Social economic costs of COPD in Extremadura (Spain): an observational study

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Purpose: COPD has been associated with a high number of comorbidities and a relatively high level of health care resource utilization. This study aimed to estimate the social economic impact of COPD in the autonomous community of Extremadura (Spain) in 2015.

Patients and methods: This is a retrospective observational study carried out using a representative sample of patients diagnosed with COPD in Extremadura. Sociodemographic data, data on health care resource utilization, formal and informal care received by the patients, and loss of labor productivity in the last 12 months were collected through an electronic data collection platform. Direct health care costs were estimated using the bottom-up approach, costs of informal care were assessed using the substitution method, and labor productivity losses were calculated using the human capital method.

Results: A sample of 386 patients was obtained (mean age: 71.8±10.3 years, males: 76.2%). The results show an average annual cost per patient of 3,077 euros. Direct health care costs represented 43.8% (1,645 euros), direct non-health care costs amounted to 38.3% (1,440 euros), and labor productivity losses represented 17.9% (672 euros) of the average annual cost. The total annual cost of patients with COPD in Extremadura reached 36.2 million euros in 2015.

Conclusion: COPD poses a significant burden for the health care system and the society of Extremadura. The implementation of preventive and control measures could result in a substantial reduction in the economic impact.

Keywords: COPD, social costs, health care resource utilization, informal care, labor productivity losses

Introduction

Although there are no recent definitive data on the prevalence of COPD in the adult population in Spain, the latest study, published in 2009, suggested a prevalence rate of 10.2% in the population between 40 and 80 years of age.¹ In Extremadura, one of Spain’s 17 autonomous communities, the prevalence rate of COPD has been estimated at 4.9% among adults aged 40–69 years in the year 2000² and at 4.4% among the population aged ≥15 years in 2012.³⁴ However, these rates may underestimate the real prevalence, for two reasons: first, they were calculated using the old European Respiratory Society criteria to define COPD⁵ and second because the findings are based on data from already diagnosed patients, while it is known that up to 73% of people with COPD have not been diagnosed yet.⁶

It is well known that COPD entails high economic costs associated to the consumption of health care resources, as well as a significant loss of health-related quality of life.⁷–¹⁰ However, the economic burden of COPD has not been assessed in Spain or any of its 17 geographical autonomous communities. The economic burden includes not only direct costs associated with the consumption of health resources but also labor productivity...
losses of patients derived both from poor health and from
time spent on medical visits or hospital stays associated with
COPD, as well as the costs of professional and informal care
(the latter defined as unpaid care that is provided by family
members or friends) that the patients may need. Additionally,
the total economic burden should also consider intangible
costs related to the negative impact that COPD has on the
quality of life of both the patients and their caregivers, even
if difficult to estimate in monetary terms.11

The objective of this study was to estimate the economic
burden associated to COPD in 2015 in the autonomous
community of Extremadura (Spain), including three main
cost categories: 1) direct health care costs (DHC), 2) direct
non-health care costs (DNHC), including both professional
and informal care, and 3) indirect costs (IC) derived from
the patient’s labor productivity losses.

Patient and methods
Subject population
The Extremadura Health Service includes eight different
health areas. Health areas are geographical divisions with a
relatively decentralized management of primary care services
in each area, as is the case across all Spanish autonomous
communities. The eight health areas of Extremadura are in
turn subdivided into a total of 114 Basic health areas. Accord-
ing to official data from the Extremadura Health System,
there were a total of 9,622 people diagnosed with COPD in
Extremadura in April 2015 (79.9% males, 79.3% ≥65 years),
spread across its eight health areas. Therefore, our population
universe was 9,622 individuals.

Study design
A retrospective cross-sectional observational study was
designed, with a probabilistic sampling stratified by Health
Area in order to obtain a representative sample of patients
with COPD in Extremadura. In the first stage, a randomized
sample representative of the adult population diagnosed with
COPD in Extremadura (n=386, 95% confidence level, 5% sam-
pling error) was calculated based on the prevalence of
COPD in the population aged ≥18 years in Extremadura.
In the second stage, two age group quotas (≤65 years of
age and ≥65) as well as quotas by gender within those
age groups were established within the sample in order to
represent different age and gender groups of prevalence
in each of the eight health areas of Extremadura. We then
randomly selected 18 Basic health areas distributed across
the eight health areas of Extremadura, proportionately to
the number of Basic health areas in each Health Area. The
number of patients and age/gender quotas to enroll in each
Basic Health Zone were assigned to each Basic Health Zone
in such a way that the theoretical sample was proportion-
ally distributed across health areas, and within each Health
Area they were proportionally distributed across age and
gender of the population with COPD residing in each of the
health areas.

Inclusion criteria were the following: people diagnosed
with COPD according to the WHO classification criteria12
at least 12 months before their inclusion in the study, being
18 years of age or older, residents of Extremadura whose
electronic medical records were available for 12 months
prior to the collection of data, and patients who provided
their informed consent to participate in the study in accord-
cance with local regulations. Patients with any limitation that
according to the researchers’ best judgement could affect the
reliability of their answers were excluded (eg, patients with-
out knowledge of the Spanish language, or patients with any
evident cognitive impairment). Patients who had participated
in any clinical trial in 12 months prior to the collection of
data and pregnant women were also excluded.

