REVIEW ARTICLE

Economic evaluation of the impact of chronic obstructive pulmonary disease and its acute exacerbations on Latin America*

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Chronic obstructive pulmonary disease is highly prevalent the world over. An estimated 7% to 10% of the global adult population is affected. In Brazil, the incidence of chronic bronchitis is 12.7% among individuals over the age of 40. Economic studies have great relevance in devising policies for dealing with diseases of such high prevalence. The majority of data related to the costs of chronic obstructive pulmonary disease is culled from national health databases. There have been only a few studies evaluating the direct public health costs of the disease. In analyzing those studies, one can conclude that a chronic obstructive pulmonary disease patient generates a direct annual expenditure of 1200 to 1800 USD. However, the cost is correlated with the severity of the disease. Patients suffering from the more severe forms can require as much as double that expenditure, and early diagnosis is therefore vital. The most cost-effective strategy is early detection of the disease, in concert with anti-smoking campaigns. In the most advanced stages of the disease, the greatest costs are incurred due to hospitalization. In such cases, correct treatment of the acute exacerbations of the disease is crucial to minimizing costs. The average cost of a hospital stay in Brazil is 2761 Brazilian reals, which is equal to that of one full year of outpatient treatment. Antibiotic therapy accounts for only a small fraction of the total cost of treating such acute exacerbations. The use of more efficacious antibiotics may represent a more cost-effective strategy for reducing the rate of treatment failure. Economic analysis should allow for the identification and implementation of the most cost-effective strategies for treating this disease.

Key words: Chronic Obstructive Pulmonary Disease. Health Care Costs. Costs and Cost Analysis.

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Abbreviations used in this paper:

COPD – Chronic obstructive pulmonary disease
FEV_1 – Forced expiratory volume in one second
IHCP – Inappropriate health care practices
CHCP – Current health care practices
RHCP – Recommended health care practices

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a social and medical problem of utmost importance. The prevalence of the disease in Spain is 9% of the adult population between 40 and 70 years of age[1,2], although it is estimated that only 22% of cases are diagnosed[2]. Moreover, in studies carried out in other developed countries, it has been shown that the number of individuals affected by the disease has increased over the past decade[3]. In a population-based study carried out in Brazil, the prevalence of chronic bronchitis among patients over the age of 40 was estimated at 12.7%[4].

Smoking is the most important etiologic factor in COPD. In a Spanish population-based study, 25% of individuals between 40 and 70 years of age were smokers and 25% were former smokers[5]. The number of smokers that develop COPD ranges from 15% to 20%. Smokers suffering from COPD are characterized by high tobacco use, high nicotine dependence, and more than one-third of this group has never tried to quit smoking. It is important to highlight the fact that this situation is more serious in Spain than in other countries. In a recent study carried out in 13 European countries and 3 non-European countries, it was shown that Spain has the highest prevalence of male and female smokers (56%) between 20 and 40 years of age. Concomitantly, Spain has the highest prevalence of chronic bronchitis (9%) among this age group[6]. In a study carried out in the Netherlands, it was estimated that the total number of years of life lost due to COPD will increase by 60%, the years of disability caused by COPD will increase by 70% by the year 2015[7]. The authors also estimate that, by that time, health costs related to COPD will increase by 90%, and that smokers will be responsible for 90% of those health care expenditures. These statistics reveal that, in the near future, the COPD problem will continue to worsen worldwide.

Periodic worsening of the symptoms, especially cough, dyspnea, increased sputum production and purulent sputum, aggravates the chronic, progressive course of the disease. Periods of worsening of symptoms are known as acute exacerbations. When outpatient treatment fails, hospitalization, which is the most important determining factor for COPD costs, may be necessary.

In this study, we analyzed the various types of pharmacoeconomic studies, costs of illness, costs attributable to acute exacerbations, available data from some Latin American countries and the efficacy of cost distribution in the treatment of patients diagnosed with COPD.

COSTS OF ILLNESS

Studies regarding the economic costs of a specific disease are designed to measure the financial onus that some of the effects of that disease put on those who suffer from the disease and on society in general. These studies have been widely used in recent years. However, in order to analyze and understand a pharmacoeconomic study, it is important that some essential aspects are taken into consideration [8]. Such aspects include whether the study is prevalence-based or incidence-based, whether a top down or a bottom up approach is necessary for data collection, and how direct and indirect costs are defined, considered and calculated.

