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Costs of chronic obstructive pulmonary disease (COPD) in Italy: The SIRIO study (Social Impact of Respiratory Integrated Outcomes)

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Summary

Chronic respiratory diseases affect a large number of subjects in Italy and are characterized by high socio-health costs. The aim of the Social Impact of Respiratory Integrated Outcomes (SIRIO) study was to measure the health resources consumption and costs generated in 1 year by a population of patients with chronic obstructive pulmonary disease (COPD) in a real-life setting. This bottom-up, observational, prospective, multicentric study was based on the collection of demographic, clinical, diagnostic, therapeutic and outcome data from COPD patients who reported spontaneously to pneumological centers participating in the study, the corresponding economic outcomes being assessed at baseline and after a 1-year survey. A total of 748 COPD patients were enrolled, of whom 561 [408 m, mean age 70.3 years (SD 9.2)] were defined as eligible by the Steering Committee. At the baseline visit, the severity of COPD (graded according to GOLD 2001 guidelines) was 24.2% mild COPD, 53.7% moderate and 16.8% severe. In the 12 months prior to enrollment, 63.8% visited a general practitioner (GP); 76.8% also consulted a national health service (NHS) specialist; 22.3% utilized Emergency Care and 33% were admitted to hospital, with a total of 5703 work days lost. At the end of the 1-year survey, the severity of COPD changed as follows: 27.5% mild COPD, 47.4% moderate and 19.4% severe. Requirement of health services dropped significantly: 57.4% visited the GP; 58.3% consulted an NHS specialist; 12.5% used Emergency Care and 18.4% were hospitalized. Compared to baseline, the mean total cost per patient decreased by 21.7% ($p < 0.002$). In

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conclusion, a significant reduction in the use of health resources and thus of COPD-related costs (both direct and indirect costs) was observed during the study, likely due to a more appropriate care and management of COPD patients.

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Introduction

Chronic obstructive pulmonary disease (COPD) is the chronic respiratory disorder that currently represents the most significant health problem at international level: its epidemiological, clinical, social and socio-economic impact is progressively rising and there are no signs of any change to this trend. Moreover, COPD represents an enormous health problem for the community, affecting patients and their families, the employment sector, the institutional network and hence society as a whole dramatically.¹⁻⁶

Cost of illness (COI) analysis, carried out by means of the measurement and estimation of the resources consumption used in disease management, is a useful methodological tool that broadens the criteria for evaluating the effects of a given disease since it provides information about the economic (as well as clinical) effects that the disease has on the entire "health system".

In face of the ever growing need to reconcile the limited available economic resources with an increasing demand for well-being from the general population, already for a number of years the health services of industrialized countries have been devoting attention to the costs generated by healthcare in their own territories. Data that permit an estimate of such costs should ideally be produced in a "real" context, if they are to reflect faithfully what is happening in everyday life: only in this way can they be fully credible and of use to the institutions for future planning.

From this arises the importance of observational studies on health outcomes, aimed not only at reducing costs but also at optimizing management and ensuring a more rationalized use of resources.

Chronic respiratory diseases, in particular, concern a large number of subjects and generate important health and social costs. The global impact of these diseases, in particular COPD, is the subject of an increasing number of pharmaco-economic studies published in the literature over the last few years.⁷⁻¹⁷ Although these studies were based on different experimental designs, they nevertheless confirm the elevated and growing impact of COPD in all countries, from the perspective both of the patient and family, and that of society as a whole. The findings that emerge highlight moreover that the attitude towards COPD management is still largely inadequate.^{7-9,13,14,17}

To provide an updated contribution in this field with regard to Italy, the Social Impact of Respiratory Integrated Outcomes (SIRIO) study was designed as a global outcome study to produce data regarding the socio-economic impact of the major respiratory diseases (bronchial asthma, COPD, community acquired pneumonia—CAP). In this article, we report exclusively data concerning COPD.

Due to the strategic value of the initiative—something of a novelty in our country—SIRIO was promoted by UIP (Unione Italiana per la Pneumologia—Italian Union for

Pneumology) and endorsed by the following scientific societies: AIPO—Associazione Italiana Pneumologi Ospedalieri (Italian Association of Hospital Pneumologists) and SIMeR—Società Italiana Medicina Respiratoria (Italian Society of Respiratory Medicine).

Materials and methods

The SIRIO/COPD study consisted in the creation of an on-line pharmaco-economic network on COPD in Italy. The study was not designed to evaluate pharmaceutical drugs, nor therapeutic strategies, nor diagnostic procedures: its aim was purely to provide an updated estimate of the economic cost of COPD in an Italian population affected by this disease. The choice of a prospective design allowed a greater precision in describing the different items for expenditure, the quality, specificity and speed of data calculation being optimized by a dedicated software system for the collection and on-line analysis of data.