A total of 18 previously trained researchers participated
in data collection, one in each of the selected 18 Basic
health areas. Researchers received a randomly ordered list
of all the patients diagnosed with COPD who resided in
their corresponding Basic Health Zone. The patients’ name,
telephone number, and address were included in the list and
disclosed to the field researchers but were never available to
the authors of this manuscript. Researchers contacted patients
over the telephone following the order in their list. Whenever
a patient was not available on the telephone, researchers
contacted the next patient on the list. After telephone contact
was established, researchers verified with the patient that
inclusion/exclusion criteria were met and, if the criteria were
met, asked the patient to meet them in person either in the
patient’s home or in their primary care center, whichever
was preferred by the patient. Patients were recruited this
way until all age and gender quotas were completed for each
Basic Health Zone.

Fieldwork was carried out between July 10 and
November 11, 2015, and included one single visit per
patient, with retrospective data collection for 12 months
prior to the date of the visit. Data were collected through
three different sources, including two closed and structured
electronic case report forms (CRFs) that were completed by
the researchers using an electronic tablet, and one microdata
database directly provided by the Extremadura Health System. The first CRF, called “the patient’s CRF,” collected information directly from the patient and included details on home respiratory therapies, institutionalization, professional care, informal care, and loss of labor productivity related to COPD in the last 12 months. The second CRF, called “the researcher’s CRF,” collected information directly provided by the patient’s electronic clinical records and included clinical data related to COPD in the last 12 months. Finally, microdata provided by the Extremadura Health System included data on medication and consumption of other health care resources in the last 12 months. Information was also collected on patients’ quality of life using the EuroQol-5D-5L questionnaire (general quality of life at the time of the visit) and the St George’s Respiratory Questionnaire for COPD patients (specific quality of life of patients with airway obstruction). Patient quality of life results will be presented in another publication.

The phases of data collection are summarized in Figure 1. Prior to data collection, patients were informed about the study objectives and data confidentiality. They provided their written informed consent to participate in the study and to release information, according to the Spanish legislation, and permission to perform the study was obtained from the Clinical Research Ethics Committee of the University Hospital Infanta Cristina (Badajoz).

### Study variables

#### Assessment of COPD severity

The electronic clinical records of a portion of the patients did not specify the severity of their COPD. In these cases, three complementary sources of information were used for the construction of a “severity” variable according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) scale. First, the GOLD classification of the patient was used, as long as it was included in their clinical history.

![Figure 1 Phases in data collection.](image-url)  
*Abbreviations: CRF-R, researcher’s case report forms; CRF-P, patient’s case report forms; SGRQ-C, St George’s Respiratory Questionnaire for COPD; EQ-5D-5L, EuroQol-5D-5L questionnaire.*
Second, in the absence of the GOLD classification, severity was calculated using the most recent forced expiratory volume (FEV%) data. Third, if both the GOLD scale and the FEV% data were missing from the clinical record, then the free description made by the doctor in the patient’s clinical history coinciding with the GOLD scale was used. Finally, if all of the previous data were lacking, an “unknown/not available” severity degree was assigned to that particular patient.

Costs methodology
Following traditional cost-of-illness studies’ methodology, we estimated DHC (those borne by the National Health System), DNHC (out of pocket expenditures borne by families, other public institutions such as social services), and cost equivalence of the time devoted to caregiving, and IC (cost equivalence of the patients’ productivity losses). Costs were estimated from a societal perspective, that is, including all available direct costs and IC associated with COPD in 12 months prior to the visit. All direct costs were estimated using the bottom-up costing method, except for the costs of informal care, for which the substitution method was used. In order to minimize recall bias related to informal care, we asked for the average hours per day devoted by caregivers to administering medication and helping in daily tasks (such as getting dressed, personal hygiene, and cooking), and average hours per month devoted to accompanying the patient to medical visits and tests, collecting medication from pharmacy, and administrative or legal tasks, and then multiplied daily care hours by 365 and monthly care hours by 12, and added them in order to obtain yearly hours. Labor productivity losses were estimated using the human capital approach. The reference year for all costs was 2015. Costs with reference years prior to 2015 were updated using the Spanish Medical Consumer Price Index (CPI) for health care costs and the Spanish General CPI for other costs.

Costs
DHC included medication linked to the respiratory system; medical visits to the pulmonology specialist; medical tests; outpatient and hospital emergencies; the use of an ambulance, both for emergency medical transportation and for on-site care; hospital admissions; and home oxygen therapy. DHC were calculated by multiplying the resources used by their unit prices.

DNHC included use of social services such as stay in nursing homes and attendance at (non-health care) day centers; professional care (defined as care provided by a professional caregiver, such as a paid domestic aid); and informal care (defined as care provided by family members or friends without remuneration) provided both by the main caregiver (the person who spent the most time caring for the patient) and by all other caregivers. The cost of informal care was estimated using the replacement cost approach, which values the time spent on caregiving at the wage rate or market price of a close substitute. In this case, we used the minimum hourly wage of a household employee (because of its nonspecialized care character). The rest of the DNHC was calculated by multiplying the resources used by their unit prices.

