AMICA

Autonomy Motivation & Individual Self-Management for COPD patients (AMICA)

DELIVERABLE D6.1

Health Economical Analisys

Workpackage WP6– Health Economics, Service & Business Models

Task T1 – Economical analysis of cost savings and quality improvement potential

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Abstract

The Autonomy Motivation & Individual Self-Management for COPD patients (AMICA) is aimed at the disease management and medical care of chronic obstructive pulmonary disease (COPD) patients. AMICA is a Research and Development project sponsored under the Europeans Commission's Ambient Assisted Living programme as well as its projects members. Its official website is http://www.amica-aal.com.

AMICA project started April 2009 and lasts for 3 years until April 2012. Seven partners spread across Europe are involved including medical companies and foundations (Vitaphone - Germany, I.S.S- Spain. and the Foundation for Biomedical Research Management- Spain), Academics (Institute of Communication and Computer Systems from the National Technical University of Athens- Greece, the Engineering School from Cádiz– Spain and the Research Centre for Information Technology from Karlsruhe – Germany) and an electronic design company (M.S.C.- Spain/Germany).

This report is part of the deliverable D1.1 belonging to the Workpackage 1. In this piece of the hole report can be found the information about the sensors and the ad-hoc designed electronic device to be used at the patient's homes.

This document has been developed by UCA.

AMICA Consortium (www.amica-aal.com)

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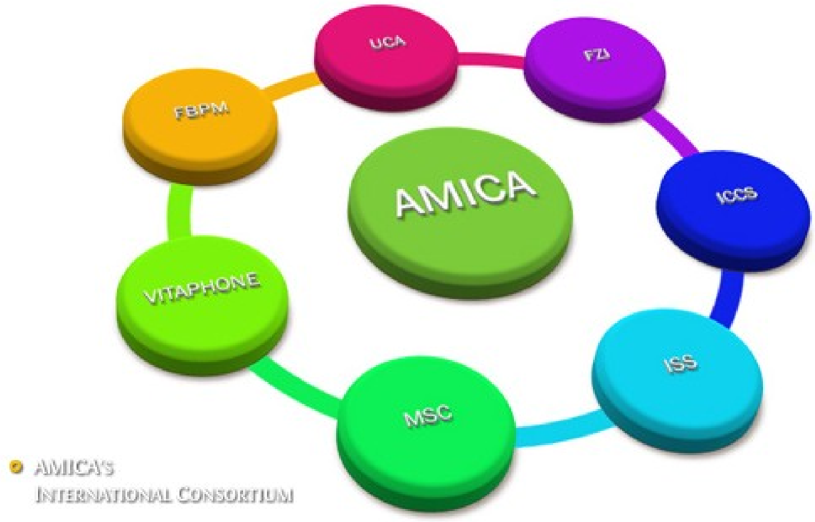
EXECUTIVE SUMMARY

AMICA PARTNERS



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0. BACKGROUND

The purpose of this section is to introduce the:

- ✓ AMICA Project
- ✓ Purpose, scope and context of this deliverable
- ✓ Intended audience for the deliverable
- ✓ Document Structure
- ✓ External References

0.1. AMICA Project

The Autonomy Motivation & Individual Self-Management for COPD patients (AMICA) is aimed at the **disease management** and **medical care of chronic obstructive pulmonary disease (COPD) patients**. AMICA is a Research and Development project sponsored under the Europeans Commission's Ambient Assisted Living programme as well as its projects members. Its official website is http://www.amica-aal.com.

It is aimed at providing medical management and medical care to patients suffering from Chronic Obstructive Pulmonary Disease (COPD). COPD is a progressive pulmonary disease characterized by reduction in airflow and is not fully reversible. COPD is the major cause of mortality and increased levels of disability, particularly in the elderly. Symptoms vary among individuals and include breathlessness, dyspnea, abnormal sputum and chronic cough. Exposure to tobacco smoke is by far the most important risk factor in the development of COPD and is associated with high levels of morbidity and mortality.

AMICA'S main objective is to develope and assess long-term COPD management solutions based on innovative Information and Communication Technologies (ICT) that:

- ✓ Allows early detection of COPD exacerbations through the use of a multifunction biomedical system able to yield continuous and sporadic data on heart, breathing and physical activity. This helps to avoid hospitalization and enhances quality of life of elderly COPD patients.
- ✓ Offers a user-friendly design for the elderly.
- ✓ Provides remote monitoring and home-based care
- ✓ Integrates a technical solution with a holistic service approach.
- ✓ Fosters prevention and self-management through immediate comprehensive feedback and efficient personalized assistance.
- ✓ Increases levels of therapy compliance providing effective incentives schemes such as health treatments abroad as an added bonus while it reduces public

health care costs and provides business opportunities on the health tourism market.

0.2. AMICA project started April 2009 and lasts for 3 years until April 2012 with a total budget budget of 2.783.139,48€. Seven partners spread across Europe are involved including medical companies and foundations (Vitaphone - Germany, I.S.S- Spain. and the Foundation for Biomedical Research Management- Spain), Academics (Institute of Communication and Computer Systems from the National Technical University of Athens- Greece, the Engineering School from Cádiz– Spain and the Research Centre for Information Technology from Karlsruhe – Germany) and an electronic design company (M.S.C.- Spain/Germany).

0.3. Deliverable purpose, scope and context

The present report is the first deliverable belonging to the Work Package number 6 “Health Economics, Service & Business Models” of the AMICA Project.

The AMICA project, “Autonomy, Motivation & Individual Self-Management for COPD patients”, is being funded by the Ambient Assisted Living Joint Programme and it is aimed at the disease management and medical care of chronic obstructive pulmonary disease patients. This management will be achieved by the means of the development of a healthcare and telemedical solution and service platform: the AMICA system.

Work Package number 6 will develop, among the whole project duration, an Economical analysis of the whole disease and system with the aim of developing a healthcare and care management service based on the AMICA system that allow the development of valuable business models for the exploitation of the project results.

To achieve this objective, the first step needed is to analyze the economical burden and economical costs caused by the illness. This is the aim of the present report.

0.4. Audience

0.5. Document Structure

The points needed to develop a “Health and Economical Analysis” are:

a) An Introduction about the illness and the burden that it causes. A description of the classification and quantification of the illnesses medical costs will also be included.

b) A description of the methodology used to find and summarize all the information obtained in order to develop the report will come next.

c) An analisys of the economical burden of the illness, based on an epidemiology description of the illness, and it will include a mortality, morbidity and prevalence analysis. This point will help to understand the importance of the illness at a global level.

d) The fourth step will be to analyze the economical costs of the illness found related to de illness. In this point, the costs per country will be analyzed. The analyzed countries have been chosen for two different reasons. On one side some of them are the countries of the partners of the consortium (Spain, Greece and Germany) and on the other side, some have been chosen as representative of the most relevant health systems in the world (USA, UK, Sweden and Norway). The costs related to the different stages of the illness will be described. The costs per treatment and programs will be also analyzed by the means of cost-effectiveness. For the last in this point, the telemonitoring existing systems will be also analyzed in terms of economical cost and economical saving.

In the last point, several conclusions about all the information included in the report will be extracted.

1. INTRODUCTION

The **Chronic Obstructive Pulmonary Disease (COPD)** is one of the leading causes of morbidity and mortality worldwide, and the functional and medical care resource consequences of COPD on individuals, families, healthcare organizations and society are substantial (Sullivan et al., 2000). It is also one of the main causes of disability in the world, particularly in developing countries. For these reasons, COPD is the chronic respiratory disease that represents the most significant, and ever increasing, world-wide public health problem; its epidemiological, clinical, social and economic impact will increase in the near future making it the third most important cause of dead in the next 10-15 years (Dal Negro, 2008). This growing of the burden of COPD is partly due to the ageing of the world's population and partly to the continued consumption of tobacco which is the most important risk factor for this disease (Buist et al., 2007).

The objective of this report is to achieve the knowledge of the social, functional and economic burden of illness and the cost-effectiveness of prevention strategies and treatments. All this information will promote the general knowledge of COPD. This knowledge is needed to better afford the needs of those who search for ways to minimize the cost impact of chronic disease (financers of health care services) and those who seek to optimize the health of those under their care (delivers of health services).

In this introduction several points will be developed with the intention to explain some concepts that will be further used in the report. Those concepts will be: **diagnosis**, due to its big importance in the definition of the number of people affected by COPD; the most important **risk factors** will be developed in order to better understand the different epidemiologic data found; and a explanation of the most frequent ways of calculation of the **economic burden** caused by COPD to the society will be made.

1.1. Diagnosis

COPD is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with abnormal inflammatory response of the lungs to noxious particles or gases. Symptoms, functional abnormalities and complications of COPD can partly be explained on the basis of this underlying inflammation and the resulting pathology. These changes may also have systemic consequences (European Respiratory Society et al., 2003).

The impact of COPD on an individual patient depends on the degree of airflow and the severity of symptoms (especially breathlessness and decreased exercise capacity). In this sense, the characteristic symptoms of COPD are **chronic and progressive dyspnea**, **cough** and **sputum production**. Chronic cough and sputum production may precede the development of **airflow limitation** by many years, but, sometimes, significant airflow limitation may develop without chronic cough and sputum production (GOLD, 2008).

All those symptoms together with the spirometry measures are used to divide the illness in four different stages (GOLD, 2008). These stages are described in chart 1. **Spirometry** is the first method used in the diagnosis of COPD. But, spirometry has been shown as a method with no relation with the ability of performing daily activities, the quality of life related to health status and the management of sanitary resources and for this reason should not be used as a daily method for the control of the illness (Ketelaars et al., 1996).

Chart 1. Description of the different stages of COPD (GOLD, 2008)

Stage I - Mild COPD: This stage is characterized by mild airflow limitation. Symptom of chronic cough and sputum production may be present, but not always. At this stage, the individual is usually unaware that his or her lung function is abnormal.

Stage II – Moderate COPD: This stage is characterized by worsening airflow limitation, with shortness of breath typically developing on extension and cough and sputum production sometimes also present. Patients in this stage typically seek medical attention because of chronic respiratory symptoms or an exacerbation of their disease.