Design and procedures

This bottom-up, observational, prospective, multicentric study was based on the collection of demographic, clinical, diagnostic, therapeutic and outcome data of COPD patients who spontaneously requested a pneumological consultation. Patients' inclusion in the study did not imply any procedure, risk or advantage other than those of routine clinical practice. Patients were enrolled in the study if they fulfilled the following inclusion criteria: males or females of adult age (18 years) with a diagnosis of COPD according to the GOLD 2001 guidelines¹⁸ in stable phase or symptomatic, who reported spontaneously to the specialist center as a first-time patient, as a previous patient coming for a scheduled check, or as a previous patient coming with symptoms of COPD exacerbation. The only exclusion criterion was that patients should not be enrolled in any clinical study. All subjects gave informed consent to participate in the study and allowed the use of their personal data for research purposes.

The study envisaged a minimum of two visits, i.e. one at baseline and the other after 12 ± 1 months; if necessary, further visits were possible during the 1-year survey. At baseline, demographics (age, sex, marital status and employment status), clinical data (symptoms; disease duration, disease severity, and frequency of exacerbations, including the presence of comorbidities), diagnostic information (type and number of specialist/non-specialist examinations performed to assess COPD in the 12 months prior to enrollment), some outcomes (GP and specialist visits, recourse to Emergency Care, hospital admissions, Day Hospital, work days off in the 12 months prior to enrollment), and information on therapeutic consumption

were collected for each patient. The majority of patients who spontaneously referred to the specialist centers had already received their diagnosis of COPD. Nevertheless, diagnosis was confirmed in the recruited patients by collecting anamnestic data, clinical information, and lung function data. In many cases, GPs' files were also consulted to clarify particular situations, e.g. concerning the number of admissions or number of diagnostic tests carried out in the 12 months prior to enrollment.

As SIRIO study was an observational survey in real life, physicians had the opportunity to prescribe the treatment they considered as most suitable for the patient's conditions; hence, no pre-set treatment was indicated to the physicians taking part in the study, nor were any management recommendations given. During the baseline visit patients were given the self-administered health status questionnaire EQ-5D (Euro-Qol, Quality of Life in Europe, 5 Dimensions) to fill in¹⁹ together with a visual analogic scale (VAS) in order to assess their health status.

The end-study visit was scheduled to take place at the end of the follow-up period, i.e. at 12 ± 1 months following the patient's recruitment. If an unscheduled visit to the specialistic center occurred within this time-frame, it could be used as the end-study visit. Other visits that occurred close to the end-date of the study, but outside the period of ± 1 month allowed, were not considered as end-study visits, and the patient was further recalled for a specific end-study visit, within the time interval established by the protocol. If the patient could not be contacted, or skipped, or had died in the interim, the specialist registered the information on the data collection card.

At the end-study visit, the same data collected during the baseline visit were updated. As this visit was part of the protocol, it was not considered in terms of resource consumption. On the contrary, if a patient made an unscheduled visit to the center for any healthcare intervention related to the COPD conditions, and if this occurred within the time-frame of the end-of-study visit (12 ± 1 months since the recruitment), that visit was calculated as additional healthcare consumption, since it was not induced by the protocol but spontaneously generated by an uncontrolled clinical change.

Data collection

Study data were collected through a dedicated software that encrypted patients' names to guarantee anonymity; data were sent via e-mail to the coordinating center which housed the central database.

The questionnaire EQ-5D was given to patients in paper form; all questionnaires were then sent by mail to the database center.

Study dimension

To ensure that data were representative of the whole of Italy Pneumological Centers were selected by the two endorsing Scientific Societies according to strict geographical criteria for distribution; moreover, the modes of data collection envisaged by the protocol made participation in

the study possible only for centers equipped with suitable computer systems.

In the global design phase of SIRIO, we hypothesized a variability of cost range of between 150% and 200% for the diseases considered, and we therefore established that a statistical sample totaling between 1000 and 1500 patients would allow an estimate with a 10% margin of error (with 95% confidence interval). Moreover, considering a drop-out percentage at follow-up of around 10–15%, each center would have to recruit a total of approximately 50 patients, variously distributed between asthma, COPD and CAP.

In each center, patients were enrolled consecutively, according to the order in which they presented to the pneumologist for consultation.

Data analysis

In order to analyze all data in the whole COPD sample, descriptive statistics were used.

Descriptive statistics were used to analyze the demographic, clinical and treatment characteristics of the total study population and of the subgroup of patients affected by COPD.

Statistical comparisons were calculated by means of non-parametrical tests (Welch test) in order to compare variations in the most relevant outcomes versus baseline values (e.g. mean costs for each level of asthma severity; mean total cost of illness), and a $p < 0.05$ was accepted as the minimum level for statistical significance.

Health costs

The healthcare interventions (e.g. visits, diagnostic tests, hospital admissions, etc.) had been valued and corresponding real costs attributed.^{20–23}

The following categories of costs were considered:

Direct

These are the costs effectively generated by the respiratory disease and/or paid for by the patient. They include direct health costs, i.e. the monetary value of the resources used in the diagnosis and treatment (therapies, hospitalization, etc.) and in general constitute an economic burden borne chiefly by the NHS.