IC included labor productivity lost by the patient in the form of absenteeism from work due to medical visits, sick leave, and hospitalizations, as well as early retirement and unemployment directly related to COPD (according to the patient’s perception). Labor productivity losses were measured using the human capital method, by which work time lost as a result of illness is valued at the market wage. Therefore, IC were estimated as the average wages forgone by the patient due to COPD.

The costs of medication consumed by the patient were provided directly by the Extremadura Health System in the form of microdata. Unit prices related to other health care resources and their source are presented in Table S1.

The total cost (TC) associated to COPD included the sum of DHC, DNHC, and IC. The cost per patient per year refers to the average cost of COPD per patient per year in Extremadura. The total annual cost refers to the cost of COPD in Extremadura in 1 year.

Statistical analysis
Descriptive statistics (number of valid cases, mean, and SD) were calculated for all continuous variables, and frequencies and percentages were calculated for categorical variables. Additionally, cost comparison was carried out by COPD severity, gender, and age group. Nonparametric techniques were used (Mann–Whitney U and Kruskal–Wallis U tests) due to the absence of a normal distribution. Statistical significance was set at \( p<0.05 \). Statistical analyses were performed using IBM SPSS Statistics V22.0 (IBM Corporation, Armonk, NY, USA).

Results
A valid sample of 386 patients meeting inclusion criteria was obtained (76.2% males, mean age 71.8±10.3 years). The sample was representative of patients diagnosed with COPD...
in Extremadura in terms of gender and age across the eight sanitary areas. Tables 1 and 2 show the sociodemographic and clinical characteristics of the sample, respectively.

**Utilization of health care resources**

The most frequently performed medical tests were blood tests (0.6±1.4 times on average), chest X-ray (0.6±1), gasometry (0.5±1.2), and spirometry without bronchodilator testing (0.3±0.6). The average number of pulmonology visits was 0.8 (±1.3) per patient per year. Averages of 0.4 (±1) visits to the hospital emergency room and 0.3 (±0.7) to the emergency room at the health center were recorded, per patient per year. The emergency ambulance was used an average of 0.3 (±1.1) times per patient, of which 0.28 (±1.1) times corresponded to unassisted emergency transportation mode. Overall, 15.4% of the patients used home oxygen therapy; oxygen concentrator was the main type (59.5%), followed by liquid oxygen (18.9%). The mean time of daily use of this therapy was 14.5 (±5.7) hours. The average number of hospital admissions per patient was 0.2 (±0.5). Within the medication related to COPD, agents against obstructive respiratory tract diseases were the most consumed (91.5%), followed by antihistamines for systemic use (5.8%), and oral preparations (2.7%) (Table 3).

| Table 1 Sociodemographic characteristics of the sample | Total |
|--------------------------------------------------------|-------|
| Gender (% males)                                       | 76.2  |
| Age in years (mean ± SD)                               | 71.8±10.3 |
| Age group (%)                                          |       |
| <65 years                                              | 20.7  |
| ≥65 years                                              | 79.3  |
| Smoking history (%)                                    |       |
| Current smoker                                         | 16.7  |
| Ex-smoker                                              | 69.6  |
| Never smoked                                           | 13.7  |
| Daily cigarettes (mean ± SD)                           |       |
| Smokers                                                | 14.1±10.3 |
| Ex-smoker                                              | 27.3±16.4 |
| Education level (%)                                    |       |
| Does not know how to read or write                     | 6.0   |
| No education                                           | 33.9  |
| Primary education                                      | 35.9  |
| Secondary education                                    | 18.5  |
| University education                                   | 5.7   |
| Employment status (%)                                  |       |
| Early retirement/retired                               | 78.9  |
| Actively working                                       | 7.9   |
| Domestic work                                          | 7.1   |
| Unemployed                                             | 3.4   |
| Permanent leave                                        | 1.6   |
| Temporary leave                                        | 1.1   |

**Abbreviation:** SD, standard deviation.

| Table 2 Clinical characteristics of the sample | Total |
|------------------------------------------------|-------|
| FEV₁/FVC (mean ± SD)                            | 60.3±18.7 |
| FEV₁% (mean ± SD)                              | 66.7±22.3 |
| COPD severity (%)                              |       |
| GOLD I                                         | 10.9  |
| GOLD II                                        | 20.5  |
| GOLD III                                       | 9.1   |
| GOLD IV                                        | 1.3   |
| Unknown/not available                          | 58.3  |
| Exacerbations in the last 12 months (% yes)     | 36.7  |
| Number of exacerbations in the last 12 months (mean ± SD) | 0.6±1.2 |
| Number of comorbidities (mean ± SD)            | 7.8±4.7 |