Prevalence-based or incidence-based approach

Prevalence-based estimations of the cost of an illness consider all existing cases during a given period of time (usually one year), as well as the resources used in prevention, treatment and rehabilitation. The effects of morbidity and mortality from the disease during that period are usually also taken into consideration. This approach can be considered numerical and macroeconomic (sectorial). On the other hand, incidence-based cost analyses concentrate on new cases of the disease diagnosed during a given year. Such

studies consider resource costs implied, from diagnosis to outcome (either cure or death). This approach demands a detailed analysis of the course of the disease and can be considered microeconomic and epidemiological.

Top-down and bottom-up analyses

Top-down and bottom-up analyses can be used to quantify disease costs. Top-down analyses are based on the total amount of money spent on all diseases at a national level, followed by a disaggregation process in which the level of the pathology studied is reached. Bottom-up analyses are usually based on financial and resource expenditures for a group of patients diagnosed with the disease under study. These results are extrapolated in order to obtain values that represent the whole population.

Direct and indirect costs

Direct costs are related to disease detection and prevention, as well as to treatment and rehabilitation of the patients diagnosed with the disease in question. Most direct costs studies concentrate on analysis of the hospital, outpatient, and pharmacological costs of the disease. Other direct costs peripheral to the health care system, such as social services, are not included because of the lack of precise data.

Indirect costs are related to morbidity and mortality caused by the disease. They are used in order to evaluate the impact of the disease on the national production capacity. The most common method is based on the human capital approach, in which the number of lost work days, due to either disease or mortality, are transformed into monetary units using mean earnings. This method has been widely criticized because, for example, it does not include the non-wage-earning population: children, the elderly, homemakers, etc.

In Spain, there have been macroeconomic (top-down) studies using statistical and epidemiological data that evaluate the costs generated by COPD. In 1994, COPD-related costs in Spain ranged from 750 million to 850 million euros[9,10]. These values included direct and indirect costs. If we used the prevalence-based approach, considering only direct health costs spent on these patients, the annual costs throughout Spain (about 40 million inhabitants) would be 260 million euros[10]. If we used the incidence-based approach, considering the actual amount spent on a cohort of patients, mean cost per patient – from diagnosis to death – would be 27,500 euros[11]. If we disaggregate costs and survival rates in relation to the severity of airflow obstruction presented at diagnosis, we see that the less severe the disease at diagnosis, the longer the survival and the lower the cost per patient. On average, patients diagnosed with mild to moderate obstruction have a survival rate of 13.9 years and a mean per-patient cost of 9,730 euros. On the other hand, patients diagnosed with severe obstruction have a mean survival rate of 10 years and a mean per-patient cost of 43,785 euros[11].

In a microeconomic (bottom-up) study comprising 1,510 outpatients diagnosed with COPD and monitored for a one-year period, it was shown that mean annual cost per patient was 1,876 US dollars (USD)[12]. Using a prevalence-based approach to analyze data from this study, we can calculate the approximate direct annual costs caused by COPD in Spain. Data from *Iberpoc*, an epidemiological population-based study carried out in 7 different geographic and socioeconomic areas[1], showed the prevalence of COPD to be 9% in the 40 to 69 age bracket[2]. According to the 1997 Spanish Census, the population between 40 and 70 years of age comprised 13,645,000 people. Using a prevalence of 9% for this age group, the total number of patients would be 1,228,000. Moreover, assuming, in a conservative fashion, that the prevalence of the disease in individuals over the age of 70 was the same, there would be a total of 1.7 million people suffering from COPD in Spain. It is extremely important to know the proportion of patients responsible for the costs related to the illness on a pharmacoeconomic basis. According to the same *Iberpoc* study, only 22% of the patients who were responsible for direct health costs had been

previously diagnosed with COPD[2]. Therefore, the total number of COPD patients treated would be 270,000. If we multiply this number by the mean annual per-patient cost, we arrive at a total of 506.52 million USD per year in direct health costs due to COPD. This sum is greater than that obtained by the previous approach, possibly due to methodological differences and, at least in part, to changes in the management of the disease that appeared between 1994 and 1998.