Stage III – Severe COPD: This stage is characterized by further worsening of airflow limitation, greater shortness of breath , reduced exercise capacity, fatigue and repeated exacerbations that almost always have an impact on patients quality of life.

Stage IV – Very severe COPD: At this stage, quality of life is very appreciably impaired and exacerbations may be life threatening.

While the importance of making an accurate diagnosis is not in doubt for patients with diabetes or chronic renal failure, it has been a slow process to adopt a similarly rigorous approach to respiratory conditions, especially COPD. Thanks to the efforts of many organisations, especially the European Respiratory Society (ERS), the American Thoracic Society (ATS) (American Thoracic Society et al., 2004), and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) programme (GOLD, 2008), there is now a much wider appreciation of the need for objective diagnosis in common conditions such as COPD (Calverley, 2008) (Chart 1).

But, there are some problems with spirometric measurements performed in the primary care settings to be used as a COPD diagnosis method. One of these is its accuracy (Zielinski et al., 2006). Several studies have found **insufficient quality** of spirometries performed in the primary care setting (Eaton et al., 1999; Schermer et al., 2003), which is in contrast with the **high repeatability** of spirometries performed by experienced personnel reported by other authors (Enright et al., 2004). Another problem is related to the **misuse of the spirometric routine** in the health care providers, mainly due to the poor recognition of the role of spirometry in the diagnosis of COPD and also the lack of knowledge in conducting and interpreting the test (Joo et al., 2009).

Despite of this, we are facing a costly but preventable disease that has substantial implications for the populations, and that is highly **underdiagnosed and overdiagnosed** both at the same time. All these problems with the diagnosis method used make that many people suffering from COPD are not properly diagnosed and at the same time, many people who has been diagnosed with COPD show other diseases that cause respiratory problems when, finally, they perform an spirometry test (GOLD, 2008; Joo et al., 2009).

All this makes the interpretation of measurements of the prevalence of disease and mortality and intercountry comparisons extremely problematic. This is mainly due to several facts:

- COPD has been **widely underdiagnosed** due to de difficulties found in the spirometric methodology (Eaton et al., 1999; Schermer et al., 2003; Joo et al., 2009).
- The existence of misuse of spirometry and, therefore, the **different methodologies used in the diagnosis** of COPD, due to de inexistence of standardized protocols (Calverley et al., 2000; Calverley, 2008). There are different ways of diagnosis focuses. These are medical diagnosis, diagnosis based in the presence of simptoms and diagnosis based in the presence of limitation in the airflow (with or without using bronchodilator). The method used in the diagnosis will produce different results in the epidemiology studies (Soriano et al., 2007).
- The **COPD term has not been widely used** by physicians or other health professionals and in many cases it has not been recognized by the public until recent years (European Respiratory Society et al., 2003). This is mainly due to the fact that COPD has been considered as a heterogeneous group of diseases with similar manifestation and includes disparate and overlapping disease processes such as chronic bronchitis, emphysema, asthma, bronchiectasis, and bronchiolitis (Stockley et al., 2009).
- The high presence of **comorbid pathologies** in COPD patients make this illness underappreciated as a contributor to mortality (Mannino et al., 2006; Mannino et al., 2007).

The importance of a correct diagnosis of the illness is out of any doubt. Setting the correct treatment program to the patient, taking into account his stage of the illness can decrease his symptoms and improve his quality of life (Joo et al., 2009).

1.2. Risk factors

The risk of developing COPD has been related to an interaction between **genetic factors** and many different **environmental exposures**, which could also be affected by comorbid disease. The risk factors are the following (Mannino et al., 2007):

- **Genetic factors:** Several genes have been implicated in COPD, and some complex relations between the lung function of parents and children have been described (Mannino et al., 2006). Also, some genes have been implicated in COPD (Keatings et al., 2000; Celedon et al., 2004).
- **Tobacco smoke:** Worldwide, tobacco smoke remains the most important cause for COPD. In this sense, genes show their importance because not all smokers develop COPD. Lately, however, a much higher proportion of smokers have been noted to develop COPD (Mannino et al., 2006).
- **Occupational dust, vapors and fumes:** Exposure to various dusts, chemicals, vapors and fumes in the workplace is a factor for many people with COPD. Available data estimates that 19,2% of COPD cases in the USA where attributable to work exposures (Hnizdo et al., 2002).
- **Indoor air pollutants:** Globally, the most important risk factor for development of COPD might be exposure to biomass fuel such as coal, straw, animal dung, crop residues, and wood which are used to heat and cook in poorly ventilated homes ()(Lopez et al., 2006b).
- **Outdoor pollutants**: The risk attributable to outdoor pollutants in development of COPD is much smaller than that for indoor air pollutants (Lopez et al., 2006b).
- **Ageing:** COPD prevalence, morbidity and mortality increase with age. Lung function reaches its peak level in young adults and starts to declines in the third and fourth decades of life. In fact, one reason for the increasing prevalence of COPD in recent years is the changing demographics of the world's population. The result is that a larger proportion of the world's population id living longer and is at risk for chronic medical disorders such as COPD (Jemal et al., 2005; Mannino et al., 2006).
- **Infections:** Infections have an important role in both development and progression of COPD. Exposure to infection in early life could predispose an individual to suffer respiratory problems during his life. Most COPD exacerbations are related to bacterial or viral infections (Wedzicha et al., 2007).

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- **Asthma:** Increased bronchial responsiveness, a hallmark of asthma, leads to development of COPD, although this topic remains controversial (Soriano et al., 2003).
- **Gender:** The role of gender in development and progression of COPD is controversial. Historically, COPD has been far more frequent in men than in women, related to patterns of smoking and occupational exposures. Lately, however, COPD prevalence seems to be becoming equal in men and in women from high income countries in which smoking habits are similar between sexes (Silverman et al., 2000; Mannino et al., 2002; de Torres et al., 2005; Lopez et al., 2006b).
- **Socioeconomic and related factors:** Poor populations tend to have a higher risk of developing COPD and its complications than their wealthier counterparts (Lopez et al., 2006b). However, poverty is regarded as a surrogate measure for many factors that subsequently increase the risk of COPD, such as poor nutritional status, crowding, exposure to pollutants including high work exposures and high smoking rates (in countries of low and middle income), poor access to health care, and early respiratory infections (Anto et al., 2001).

1.3. The burden caused by illnesses: how to quantify it.

Several aspects can be taken into account when defining the burden that an illness causes to the society. In one side, the epidemiology studies analyze how the illness affects the population. This analysis is based on public health and preventive medicine and it is used in health research for identifying risk factors for disease and determining optimal treatment approaches to clinical practice. Some definitions related to epidemiology terms can be found in chart 2.

Chart 2. Epidemiology definitions

Epidemiology *is the scientific study of the causes, distribution, and control of disease in populations.*

Mortality *is the ratio of deaths in a population during a determined period of time.*

Morbidity *is the Ratio of people who fall ill in a defined time and place*

Prevalence *is the ratio (for a given time period) of the number of occurrences of a disease or event to the number of units at risk in the population.*

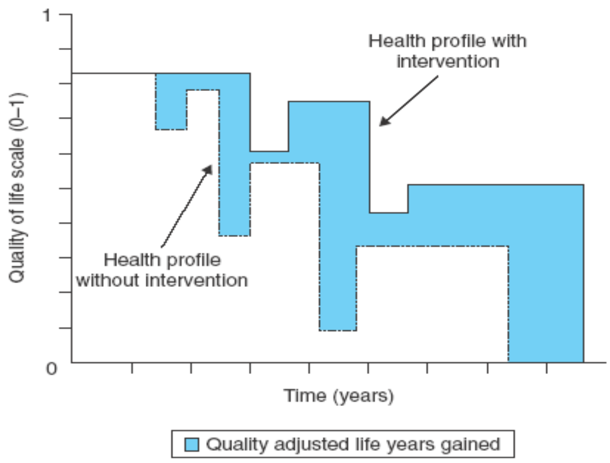
On the other side, also the economical cost of an illness is calculated, studied and evaluated. The concept of Economic burden, or cost-of-illness, and the studies related to it provide insight into the economic impact that illness has on society as well as on individuals and families. This approach separates economic burden into disease direct and indirect costs (Sullivan et al., 2000).

Direct costs are associated with medical treatments and care, representing the direct burden of COPD on the healthcare system. These costs include the cost of medicines, care providers, hospitalizations, appointments, ambulatory care, and more. These costs are related to the health service and societal perspective (Dal Negro, 2008).

Indirect costs, on the other hand, are less tangible, associated with the costs of morbidity and premature mortality; these costs include the loss of productivity or work time as a result of illness or premature death as well as costs to the families of those affected by COPD; in other words, the value of what could have been accomplished if the disease was not present. These costs are related to the societal and patients perspective.

For the calculation of **direct costs**, the outcome measures should be based upon the aim and intended use of the evaluation. The National Institute for Health and Clinical Excellence (NICE) recommends the QALY analyses as the appropriate way to make comparative assessments of value for money within a health system. Although not universally accepted, the QALY is nevertheless acknowledged as the most popular measure of utilities for making comparative assessment of the value for money of alternative treatment choices. The QALY quantifies changes in utility over the life of the patient and has two components: quality and quantity of life. A graphic representation of the QALY concept is shown in figure 1.

Figure 1. Quality Adjusted Life-Year profiles for a hypothetical patient with and without a treatment intervention. Profiles weight length of life by quality of life on a zero-one scale where one represents perfect health and zero death. In a chronic disease such as COPD, exacerbations might result in reduced quality of life for a period of time with incomplete recovery (Briggs et al., 2009).



The QALY is, thus, a measure of disease burden, including both the quality and the quantity of life lived (National Institute for Health and Clinical Excellence, 2009). It is used in assessing the value for money of a medical intervention. The QALY model requires utility independent, risk neutral, and constant proportional tradeoff behavior (Pliskin et al., 1980). This concept is based on the number of years of life that would be added by the intervention. Each year in perfect health is assigned the value of 1.0 down to a value of 0.0 for death. If the extra years would not be lived in full health, for example if the patient would lose a limb, or be blind or have to use a wheelchair, then the extra life-years are given a value between 0 and 1 to account for this.

