for informed decision making have been conducted since the early 90ties. Health system itself has been ranked 21st in the world by overall quality of care by WHO estimates in 2000 [9,11,12].

OBJECTIVE

Our comparison of COPD burden estimates was conducted with the two aims:

1. Evaluate the annual national costs of COPD in Serbia and Belgium and structure of services and goods needed to deal with them;
2. Try to define differences in cost matrix and in total cost due to existing differences in societal milieu and health care system.

METHODS

The Authors used available data acquired through prospective (Belgium) and retrospective (Serbia) research approach.

Serbian cost of illness analysis was conducted as observational, retrospective, bottom up, third party payer's perspective, case study. It used clinical centre invoice registry for 2008 with invoices (imposed to state Health Insurance Fund) for given services and goods consumed by patients, including drugs. These economic data originated from ward clerks regular updating of electronic payment invoices given to the patient at the discharge from hospital. Medical and economical data related to patients with clinically and spirometrically confirmed COPD (ICD J40-J47) were retrieved. Sample size was 322 patients of both sexes and aged above 40. Clinical data relied on patient's medical records taken from The Pulmonary Diseases Clinic archive, Clinical Center Kragujevac, in Kragujevac, Serbia, the main one in the region with approximately 600,000 inhabitants. All attending physicians were specialist pulmonologists. Diagnostic criteria and grading were used in line with Global Initiative for Chronic Obstructive Lung Disease recommendations. They commonly also had positive history of productive chronic cough and auscultatory signs of irreversible bronchial obstruction [13]. Clinical outcomes of interest were: exacerbation, hospitalization and death. The utilization of resources imposed by patient who deceased during the course of the study was added to the overall costs because they contribute to the costs attributable to COPD in a given year. There were 15 such cases. Although some exacerbations could be suc-

cessfully treated out of hospital, majority of others required necessary ICU and pulmonology department admission. These were expected to be major drivers of increased health services utilization (previous experiences of other authors) and were carefully noticed. Recording of utilized health services was limited to inpatient diagnostic procedures and treatments and specialist physician's outpatient services at the clinic. Number of hospital admissions, their duration and number of outpatient consultations were also evidenced in unit amounts (days and absolute numbers). Costs were separated into following classes: hospital admission charges (including Intensive Care Unit and inpatient consultations), laboratory diagnostic procedures, imaging diagnostic procedures, interventions, drugs and outpatient chest physician consultations. Non-pharmacological therapeutic interventions ranging from surgery, physiotherapy to complementary medicine treatments were suited into a single file together. The practice of including physician's consultations in the charge of daily inpatient care is today common to many hospital management systems. Neither primary care nor home occurring direct medical expenses were considered.

Belgian cost of illness analysis was an in-depth, prospective, observational, bottom up, third party payer's perspective, case clinical study. 41 general practitioners and 21 pulmonologists participated in the survey. The physicians have completed one survey per each patient providing all the necessary data. The study included 433 patients with COPD (195 patients from GPs, 238 from pulmonologists), aged above 40 in 2006, with detailed evidence on their medical treatment needs and consumption. There was an equal distribution of patients among the GPs/pulmonologists. Basic method to acquire these data was structured questionnaire delivered to physicians in charge, in order to report all direct medical costs associated with this diagnosis in 2006. The physician sample was representative in terms of regional and urban versus non-urban distribution. Patients were not assigned due to their place of residence but were rather scattered all around the country. Clinical outcomes of interest and diagnostic inclusion/exclusion criteria remained the same as in Serbian twin study. Drug acquisition costs in both samples were related only to the medicines necessary to treat COPD or associated clinical conditions (anticholinergics, beta2 agonist, inhaled corticosteroid, antibiotics, methylxantine, etc). Cost calculation in both countries was based on respective official pricelist of national health insurance funds.