Both treatment for COPD and that for comorbidities were calculated as direct costs. Concomitant pharmacological treatment was defined as "any treatment needed to treat any disease different from COPD or comorbidity which the patient is suffering from".

Furthermore, the direct non-medical costs of different origin (e.g. transfers of patient and caregivers for examinations and/or hospitalization, home care, etc.) were calculated using average unitary costs of different types, according to the case (transport tariffs, tariffs for paid caregivers, etc.).

Indirect

These are costs corresponding to the loss of productivity occurring as a result of a patient's inability to work (or death) on account of the disease. The economic burden of indirect costs is borne essentially by the society.

To evaluate the indirect costs, we referred to the activity carried out by the patient, considering the average daily wage that such activity implies.

Intangible

These are costs not convertible in monetary terms, in that they relate specifically to the distress and suffering caused by the disease. Measurement of the patient's self-perceived health status is performed by means of quantitative scales. The perception of a poorer health status due to the disease, compared to a conventional value indicating full health, was considered as a proxy of the intangible costs.

Health status

Measurement of health status was performed by means of the questionnaire EQ-5D, in the official Italian version,¹⁹ which is a simple generic instrument of general applicability to diseases and treatments. Patients identify their own health status indicating on the first page of the questionnaire which level of attitude (of the three given) best corresponds to their situation for each of the five dimensions: (1) movement capacity, (2) personal care, (3) habitual activities, (4) pain or irritation, (5) anxiety and depression. Each dimension has three response levels, giving thus 243 possible health statuses. The information gathered is synthesized by an algorithm into a score ranging from 0 to 1.

On the second page of the questionnaire patients are required to indicate on a VAS their currently perceived health status: the linear VAS grade was from 0 (worst health status imaginable) to 100 (best health status imaginable).

As the instrument's output is a single numerical value that expresses the health-related quality of life, it can be used in cost-utility analyses. Generally, it takes just a few minutes to complete the EQ-5D.

Ethical issues

The study was approved by the Ethics Committee of the Coordinating Center which notified all participating centers.

Results

Of the 37 Pneumology Centers distributed throughout Italy initially involved in the study, 32 of them enrolled subjects with COPD effectively. The five centers which did not recruit any subjects had severe bureaucratic delays with their local ethical committees and missed the deadline for entering the study: there was no particular geographic bias in the distribution of these centers.

Demographic, clinical and diagnostic data

In the period November 2001–December 2003, 748 COPD patients were enrolled, but only 561 of them (408 males; mean age 70.3 years \pm 9.2 SD) fully completed the 1-year survey and thus were considered eligible for analysis (those patients who spontaneously interrupted their participation, were never seen, or whose forms were incompletely filled in were considered ineligible). In the course of the survey a

total of 11 patients died: all were severe COPD patients (in stage 3 category which represented 16.8% of the overall group). No deaths were observed in the other groups. The geographical distribution of the 561 patients who underwent analysis is reported in Table 1. The most represented category was that of retired, while the least represented was that of full-time employees; current and ex-smokers were the majority of the patient sample (Table 1).

The average distance traveled by patients to reach the specialist center was 27.4 km, with a maximum of 122.9 km and a minimum of 4.9 km in two centers, respectively, in south and central Italy.

In the vast majority of patients (91.1%), COPD had been already diagnosed, the mean duration of COPD being on average 13.3 years. At enrollment, mean lung function (FEV₁) in the clusters of patients with different COPD severity according to the GOLD 2001 guidelines was as follows: level 0, 88.1% \pm 9.8 (mean FEV₁% pred. \pm SD); level 1, 86.0% \pm 7.9; level 2, 54.2% \pm 10.1; level 3, 22.3% \pm 7.6 (Figure 1A).

At the time of enrollment, almost all patients (94.7%) with a previous diagnosis of COPD had already performed at least one spirometry test; 1.8 years was the average time lapsed since the last spirometry. In patients with a first-time diagnosis of COPD, spirometry had already been performed in 64% of subjects.

At least one comorbidity was present in 67.7% of patients, and their frequency is reported in Figure 2: cardiovascular comorbidities were the most represented.

Table 1 Characteristics of study population.