Recently, the meaning and usefulness of the QALY is being debated (Prieto et al., 2003; Schlander, 2007; Mortimer et al., 2008). These authors claim that perfect health is hard, if not impossible, to define. Some argue that there are health states worse than death, and that therefore there should be negative values possible on the health spectrum (indeed, some health economists have incorporated negative values into calculations). Determining the level of health depends on measures that in some cases place more importance on physical pain or disability than in mental health. In addition, the effects of a patient's health on the quality of life of others (e.g. caregivers or family) do not figure into these calculations.

Once the QALY measurement has been used to compare how much someone’s life can be extended and improved, the cost effectiveness can be calculated. Cost effectiveness means how much the drug or treatment costs per QALY. In other words, cost-effectiveness is the cost of using the drugs to provide a year of the best quality of life available. This term can be calculated for one person receiving one QALY, but is more likely to be calculated as a number of people receiving a proportion of a QALY. Cost effectiveness is then expressed as monetary unit per QALY (National Institute for Health and Clinical Excellence, 2009).

An example of the calculation of the cost effectiveness for a treatment is shown in chart 3.

Chart 3. Example of QALY calculation (National Institute for Health and Clinical Excellence, 2009)

Patient x has a serious, life-threatening condition.

If he continues receiving standard treatment he will live for 1 year and his quality of life will be 0.4 (0 or below = worst possible health, 1= best possible health)

If he receives the new drug he will live for 1 year 3 months (1.25 years), with a quality of life of 0.6.

The new treatment is compared with standard care in terms of the QALYs gained:

Standard treatment: 1 (year’s extra life) x 0.4 = 0.4 QALY

New treatment: 1.25 (1 year, 3 months extra life) x 0.6 = 0.75 QALY

Therefore, the new treatment leads to 0.35 additional QALYs (that is: 0.75 –0.4 QALY = 0.35 QALYs).

The cost of the new drug is assumed to be £10,000, standard treatment costs £3000.

The difference in treatment costs (£7000) is divided by the QALYs gained (0.35) to calculate the cost per QALY. So the new treatment would cost £20,000 per QALY.

In the calculation of the cost effectiveness, each drug is considered on a case-by-case basis. Taking into account that the reimbursement of one treatment will displace health care resources spent on other treatments within the health system (so called opportunity cost), it is important to ensure that the treatment reimbursed provides sufficient value for money. For this reason, a "guide price" or a threshold from which it can be decided whether or not any one treatment should be reimbursed by the health care system is necessary. In the United Kingdom, NICE's documented threshold is said to be between £20,000 and £30,000 per QALY (Rawlins et al., 2004). This means that below £20,000 per QALY there is a high probability of the technology being accepted and that above £30,000 per QALY there is less chance of the technology being accepted.

Another concept quite used in the cost-effectiveness calculation is the so called **incremental cost-effectiveness ratio**, or iCER ratio, which represents the additional cost of one unit of outcome gained, for example a QALY, by a healthcare intervention or strategy, when compared to the next best alternative, mutually exclusive intervention or strategy. The iCER is calculated by dividing the net cost of the intervention, by the total number of incremental health outcomes prevented by the intervention (for example calculated QALYs).

On the other hand, and regarding **indirect costs**, those are referred to the morbidity and mortality caused by the disease. They establish the impact that the disease may have on national production. The most commonly used method of calculation is based on human capital in which days of work, whether due to disease or death, are transformed into monetary units by the application of the mean returns. This method has been extensively criticized. One of the reasons for the criticism is that this method does not include the collectives that are not integrated in the labor market, such as children, the elderly, housewives, etc. In those groups can be included people affected by COPD, for example.

The understanding of the epidemiology of a disease, as well as the estimates of the disease costs is important for appreciating the overall disease burden and is useful for estimating the disease effects in both the patients themselves and society. Estimates of the economic burden of a disease are important for informing policy decisions. Healthcare decision makers use information on the magnitude of cost associated with a disease and what might reasonably be expected in the future when making resource-allocation decisions. The cost estimates of the components of a disease are vital for developing health economic models of diseases (Chapman et al., 2006).

In this report a whole analysis of the economical burden and economical costs of the COPD illness will be developed with the aim of developing a healthcare and care management service based in the AMICA system that allow the development of valuable business models for the exploitation of the project results.

In order to develop the present report, the methodology used has been the following.

2. METHODOLOGY

The methodology that has been followed in order to achieve the planned objective of this report started with an exhaustive search of bibliography in different sources:

- Medical and scientific journals and books (Chest, European respiratory Journal, Thorax, Respiratory Medicine, etc.).
- National and International databases (WHO, Eurostats, etc.).
- National health system web pages (NICE, Department of Health and Human Services. Centers for Disease Control and Prevention, etc.).
- Results form other European and National research projects (6th Framework Programme, 7th Framework Programme, National projects, etc.)
- National and International COPD management guidelines (GOLD Guidelines, European Lung White Book, GARD Book, ATS-ERS Guidelines, etc.).

The performed search has been focused in some parameters:

- Some key words have been used: COPD; pulmonary; obstructive; costs; burden; chronic; epidemiology; cost-effectiveness.
- The information has been centred in some countries (USA, UK, Norway, Sweden, Germany, Spain and Greece).
- It has been selected the most recent information available.
- Once all the relevant information was found, a systematic work was made in order to resume the information and summarize it in the present report.

The summary of all the information recorded, will start with the description of the Economical burden of the illness.

3. EPIDEMIOLOGY

Epidemiology is the study of diseases from a population-based perspective; it involves the factors affecting disease rates and the distribution of disease and disabilities in populations. Thus, it can be divided into mortality, morbidity, prevalence and incidence.

Epidemiology studies give an idea of the health status of the population in relation to the illness studied. They are also used for the inference of economic costs and burden that such illness causes to the patients themselves and the society.

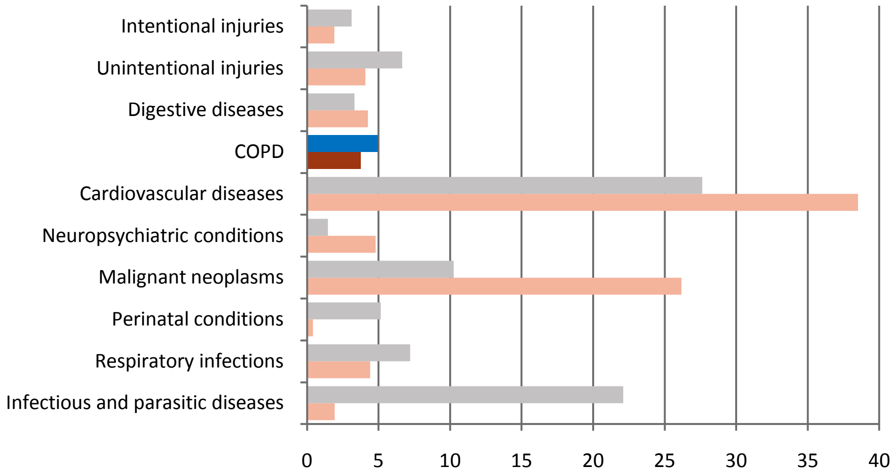
In this point, the three main components of the epidemiology will be analyzed regarding to COPD: mortality, morbidity and prevalence. Besides, the most important risks factors of the illness will be taken into account in the analysis of the situation.

Before starting with the analysis of the epidemiology, it must be highlighted that the true rate of COPD within the general population is likely to be greater than that recorded (see point 1.1 Diagnosis). As said before, on one side, there is much evidence that suggests COPD is heavily underdiagnosed worldwide (Calverley et al., 2000);(Fukuchi et al., 2004; Zielinski et al., 2006) and in the other side, the rates of COPD in the different countries are affected by the different methods used in the diagnosis in each of them, and this is likely to be the situation, particularly among mild cases of COPD. This mixture in the existing data explains the great difference between the different statistics of organizations and countries.

3.1. MORTALITY.

The World Health Organisation estimates that deaths attributable to COPD are the fifth largest killer globally in developed countries and they accounted for 5% of adults deaths worldwide in 2001 (figure 2) and 2005, meaning between 2,75 to 3 million of deaths due to COPD those years (US Department of Health and Human Services., 2004; Lopez et al., 2006b; GOLD, 2008);(Soriano Ortiz et al., 2009) but the forecasts say that will become the third leading cause of death worldwide in 2020 (GOLD, 2008). In fact, COPD is the only leading cause of death that still has a rising mortality rate (Gudmundsson et al., 2006). This increasing mortality is driven by the expanding epidemic of smoking and the changing demographics in most countries with more of the population living longer.

Figure 2. Percentages of deaths respect total deaths by cause in the world in 2001. It is represented in red high income countries and in blue low and middle income countries. Data source (Lopez et al., 2006b)



Mortality data are rarely available and when available they usually underestimate COPD as a cause of death by around 50% (World Health Organization, 2007). This is due to several factors. On one side, it has been sown that COPD is highly underdiagnosed all over the world (Eaton et al., 1999; Schermer et al., 2003; Joo et al., 2009) and on the other side, frequently, the final defined cause of death is not COPD, even if the person was diagnosed with COPD, rather that the defined cause is frequently respiratory failure or even heart failure, etc. (Sin et al., 2006; Soriano Ortiz et al., 2009; Terzano et al., 2010). In fact, some available data suggests that COPD might be underappreciated as a contributor to mortality, particularly when it could be an important comorbid disorder that leads to development of a lethal disease, such as lung cancer or stroke (Chapman et al., 2006; Mannino et al., 2006; Mannino et al., 2007);(World Health Organization, 2007) World Health Organization, 2007).

The population risks and mortality rates are usually difficult to be interpreted at individual level. Many people do not feel them as a near real personal risk. Table 1 shows a recent modeling approach to the mortatity risk for non-smokers, smokers and by age (Woloshin et al., 2008). Table 1 shows that COPD has the third higher risk after lung cancer and heart disease in smokers older than 60 years old but it is the last one in non-smokers.