It is interesting to compare the distribution of estimated costs in both models. Therefore, in the top-down approach, hospital costs accounted for 36.3% of the total, medication costs for 42.2%, and visits and diagnostic tests for 22.5%[10]. In the bottom-up study, hospital costs accounted for 43% of the total, medication costs for 43%, and visits and complementary tests for 17%[12]. Although absolute values between the two types of study were very different, cost distribution was quite similar in both studies. If we divide the total direct costs due to COPD by the total national population, the amount of money spent per citizen due to COPD is about 13.32 USD per year. In a study carried out in the Netherlands, Rutten van Mölken et al. reported costs due to asthma and COPD of 23 USD per capita[13]. Differences may be due to, among other reasons, the inclusion of asthma in this study and to a minimal amount of underdiagnosis in the Netherlands.

Another important aspect is the fact that cost increases in parallel with increased disease severity. If we categorize patients into distinct severity levels, the annual cost per patient diagnosed with severe COPD is 2,911 USD, cost per patient with moderate COPD is 2,047 USD, and cost per patient with mild COPD is 1,484 USD[12].

It is interesting to compare these costs with those obtained in studies carried out in other countries. In a recent bottom-up study carried out in the USA, Hilleman et al. evaluated a cohort of 413 patients diagnosed with COPD and classified as either stage 1, stage 2 or stage 3, as defined by the American Thoracic Society (ATS) guidelines. The authors reported direct health costs ranging from 1,681 USD for stage-1 patients, to 5,037 USD for stage-2 patients and 10,812 USD for stage-3 patients[14]. These costs are considerably higher than those in Spain, which can be explained by various factors, such as the fact that doctor fees in Spain are lower than in most western countries, as are medication and hospital costs. A crucial factor to be considered is the fact that patients in the American study were selected from a population of COPD inpatients in a hospital, whereas the patients evaluated in the Spanish study were treated by their primary-care physicians. We can infer that the patients included in the American study suffered from more severe and complex forms of the disease. Other COPD cost-analysis studies carried out in various countries are shown in Table 1.

Another alternative in the analysis of costs due to COPD is to compare them to costs due to asthma. Asthma has traditionally received more attention than COPD. However, since COPD is more prevalent in the adult populations, the demands it places on the health care system must, perforce, be greater. In another study carried out in Spain, Serra-Batlles et al.[15] evaluated a cohort of 385 adult patients and reported that direct costs due to asthma were approximately half those due to COPD – a mean per-patient cost of 885 USD, ranging from 532 USD for patients with mild asthma to 1,044 USD for patients with moderate asthma and 1,276 USD for patients with severe asthma.

In addition to the increase in costs due to the disease itself, COPD also causes an increase in general health costs. Patients diagnosed with COPD are frequently smokers or former smokers, usually present with other diseases and may be receiving various medications. Therefore, COPD worsens patient quality of life[16] and costs increase as a consequence. In a study carried out in the USA, Mapel et al. reported that COPD patients required twice the expenditure of health resources as that required by those in a control group (age and gender adjusted), and most of the costs were due to smoking-related diseases[17].

Incidence and evolution of acute exacerbations

Acute exacerbations are frequent over the course of disease evolution in COPD patients. In addition, these exacerbations are the most frequent motive for visits to the doctor, hospitalization and mortality in these patients[18]. It is difficult to define exacerbations since there is no consensus on the clinical criteria, although the combination of symptoms described by Anthonisen et al.[19] (increased dyspnea, sputum production and purulent sputum) has been widely adopted. Based on this combination of symptoms, patients diagnosed with moderate COPD and included in clinical studies presented from 1.9 to 2.1 exacerbations per year, with a forced expiratory volume in one second (FEV_1) between 50% and 55% of predicted values[20,21]. In an observational study, patients diagnosed with severe COPD (mean FEV_1 of 47% of predicted values) also presented an average of 2 exacerbations per year. Patients with FEV_1 < 40% presented an average of 2.3 exacerbations a year and those with FEV_1 > 60% presented an average of only 1.6 exacerbations a year[22]. It is important to emphasize that the incidence of repeated exacerbations is typical of the disease. According to follow-up studies, patients that had a great number of exacerbations during a certain amount of time are likely to have others in the future [23]. Therefore, as will be explained further, the number of acute exacerbations that a patient had in the past is one of the most important predictive risk factors for acute exacerbations in the future[24].