**Main comorbidities (%)**

- Cardiovascular comorbidity
- Dyslipidemia/lipid metabolism disorder
- Noncomplicated hypertension
- Diabetes mellitus (type 1 + type 2)
- Arthritis/arthrosis
- Cancer/malignancy
- Hypertension with target organ involvement
- Anemia
- Depression
- Asthma
- Osteoporosis

| BMI (mean ± SD) | 30.0±5.0 |

| BPI classification according to WHO (%) |       |
|-----------------------------------------|-------|
| Insufficient weight                     | 0.8   |
| Normal weight                           | 3.4   |
| Overweight                              | 16.1  |
| Obesity                                 | 18.4  |
| Unknown/not available                   | 61.4  |

**Notes:** 
1. Number of valid cases: 123, number of missing values: 263. 
2. Number of valid cases: 140, number of missing values: 246. 
3. Number of valid cases: 215, number of missing values: 171. 
4. Includes cerebrovascular accident/ictus/apoplexy, unspecified cardiac arrhythmia, atherosclerosis or peripheral arterial disease, valvular heart disease, atrial fibrillation/atrial flutter, acute myocardial infarction, heart failure, cardiac ischemia with angina, cardiac ischemia without angina, transient cerebral ischemia, other cardiac diseases, other cardiovascular diseases, other cardiovascular signs/symptoms, and paroxysmal tachycardia. 
5. Number of valid cases: 149, number of missing values: 237.

**Abbreviations:** SD, standard deviation; BMI, body mass index; WHO, World Health Organization; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

**Utilization of non-health care resources**

Overall, 3.8% of patients were living permanently in a home or residential center. In 21.9% of these cases, admission was specifically due to COPD. A total of 5.3% of patients needed professional care at home due to their illness, and received an average of 12.7 (±16.1) hours of care per week. A total of 17.4% of the patients received informal care due to their illness. In 63.4% of these cases there was only one caregiver, while in the remaining 36.6% there were two or more caregivers. The informal caregiver profile was female (84.3%), aged 61.3 (±14.2), and partner (44.8%) or
Table 3 Utilization of health care resources in the last 12 months

| Resource typology                          | Total | N (valid cases)* |
|--------------------------------------------|-------|------------------|
| Medical tests (mean ± SD)                  |       |                  |
| Blood analysis                             | 0.6±1.4| 292              |
| Spirometry with bd test                    | 0.1±0.4| 280              |
| Spirometry without bd test                 | 0.3±0.6| 271              |
| Alpha-1 antitrypsin                        | 0.0±0.2| 254              |
| Chest X-ray                                | 0.6±1.0| 299              |
| CAT                                        | 0.1±0.3| 289              |
| Gasometry                                  | 0.5±1.2| 276              |
| Pulmonology visits (mean ± SD)             | 0.8±1.3| 386              |
| Visits to the emergency room (mean ± SD)   |       |                  |
| Health center emergencies                  | 0.3±0.7| 284              |
| Hospital emergencies                       | 0.4±1.0| 302              |
| Use of ambulance (mean ± SD)               |       |                  |
| Total times                                | 0.30±1.1| 381             |
| Times when used as non-assisted emergency  | 0.28±1.1| 381             |
| health transport                          |        |                  |
| Use of home oxygen therapy (%)             | 15.4  | 386              |
| Use of home oxygen therapy (only users) (mean ± SD)\* | | |
| Hours per day                              | 14.5±5.7| 57              |
| Months (over the past year)                | 10.6±3.2| 57              |
| Hospital admissions (mean ± SD)            | 0.2±0.5| 328              |
| Medication consumed (%)                    |       |                  |
| R01 nasal preparations                     | 2.7   |                  |
| ICS                                        | 2.7   |                  |
| R03 agents against obstructive respiratory diseases | | |
| Short-acting beta agonists                 | 6.2   |                  |
| Long-acting beta agonists                  | 6.9   |                  |
| Short-acting muscarinic agonists           | 3.3   |                  |
| Long-acting muscarinic receptor antagonists| 32.0  |                  |
| ICS                                        | 2.9   |                  |
| Fixed combinations                         | 31.7  |                  |
| Leukotriene receptor antagonist            | 3.8   |                  |
| Interleukin inhibitors phosphodiesterase   | 3.4   |                  |
| Methylxanthines                            | 1.4   |                  |
| R06 antihistamines for systemic use        | 5.8   |                  |
| Antihistamines for systemic use            | 5.8   |                  |

Notes: *Valid cases refer to all cases (386) minus missing values. Results calculated only for users of home oxygen therapy (59 patients).