Table 1. Risk chart for smokers and non-smokers. The numbers on each cell mean the number of 1000 men who will die in the next 10 years from each of the illnesses listed. Adapted from (Woloshin et al., 2008).

Age	Smoking status	COPD	Heart disease	Stroke	Lung Cancer	Pneumonia	Accidents	All causes combined
Men								
45	Non-smoker	**<1**	6	1	1	1	6	35
	Smoker	**1**	21	3	8	1	6	91
60	Non-smoker	**1**	32	5	2	2	5	115
	Smoker	**16**	56	11	59	3	4	256
75	Non-smoker	**6**	137	32	8	11	11	449
	Smoker	**60**	140	39	109	16	9	667
Women								
45	Non-smoker	**<1**	2	1	1	<1	2	25
	Smoker	**2**	9	3	7	<1	2	45
60	Non-smoker	**2**	14	4	3	1	2	84
	Smoker	**18**	31	8	41	2	2	167
75	Non-smoker	**6**	89	30	7	8	7	335
	Smoker	**61**	99	34	58	14	7	463

Differences between geographic origins

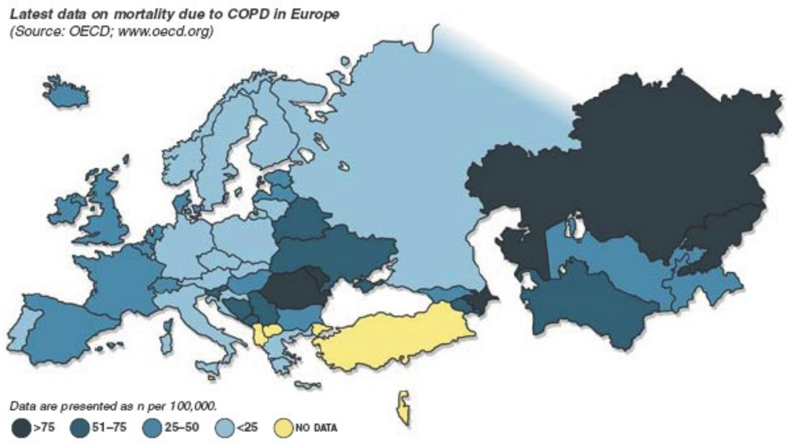
Making a geographical comparison can be seen that the proportion of deaths for COPD varies significantly between regions of the world. Of particular concern is the East Asian and Pacific region where COPD accounts for 10.8% of all deaths and where COPD is ranked as the second leading cause of death (table 2)(Lopez et al., 2006b).

Table 2. Percentages of total deaths and number of position in the 10 leading causes of deaths ranking in 2001 per origin. Adapted from (Lopez et al., 2006b).

Region	Percentage of total deaths	Number of position
High income countries	**3,8**	**5**
Low and middle-income countries	**4.9**	**6**
East Asia and Pacific	10,8	2
Europe and Central Asia	2,3	4
Latin America and the Caribbean	3	7
Middle East and North Africa	2,1	10
South Asia	4,3	7
Sub-Saharan Africa	-	-

The distribution of the mortality rates in Europe is also shown in figure 3. Comparing data from USA and Europe it has been shown that while the mortality rate trend in USA and Canada is increasing, in Europe is decreasing. There is no obvious reason for this difference but, presumable factors such as awareness, changing terminology and diagnostic bias may contribute to these differences (GOLD, 2008).

Figure 3. Mortality rates of COPD in Europe (European Respiratory Society et al., 2003).



The data for the countries relevant for the AMICA project, is shown in table 3. This table shows a great difference between Europe and the USA, where USA (41,6) doubles the European ratio (18,7). This can be due to the different methodologies used for the calculations and the estimates made. The American ratio is even bigger if the number of deaths is calculated taking into account any mention of the Chronic lower respiratory disease cause on the death certificate reaching 84 deaths each 100.000 inhabitants. America, which has the higher ratio, is followed by UK and Norway, having both of them ten points more than the rest of the countries (29 and 28 respectively). All the rest, Spain, Germany, and Sweden have all nearly the same ratio between 15.9 to 19,5) and the lowest belongs to Greece (11,1)

Table 3. Number of deaths in absolute number and by ratio (number of deaths per 100.000 inhabitants)

	Period	Absolute number	Ratio
European Union[a]	2007	154.277	18,7
Spain[a]	2007	15.699	19,5
Greece[a]	2008	2.173	11,1
Germany[a]	2008	26.235	17,3
Sweden[a]	2007	2.710	15,9
Norway[a]	2008	2.103	28
United Kingdom[a]	2007	29.473	29
USA[b]	2004-2006*	125.834	41,6

*Estimates are presented as three-year annual averages to obtain stable estimates.
Source: [a](European Commission Eurostat, 2010); [b](Centers for Disease Control and Prevention. National Center for Health Statistics., 2010) Data correspondent to the J40-47 “Chronic lower respiratory diseases” of the ICD10 codification.

Regarding the different developing status of the regions in the world, other data show that in 2001, COPD was the fifth leading cause of death in high-income countries, accounting for 3,8% of total deaths and it was the sixth leading cause of death in nations of low and middle income, accounting for 4,9% of total deaths (figure 2, table 2) (Lopez et al., 2006b). On the other side, WHO estimates that in high-income countries, 73% of COPD mortality is related to smoking while low and middle income countries account for only a 40% (Lopez et al., 2006b). This data shows the great importance of smoking in the development of COPD in high income countries but, it is not so important in low and middle income countries where other risk factors have to promote the development of the illness. These differences are mainly due to the fact that occupational and environmental exposures are in general more frequent in countries of low and middle income than in those with high income. In addition, the existence of early respiratory infections, tuberculosis and malnutrition, also have influence in the development of the illness (Mannino et al., 2007).

Differences between sexes:

Comparing the mortality rates due to COPD in European countries between men and women, it is shown that in 1990 it was two or three times higher in males than in females (70% in men against 30% in women), nevertheless, these differences are getting smaller recently (European Respiratory Society et al., 2003; Chapman et al., 2006) and in fact, 50,3% of the deaths attributable to COPD in 2000 in the USA where among women. This means a significant increase comparing with the data in 1990 (World Health Organization, 2007).

Even more recent data shows that in 2001, the number of deaths between men and women where nearly the same being due to COPD 4,7% and 5.1% respectively of the total deaths. The higher percentage shown in women in both studies is attributed to the higher expectancy of life of women, it makes them to live longer and therefore, have more illnesses related to age. In number of people these data mean 1,21 millions of men versus 1,17 millions of women (Lopez et al., 2006b). Also, the estimated risk of dying between men and woman is nearly the same in COPD both in smokers and non-smokers (table 1).

3.2. PREVALENCE.

In epidemiology, the prevalence of a disease in a statistical population is defined as the total number of cases of the disease in the population at a given time, or the total number of cases in the population, divided by the number of individuals in the population (chart 2). It is usually shown as a percentage.

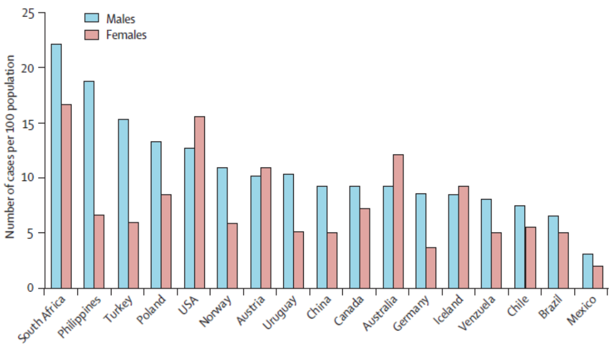
Until recently, most of the information available on COPD prevalence came from high income countries. Even in these countries, data greatly underestimate the total burden of COPD because the disease is usually not diagnosed until it is clinically apparent and moderately advanced and the definition of COPD varies between studies (World Health Organization, 2007). Another relevant problem in the prevalence calculation of COPD is the different methods for the diagnosis that can be used (GOLD, 2008) (see point “1.1 Diagnosis”) and the different methods used in the data calculation (Mannino et al., 2007).

The Global Burden of Disease Study has estimated the worldwide prevalence of COPD as 834 per 100.000 people. This means that approximately 44 million cases of people suffering COPD worldwide, or in other words, the same number of people as the whole Spanish population (European Respiratory Society et al., 2003). Other authors estimate the prevalence of physiologically defined COPD in adults aged 40 or more in between 9-10% (Halbert et al., 2006) .

Differences between geographic origins

Great differences between countries have been found worldwide ranging from values of 3 to 23% (figure 4). These differences have been reported by several authors (Lopez et al., 2006a) and may be due to many factors including differences in diagnostic methods (see point "1.1 Diagnosis"), year of study, age of the population, case definition, study design, sample size, data analysis and prevalence of the main risk factors such as tobacco smoking.

Figure 4. Estimated prevalence of GOLD stage 2 or higher COPD. Estimates have been made in small regions of the listed countries and do not necesarily represent national prevalence estimates. Source: (Mannino et al., 2007)



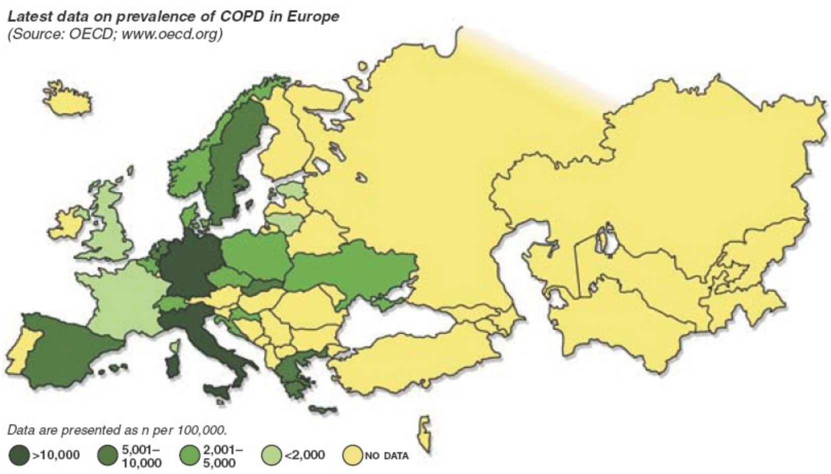
By regions, the highest values of prevalence have been found in **South-East Asia** followed by the **Western Pacific** (table 4). This data agrees with the mortality (see point 3.1 "Mortality") where the highest values were found in East Asia and Pacific (table 2). Both of these data show the high number of people affected by this illness in the Asian countries. Some authors explain this fact by the phase of the tobacco epidemic in the region and the importance of other risk factors in these countries. Regarding the first point, the highest prevalence of smoking has been found in Asia, which is experiencing a smoking epidemic at the same time as the prevalence for smoking is falling in the Western world. Other risk factors such as occupational exposures to dust, vapors and fumes can cause specific occupational respiratory diseases. Another important risk factors quite frequent in Asia are the combustion of biomass fuel for heating or cooking in poorly ventilated homes, the ambient air pollution and the high prevalence of other respiratory illnesses in early childhood such as pulmonary tuberculosis and HIV positive status (Tan et al., 2008).