Various studies have reported a consistent failure rate between 15% and 26% in the treatment of acute exacerbations in outpatients[25-27]. Worsening of symptoms after initial treatment of acute exacerbations may result in prolonged incapacitation, the need for a second course of antibiotics, subsequent visits to emergency rooms or even hospitalization. Therefore, it is essential to identify patients who are likely to present worsening of the disease.

The identification of risk factors for outpatient treatment failure would allow the adoption of more aggressive therapies as well as stricter patient follow-up treatment. Table 2 details risk factors for recurrence and hospitalization as reported in the literature[28].

COSTS RELATED TO ACUTE EXACERBATIONS CAUSED BY COPD

Acute exacerbations and, in particular, hospitalization are the most important factors in increasing direct health costs due to COPD. In 1993, the economic impact due to COPD in the USA was more than 15.5 billion USD, 6.1 billion of which were hospitalization costs[14]. It has been reported that hospitalization is responsible for 40% to 57% of total direct costs incurred in the treatment of COPD patients, soaring to 63% in severe cases[8,14,29]. In a cohort study of patients with severe COPD, mean hospitalization costs due to COPD in the USA were estimated at 7,100 USD[30]. In a study carried out in Spain, a large cohort of primary-care COPD patients was studied[12]. In that study, mean annual cost per patient was estimated at 1,876 USD, and costs due to hospital care and acute exacerbations represented 43.8% of total costs. Since acute exacerbations are the main cause of hospitalization among patients with COPD[18,30], we can conclude that economic costs due to acute exacerbations are considerable.

Although COPD patients suffer an average of two acute exacerbations per year, only a small number of patients require hospitalization[22]. In an observational study on primary care, Miravittles et al. reported that only 22% of COPD patients were hospitalized during a one-year period[24]. In another study, of all outpatients presenting acute exacerbations, only 3.4% were hospitalized[27]. Inappropriate pharmacological treatment of exacerbations, primarily due to incorrect antibiotic prescription, represents only 4.3% of the costs due to inappropriate practices in COPD management[31]. However, the consequences of inappropriate antibiotic regimens resulting in hospitalization represent the most significant expenditures in the treatment of such patients. In a pharmacoeconomic study in which 2,414 occurrences of acute exacerbation were treated in outpatient settings, mean direct cost of an exacerbation episode was estimated at 159 USD[32], whereas the cost of therapeutic failure was estimated at 477.50 USD per occurrence. Therefore, 63% of the

total cost of acute exacerbation management was caused by therapeutic failure. If we hypothetically reduced failure to zero, the mean per-occurrence cost of an acute exacerbation would be reduced from 159 USD to only 58.7 USD (Figure 1)[32]. Moreover, in a study on respiratory infections treated in a general clinic, Davey[33] reported that repeated visits due to therapeutic failure would cost, including indirect costs, 28.45 British pounds per visit. We must emphasize that this value is much lower than that estimated in the former study because patients of all age groups were included and there was a wide variety of respiratory infections.

As a consequence, we can conclude that reducing hospitalization would be the most efficacious means of economizing resources. Since hospitalization rates are low among COPD patients, studies comprising large populations are necessary in order to demonstrate economic advantages of a specific treatment. Although financing a study of that magnitude is a great challenge, the benefits of devising a practical clinical and economic approach to COPD treatment would be considerable[34,35].

The most recent studies comparing various antibiotics used in the treatment of acute exacerbations are designed to show differences in how fast symptom resolution is achieved, since faster resolution allows patients to return to their personal and professional activities more rapidly, which equals lower costs (especially indirect costs)[36]. It has also been shown that antibiotics that are more efficacious (and costly) may be cost-effective in the treatment of patients with severe COPD, since COPD patients present acute exacerbations caused by microorganisms that are more aggressive and more often resistant to traditional antibiotics[38]. Some guidelines on antibiotic treatment of exacerbations due to COPD have taken this knowledge into account, recommending that antibiotic choice be based on the degree of pulmonary function alteration[39].