	No. (%)
Total	561
Mean age _{years} (S.D.)	70.3 (9.2)
Sex	
Males	408 (73.0)
Females	153 (27.0)
Geographic distribution	
North	174 (31.0)
Centre	156 (28.0)
South	231 (41.0)
Occupational status	
Retired	431 (76.8)
Housewife	51 (9.1)
Full-time employee	43 (7.7)
Self-employed	28 (5.0)
Other	8 (1.4)
Smoking habit	
Non smoker	86 (15.2)
Smoker	60 (11.0)
Ex-smoker	265 (47.2)
N/A	150 (26.6)
Respiratory therapy	
Yes	541 (97.0)
No	20 (3.0)

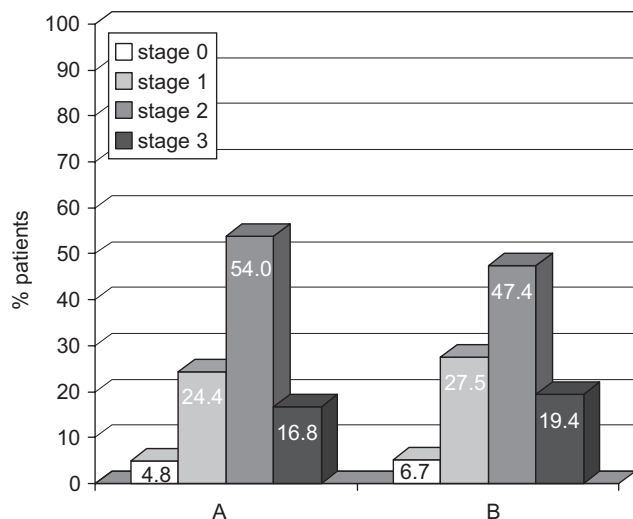


Figure 1 (A and B) Distribution of COPD patients according to their clinical severity (GOLD 2001): (A) baseline; (B) follow-up.

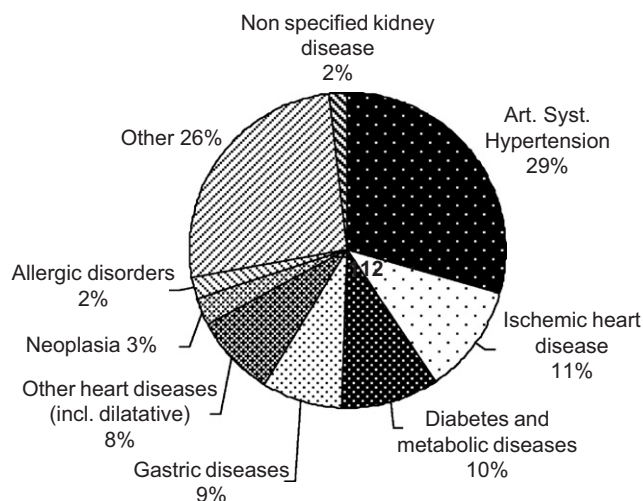


Figure 2 Distribution of concomitant diseases. Total patients with at least one comorbidity ($n = 380$).

In the 12 months preceding enrollment, subjects had carried out a total of 2385 diagnostic tests. A list of those most frequently performed ($> 1\%$) is reported in Figure 3. Of note, the total value spent for diagnostic procedures was quite low (6% of total cost).

Outcome data

The absolute number and corresponding percentage of subjects who visited the GP, consulted an NHS specialist, utilized Emergency Care, or who were hospitalized at least once during the 12 months prior to enrollment are reported in Table 2A, together with the overall number of work days lost (5703).

Changes in COPD severity as assessed at the end of the survey are reported in Figure 1B. Changes in all outcomes monitored during the study (e.g. number of visits, number of

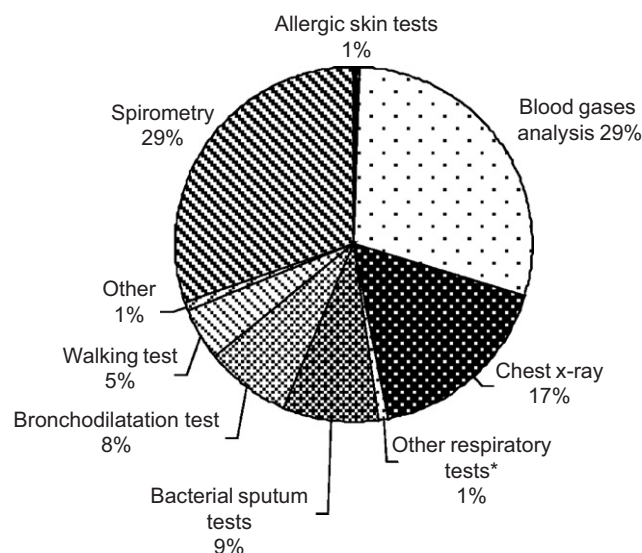


Figure 3 Distribution of diagnostic tests performed in the 12 months preceding enrollment.

hospitalizations, etc.) are reported in Table 2B analytically, together with the corresponding number of work days off. All these figures dropped dramatically at the end of the survey.

Evaluation of costs

The mean total direct costs per patient are reported in Table 3; in general, total cost of illness dropped significantly at the end of the 1-year survey ($p < 0.002$). Mean total cost in females was significantly higher than that calculated in males ($\text{€}2191.73 \pm 3098.66$ versus $\text{€}2923.16 \pm 4057.60$ SD, respectively; $p = 0.022$).

Of note, in spite of the substantial increase in pharmaceutical costs, there was a significant drop in all other direct costs: in particular, there was a substantial reduction in costs due to hospitalizations and Emergency Care. Indirect mean costs also decreased significantly during the 12-month survey (Table 3).