Table 4 Utilization of non-health care resources in the last 12 months

| Resource typology                          | Total | N (valid cases)* |
|--------------------------------------------|-------|------------------|
| Permanent stay in housing or residential center |       |                  |
| Yes                                        | 3.8   | 386              |
| Due to COPD                                 | 21.9  |                  |
| Attendance at day center                    |       |                  |
| Yes                                        | 0.3   | 372              |
| Due to COPD                                 | 0.0   |                  |
| Professional care at home                  |       |                  |
| Due to COPD                                 | 5.3   | 371              |
| Months over the past year (only users)\*    | 10.8±3.1| 18              |
| Hours of weekly care (only users)\*         | 12.7±16.1| 18             |
| Informal caregiving                        |       |                  |
| Due to COPD                                 | 17.5  | 371              |
| Months over the past year (only users)\*    | 11.0±2.7| 18             |
| Hours of care per month                     |       |                  |
| Principal caregiver\*                       | 19.0±53.0| 386           |
| Other caregivers                            | 2.5±21.9| 18              |
| Number of informal caregivers\*             |       |                  |
| One caregiver\*                             | 63.4  | 63               |
| Two or more caregivers                      | 36.6  |                  |
| Profile of principal informal caregiver\*   |       |                  |
| Gender                                     |       |                  |
| Female                                     | 84.3  | 64               |
| Male                                       | 15.7  |                  |
| Age (years)                                | 61.3±14.2| 386             |
| Relationship with the patient               |       |                  |
| Spouse/partner                             | 44.8  |                  |
| Daughter/son                               | 44.5  |                  |
| Other                                      | 10.7  |                  |

Notes: *Valid cases refer to all cases (386) minus missing values. Results calculated only for users of professional care at home (20 patients). Results calculated only for users of informal caregiving (65 patients). Censored to a maximum of 8 hours per day.

Abbreviations: SD, standard deviation; COPD, chronic obstructive pulmonary disease.

daughter (44.5%) of the patient. The monthly average hours of informal care amounted to 19 (±53) hours provided by the main caregiver and to 2.5 (±21.9) hours provided by other caregivers (Table 4).

Labor productivity losses

The vast majority of patients (78.9%) were retired or early retirees at the time of the survey. In 3.7% of cases, early retirement was due to COPD. Overall, 16.7% of working patients had seen their work affected by COPD, having to be absent from work on occasion due to the disease. In addition, 7.4% of people engaged in domestic work did not work outside their home because of COPD. Among the patients who were unemployed, 7.7% considered that they had lost their jobs due to their illness, and 38.5% perceived having difficulties in accessing a job for the same reason.

Cost estimations

The average annual cost per patient with COPD in 2015 amounted to 3,757 (±6,800) euros and was distributed as follows: DHC accounted for 43.8%, DNHC for 38.3%, and IC for 17.9%. The average annual DHC per patient was 1,645 (±2,240) euros; of these, medication accounted for the largest amount (44.5%), followed by hospital admissions (23.1%),
and home oxygen therapy (11.3%). The annual average DNHC amounted to 1,440 (±4,068) euros. Most of DNHC corresponded to informal care (81.9%), followed by formal care (13.1%), and residential care (5%). The IC attributable exclusively to COPD amounted to 672 (±3,744) euros per patient per year (Table 5).

Table 6 shows the average annual costs per patient according to severity, gender, and age group. The TC and DHC per patient showed statistically significant differences between severity groups (p<0.05), revealing in both cases a progressive rise in cost from the initial stages (I and II) to the most advanced stages (III and IV) of COPD. Regarding DNHC, there were no significant differences between the two initial stages (I and II), although there were significant differences between these two stages and stages III and IV (p<0.05). IC did not show statistically significant differences between the different severity categories. Differences in costs were not statistically significant by gender, although there were differences by age group, with patients aged ≥65 years presenting higher direct costs (both DHC and DNHC) but lower labor productivity losses and lower TC.

As our sample was representative of the Extremadura population, we extrapolated the average costs per patient to the population with COPD in Extremadura. The TC of COPD in Extremadura was 36,152,319 euros per year. Of these, 15.83 million euros corresponded to DHC, 13.86 million euros to DNHC, and 6.47 million euros to IC (Figure 2).

### Table 5 Annual average costs per patient (euros 2015)

| Cost typology                                      | Mean ± SD   | 95% CI       | % of subcategory | % of TC |
|---------------------------------------------------|-------------|--------------|------------------|---------|
| Direct health costs                               | 1,645 ± 2,240 | 1,421–1,869  | 100              | 43.8    |
| Medical tests<sup>a</sup>                          | 47 ± 121    | 2.9          | 1.2              |
| Pulmonology visits                                | 89 ± 157    | 5.4          | 2.4              |
| Emergency visits<sup>b</sup>                       | 102 ± 439   | 6.2          | 2.7              |
| Use of ambulance<sup>c</sup>                       | 108 ± 433   | 6.6          | 2.9              |
| Use of home oxygen therapy<sup>c</sup>             | 187 ± 459   | 11.3         | 5.0              |
| Hospital admissions                               | 380 ± 1,387 | 23.1         | 10.1             |
| Medication (total)                                | 732 ± 626   | 44.5         | 19.5             |
| R01 nasal preparations                            | 5 ± 20      | 0.3          | 0.1              |
| R03 agents against obstructive respiratory diseases| 367 ± 407   | 22.3         | 9.8              |
| Short-acting beta agonists                         | 13 ± 51     | 0.8          | 0.3              |
| Long-acting beta agonists                          | 49 ± 142    | 3.0          | 1.3              |
| Short-acting muscarinic agonists                   | 236 ± 258   | 14.4         | 6.3              |
| Long-acting muscarinic receptor antagonists        | 13 ± 56     | 0.8          | 0.3              |
| ICS                                               | 1 ± 6       | 0.1          | 0.0              |
| Fixed combinations                                | 28 ± 133    | 1.7          | 0.7              |
| Leukotriene receptor antagonist                    | 5 ± 15      | 0.3          | 0.1              |
| Interleukin inhibitors phosphodiesterase          | 6 ± 27      | 0.3          | 0.1              |
| R06 antihistamines for systemic use                | 9 ± 29      | 0.6          | 0.2              |
| Direct non-health costs                            | 3,757 ± 6,800 | 3,077–4,438  | 100              | 38.3    |
| Stay in residential center                         | 73 ± 797    | 5.0          | 1.9              |
| Attendance at day center                           | 0.0 ± 0.0   | 0.0          | 0.0              |
| Formal care in home                                | 189 ± 1,287 | 13.1         | 5.0              |
| Informal care                                      | 1,179 ± 3,749 | 81.9        | 31.4             |
| Principal caregiver<sup>d</sup>                    | 1,036 ± 3,051 | 71.9        | 27.6             |
| Other caregivers                                   | 143 ± 3,333 | 10.0         | 3.8              |
| Indirect cost<sup>e</sup>                          | 672 ± 3,744 | 298–1,047    | 100              | 17.9    |
| Total cost/patient/year                            | 3,757 ± 6,800 | 3,077–4,438  | –                | 100     |