COSTS OF ACUTE COPD-RELATED EXACERBATIONS IN LATIN AMERICA

Estimates of costs related to exacerbations due to chronic bronchitis and COPD in Latin America have been made thanks to the cooperative effort of various professionals in the region[40]. Researchers in Argentina, Brazil, Colombia, Ecuador, Mexico, Peru, and Venezuela have shared their data. Wide variability of health resource costs was the first relevant observation made in the analysis of the data. This was mainly due to various health care systems, price ranges and the degree of development of each country, as well as exchange rate fluctuations in relation to US currency. The highest mean cost per outpatient visit was in Peru (124 USD vs. 25 USD in Brazil). In addition, the highest mean cost per emergency room visit was in Venezuela (310.48 USD vs. 65.50 USD in Brazil), and the highest mean cost of hospitalization was in Argentina (3,120 USD vs. 2,761.10 USD in Brazil)(Table 3).

Resource use expressed in USD is shown in Table 4. The mean per-patient cost of treatment failure ranged from 28 USD in Colombia (representing 28.6% of total costs due to exacerbations) to 136 USD in Venezuela (48% of total costs due to exacerbations). In Brazil, the mean per-patient cost of treatment failure was estimated at 102 USD (representing 48.3% of total costs). The highest percentage of costs attributable to treatment failure was in Ecuador, where it represented 62.8% of total costs due to acute exacerbations.

In the group of Latin American countries studied, it has been demonstrated that therapeutic failure is responsible for the greatest proportion of total costs (51.9%), followed by antibiotic therapy (19.7%), other medication therapies (16.3%) and preliminary medical visits (11.9%)(Figure 2).

Unequal economic expenditure due to health activities has been demonstrated in various countries. We highlight the low mean hospitalization costs in Colombia, where therapeutic failure represents only 28.6% of total costs due to acute exacerbations. On the other hand, mean hospitalization costs in Argentina are high. These differences may be due to various factors, such as technological level of hospitals, drug purchasing policies and staff salaries, as well as to factors related to economic conditions each country, such as inflation, and

exchange rates in relation to the US currency. These and other unidentified factors, alone or in combination, may explain the differences found among countries. Mean prices in each country were used, and fluctuations may be significant depending on the type of center (public or private). Therefore, these results can not be applied to a specific center. They must be considered as an approximation.

These studies have highlighted the significance of economic costs due to COPD exacerbation management. From a pharmacoeconomic perspective, the most efficacious alternative would be to reduce therapeutic failure, especially in patients with severe COPD, who are more likely to be hospitalized if initial treatment fails.

COSTS RELATED TO INAPPROPRIATE PRACTICES

In addition to disease costs, it is important to evaluate whether resources have been used as efficiently as possible. In a recent study, the costs due to inappropriate practices in the treatment of COPD were estimated[31]. With that in mind, other studies have estimated the cost of inappropriate health care practices (IHCP), defining that cost as the difference between the costs incurred through current health care practices (CHCP) and those that would be incurred through the use of recommended health care practices (RHCP)[41,42].

The general scenario for COPD patients was defined based on results obtained from various studies on outpatient care[16,22,43]. Subsequently, RHCP were identified through analysis of the documented recommendations of various scientific societies[41,42]. The CHCP were identified and rated based on descriptive studies. The IHCP were identified and modified so that they were adjusted in relation to the recommended guidelines. Therefore, an ideal management scenario was created for every type of practice. Hence, costs were estimated. Finally, IHCP cost was obtained by subtracting the cost of RHCP from that of CHCP, and the result was multiplied by the number of patients with COPD.

Table 5 shows the CHCP costs. We highlight the fact that 81% of total costs are due to fact that COPD often goes undiagnosed during the early stages of the disease. Strictly speaking, this cost would be nonexistent during the reference year of the study. However, an incidence-based study on costs due to COPD showed that delayed (severe-stage) diagnosis is predictive of higher long-term health care costs and poor survival rates when compared to early (mild-stage) diagnosis[11]. This is due to the fact that patients with mild COPD benefited from smoking cessation counseling (5% of COPD patients quit smoking every year) and were therefore able to retard disease progression.