Methodology	Serbian data	Belgian data
Study design	Observational, retrospective, bottom-up, case study	Observational, prospective, bottom-up, case study
Perspective	Third party payers	Third party payers
Source of data	Clinical files, invoice registry	GPs and specialists survey
Sample size	322	433
Inclusion criteria	COPD spirometry and clinically confirmed	COPD spirometry and/or clinically confirmed

Table I. Short overview of both study designs

Chosen time horizon believed to be enough long to cover most outcomes of interest, in both of them, was one year. Authors needed to make economic outlook truly comparable due to two year gap between studies. Discount rates used for this purpose were derived from "Health Index" and found to be around 104. Third party payer's or health insurance fund's perspective was adopted for this research for few reasons. In general, major part of COPD-related expenses occur due to inpatient treatment of exacerbations therefore direct medical costs would probably be sufficiently representative for the entire cost of illness. Except that, societal perspective would require an in-depth estimate of indirect costs attributable to lost productivity: absenteeism, impaired working ability, early retirement, premature mortality which would have been out of the scope of this paper and the available budget. See Table I for methodological comparison.

Health care costs are given in a parallel manner, sorted for both samples. Serbian part of calculation was done in national currency (Central Serbian Dinar, CSD) converted to Euro relying on an official exchange rate of National Bank of Serbia for 2008 (1€ = 78.9 CSD). Market values of health care goods and services provided was in both countries overtaken from an official pricelist given by National Health Insurance Funds.

Graphical analysis of data was conducted by means of Microsoft Office Excel 2010 and with Systat Software SigmaPlot commercial package version 11.2 s for which The Medical Faculty University of Kragujevac, Serbia has purchased institutional license number E08A6986 - C790C936.

Study limitations

Methodological weaknesses of this comparative economic evaluation stands for time gap 2006 for Belgian and 2008 for Serbian data but we could justify it by the fact that discount rates were applied and respective inflation rates were taken into account. Ano-

ther issue is quite a different way of obtaining data implying highly likely different quality and reliability of the same ones. Methodological differences could be regarded as the source of bias. Nevertheless an ambitious task of comparing such large samples (752 in

both countries) in an academic twin clinical trial justifies the efforts. An additional issue was the fact that Serbian patients originate from central region and single large specialist clinic while Belgian ones were dispersed across the country.

Our idea is quite an unexploited one in the field of health economics, to compare to substantially different health care markets not only in terms of their level of development but quite a lot in sense of health policy strategies and financing approach too. Most of costs subdomains were carefully collected and split to be attributable particularly to the COPD morbidity (drugs, examinations and treatments outsourcing from comorbidities were excluded) in both samples. Those domains are truly comparable and refer to the equivalent values in two societies. We believe that uneasy task we decided for, will meet the needs of both policy makers and health practitioners making real-time clinical decisions.

Serbia			Belgium		
Severity stage	N.	%	Severity stage	N.	%
I	68	21.3	I	62	(14.3)
II	54	16.9	II	190	43.9
III	123	38.6	III	140	32.3
IV	74	23.2	IV	41	9.5
All stage	319	100	All stage	433	100

Table II. Severity grade structure, according to GOLD classification of COPD

Direct medical cost (€)	Serbia	Belgium
Laboratory diagnostics	120.37	Unavailable data
Imaging techniques	171.79	Unavailable data
Drug acquisition costs (inpatient expenditure)	980.22	799.7
Hospital admission*	493.02	744.1
Outpatient consultations	47.44	196.2
Cost/patient/year without diagnostic services included	1,520.68	1,738.13
Total cost/patient/year (average +/- standard error)	1,812.84	1,738.13

Table III. Measured costs of consumed medical goods and services in a given year for both samples of general COPD population (€/patient/year)

* Specialist's consultations, Intensive Care Unit admissions included

Statistical analysis

Statistical analysis of data was conducted by means of IBM SPSS commercial software package version 18, for which The Faculty Medical Sciences University of Kragujevac, Serbia has purchased institutional license number, SPSS ID: 729157.

By means of Spearman's rho nonparametric correlation test we probed significance of several hypothetical causal relationships:

- Summary duration of exacerbations (days) towards amount of costs incurred per particular patient;
- Severity of disease (according to GOLD classification stage) towards amount of costs incurred per particular patient. Within 95% confidence interval and p value ≤ 0.05 we found out that both supposed relationships could be considered significant in both populations.