**Notes:** All costs have been rounded to the nearest unit. *Zero cost (0 euros) has been assigned to patients without available information; the cost of additional tests specified in the CRF-R is included. †Zero cost (0 euros) has been assigned to patients without available information. ‡The cost has been calculated assuming the use of full months of oxygen therapy; in cases without information on the months of use, the average time of use of the rest of the patients has been assigned. §Cost calculated assuming 8 hours a day of informal care. ¶All cases were included; zero cost (0 euros) has been assigned to patients ≥65 years of age (age of retirement) and to labor productivity losses that were not a consequence of COPD.

**Abbreviations:** SD, standard deviation; CI, confidence interval; ICS, inhaled corticosteroid; COPD, chronic obstructive pulmonary disease; CRF-R, researcher’s case report forms.
Discussion

To our knowledge, this is the first study to estimate the social economic cost of COPD on a representative sample of adult patients in a Spanish autonomous community. Extremadura is only one of the 17 autonomous communities in Spain and gathers only 2.35% of the total Spanish population. Although this may limit the generalizability of our results to the rest of the country, the ratios of professional, structural, and technological health care resources in Extremadura are in line with average values in Spain,19 and the random selection of the Basic health areas where patients were recruited reflects potential differences in diagnostic and therapeutic patterns. Therefore, there is no reason to assume that the use of the resources consumed by the patients and the cost of these resources differ substantially from use and costs elsewhere in Spain. Moreover, the fact that Extremadura is an autonomous community with a relatively old population and a low population density20 makes it an optimal population for the development of this study as a pilot experience for future analyses in other autonomous communities that could serve to update national data on COPD economic burden.

Previous studies have estimated that the annual costs of COPD range between 675 and 775 million euros (of 1994) for Spain, including direct, indirect, and intangible costs.21 Other Spanish studies focus on the calculation of direct health costs, which range between 911 and 3,238 euros per patient per year.7,9,22–25 Despite the broad range of this interval, the studies agree that most DHC correspond to hospitalizations (40%–45%), followed by pharmacological costs (35%–40%), and visits and diagnostic tests (15%–25%).7,9,23,24 Our results indicate that in Extremadura, the proportion of DHC corresponding to pharmacological costs is slightly higher than these estimates (44.5%), and that hospital admissions are significantly lower than previous findings (23.1%).

One of the main strengths of our study is the estimation of the costs of informal care for COPD, as data published on this type of cost are scarce. A study conducted using the Spanish Survey on Disabilities, Personal Autonomy and Dependency (EDAD-08) estimated that ~48% of patients with COPD received informal care, which was valued between 24,549 and 40,681 euros per patient per year.26 These values are higher than our estimates, mainly because the EDAD-08 survey only includes individuals with a declared disability, with a greater need for care, and is not representative of COPD patients. Our results show that informal care accounts for 81.9% of the DNHC and 31.4% of the TC, indicating the incapacitating nature of COPD.

| Subgroups            | Valid N | DHC     | DNHC    | IC      | TC      |
|----------------------|---------|---------|---------|---------|---------|
| **GOLD severity scale** |         |         |         |         |         |
| GOLD I               | 41      | 1,246*  | 1,004   | 550     | 2,800*  |
| GOLD II              | 79      | 2,123*  | 1,042   | 1,120   | 4,285*  |
| GOLD III             | 35      | 2,430*  | 3,507*  | 1,905   | 7,842*  |
| GOLD IV              | 5       | 5,669*  | 7,691*  | 4,298   | 17,658* |
| Unknown              | 226     | 1,334   | 1,189   | 261     | 2,784   |
| **Gender**           |         |         |         |         |         |
| Male                 | 308     | 1,682   | 1,456   | 678     | 3,816   |
| Female               | 78      | 1,500   | 1,376   | 649     | 3,525   |
| **Age range**        |         |         |         |         |         |
| <65 years            | 80      | 1,261*  | 560     | 2,650*  | 4,471*  |
| ≥65 years            | 306     | 1,745*  | 1,670*  | 157     | 3,571*  |
| **Total**            | 386     | 1,645   | 1,440   | 672     | 3,757   |

**Notes:** All costs have been rounded to the nearest unit. *The low number of valid cases in this category suggests caution in the interpretation of its results. **This category was not included in the analysis of differences (Kruskal–Wallis test). ***Corresponds to labor productivity losses in the last 12 months for people up to 65 years of age. +Statistically significant differences (p<0.05) within each type of cost between the categories of each variable.