Due to the importance of early diagnosis in achieving lower morbidity and lower health care costs, various programs to increase diagnosis rates, especially during the early stages of the disease, have been tested, with varying results. In the Netherlands, the population-based project *Dimca* involved 1,155 individuals between 25 and 70 years of age. The authors reported that 7.7% of subjects presented reduced pulmonary function or increased nonspecific bronchial responsiveness, and that another 12.5% of subjects presented a sharp decrease in FEV_1 (> 80 mL/year)[44]. The Lung Health Study demonstrated that more than 20% of smokers between 35 and 59 years of age presented altered spirometry findings[45]. If we consider that 78% of COPD in Spain go undiagnosed[2], the importance of COPD awareness programs targeted at the population and at primary care physicians becomes obvious.

The poor use of respiratory function tests in the follow-up treatment of patients with COPD is also responsible for the low efficiency in the management of the disease. In a recent study on primary care, the difference in the use of health resources between patients who had been submitted to respiratory function tests at least once and those who had never been submitted to the tests has been reported[43]. These data, together with the knowledge that spirometry figures prominently in efficient follow-up management of these patients, were used to determine the costs due to follow-up treatment of patients with COPD. Patients who had never been submitted to respiratory function tests had a

treatment profile less in accordance with present recommendations. Possible explanations for this are that the lack of respiratory function tests would cause more frequent use of health care resources due to poorer health care quality, or that physicians who tend not to follow guidelines and make less use of respiratory function tests are those who have poorer prescription practices. In this sense, Hilleman et al., in a recent study involving COPD patients categorized as stage 2 or stage 3, according to the ATS guidelines, reported that direct health costs were lower for patients treated by pulmonologists than for those treated by primary-care physicians. The direct annual per-patient cost for stage-2 patients treated by pulmonologists was 4,439 USD, compared with 5,270 USD for stage-2 patients treated by primary-care physicians ($p < 0.01$). Direct annual per-patient cost for stage-3 patients treated by pulmonologists was 10,226 USD, whereas that for stage-3 patients treated by primary care physicians was 11,105 USD ($p < 0.01$)[14].

Pharmacological treatment represents 14.6% of CHCP costs, 28% of RHCP costs and 6.2% of IHCP costs. It is one of the interventions on which resources are spent most inappropriately, surpassed only by diagnosis. The determination of CHCP was based on studies of medication use in the treatment of stable COPD[16,22,43]. We determined RHCP based on published guidelines. The administration of theophylline in patients presenting FEV_1 > 50% was considered inappropriate, since, due to its limited efficiency and narrow margin for error, it is the bronchodilator of last resort. We considered the use of inhaled corticosteroids to be improper in 30% of cases. We based this viewpoint that their potential effect is not related to slowing disease progression, but to a possible decrease in the incidence or severity of acute exacerbations in patients with severe COPD, although they may be beneficial for patients who also present asthma symptoms[20,21]. We consider 30% to be a reasonable estimate, although some authors have reported that only 10% of the patients would benefit from the administration of inhaled corticoids[47].

Costs incurred when health care practices were in accordance with guidelines (RHCP) are shown in Table 6. The overall RHCP costs were 417 million euros, much lower than those of CHCP in any of the approach categories selected. Therefore, subtracting RHCP costs from CHCP costs rendered the effective IHCP costs, which were 670 million euros (Table 7).

In relative terms, costs due to a delay in the diagnosis of COPD still represent the greater part of costs attributable to inappropriate use of resources, followed by costs due to pharmacological treatment. In COPD patients, follow-up treatment and oxygen therapy were found to be, in relative terms, less relevant.

CONCLUSIONS

COPD has high prevalence and places many demands on a health care system. Direct annual health care costs incurred from treating a patient diagnosed with COPD may range from 1,000 to 10,000 USD, depending on the severity of the disease and costs of health care in each country. Early diagnosis of the disease is the most important factor for reducing resource use. Therefore, the implementation of early-detection and smoking-cessation programs must be stimulated.

Among patients diagnosed with COPD, hospitalization costs are the most relevant, and they are frequently due to acute exacerbations. Mean per-occurrence cost of exacerbations is approximately 159 USD. However, if initial treatment of exacerbations fails, the mean per-patient cost is 477.50 USD. Pharmacotherapy for the prevention of acute exacerbations or to avoid treatment failure is a cost-effective alternative.

Cost differences among Latin American countries are due to differences in the price of resources, health care system organization, and exchange rates in relation to US currency. However, treatment failure in acute exacerbations is a decisive factor in direct costs due to COPD in all of the countries analyzed.