Number of observations was 319 for Serbian and 433 for Belgian side. According to Kolmogorov Smirnov test results (p < 0.05, p = 0.000), we considered data to be nonparametric. We used Spearman's rho nonparametric correlation test (significant correlation was for P value < 0.05) to test the impact on total direct medical costs of different variables (male sex, age, GOLD severity stage, number of hospitalizations, duration of hospitalizations, pack years, smoker).

RESULTS

Severity stage structures of population observed is given in the Table II because it is considered to have a decisive impact on overall cost of disease.

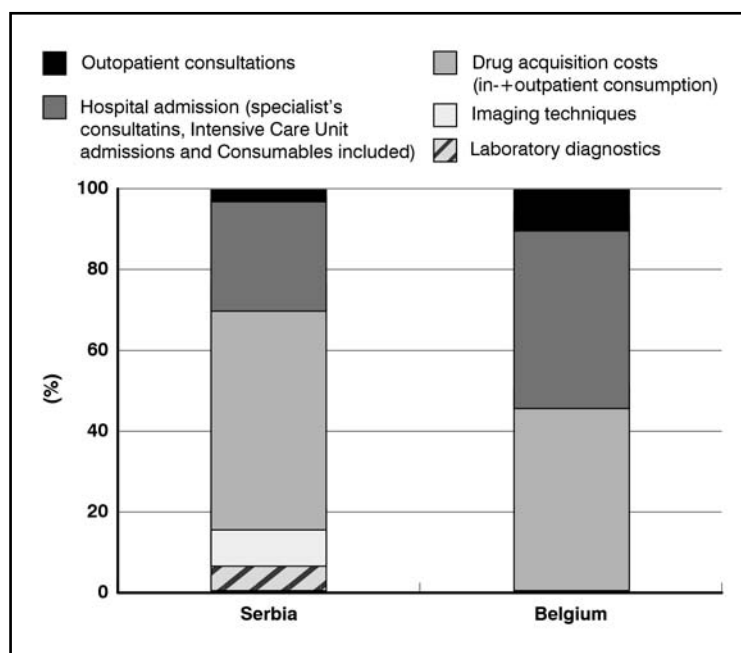


Figure 1. Stratified column chart presenting cost matrix comparison between countries, created using comparable set of respective data, acquired through similar methodological framework

Dependent variable-covariate	Total cost			
	Serbia		Belgium	
	Coefficients (95% CI)	P value	Coefficients (95% CI)	P value
Male sex	0.077 (-0.036:0.193)	0.170	-0.070 (-0.159:0.034)	0.148
Age	-0.77 (-0.192:0.035)	0.170	0.108 (0.013:0.200)	0.025
GOLD severity stage	0.458 (0.355:0.556)	0.000	0.478 (0.406:0.545)	0.000
Number of hospitalizations	0.437 (0.349:0.524)	0.000	0.262 (0.179:0.341)	0.000
Duration of hospitalizations	0.422 (0.319:0.510)	0.000	0.254 (0.167:0.339)	0.000
Pack Years	Data not available		0.007 (-0.163:0.179)	0.934
Smoker	Data not available		-0.118 (-0.223:-0.015)	0.014

Table IV. Linear regression analysis results of different variables impact on total direct medical costs (Spearman's rho nonparametric correlation test used)

It is easily demonstrated that other, so called “prosperity diseases” like diabetes mellitus 2, essential hypertension, cardiomyopathy, arrhythmias etc. arising from sedentary life styles, are present in majority of these patients. The most are proven to be related to tobacco consumption, are incurable life time disorders and significantly contribute to patient’s medical needs [5].

Next part of measurements deals with number of hospital admissions due to COPD exacerbations at the population level. Average number of hospitalizations per person was 1.5 times vs. 0.24 and its duration 14 vs. 2.83 days (Serbia vs. Belgium). An average cost of exacerbation treated was € 322.5 vs. € 1,336.82, and average number of outpatient visits was 2.9 for the Eastern European and 3.9 for Western European population. Please see Table III and Figure 1 for more details.