**Abbreviations:** DHC, direct health costs; DNHC, direct non-health costs; IC, indirect costs; TC, total cost; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

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**Abbreviations:** DHC, direct health costs; DNHC, direct non-health costs; IC, indirect costs; TC, total cost; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

**Figure 2** Total annual cost of COPD in Extremadura in 2015 according to cost typology.

**Abbreviation:** COPD, chronic obstructive pulmonary disease.
Our results on labor productivity lost by patients also shed light on the work disability linked to COPD, representing 17.9% of the TC.

Previous studies have documented the direct relationship between the level of severity of COPD and the derived costs. Our analysis found that patients with the highest COPD severity (classified as GOLD IV) had an average TC six times higher than that of the patients classified as GOLD I (17,658 vs 2,800 euros per year), four times higher than the patients classified as GOLD II (4,285 euros), and twice that of patients classified as GOLD III (7,842 euros). Gender did not account for significant differences in any of the cost categories, while analyses by age groups showed that patients ≥65 years of age incur higher direct costs, which is likely due to complications and/or comorbidities of COPD.

Regarding productivity losses, those of working patients (<65 years of age) accounted for 60% of their TC. This percentage is higher than that represented by the productivity losses of other chronic diseases, even those that affect younger population groups, such as depression, diabetes mellitus, HIV-AIDS, ankylosing spondylitis, heart failure, and multiple sclerosis.

This study is not without limitations. First, the severity level of the patient’s COPD corresponds to a variable constructed from information provided by the clinical history. However, this information was missing for the majority (58.3%) of the participants, for primary care records only collect information on the number of spirometries the patient had in the past 12 months, but do not necessarily provide the results of the spirometries, nor the GOLD classification of the patient. Therefore, the relationship between lung function impairment and costs that is presented in Table 6 may not reflect the actual relationship in the population. Had data been collected from pulmonology services’ clinical records, information on lung function impairment would be available for all patients. Second, the use of resources corresponds to resources associated with COPD in the past 12 months but it is possible that a proportion of these resources may not be strictly associated to COPD but to its related comorbidities. Thus, a clear distinction between costs strictly COPD related and costs related to its comorbidities cannot be made from our database, and results show all costs associated with COPD and its comorbidities. Third, working patients (7.9% of the sample) had to recall lost working hours in the past 12 months due to medical visits, tests, hospitalization, or feeling poorly, while patients on early retirement, temporary or permanent leave due to COPD, had to recall the length of time they had been in that situation. Therefore, results for productivity losses may be subject to some degree of recall bias. Finally, due to the difficulty in estimating in monetary terms the intangible costs associated with COPD – such as the loss of quality of life, and pain and suffering of both patients and informal caregivers – intangible costs were not taken into account in our calculations. The latter, together with the high rate of underdiagnosis of COPD in the general population, might imply that the real socioeconomic impact of COPD in Extremadura exceeds the figures estimated in this study.

Conclusion

Despite these limitations, this work represents the most complete and realistic economic estimate of the burden of COPD in Extremadura to date and can serve as an example for future cost estimations in other autonomous communities or nationwide, with the aim to enlighten the real magnitude of the socioeconomic impact of COPD in Spain.

In the context of permanent competitive demands due to the scarcity of health care resources, information on economic burden is necessary and important to make informed resource allocation decisions in the areas of prevention, early diagnosis, and management of COPD. Likewise, cost estimations might be valuable for future economic evaluations of new treatments for the disease. In addition, any program, strategy, or health care policy aimed at COPD patients should not overlook the importance of informal care. In brief, estimations of direct costs and IC of COPD might provide valuable information for decision making based on empirical evidence that will favor not only patients but also society in general.

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Author contributions

MM, RV, and AHV participated in the conception and design of the study. CC participated in the acquisition of data. MM and RV participated in the analysis and interpretation of data. MM wrote the draft of the manuscript. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work. All authors critically revised the manuscript for important intellectual content and approved the final version to be published.

Disclosure

The authors report no conflicts of interest in this work.