Guidelines for the diagnosis, treatment, and follow-up management of COPD have not been adequately implemented. Professionals involved in the treatment of these patients should be aware of new diagnostic and treatment alternatives in order to reduce morbidity and mortality, as well as the costs related to the disease.

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TABLE 1
Costs related to COPD as reported in various international studies

Study[Reference]	Country	Approach	Costs	Costs per patient/year	Total costs/year
Morera, 1992[9]	Spain	Top-down	Direct and indirect	959 €	Direct: 319 million € Indirect: 541 million €
B. Krief, 1995[10]	Spain	Top-down	Direct and indirect		Direct: 260 million € Indirect: 492 million €
Hilleman, 2000[14]	USA	Bottom-up	Direct	Stage 1: 1,681 USD Stage 2: 5,037 USD Stage 3: 10,812 USD	
Jacobson, 2000[48]	Sweden	Top-down	Direct and indirect		Direct: 109 million € Indirect: 171 million €
Wilson, 2000[29]	USA	Top-down	Direct	Emphysema: 1,341 USD Chronic bronchitis: 816 USD	14,500 million USD
Rutten van Mölken, 2000[13]	Netherlands	Top-down	Direct	876 USD	
Dal Negro, 2001[49]	Italy	Bottom-up	Direct	Stage 1: 151 € Stage 2: 3,001 € Stage 3: 3,912 €	
Jansson, 2002[50]	Sweden	Bottom-up	Direct and indirect	1,284 USD	871 USD
Miravitlles, 2003[12]	Spain	Bottom-up	Direct	Stage 1: 1,185 € Stage 2: 640 € Stage 3: 2,335 €	427 million €

COPD: chronic obstructive pulmonary disease; €: euros; USD: US dollars.

TABLE 2
Risk factors found for treatment failure and hospitalization in COPD patients in a follow-up study*

1. **Risk factors for treatment failure:**
   - High number of visits due to respiratory symptoms (more than 3 visits a year)
   - High number of previous acute exacerbations
   - Moderate to severe baseline dyspnea
   - Significant changes in pulmonary function (FEV_1 < 35%)
   - Improper antibiotic therapy
   - Home oxygen therapy

2. **Risk factors for hospitalization:**
   - Significant changes in pulmonary function (FEV_1 < 35%)
   - Significant comorbidity: insulin dependent *diabetes mellitus*; cardiac insufficiency; ischemic cardiopathy
   - More than 70 years old
   - High incidence of hospitalization due to previous acute exacerbations

*data obtained from reference 28
COPD: chronic obstructive pulmonary disease; FEV_1: forced expiratory volume in one second

TABLE 3
Costs (in US dollars) related to various health care activities in some Latin American countries*

Country	Ambulatory visit	Emergency room visit**	Hospitalization***
Argentina	40.00	97.60	3,120.00
Brazil	25.00	65.50	2,761.10
Colombia	17.10	52.70	641.30
Ecuador	30.00	82.00	2,800.00
Mexico	32.00	240.00	2,595.00
Peru	124.00	225.00	1,688.00
Venezuela	70.10	310.50	3,086.00
Spain*	7.50	103.60	2,652.60

*data obtained from reference 40
**Emergency room visit costs include a chest X-ray and blood cell counts
***Hospitalization costs are based on a 7-day stay on a respiratory ward

TABLE 4
Direct health care costs (in US dollars) due to treatment failure and acute exacerbations

Country	Failure costs	Exacerbation costs	% of costs*
Argentina	118	329	35.8
Brazil	102	211	48.3
Colombia	28	98	28.6
Ecuador	105	177	59.3
Mexico	109	215	50.7
Peru	90	302	29.8
Venezuela	136	283	48.0
Spain**	100	159	62.8

*percentage of total costs due to treatment failure. Adapted from reference 40
**data obtained from reference 32

TABLE 5
Annual costs (in millions of euros) and percentages of overall costs for current health care practices*

	CHCP	%
Diagnosis of COPD	882	81.1
COPD follow-up	11	0.99
Pharmacotherapy during Stable phase	133	12.3
Pharmacotherapy during Acute exacerbations	25	2.3
Home oxygen therapy	36	3.3
Custo total	**1,087**	**100**

*data obtained from reference 31
CHCP: current health care practices; COPD: chronic obstructive pulmonary disease