See Table IV for the linear regression analysis results of different variables impact on total direct medical costs.

DISCUSSION

At first, we were thinking of what could be the optimal approach when faced to such research question. In basic, most appropriate to counting real world expenses would be retrospective study design. This is so, due to lack of researcher’s subjectivity and no need for blinding, for we explore things that happened in the past. Protocol is also not interfering into physician’s practices, which commonly much differ from good clinical practice guidelines [12]. For an example in one large sample study, inhaled corticosteroids were prescribed twice as much as first line recommended ipratropium [14]. Disadvantage of

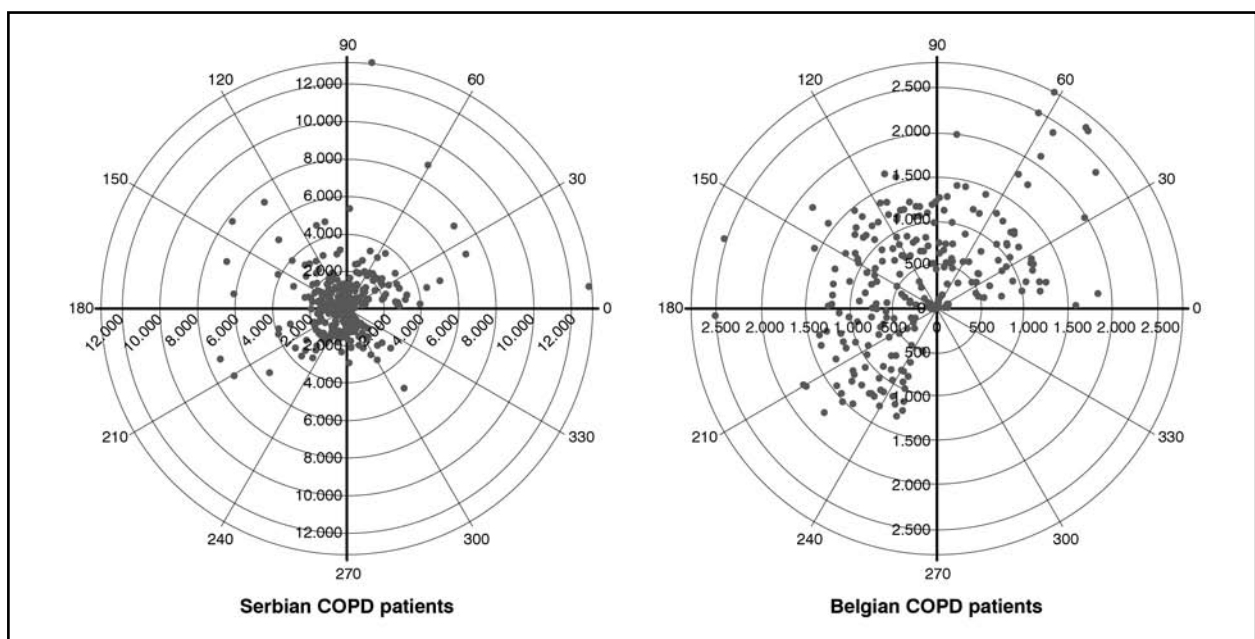


Figure 2. Scatter plots of COPD medical care costs in patients compared between countries (Serbian sample exhibits more central tendency but several extreme values, Belgian ones more overall heterogeneity inside sample)

this half of our design was of course lack of some important data e.g. professional toxic exposure, tobacco smoking habit details.

Our second half, prospective clinical case study design, while limited by certain inclusion criteria, did not define schedule of consultations and interventions in its protocol and thereafter provided plenty of highly reliable data. Here we do miss diagnostic resources consumption but have an in-depth data regarding other sorts of costs and patient's medical background.