Total mean cost proved proportional to the severity of COPD, varying from $\text{€}1314.94 \pm 1830.61$ SD for mild disease to $\text{€}5451.66 \pm 5312.67$ SD for more severe COPD (Figure 4A and B) ($p < 0.01$). Moreover, the statistical comparisons between costs calculated for the corresponding COPD stages before and after the survey were: stage 0, $p = \text{ns}$; stage 1, $p = 0.05$; stage 2, $p = 0.004$; $p = 0.056$, respectively. In other words, only stages 2 and 3 showed that they can in real life be influenced by a more strict control of COPD patients. In total, the mean cost per patient decreased by $\text{€}590.79$ at the end of the survey ($p < 0.001$) (Table 3).

Treatment data

Both at baseline and at the end of the study, 97% of patients were pharmacologically treated for their COPD, thus supporting the hypothesis that the clear improvement in

Table 2 A and B—visits and/or hospital admissions and/or Emergency Care use by patients: (A) baseline; (B) follow-up.

Visits/admissions	A (n = 561)				B (n = 561)			
	Total, n	n	No. of patients	% Patients	Total, n	n	No. of patients	% Patients
Visits to GP	2541	358	63.8		1361	322	57.4	
Visits to NHS specialist	1335	431	76.8		812	327	58.3	
Visits to private specialist	123	56	10.0		108	51	9.1	
Access to Emergency Care	207	125	22.3		104	70	12.5	
Hospital admission	268	184	33.0		148	103	18.4	
Day Hospital		199	32	5.7		158	30	5.3
Total work days off	5703				5212			

Table 3 Direct, indirect and total mean costs per patient.

Parameters	Baseline		Follow-up	
	Mean cost per patient (n = 561)		Mean cost per patient (n = 561)	
	Value in €	%	Value in €	%
Principal pharmacological therapy	347.23	12.7	663.78	31.1
Concomitant pharmacological therapy	186.82	6.9	256.44	12.0
Hospital admissions	1519.67	55.8	823.12	38.6
Day Hospital	88.68	3.3	70.41	3.3
Access to Emergency Care	7.62	0.3	3.83	0.2
Visits to GP and specialist	150.59	5.5	93.99	4.4
Examinations*	162.68	6.0	124.66	5.8
Verifications of side effects	0.70	0.0	0.12	0.0
Environmental preventive therapy and home help	3.07	0.1	2.35	0.1
Alternative therapy†	39.77	1.5	5.88	0.3
Total direct costs	2506.84	92.0	2044.58	95.9
Work days lost	216.84	8.0	88.31	4.1
Total indirect costs	216.84	8.0	88.31	4.1
Total costs	2723.68 ± 3831.24	100	2132.89 ± 2776.30‡	100

*Spirometry, blood gases analysis, allergic skin tests, chest X-ray, sputum test, strength test, Walking test, bronchial provocation test, bronchodilatation test, bronchoscopy, etc.

†Thermal cures, homeopathy, etc.

‡ $p < 0.002$.

economic outcomes is not due to a higher percentage of treated patients at the end of the 12-year survey (Table 1).

In the 12 months prior to enrollment, respiratory drugs accounted for 12.7% of the total cost of the disease, while those prescribed for the management of concomitant diseases represented 6.9%. Costs related to alternative therapies (homeopathy, etc.), environmental preventive treatments, and to the performance of medical procedures secondary to negative side effects consequent upon the assumption of therapeutic drugs (both for basic and concomitant therapy) were completely marginal (Table 3). At the end of follow-up, a notable increase was observed in pharmaceutical costs (31.1% in those for respiratory drugs and 12.0% in those used to treat comorbidities). This occurred without any increase in the percentage of subjects treated for COPD, which was unchanged.

However, as mentioned above, the increase in costs of basic therapy was offset by a marked, systematic decrease in all other direct costs as well as in the indirect costs induced by the disease.

The total mean cost of COPD showed some variations according to the geographical zone of patient recruitment. Even though statistically not significant ($p = ns$), the cost in the central Italian regions was lower than the mean national cost, while in the southern regions it was higher (Figure 5). This gradient persisted also when subjects were subdivided according to clinical severity. Moreover, in the 12 months prior to enrollment, northern regions produced the lowest mean indirect costs in the same period. At the end of the survey, a significant reduction of both direct and indirect costs was in any case observed in all the three macro-regions considered in the study.