Table 4. Pooled prevalence estimate from different epidemiologic studies (95% confidence interval). Adapted from (Halbert et al., 2006).

Pooled prevalence	
Africa	no data available
Americas	4.6 (2.8-7.6)
Eastern Mediterranean	no data available
Europe	7.4 (5.9-9.3)
South-East Asia	11.4 (4.4-26.4)
Western Pacific	9.0 (3.0-24.1)

Regarding the **European countries**, it has been calculated that the prevalence of clinically relevant COPD patients varies from 4 to 10% of the adult population with a considerable increase with age, particularly among smokers (Lopez et al., 2006a). Figure 5 shows the prevalence found in the different European countries (European Respiratory Society et al., 2003). The figure shows that Germany and Italy are the countries with higher COPD prevalence (more than 10%) followed by Spain, Greece, Norway, Netherlands and Slovakia (between 5 and 10%) . The lower rates were found in France, UK, Estonia and Lithuania (less than 2%). It has to be taken into account the high number of countries which have no data available about their prevalence on COPD.

Figure 5. Prevalence rate (/100.000) of COPD in Europe (European Respiratory Society et al., 2003).



For example, in Spain, the IBERPOC study, performed between 1996 and 1997, quantified in a 9,1% the prevalence of COPD in the Spanish population with ages comprised between 40 to 69. This data is not complete since the prevalence continues growing after the 70's. Even that this data is quite old, the situation has not improved (Izquierdo, 2003).

In general, it has been detected a lack of good quality prevalence data from outside Europe and North America (Halbert et al., 2006). In this sense, The Burden of Obstructive Lung disease (BOLD) study is currently being carried out in different parts of the world including low and middle income countries in order to improve the data regarding the burden caused by COPD (Buist et al., 2007). This study compares the prevalence and burden of COPD across the world using the same protocol, including the BOLD questionnaire and spirometry. Some data are already available and show that the prevalence of COPD is far higher than is recorded.

Differences between sexes

In general, the prevalence of COPD is higher in men than in women (table 5) (Chapman et al., 2006; Lopez et al., 2006a). That is because smoking is a major risk factor in men but recently, some studies have found high rates non-smoking women in low and middle income countries. These rates may be associated with the use of biomass fuel (World Health Organization, 2007). In fact, many studies have identified biomass smoke as a primary risk factor for COPD in rural areas. It has been shown that women using biomass fuel for cooling have increased prevalence of respiratory symptoms attributable to COPD and substantially greater decline in lung function than women who do not use these fuels (Lopez et al., 2006a; Salvi et al., 2009).

Table 5. Pooled prevalence estimate from different epidemiologic studies (95% confidence interval). Adapted from (Halbert et al., 2006).

	Pooled prevalence
Male	9.8 (8.0-12.1)
Female	5.6 (4.4-7.0)

Effects of smoking

The prevalence of COPD is appreciately higher in smokers and ex-smokers than in non smokers (table 6) (Chapman et al., 2006; Chapman et al., 2006; Halbert et al., 2006).

Table 6. Pooled prevalence estimate from different epidemiologic studies (95% confidence interval). Adapted from (Halbert et al., 2006).

	Pooled prevalence
Smoker	15.4 (11.2-20.7)
Ex-smoker	10.7 (8.1-14)
Never-smoker	4.3 (3.2-5.7)

Effects of age

It has been widely demonstrated that the prevalence is higher in people over 40 years old than those under 40 (table 7) (Chapman et al., 2006; Halbert et al., 2006).

Table 7. Pooled prevalence estimate from different epidemiologic studies (95% confidence interval). Adapted from (Halbert et al., 2006).

	Pooled prevalence
<40 years	3.1 (0.8-5.0)
≥40 years	9.9 (8.2-11-8)

40-64 years	8.2 (6.5-10.3)
≥65 years	14.2 (11.0-18.0)

In fact, data from both the **United States** and the **United Kingdom** show that the prevalence of COPD is comparatively small among the under 45 years old but increases markedly throughout later years (US Department of Health and Human Services., 2004). For example, in UK, prevalence is approximately 1% of the general population, increasing with age to around 5% of men between 65 and 74, rising to 10% in men over 75 (Calverley et al., 2000).

3.3. MORBIDITY.

As said in chart 2, morbidity refers to the ratio of people who fall ill in a defined time and place. Morbidity measures traditionally are based in **physician visits, emergency department visits and hospitalizations** and in general, morbidity from COPD is high, compared to other illnesses. Patients need frequent primary and secondary care input. In fact it is predicted that COPD will rank seventh in 2030 as worldwide burden of disease (World Health Organization, 2007).

COPD morbidity data are no more reliable than mortality or prevalence, since the various ways of measuring morbidity are prone to external factors such as the availability of hospital beds, local and regional use of filters from primary to secondary care, the coding for utilization being affected by reimbursement patterns and other such potentially biasing factors (Chapman et al., 2006). Despite this, the access to reliable morbidity data is of great importance because it can be used as a measure of health services needs and the costs related to them. In fact, Due to the main characteristics of the illness and the difficulty found in the differences of its diagnosis, the limited data available about morbidity due to COPD is that it increases with age and it is greater in men than in women. In fact, COPD in its early stages is usually not recognized, diagnosed and treated, and therefore may not be included as a diagnosis in a patients medical records (GOLD, 2008).

Hospitalizations attributable to COPD, as said before, are common and their frequency is recognized as a prognostic marker (World Health Organization, 2007). In fact, the European Respiratory Society White Book (European Respiratory Society et al., 2003) states that the number of hospitalizations for COPD in 1993 in Germany was 125.000, in Italy 40.000 and in the United Kingdom 73.000. Hospitalizations attributable to COPD are sharply increasing in most countries (World Health Organization, 2007).

Table 8 shows the number of hospital discharges in the AMICA project relevant countries.

Table 8. Numer of hospital discharges by absolute number and by ratio (number of hospital discharges per 100.000 inhabitants).

	Period	Absolute number	Ratio
European Union	-	-	-
Spain[a]	2007	85.020	189.4
Greece	-	-	-
Germany[a]	2007	209.192	254.3
Sweden[a]	2006	17.041	187,7
Norway[a]	2007	137.907	220.9
United Kingdom[a]	2007	10.402	226.1
USA[b]	2006	557.000	187

Source: [a](European Commission Eurostat, 2010); [b](Centers for Disease Control and Prevention. National Center for Health Statistics., 2010) [a]Data correspondent to the J40-44,47 "Chronic obstructive pulmonary disease and bronchiectasis" of the ICD10 codification.
[b]Data corresponding to "Chronic Obstructive pulmonary disease"

The higher ratio for hospital discharges belongs to Germany, followed nearly by UK and Norway. Susprisingly and despite the high level of mortality found in the USA, the hospital discharge there is not that high. Greek and European data for hospital discharge is not available (European Commission Eurostat, 2010).

4. ECONOMICAL DATA

Taking into account the difficulties found in the study of the epidemiology of the illness due mainly to the different methodologies for the diagnosis, the available economical data is very heterogeneous and variable depending on the year and the origin of the study. In different countries has been shown that the mean annual cost of COPD has progressively increased over the last few years and this increase has been shown as a general trend in different countries.

Besides, great costs per patient variations can be found across countries since these costs depend on how health care is provided and paid (Chapman et al., 2006). In fact, there is a direct relation between the severity of COPD and the costs of care This means that the distribution of costs change as de disease progresses (GOLD, 2008) making the stage of the illness another source of costs variability. This point will be further developed in point “4.2 Costs per stage of the illness”.

In this section the report will approach the costs of the illness from four different perspectives. First, the costs in the different countries and the variability in the data available from each of them will be discussed. Some countries have been selected to be included in the report as it is explained in sections 0.4 “Document structure” and 2. “Methodology”. Secondly, the importance of the stage of the illness in the increase of costs will be analyzed. For the last, both COPD treatments and programs will be described from the point of view of the cost effectiveness related to them.

4.1. COSTS PER COUNTRY

It is well-known that COPD is a very costly disease, but as COPD is frequently not listed as the underlying cause of death or the primary reason for hospitalization, as noted above (see point “3.1 Mortality”), these costs estimates may make the true cost of COPD underestimated (Mannino et al., 2006).

The situation of the selected countries is the following:

United States of America

COPD is a leading cause of death, illness, and disability in the United States. Between 2004 and 2006 the annual average of deaths was calculated in more than 125,000 (table 3) and 557,000 hospital discharges being COPD the main cause of admission in hospital in 2006 (table 4). An additional 8 million cases of hospital outpatient treatment or treatment by personal physicians were linked to COPD in 2000 (Department of Health and Human Services. Center for Disease Control and Prevention, 2009).

The evolution of the estimated total annual costs of the illness in the USA in recent years has been the following:

- In 1993 (Sullivan et al., 2000) the United States' economic costs of morbidity and mortality where estimated in US$23.9 billion (approx. more than 18.4 billion Euros). From these, US$14.7 billion (approx. 11.3 billion Euros) were due to direct costs and US$9.2 billion (approx. 7.1 billion Euros) were due to Indirect Costs shared in US$4.7 billion (approx. 3.6 billion Euros) in indirect morbidity and US$4.5 billion (approx. 3.5 billion Euros) in costs related to premature mortality.