TABLE 6
Annual costs (in millions of euros) and percentages of overall costs for recommended health care practices*

	RHCP	%
Diagnosis of COPD during mild phase of the disease	265	63.7
Follow-up management with regular spirometry	5.6	1.3
Recommended pharmacotherapy during stable phase	99	23.7
Recommended pharmacotherapy during acute exacerbations	18	4.3
Properly prescribed home oxygen therapy	29	6.9
Total costs (RHCP)	**416.6**	**100**

*data obtained from reference 31
RHCP: recommended health care practices; COPD: chronic obstructive pulmonary disease

TABLE 7
Annual costs (in millions of euros) and percentages of overall costs for inappropriate health care practices*

	IHCP**	%
Delayed diagnosis of COPD	616	91.9
No spirometry during follow-up treatment	5.2	0.8
Inappropriate pharmacotherapy during stable phase	35	5.2
Inappropriate pharmacotherapy during acute exacerbations	6.5	0.9
Inappropriate use of home oxygen therapy	7.2	1.1
Total costs	**669.9**	**100**

*data obtained from reference 31
**(IHCP = CHCP – RHCP)
COPD: chronic obstructive pulmonary disease; IHCP: inappropriate health care practices; CHCP: current health care practices; RHCP: recommended health care practices

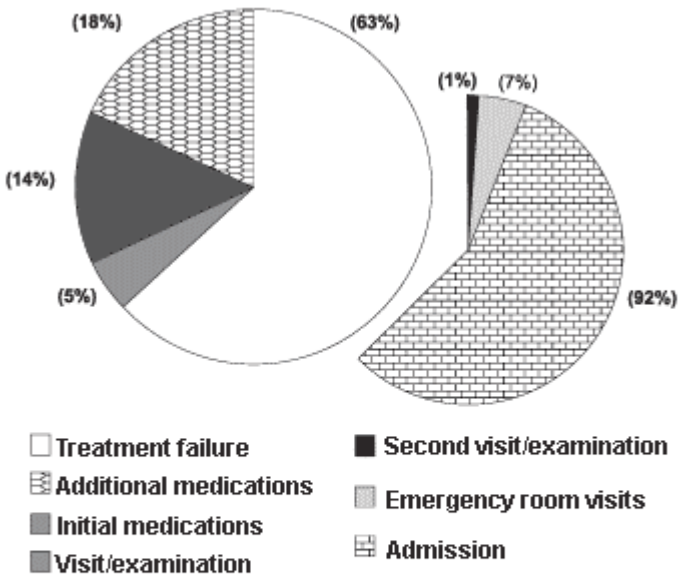

Figure 1. Percentage distribution of costs due to acute exacerbation treatment of COPD.
Diagram on the left shows cost distribution due to acute exacerbations. Diagram on the right shows cost distribution due to treatment failure. Adapted from reference 32.

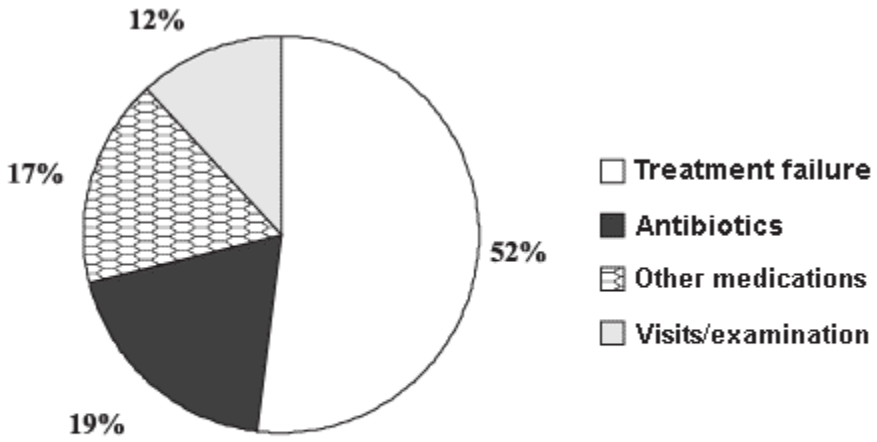

Figure 2. Direct health care cost distribution due to treatment of patients presenting acute exacerbations in various Latin American countries combined.