Discussion

The awakening of international focus on COPD dates back to just a few years ago, in response to its ever growing prevalence and increasing incidence. The concern about COPD is in fact of more recent date than that about bronchial asthma, which first began to cause alarm about 15 years ago. It is in fact just a few years ago that the study was published which forecast that, in 2020, COPD would represent the third-ranking cause of mortality in the world.¹

Awareness about the global problem of COPD was subsequently promoted also by the European Respiratory Society which, in 2003, published the first European report on respiratory diseases by proposing its importance as a health and social issue to all European citizens and invoking the attention of political leaders.^{24,25} Even if the importance of COPD still does not appear to be fully grasped by all parts of the social and institutional infrastructure, the European report in any case helped draw attention to the elevated impact of COPD as a disease in the community. The report moreover evidenced the distribution of COPD in the different European countries, with up-to-date data on the costs, risk factors, diagnostic techniques and therapeutic options (pharmacological and non-pharmacological).

Generally, the impact of COPD is high in all countries, particularly in the more industrialized ones.^{8,13–16,25} Nevertheless, as for asthma, also for COPD the global impact has been demonstrated to be independent of the specific health and welfare models adopted in the each single country.

In USA, the country that first undertook to analyze the economic impact of the disease, the total cost of COPD was recently estimated at \$24 billion, more than 60% of which was due to direct costs, 18% to loss of earnings due to early death, and 20% to morbidity.²⁵

In Italy, in 1997, COPD represented the fifth cause of hospitalization for non-surgical causes, determining more than 1 million days of hospital stay (data ISTAT). In 1999, ISTAT also documented that 2.6 million Italian citizens were affected by COPD, with a mortality of approximately 18,500 individuals, which represents more than 50% of all causes of death for respiratory causes. From more recent data, it

appears that 6% of individuals aged between 46 and 55 years, and 11% of individuals over 55 years of age, are affected by COPD in our country.²⁴

Unfortunately, not a lot of data are available in Italy concerning the prevalence of different classes of COPD severity. In particular, the only data available derive from epidemiologic studies carried out by means of questionnaire investigations. Even though the present study was carried out in a different setting (the target was patients recruited in hospital outpatient clinics, and COPD prevalence was 24.2% mild, 53.7% moderate and 16.8% severe), corresponding results were found in two other previous Italian studies.^{7,27} In these studies, mild COPD was around 30%, while moderate around 55%, and severe around 12%.

SIRIO results are in good agreement also with the most recent data on distribution of different stages for COPD severity, which are based on national epidemiological data.^{25,27} Also in Italy COPD has been demonstrated to have an extremely significant socio-economic impact. In our study, the mean annual cost per patient was €2133, corresponding to a 20% increase with respect to the cost calculated 5 years previously in a similar, but not identical study (a *bottom-up* pilot study based on a national population of more than 5 million inhabitants based on telephone interviews).²⁶ Significant differences were registered according to the clinical severity of the disease, the cost varying from €1500.8 for the milder forms (65% of cases) to €3001.1 for moderate forms (30% of cases) to €3911.7 for severe COPD (5% of cases).⁷

The above-mentioned nation-wide survey based on telephone interview, showed that in Italy there is still a long road to go before we reach an acceptable management control of COPD. In this study, in fact, 28% of the subjects interviewed declared to be little or not at all clinically controlled by their current therapy and more than 60% of these subjects reported they had had to consult their GP at least three times in the last 12 months on account of COPD: added to this were, on average, two more specialist consultations effectuated in the same period. Moreover, 19% of the visits performed resulted unscheduled and were related to a sudden worsening of the disease. Finally, in the

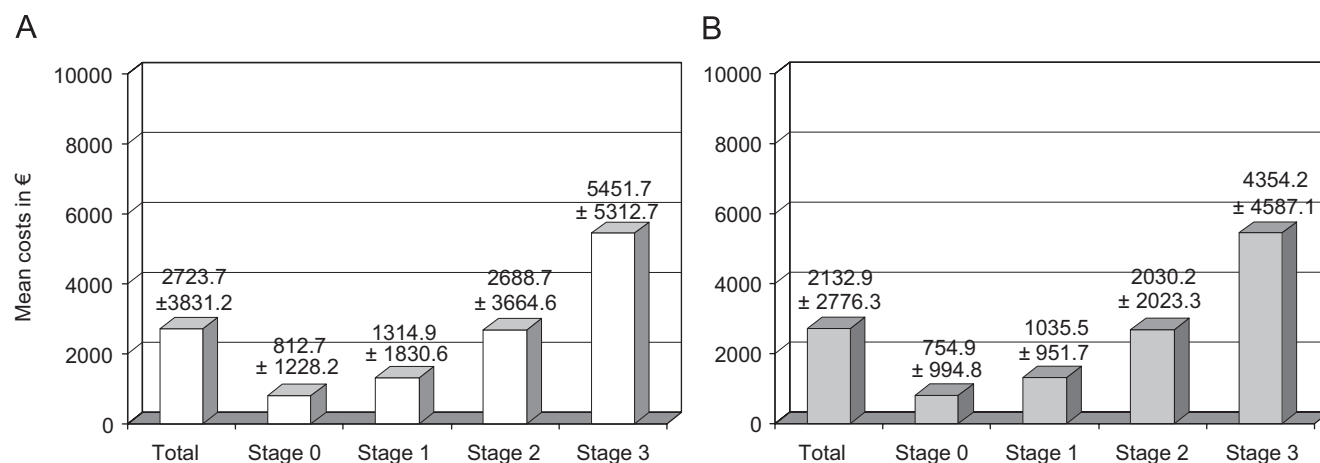


Figure 4 (A and B) Mean annual cost per patient and subdivided according to stage of COPD severity: (A) baseline; (B) follow-up. Statistical comparisons between costs for corresponding COPD stages were: stage 0, $p = ns$; stage 1, $p < 0.05$; stage 2, $p < 0.004$; stage 3, $p < 0.056$.