  The same study determined that the largest contributor to the cost of COPD is hospitalization. Combining disease prevalence and illness burden, COPD costs an average of US$1,522 (approx. 1,150 Euros) per person per year or almost three times the per capita cost of asthma.
- In **2000**, the total annual costs of COPD in the US increased by more than 30%, reaching US$31 billion (approx. 51.6 billion Euros), with a substantial increase in indirect costs (Ramsey et al., 2004).
- In **2002**, the direct costs of COPD totaled US$18 billion (approx. 19.3 billion Euros) and the indirect costs totaled US$14.1 billion (approx. 15.1 billion Euros) (GOLD, 2008) making a total of US$32.1 billion (approx. 34.4 billion Euros).
- In **2003**, the US National Heart, Lung, and Blood Institute estimated that total costs (direct and indirect) of COPD where US$32.1billion (approx. 27.3 billion Euros) with direct costs of US$18.0 billion (approx. 15.3 billion Euros) (Mannino et al., 2007).
- A further increase was assessed in **2004**, with an estimated cost of US$37.2 billion (approx. 30.5 billion Euros) (Ramsey et al., 2004)

Taking into account this data, the **distribution of costs** of the USA total expenditures in COPD are the following (Sullivan et al., 2000):

- **Inpatient hospitalization** and **emergency department** accounted for the 72.8%;
- **outpatient clinic** and **office visits** accounted for the 15%.
- **drug prescription** accounted for the 12.2%.

In 2005, the **cost per patient** was estimated at US$2,700-5,900 (approx. 2,194-4,794 Euros) for attributable costs and at US$6,100-6,600 (approx. 4,956-5,362 Euros) for excess costs (Mannino et al., 2007).

United Kingdom:

As seen in the previous section, in the United Kingdom, the number of deaths accounted for COPD were more than 29,000 (Table 3) and the number of hospital discharges reached 10,000. (table 4).

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In **1996** (Sullivan et al., 2000), the National Health Service Executive published data showing that the medical cost of COPD in the UK was approximately £846 million (approx. 1 billion Euros) or £1154 (about US$2300) (approx. 1,300 Euros) per person per year.

In **2000**, the estimated annual cost of COPD was £982 million (approx. 1.6 billion Euros) (Britton, 2003).

Distribution of costs calculated is the following (Sullivan et al., 2000).:

- **Expenditures for pharmaceutical treatments** accounted for the 47,5%;
- **Ambulatory oxygen therapy** accounted for the 24,5%;
- **Hospital-based care** accounted for the 17,8%;
- **Primary care and community based services** accounted for the 10,2%.

The annual direct **cost per patient** of COPD in the UK was estimated at £819.42 (approx. 1,300 Euros) in a study performed between 2000 and 2001 with 3,265 patients from the UK (Britton, 2003) In the same study, the indirect costs were estimated in £819.66 (approx. 1,300 Euros) making a total of £1639.08 (approx. 2,600 Euros).

The average **length of the stay** among those admitted for a COPD diagnosis was 9.9 days (Sullivan et al., 2000).

Sweden and Norway:

In 1991 (Sullivan et al., 2000), the **expenditures for COPD** related medical care in Sweden were estimated in £115 million (approx. 125 million Euros). The estimated indirect cost was an additional £152 million (approx. 165 million Euros). The total amount reached that year £267 million (approx. 290 million Euros).

Spain:

Different studies performed in Spain between the years 2003 and 2004 have studied the costs related to the illness to the Spanish healthcare system.

In one of these studies (Masa et al., 2004), performed with 363 COPD patients, the **estimated annual cost** of COPD in Spain was calculated in €238.82 million (Masa et al., 2004).

Other study has calculated these costs in approximately €800 million in 1994 in Spain, including both direct and indirect costs. If only healthcare resources (direct healthcare costs) for COPD patients are examined, €319 million are spent annually from the focus of prevalence (Morera, 1992).

On the other side, the same study made a calculation of the **distribution of costs** (Masa et al., 2004). This study concluded that two where the main items responsible of the medical COPD costs in Spain:

- **Hospitalization** accounted for the greatest expenditure (41% of total),

- **Drug therapy** accounted for 37%.

The **cost per patient** was estimated in €198.17 per year, and €910.57 per previously diagnosed patient and year in the same study (Masa et al., 2004). Despite this, other study made among 192 COPD patients estimated the medium cost per patient and year in 1.712€ (García-Ruiz et al., 2003).

There are some other studies performed in Spain in the same years (Izquierdo, 2003; Miravitlles et al., 2003; Izquierdo-Alonso et al., 2004) and all this studies show remarkable variation in the ,medium cost per patient and year estimated. The values shown vary from 910€ to 3238€.

Germany

The **total direct costs** in 2003 in Germany have been calculated in more than 32.000 million € (Freytag et al., 2007).

The **cost per patient** in Germany has been calculated in 664€ (836€ if ambulatory care is included) (Freytag et al., 2007). Even thought another study published earlier estimated the annual cost per patient in 3027€ (Nowak et al., 2004).

The **distribution of costs** has been calculated as follows (Freytag et al., 2007):

- **Drug prescriptions** accounted for the 50,6%
- **Hospital care** accounted for the 17,8%
- **Remedies** accounted for the 6%
- **Medical devices** accounted for the 5%
- **Ambulatory care** accounted for 20,6%

The **average length of hospital sta**y for stages I, II and III was between 12,8 and 13,6 days. For stage IV the length of stay is considerably higher reaching 15,9 days(Freytag et al., 2007).

Greece

There is no data available about the costs of COPD in Greece

4.2. COSTS PER STAGE OF THE ILLNESS

Costs increase as disease severity moves from moderate to severe (with a much smaller increase between mild and moderate). As FEV deteriorates a general shift from outpatient care to hospitalization, an increase in the use of oxygen therapy and a subsequent increase in total costs occurs, especially in the most advanced stages of the disease (Briggs et al., 2009); (Chapman et al., 2006).

The increasing cost associated with the advanced stage of the disease is well illustrated in several studies. In a Swedish study performed with 212 patients with COPD, the smallest percentage (4%) of patients with severe disease accounted for 30% of the total costs, whereas 83% of patients with mild disease generated only 29% of costs (Jansson et al., 2002). In other study performed in Spain, the cost per person of severe COPD was more than 3 times that of moderate COPD and more than 7 times that of mild COPD (55,67€ for mild, 114,98€ for moderate and 413,52€ for severe)(Masa et al., 2004).

Exacerbations are the leading drivers of cost in COPD. A serious exacerbation will lead to hospitalization; indeed an exacerbation is the main reason why a COPD patient would attend hospital. COPD patients take up around 1 million bed days per year in the United Kingdom alone (Briggs et al., 2009).

In this sense, exacerbations and hospitalizations, in particular, constitute the most important direct healthcare costs associated with COPD. In fact, some studies have shown that the cost of hospital stay represents 40–57% of the total direct costs generated by patients with COPD, reaching up to 63% in severe patients (Chapman et al., 2006); (Mannino et al., 2007). Moreover, it has been calculated that only the 10% of the people with COPD account for more than the 70% of the total medical care costs (Sullivan et al., 2000).

For this reason, reducing or preventing disease progression and/or an exacerbation, (particularly severe exacerbations), will have a direct effect on the total cost of COPD. In England and Wales, McGuire calculated that for every exacerbation related hospital admission avoided, a total saving of approximately £1200 would be made (Briggs et al., 2009).

4.3. TREATMENTS AND COST-EFFECTIVENESS RELATED TO THEM

The aim of the existing treatments for COPD, in the absence of a disease cure is to prevent and control symptoms, reduce the frequency of exacerbations, improve health status and improve exercise tolerance (GOLD, 2008).

As seen in point 1.3 "The burden caused by illnesses: how to quantify it" one mean of measuring costs is to ascertain how expensive a specific intervention would be per quality-adjusted life year of improvement. Using this approach, WHO estimates that costs per quality-adjusted life year for COPD range from US$6,700–8,900 (approx. 5,000-6,600 Euros) for inhaled ipratropium to US$13,400 (approx. 10,000 Euros) for inhaled corticosteroids to US$238,200 (approx. 18,000 Euros) for lung transplantation, which are the most frequent treatments used (Mannino et al., 2007).

Taking into account that the COPD management is additive, this means, as the disease progresses more treatments are added (Briggs et al., 2009). The treatments usually recommended for the stages of the illness and their cost-effectiveness are the following (Briggs et al., 2009):

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Mild COPD:

Influenza vaccines are recommended to treat all COPD patients, regardless of severity. The cost for the vaccine for high risk people was found to be US$570 (€392) per life year saved. The **Pnuemococcol vaccine** is recommended for patients aged 65 years or over. For this subgroup, the cost-effectiveness ratio has been found to be between US$1.800 to US$2.200 (€1.238–1.513) per life year. Both vaccines represent good value for money.

Use a **short-acting bronchodilator**, short-acting anticholinergic when necessary: One study modelled the costs and cost-effectiveness of theophylline compared to ipratropium in moderate to severe COPD. In this case no Incremental Cost-Effectiveness Ratio (ICER) was calculated since ipratropium was found to be both less costly and more cost-effective than theophylline. Sometimes these products are combined and evidence exists to support one such combination. One study examined the efficacy of ipratropium combined with albuterol, compared to each monocomponent in moderate to severe COPD patients. The ICER for the combination product was not calculated: combining ipratropium with albuterol compared to albuterol alone was found to strictly dominate.

Moderate COPD:

Rehabilitation is a multifaceted approach which incorporates a wide range of programs to improve quality of life and functional independence and to reduce symptoms and disability for the patient. Areas within the rehabilitation program can include exercise and physical training, psychological, social interactions, education around the disease, and about nutrition. A recent US study found a marked reduction in cost following a rehabilitation program in terms of a reduction in health care utilization after 1 year of treatment compared to the previous year of no treatment (Raskin et al., 2006). Another study reports that the cost-effectiveness of a rehabilitation program leads to overall gains in utility in the patients receiving rehabilitation and also a drop in total costs, compared to the control group. The probability that rehabilitation was cost-effective was 90% at £10,000 and 95% at £17,000 (€ 24,405) (Griffiths et al., 2001). Given the data, rehabilitation seems to represent a cost-effective treatment.