We could see that diagnostics account for 16.12% of all costs in eastern European sample (Figure 1). This is in line with findings of Coleva et al. in Italian population on 2007 [15]. Treatment costs of up to 54% in Serbian and 46% in Belgian sample (diagnostics was excluded for comparability) declines from the dominant assumption that drug acquisition costs should be expected at 16% level [16]. It is probably due to the fact that better funded multicenter COPD cost of illness trials often included indirect expenses too in the overall picture. Relative number of hospital admission days due to sickness exacerbation, calculated per person, is significantly smaller in Belgian population and overall admission is much more seldom than in Serbian setting. At the same time, price of an average hospitalization is even four times higher. This could be explained by higher level of patient compliance to treatment or regularly scheduled consultations which succeeded to diagnose it earlier in stage easier to be treated. Severity grade spectrum shows that eastern European sample was dominated by more severe disease forms more than western one. This fact exhibits impact to total costs if we observe level of dissipation shown in scatter plots (Figure 2).

More extreme values in Serbian patients are accompanied by other findings showing that tobacco consumption and nicotine dependence is deeply rooted in Balkans countries and related to COPD prevalence [17]. When we consider hypothesis that severity grade influences costs, it's inevitable to mention earlier efforts in regard to this matter of Jansson et al. They approved that there is certain predictability [18]. More gravely ill patients are likely to often suffer from bronchial obstruction, productive cough and breathing difficulties and be hospitalized because of these symptoms. They will also be probably more expensive to society than others. It will be necessary for them to conduct extensive lab monitoring e.g. partial blood pressure of gasses. Many of them will receive simultaneously several drug treatments e.g. anticholinergic + beta2 agonist + inhaled cortico-

steroid + antibiotic + methylxantine. Some of these patients will even undergo surgical removal of hyperinflated lung tissue. We observed that patients in later stages of natural disease progression would probably cost even 2-3 times more than average [19].

Services provided by means of outpatient visits were usually GP's and chest physician consultations mostly, basic lab and spirometry controls. They fall in range of 2-3% of all costs. This is in accordance with different findings elsewhere [14,16, 20-28].

CONCLUSIONS

Both epidemiological and financial burden of chronic obstructive pulmonary disease on contemporary health budgets is enormously heavy. With 9% prevalence after the age of 40, massive professional risk exposure and tobacco smoking lifestyle, traditionally favored in Balkans region and Turkey, it is even expected to rise further. We decided to compare two different health care settings faced with the same problem. They had very different economic background and health care sector financing and management in recent past – state controlled as opposed to free market model.

One can notice that an average GDP per capita (Purchase Power Parity basis) income was 3.6 stronger in the West, but disease (compared as average COPD cost per patient per year) is likely to be only some 12.5% less expensive in the East. According to this fact we have the paradox of this illness currently being more affordable to combat with, in high-income societies. Human labor wages rose continually in eastern European and Balkans countries during past two decades. Anyway they remain at pretty lower level than in the West. The truly comparable part of COPD expenses mentioned between our samples, are drug acquisition costs. Among drugs we may see that, when of DDD units (defined daily doses) consumption is considered, patterns of prescription do not differ significantly. Also unit prices provided by national insurance funds could be treated similar.

From overall picture provided by these two observational studies we can conclude several facts:

- Hospital admissions due to exacerbations are major driver of costs incurred;
- Drugs consumption has similar structure in both societies;
- Services relying on human labor (unlike lab analysis. an example of physician consultations) are still significantly more expensive in western European conditions.

Serbian part of this research, together with one Romanian and few Polish studies published in native languages was probably one of few pioneering cost of illness determination efforts related to prosperity diseases in Eastern Europe [29-36]. This could be conducted from the huge lack of knowledge on costs of most important prosperity diseases in this part of the world. We assume that further in-depth evidence on indirect costs of COPD, would still be needed in future, especially in order to reveal true picture in middle and lower income so-

cieties. Health care budgets are evidently more threatened by chronic diseases in an economic environment with scarcer resources.

ACKNOWLEDGEMENTS

The authors would like to thank to the BASILEUS program approved by The European Commission, and Ministry of Science and Technological Development of The Republic of Serbia (grant N° 175014) who partially supported this research.

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