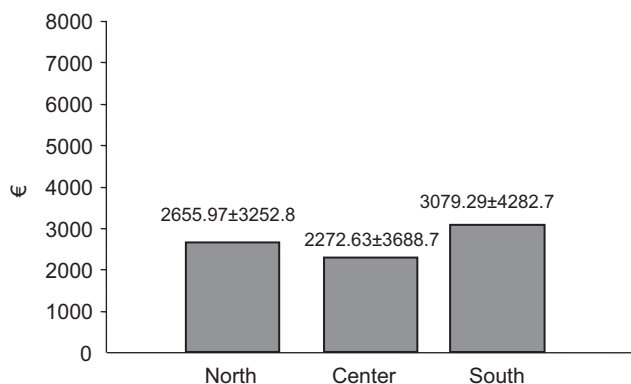


Figure 5 Regional distribution in mean total annual cost per patient (€).

last 12 months, 11% of the subjects had been admitted to hospital, and 6% had passed through an emergency or intensive care unit. Only 35% of subjects had been regularly prescribed respiratory drugs, and in more than 50% of these the treatment had consisted in the sole repeated assumption of antibiotics, in some cases up to 20 cycles in the 12 months. In the same study, the hospitalization phenomenon had been found to account for 3/4 of the total cost. Once again, the cost varied as a function of clinical severity, reaching an approximate cost of €7000 per patient per year in the more severe stages of COPD. Furthermore, the mean costs were far higher in males (+160%), in subjects with comorbidities (+82%), and in those not enrolled in specific educational programs (+42%). In any case, the incidence of costs related to diagnostic procedures and therapeutic treatment resulted very low (globally only 17%).²⁶

It is known that, in the course of COPD, the most frequent cause of hospitalization, and thus the most significant item of cost, is the event of *exacerbation*.^{13,14,17,28–30} Patients can experience up to three or four exacerbations per year, of varying degrees of severity. The causes of exacerbation are multiple, and include late diagnosis of COPD, a healthcare organization still based on hospitalization, and inappropriate treatment and management. In this regard, it should be noted that treatment failure of an exacerbation (due to underestimation and/or inappropriateness) leads, in economic terms, to a far higher consumption of resources than that required for the exacerbation itself.^{13,14,30} Generally speaking, in order to provide information that is reliable and able to effectively influence the strategic decisions aimed at controlling an expanding disease like COPD, epidemiological and pharmaco-economic studies need to be conducted more frequently, so as to render more stable the available data and, at the same time, monitor eventual management or behavioral constraints on the state of control of the disease.

Actually, the SIRIO study seems to fit well this bill, aimed as it is to produce up-to-date data on the health resources consumption and costs generated by COPD in Italy. The study design (observational, prospective, multicentric) was chosen precisely to allow a comparison between current data and historical data previously collected through the same bottom-up methodology.

In our study, COPD was confirmed in our country to be still most prevalent in males, in smokers (ex or current), and in the older age groups, i.e. in those subjects who represent the weakest and the least active individuals in socio-economic terms, but without any significant regional differences.

In our study group, the incidence of clinically important concomitant diseases emerged as very significant. Heart diseases (in particular hypertensive and ischemic heart disease), dysmetabolic diseases (diabetes, dyslipidemia), gastric diseases and cancer resulted the most prevalent comorbidities.

Actually, COPD patients appear to be a particularly fragile population in which the effects of disability induced by precarious clinical conditions involving diverse organs and systems interact, in an additive and/or synergic way, with those of the basic disability determined by COPD. It however should be emphasized that in the representative sample COPD resulted of moderate severity in more than 50% of cases, but that, on the other hand, severe COPD showed an incidence of 16% in the recruited subjects. This clinical impact appears further confirmed by the poor quality of life that characterized, on the basis of data collected from both questionnaires used (VAS and EQ-5D), our COPD subjects: this finding was independent of the age class of single subjects (Table 4).³

From the above evidence one cannot but deduce that COPD still has a very high socio-economic impact in Italy, which society will have to face in the near future if it wants to avoid the health system getting “out of control”.

The consumption of resources and health goods was found to be consistent with a frequent recourse to GP and specialist consultations, hospitalization, and use of urgency-emergency facilities. In other terms, at a distance of only a few years from the two previous Italian studies on COPD,^{7,26} data of the SIRIO study document a further, not negligible increase in the impact of COPD and indicate that the disease control is still a long way from being adequate at territorial level.