Add **regular treatment with one or more long-acting btonchodilators/ anticholinergic**: Different studies have compared different existing treatments (Hogan et al., 2003; JONES et al., 2003; Oostenbrink, 2004; Oostenbrink et al., 2005; Maniadakis et al., 2006; Rutten-van Molken et al., 2007). In those studies, formoterol, salmeterol, tiotropium and ipratropium have been evaluated for their cost-effectiveness using the ICER ratio. The better cost-effectiveness was found in tiatropium in several of these studies (Oostenbrink, 2004; Oostenbrink et al., 2005; Maniadakis et al., 2006; Rutten-van Molken et al., 2007)

Severe COPD:

Add **inhaled corticosteroids** if exacerbations are repeated: This kind of treatment has been found to be cost-effective when given to patients with stages of the illness moderated and severe.

Concretely, Fluticasone has been found to improve several clinical outcomes, including FEV and in the proportion of patients remaining exacerbation free compared to placebo (Ayres et al., 2003).

Different studies have investigated the effects of joining a a β2-antagonist and a inhaled corticosteroid.

The first one studied the joining of Fluticasone and Salmeterol and concluded that the addition of a β2-antagonist to an inhaled corticosteroid may represent a cost-effective treatment in those patients who have a history of frequent exacerbations and poorly reversible COPD (Spencer et al., 2005).

Another studied the combination of Budesonide and Formoterol and found this treatment cost-effective. In fact, improvements were observed in terms of fewer accident and emergency admissions, hospitalizations and specialist visits. This treatment supposes the payment of $2 (approx. 1.6 Euros) per day per avoided exacerbation (Lofdahl et al., 2005).

Other study found that the addition of an inhaled corticosteroid to a β2-antagonist led to significant benefits in respiratory function and reduced the number of restricted activity days. On the other hand, the addition of an anticholinergic was found to be both expensive and of no long-term value (Rutten-van Molken et al., 1995).

Very severe COPD:

Oxygen therapy is recommended for use in some very severe patients in order to increase the partial pressure of oxygen in the arterial blood (PaO2) and has three different uses: to relieve dyspnea, to aid oxygen intake during exercise and for long term continuous treatment (GOLD, 2008). This kind of treatment causes a high proportion of outpatients costs for COPD patients but, its cost-effectiveness have not been studied in depth.

Surgical treatments: There are several options including surgery between the available treatments for very severe COPD patients.

<u>Lung volume reduction surgery (LVRS)</u> has become an available option for treating severely disabling emphysema. It has been projected that widespread adoption of this procedure could cost the US health economy more than $6 billion (approx. 10 billion Euros) in the first several years of adoption (Sullivan et al., 2000).

This kind of intervention involves cutting away around 30% of the diseased lung tissue in order to increase the effectiveness and efficiency of the remaining lung and surrounding muscle. It is only suitable for some patients with very severe COPD (Briggs et al., 2009). Because of the high cost effectiveness ratios calculated for this type of interventions ($190,000 [approx. 161,000 Euros] per QALY for three years or $53,000 [approx. 45,000 Euros] per QALY for 10 years) (National Emphysema Treatment Trial Research Group, 2003) patients undergoing LVRS must be carefully selected taking into account the potential benefit of the intervention versus the possible risks and complications of the patient.

A number of studies have estimated costs for LVRS. Total hospital costs ranged from $11,712 to $121,829 (approx. 19,500 to 200,000 Euros) and were significantly associated with length of stay in the hospital, both in the ICU and in total length of stay. A small number of individuals incur extraordinary costs because of complications. The mean cost was $30,976 (approx. 51,600 Euros), and the median cost was $19,771 (approx. 33,000 Euros). Advanced age was a significant factor leading to higher expected total hospital costs (Sullivan et al., 2000).

Lung transplantation is a costly but often effective therapy for severe emphysema. The lifetime expenditures for lung transplantation have ranged from $110,000 (approx. 183,000 Euros) to well over $200,000 (approx. 333,000 Euros). In this case, unlike LVRS, the cost associated with lung transplantation remains elevated for months to years after surgery because of the high cost of complications in immunosuppression regimens (Sullivan et al., 2000).

Even though that Several studies (Ramsey et al., 1995; Al et al., 1998 and Anyanwu et al. 2002) have found substantial gains in quality of life following lung transplantation, the evidence of an effect on survival was mixed.

Bullectomy may be an option when a large air filled bulla exists that fills half of the thoracic volume and compresses the relatively normal adjacent parenchyma (Meyers and Patterson 2003). There is no cost-effectiveness information on this surgery option.

4.4. COPD PROGRAMS: COST EFFECTIVENESS

Some programs have been developed to complement the pharmacological treatments for the patients. The most important are the following:

Smoking cessation:

Investing resources in smoking-cessation programs is cost-effective in terms of medical costs per year of life gained. In fact is the single most cost effective way to reduce exposure to COPD risk factors (GOLD, 2008) and it is recommended at all stages of the disease.

Interventions to assist individuals in quitting smoking include: counselling, nicotine replacement products and drug therapies (Bupropion, Nortriptyline and Varenicline) (Briggs et al., 2009).

The median societal cost of various smoking-cessation interventions was approximately £17,000 (approx. 20,000 Euros) per year of life gained. The literature on smoking-cessation cost effectiveness studies reports on face-to-face interventions such as nicotine transdermal patches, physician and other health professional counseling with and without patches, self-help and group programs, and community-based stop-smoking contests.

Smoking-cessation programs produced cost-effectiveness ratios that ranged from £212 (€304) to £873 (€1253) per year of life gained and were, thus, a very good health-care value for the National Health Service (Briggs et al., 2009).

Supplemental home oxigen:

Supplemental home oxygen is usually the most costly component of outpatient therapy for adults with emphysema who require this therapy. Reviews of the cost-effectiveness of alternative outpatient oxygen delivery methods suggest that oxygen concentrator devices may be cost-saving compared with cylinder delivery systems (Pelletier-Fleury et al., 1996).

Education and pulmonary rehabilitation programs

Education and pulmonary rehabilitation programs have been shown to have beneficial effects in patients with COPD. Education programs have been promoted as an economically attractive intervention for individuals with COPD (Ries et al., 1995). Some studies have shown an statistically significant improvements in dyspnea, fatigue, emotional health, and mastery (Goldstein et al., 1997).

An observational study with a small number of subjects found that patients in a pulmonary rehabilitation program used fewer health-care services compared with those without rehabilitation. Because of study design limitations, it is unclear whether these results can be generalized to a larger, more diverse group of patients. The initial costs of the rehabilitation program may be offset if urgent care and emergency department visits or hospitalizations are subsequently reduced (Ries, 1990).

4.5. EFFECTS OF TELEMONITORIZATION IN COPD COSTS AND BURDEN

As seen before, in point 4.2”Costs per stage of the illness”, the most important COPD costs are due to the hospitalization needs caused mainly by the exacerbations events. Most of these hospitalizations could be avoided through the development of more responsible models of care that allow earlier recognition and treatment of exacerbations (McKinstry et al., 2009). The telemedicine and telemonitoring systems are believed to be a proper way of reducing the hospitalizations in several illnesses. In fact, it is increasingly accepted that changes in the way care is provided are needed to ensure quality and cost containment (de Toledo et al., 2006).

In this point an analysis of effects of these systems in the control and monitorization of chronic illnesses in general and COPD in particular will be developed. In this sense, it will be developed the acceptance of this systems by users with special stress in the elderly, the economic impact of these systems at the moment and future perspectives and the benefits that they give to the society.

Users' acceptance

Several studies have been performed with different telemedicine systems and different pulmonary illnesses ((Jaana et al., 2009). In general, most of the telemonitoring studies presented positive results in relation to acceptance of the systems and telemonitoring programs (Maiolo et al., 2003; Pare et al., 2007). Patients showed a positive attitude, an increased feeling of security and reassurance and control over their medical condition, better knowledge and awareness about their disease, improved communication with health professionals and improvements in their caregivers' knowledge and quality of life were reported.

In this sense, the patient empowerment is one of the most important effects observed. This empowerment can be created by the direct involvement of patients in the care process and the associated increase in their knowledge and awareness about their respective medical condition (Pare et al., 2007).

Some other benefits have been identified in other illnesses. For example, patients with heart failure indicate that a major issue in their care is the need for better access to specialist advice, including an identified contact for support with who is familiar with their medical condition. This wish can be at least partially addressed through telemonitoring, which both directly and indirectly increases contact with the health professional, and leaves the patient and their family less isolated. In this kind of systems, when help is sought the professional has easy access to up-to-date clinical information upon which to base their advice. In addition to this, the patient gains confidence that if there is a medical problem the healthcare professional is more likely to contact him (Riley et al., 2009).

Regarding privacity, users present two different positions. On one side, people who have experience of being continuously activity monitored in their own homes can perceive electronic care surveillance as freeing and as protecting their privacy, as it enables them to continue living in their own home rather than moving to a nursing home. On the other side, few individuals, however, can experience a privacy violation (Essen, 2008).

Nevertheless, a decrease in adherence and compliance of patients with time has been detected in several studies (Pare et al., 2007).

Potential benefits

At **clinical level**, it has been shown some positive effects of home telemonitoring on patients' medical conditions, as for example, detection of complications, better disease control, inmediate feedback and adequate medication use. These positive effects of telemonitoring on patient condition and the overall process of care were also highlighted in several studies across several types of chronic conditions, including pulmonary diseases. Specifically in these, where found in several studies the ability to identify early changes in the condition of patients, thus supporting immediate intervention and avoiding exacerbations. This clinical effectiveness of telemonitorization can be translated into a significant decrease in the hospital admissions, emergency departments visits and hospital length of stay (Pare et al., 2007). Nevertheless, there is not any study where these results are clearly demonstrated (Jaana et al., 2009).