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## Table S1 Unit prices of resources related to COPD

| Resources                               | Euros (2015) | Reference                                      |
|-----------------------------------------|--------------|------------------------------------------------|
| Visits to the pulmonology specialist    |              |                                                |
| First visit                             |              |                                                |
| Section 1                               | 201.82       | Section 1: HA of Badajoz¹                       |
| Section 2                               | 183.57       | Section 2: HA of Cáceres¹                       |
| Section 3                               | 145.69       | Section 3: HA of Don Benito-Villanueva, Mérida, Llerena-Zafra, and Plasencia¹ |
| Section 4                               | 131.13       | Section 4: HA of Navalmoral and Coria¹         |
| Subsequent visit                        |              |                                                |
| Section 1                               | 121.09       | Section 1: HA of Badajoz¹                       |
| Section 2                               | 110.15       | Section 2: HA of Cáceres¹                       |
| Section 3                               | 87.42        | Section 3: HA of Don Benito-Villanueva, Mérida, Llerena-Zafra, and Plasencia¹ |
| Section 4                               | 78.68        | Section 4: HA of Navalmoral and Coria¹         |
| Medical tests                           |              |                                                |
| Blood analysis                          | 72.45        | ¹                                               |
| Spirometry with bd test                 | 84.16        | ¹                                               |
| Spirometry without bd test              | 42.08        | ¹                                               |
| Alpha-1 antitrypsin                     | 10.29        | Average price 2–4                               |
| Chest X-ray                             | 17.08        | ¹                                               |
| CAT                                     | 93.97        | ¹                                               |
| Gasometry                               | 7.88         | ¹                                               |
| Other medical tests                     |              |                                                |
| Ag1 Legionella urine                    | 21.03        | ¹                                               |
| Anti-biogram                            | 37.58        | ¹                                               |
| Diffusing capacity                      | 133.17       | ¹                                               |
| Co-oximetry                             | 11.60        | 5                                               |
| Sputum culture                          | 37.58        | ¹                                               |
| Streptococcus pneumoniae culture        | 23.20        | ¹                                               |
| 6-minute walk test                      | 126.66       | ¹                                               |
| Electrocardiogram                       | 30.24        | ¹                                               |
| Echocardiogram                          | 168.83       | ¹                                               |
| Abdominal ultrasound                    | 54.79        | ¹                                               |
| FeNO                                    | 17.19        | 2                                               |
| Pulmonary scintigraphy                  | 272.49       | ¹                                               |
| Thyroid hormones                        | 26.12        | ¹                                               |
| Cardiorespiratory polygraphy            | 192.79       | Average price 2,4,6,7                           |
| Oxygen saturation/pulsometry            | 2.81         | 4,5                                             |
| Visits to the emergency room            |              |                                                |
| Emergency consultation in primary care  | 54.88        | ¹                                               |
| Emergency consultation in hospital care  | 218.61       | ¹                                               |
| Use of ambulance                        |              |                                                |
| Use of non-assisted emergency health transport | 273.23       | Average price 4,5,8–15                        |
| Use of emergency ambulance (medicalized) in situ | 1,076.46     | ¹                                               |
| Hospital admissions                     |              |                                                |
| GRD 85: pleural effusion with CC        | 4,533.10     | 16                                              |
| GRD 88: COPD                            | 2,652.45     | 16                                              |

(Continued)
Table S1 (Continued)

| Resources                                                                 | Euros (2015) | Reference |
|---------------------------------------------------------------------------|--------------|-----------|
| grD 89: simple pneumonia and pleuritis age &gt;17 with CC                | 3,581.46     | 16        |
| grD 99: respiratory signs and symptoms with CC                            | 3,221.03     | 16        |
| grD 101: other respiratory system diagnoses with CC                       | 3,495.95     | 16        |
| grD 143: chest pain                                                       | 2,338.61     | 16        |
| Home oxygen therapy                                                       |              |           |
| One day of use                                                            | 3.74         |           |
| Stay in housing or residential center                                      |              |           |
| One month of stay in nursing home                                         | 732.91       | 1         |
| Day care center                                                           |              |           |
| Care/eye/user                                                             | 6,145.35     | 18        |
| Professional care at home                                                 |              |           |
| One hour of formal care                                                   | 6.14         | 18        |
| Informal care                                                             |              |           |
| One hour of informal care                                                 | 5.08         |           |
| Wage for every hour worked                                                |              |           |
| Females                                                                   |              |           |
| Occupation high                                                           | 16.88        | Large occupation groups 1–3<sup>20,21</sup> |
| Occupation medium                                                         | 9.90         | Large occupation groups 4–7<sup>20,21</sup> |
| Occupation low                                                            | 9.38         | Large occupation groups 8 and 9<sup>20,21</sup> |
| All occupations                                                           | 11.81        | 20,21     |
| Males                                                                     |              |           |
| Occupation high                                                           | 20.05        | Large occupation groups 1–3<sup>20,21</sup> |
| Occupation medium                                                         | 11.45        | Large occupation groups 4–7<sup>20,21</sup> |
| Occupation low                                                            | 9.67         | Large occupation groups 8 and 9<sup>20,21</sup> |
| All occupations                                                           | 13.39        | 20,21     |

Abbreviations: HA, health area; bd, bronchodilator; CC, complications and/or comorbidities; FeNO, fractional exhaled nitric oxide; grD, related groups by diagnosis; ref, reference; CAT, computerized axial tomography.

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