Table 4 Health questionnaire EQ-5D and VAS scores in all patients and in patients subdivided by age category.

	No. of patients	Score*			
		Mean	S.D.	Minimum	Maximum
EQ-5D	414	0.683	0.255	−0.429	1.000
19–64 years	107	0.693	0.275	−0.358	1.000
>65 years	307	0.680	0.249	−0.429	1.000
VAS	414	0.588	0.183	0.000	1.000
19–64 years	107	0.623	0.203	0.000	0.960
≥65 years	307	0.576	0.175	0.000	1.000

*Normal references for Euroqual User Guide values: total = 0.856; subject <65 years = 0.885; subject >65 years = 0.740.

In economic terms, at the time of enrollment (reflecting thus principally the state of local management), the total annual mean cost of COPD was more than €2700 per patient: in fact a mean cost of approximately 22% more than what was documented only a few years ago in a comparable bottom-up study. This preoccupying development in costs was confirmed also when the different levels of clinical severity of COPD were considered, in particular for the more severe clinical conditions.

What once again emerges from the present findings is the dramatic incidence of direct costs, mainly due to hospitalizations, which is in contrast to the modest incidence of treatment costs and a negligible role of diagnostic costs.

As in several other countries, also in Italy the present diagnostic approach to COPD is still far from the GOLD standard. Spirometry still is used only in the vast minority of patients (20–25% of cases) both for diagnostic and for monitoring purposes. Furthermore, the therapeutic approach is mainly based on short-acting beta-agonists as required; moreover, LABA (alone or in combination with ICS) and/or anticholinergics are also used but off label in the majority of cases (particularly in mild-to-moderate COPD), where the correspondance with COPD severity is very poor.

The aim of SIRIO was also to estimate the resources expenditure over the follow-up period. At the end of the study, we observed a significant, consistent decrease in the total mean cost (–17%), correlated in particular to an equally significant reduction of the direct mean costs (–18.4%). As the number of subjects in treatment for COPD remained absolutely unmodified (97% before and after follow-up), this management finding is probably attributable to the sole fact of more appropriate therapeutic interventions during the period of follow-up (ICS, LABA, etc.). On the other hand, corresponding to a significant increase in the cost for pharmaceutical drugs (both those of principal therapy and those for concomitant diseases) there was in fact a net decrease in visits made to the GP and specialist, use of emergency structures, hospitalization, work absenteeism, and use of alternative therapies. Even if indirectly, the picture that clearly emerges at the end of the survey is of an improved general respiratory health status of the COPD patients recruited, thus confirming the partial treatability of COPD and the possibility to minimize related costs.

These positive results in terms of direct and indirect savings remained equally significant when COPD patients were divided by the level of their clinical severity and by geographical zone of enrollment.

Generally, this confirms once again that an attentive and appropriate use of the therapeutic resources currently available represents the key point on which to base the management of COPD (a disease in itself difficult to control), both in terms of efficacy and efficiency. It should not come as a surprise that the findings emerging from SIRIO highlight the fact that outcome optimization and reduction of costs are obtainable simply through a more appropriate utilization of the available resources. This finding is confirmed by a recent study carried out in subjects with severe and very severe COPD which showed the possibility to optimize clinical outcomes maintaining the same level of health resources and costs.³⁰

However, it still emerged as critical the situation of COPD patients who come too late to the attention of the medical

specialist and whose disease continues to be underestimated both from a diagnostic (there is still inadequate recourse to suitable and appropriate investigations) and therapeutic point of view.

Globally, the findings of the SIRIO study show that today, and in the near future, to implement the best strategies of intervention it is fundamental to have periodic recourse to analyses on the impact of the most frequent chronic/persistent respiratory diseases, in particular COPD. If effective and credible study models are used, these evaluations based on the estimate of resources consumption required for disease management will increasingly represent an indispensable decisional tool that can guide decision makers in future health policies, both at local and national level. Vice versa, if such information is not available, this will inevitably end by negatively affecting the quantity and quality of the efforts to manage the disease, as well as the sensitivity and specificity of the markers used to monitor outcomes. It is equally inevitable that, in the final analysis, what will suffer most will be the effectiveness and tempestivity of the healthcare planning to cope with this growing and challenging respiratory disease.

The message for the Italian healthcare system is that COPD continues to rise and that it is causing an ever increasing economic burden for society and the patient. A second message is that more effective territorial strategies for controlling COPD should be implemented in the very near future in order to avoid an uncontrolled explosion of health costs in the most ageing country in Europe. Data in real life point to this dangerous drift in healthcare costs.

In fact, only by following management programs inspired from the knowledge and objective documentation of the events driving COPD management at local level is it possible to obtain reliable data, on the basis of which decision-makers will be able to plan more useful, incisive and realistic interventions for the benefit of the whole community.

Conflict of interest

The authors all declare that there are no conflicts of interest related to the contents of this paper.

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