A good **accuracy and reliability of the transmited data** has been consistently reported in several studies, and the process of data transfer was performed successfully in most cases with minimal technical problems and errors (Pare et al., 2007).

Other studies have found that long-term disease monitoring of patients at home is the most promising application at this time for delivering cost-effective quality care (Meystre, 2005); a home telehealth system consisting of vital sign monitors and patient questionnaires **reduced cost** and **improve quality-of-life** for elderly users (Noel et al., 2004); there is no difference in quality indicators between home patients receiving traditional home healthcare and those in telehealth intervention. Telemedicine has the potential to affect cost savings when use to substitute for some in-person visits (Johnston et al., 2000). Also, some other benefits have been detected in the use of telemonitoring systems with elderly people, such as the prevention of falls (Horton, 2008).

Economic viability

In general, the assessment of the effects of telemonitoring on the use of health services has been very poorly studied. There is no solid evidence about effects of home telemonitoring on the utilization of healthcare resources, and no in-depth analyses were conducted in most instances (Jaana et al., 2009). Besides, there isn't any study regarding the comparison of time spent by healthcare professionals in one or the other way.

Some analysis have showed promising results and affordability of the telemonitoring systems related to respiratory illnesses, especially with technology advancement and decreased cost over the years (Jaana et al., 2009) and also, some of them presented evidence on its ability to produce savings (Maiolo et al., 2003; Pare et al., 2006).

Between the available bibliography, there can be found studies assessing the economic viability of the telemonitoring and telemedicine systems used. For example, a study performed with COPD patients quantifies the net gain in a 15% by the means of the lower hospitalization rate found and less frequent home visits (Pare et al., 2006). In other study (Maiolo et al., 2003), performed with 20 COPD patients, the results show a significative reduction of hospital admissions (50%) and a significant decrease of acute home exacerbations (55%) when the telemonitoring system was being used. The economic saving in this study was calculated in 17%.

On the other hand, there are some other examples that raise doubts about the cost effectiveness of the telemonitoring systems. For example, a cost-benefit analysis involving patients with asthma suggested that telemonitoring will have limited cost-effectiveness unless the cost of the technology decreases (Willems et al., 2007). In other study performed with a heart failure telemonitoring system that suggested a mean incremental cost per patient for the telemonitoring system in comparison to the control group, although the overall costs were not statistically significantly (Dar et al., 2009). Some other studies performed to evaluate the effectiveness of telemonitoring systems can be found in chart

Despite this, it is expected that with the development of technologies and infrastructures to support telemonitoring the incremental cost will decrease.

Chart 4. Examples of studies performed with telemonitoring systems in several illnesses.

Due to the lack of general studies reporting the cost-effectiveness of the telemonitoring and telemedicine systems at general level, some more specific studies have been used in the analysis of the situation. Despite this, it must be taken into account the limitations of the methods used.

In this line, several studies have been made in order to determine the real benefits of the telemonitoring systems.

Between 2003 and 2007, the census for Veterans Health Administration, within the Care Coordination/Home Telehealth (CCHT) program noticed an increase of patients from 2,000 to 31,570 (1,500% growth), predominantly male (95%) and aged 65 years or older. Data analyzed from 17,025 CCHT patients showed a reduction in the number of bed days of care (25%), a reduction in the number of hospital admissions (19%), and satisfaction score rating of 86% after enrolment into the program (Darkins et al., 2008).

In other study, patients received a disease-specific COPD self-management program ("Living Well with COPD"; Boehringer Ingelheim Canada, Burlington, Ontario) consisting of approximately 1 hour per week of teaching at home for 7 to 8 weeks. The program was supervised by experienced and trained health professionals (nurses, respiratory therapists, and a physiotherapist). Follow-up was conducted with patients by weekly telephone calls for 8 weeks (educational period) and then monthly calls for the remainder of the study. The results showed that hospital admissions for exacerbation were reduced by 39.8%, admissions for other health problems by 57.1%, emergency department visits were reduced by 41.0% and unscheduled physician visits by 58.9%. Also, greater improvements in the quality-of-life were observed (Bourbeau et al., 2003).

In 2002, a telemonitoring platform specific for COPD was developed (de Toledo et al., 2006)*. It included several services specially designed for COPD patients (for example* *ubiquitous access to an electronic chronic patient record and telephone support to patients). After the experience of the use of the platform with 157 COPD patients authors of the study observed the following results: A significant reduction in the number of readmissions; This was mainly due to the prevention of exacerbations achieved by the early detection of symptoms. The system was well-accepted by both patients and professionals; In the evaluation of costs, it was seen that the cost of the system can be paid before the end of the first year.*

5. CONCLUSIONS

During the whole report it has been highlighted that COPD is a leading cause of death worldwide. In addition to generating high healthcare costs, COPD imposes a significant burden in terms of disability and impaired quality of life. Unlike many leading causes of death and disability, COPD is projected to increase in much of the world as smoking frequencies rise and the population ages.

Despite the great importance of COPD, the knowledge regarding the situation of people affected by COPD and the epidemiology of the illness is vague. There are identified different causes for this. The most important one is related to the different ways of diagnosis used in the different countries. The use of spirometry is the most recognized way of diagnosis of the illness (GOLD, 2008) but, the unavailability of spirometer in the primary care centers and the misuse of it, makes the differences exist. In fact, there have been identified in many studies a great number of underdiagnosis but also, wrong made diagnosis (Eaton et al., 1999; Eaton et al., 1999; Calverley et al., 2000; Schermer et al., 2003; Fukuchi et al., 2004; Halbert et al., 2006; Lindberg et al., 2006; Zielinski et al., 2006; Zielinski et al., 2006; Calverley, 2008; GOLD, 2008; Joo et al., 2009). However, the situation is expected to improve due to the development of internationally accepted guidelines (American Thoracic Society et al., 2004; National Institute for Clinical Excellence, 2004; GOLD, 2008).

In order to have a closer look into the COPD worldwide situation an analysis of the mortality, morbidity and prevalence of the illness has been made.

Regarding mortality, COPD is at the moment the fifth leading cause of deaths in the world, but it is predicted to become the first one in 2020. Besides this statistical data, other factors such as comorbidity make COPD even more mortal than expected. It has been seen that in many cases, patients officially dead by other causes (like lung cancer, heart stroke, respiratory failure or heart failure) suffered also COPD (Chapman et al., 2006; Mannino et al., 2006; Sin et al., 2006; Mannino et al., 2007; Soriano Ortiz et al., 2009; Terzano et al., 2010). In these cases, it is difficult to define whether COPD was the turning point in the development of the other illness or it COPD was the real cause of death. Anyway, any of these cases is taken into account when defining the real burden of the illness.

The comparison between sexes has show that in the past, males were much more affected by COPD than females. Despite this, with the increasing consumption of tobacco of women, who are reaching male’s levels and the higher life expectancy of women comparing with men, are making these differences have disappeared.

Regarding geographic origins, it must be highlighted the high mortality and prevalence of the illness found in Asia. Besides, it has been noticed that while in Europe the illness trend is decreasing, in the USA is increasing. In fact, it has been found a higher mortality in USA in comparison to Europe. The differences found in mortality and prevalence between developing and developed countries are not too high, but they are bigger in low and middle income countries, even though that the smoking prevalence is bigger in high income countries, the awareness is making it decrease while this awareness is not so evident in middle and low income countries. On the other side, other risk factors are quite evident in low and middle income countries such as the use of biomass fuel or occupational exposures to dust, vapors and fumes. The use of biomass fuel for cooking has been detected as a causing factor of the increasing levels of COPD between women from low and middle income countries (Lopez et al., 2006b; Salvi et al., 2009).

Comparing mortality and morbidity it is surprising that in USA, the mortality rates are much bigger in comparison to the European countries while the morbidity is not so high. It is the contrary in Germany, where the morbility found is high but the mortality rates are in the same level as other European countries (tables 3 and 8).

In the economical analysis, and as it happened with the epidemiological analysis, it was difficult to establish comparisons between countries. This was due to the same factors as in epidemiology (different methods used in the diagnosis, underdiagnosis and overdiagnosis, etc.) added to the difficulties in the comparison between different currency and the different years when the studies where performed.

In this sense, many economical data from USA, UK and Spain was available from different years, little economical data has been found from Germany, Sweden and Norway and no data is available from Greece.

Great differences have been found in terms of costs per COPD patient between the USA and other countries (USA: 5000€ approx; UK: 2600€ approx.; Spain: 1712€; Germany: 836€). This difference has been justified by the very big difference between the unit costs of days in hospital between USA and the other countries (Chapman et al., 2006).

On the other side, big differences have been found even within country when different studies are taken into account. This is due to the different methods used in the costs estimation and the high variability in terms of epidemiology and diagnosis found in the different studies available.

The stage of the illness is also another parameter that increases the variability found in the several studies analyzed. In fact, the costs of the illness have a great variability depending on the stage of the illness of the patient. Exacerbations and as a result of them hospitalizations have been identified as the main responsible of the COPD costs.

Regarding treatments and programs for the management of COPD, some of them of them have been analyzed in terms of cost-effectiveness. The available treatments have been found to be accumulative as long as the illness progresses in the patient. This means that new treatments do not replace others rather that are added to them.

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In terms of programs, three are the most important: smoking cessation, supplemental home oxygen and education and pulmonary rehabilitation programs. The most cost-effective is the smoking cessation programs which are strongly recommended by experts and pulmonologists at any stage of the illness.

For the last, several studies have been found regarding the use of telemonitoring and telemedicine programs specific for COPD. Most of them have found to be cost effective as they have been found to be able to reduce the number of hospitalizations and prevent exacerbations. Despite the data available it must be taken into account that any of these studies has made a deep analysis of the cost savings and their results have not been clearly demonstrated. Even thought, cost-effectiveness of the telemonitoring systems is expected to increase as the development of the technologies increases and their cost decreases.

The acceptance of this kind of systems is positive, increasing the self-empowerment of patients, giving them more confidence, feeling of security, better knowledge about their illness and their health condition, etc. Regarding the clinical effects they have been found to be also positive as the systems have been found to be able of detecting complications in early stages of the change produced. The systems have also shown a good accuracy and reliability of the transmitted data.

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