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# Primary care of the patient with chronic obstructive pulmonary disease in Italy

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## KEYWORDS

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## Summary

Using a general practice research database with general practitioner (GP) clinical records, it has been observed that among the 617,280 subjects registered with 400 Italian GPs, 15,229 (2.47%) patients were suffering from chronic obstructive pulmonary disease (COPD). Of these, 67.7% had a chest radiograph at least once in a period of 10 years (1997–2006), while in the same period only 31.9% had a spirometry, 29.9% had a visit to a specialist, and 0.94% had a visit to an allergologist. From 1997 to 2006, 7.5% of patients with COPD, especially the oldest ones, were hospitalized at least once for the disease, although 44.0% of all patients with COPD were hospitalized for other pathologies. With regard to treatment, in 2006, 10,936 (71.1%) of COPD patients received at least one drug for their disease (drugs classified within the R03 therapeutic pharmacological subgroup of the Anatomical Therapeutic Classification). In particular, salmeterol/fluticasone was prescribed 6441 times, tiotropium 4962, theophylline 3142, beclomethasone 2853, salbutamol 2256, formoterol 2191, salbutamol/beclomethasone 2129, oxitropium 1802 and formoterol/budesonide 1741 times. Based on these findings, the level of COPD management in Italy seems to fall short of recommended international COPD guidelines. In particular, it appears that GPs usually prescribe treatment without the use of spirometry, and/or without taking into account the severity of airway obstruction. It must also be noted that, in general, patients with COPD are undertreated.

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## Introduction

Treatment of chronic obstructive pulmonary disease (COPD) is codified by national and international guidelines.<sup>1–3</sup>

These guidelines have been widely disseminated,<sup>4</sup> but, unfortunately, they do not seem to have an impact on clinician behaviour<sup>4,5</sup> and evidence suggests that COPD still remains an underdiagnosed and undertreated disease worldwide.<sup>6–14</sup>

Some of the factors contributing to this are a poor knowledge and low adherence to guideline recommendations, on the part of some health care professionals, and

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a lack of understanding of the significance and severity of the disease, on the part of patients.<sup>15</sup> However, COPD is both preventable and treatable when it is diagnosed early and treated effectively.<sup>1,2</sup>

Primary care clinicians can play a crucial role in early diagnosis of at-risk subjects.<sup>15</sup> They have a unique opportunity to identify patients at risk through directed screening, to implement primary and secondary prevention strategies, and to provide care that encompasses a holistic approach to management.<sup>16</sup> Nonetheless, even after the publishing and distributing of guideline documents, there is a very poor understanding of COPD in primary care,<sup>17</sup> with important deviations from current guidelines in general practitioners (GPs).

Since the impact of national education and literature in the native language is important and implementation projects of COPD guidelines should take deviations from the guidelines that may be specific for each country into account,<sup>6</sup> the aim of this research was to assess whether current primary care practice in Italy is consistent with the guidelines for COPD management.

## Material and methods

### Collection of information

We conducted a population-based retrospective study using information obtained from the Health Search database (HSD) owned by the Italian College of General Practitioners (SIMG). The HSD contains patient demographic details, medical records (e.g. diagnoses, tests and tests results, hospitalization, etc.), drug history and prevention records. The software system used codes all the diagnostic records using the ninth revision of the International Classification of Diseases (ICD-9).<sup>18</sup> The participating GPs use the same software to record data during their daily practice, and they agree to send periodically complete, but anonymous, records of their patients to the HSD. A unique patient code links demographic and prescription information, clinical events and diagnoses, hospital admission, and cause of death. Prescription records are coded according to the last version of Anatomical Therapeutic Chemical classification system.<sup>19</sup> Data are subject to a range of quality checks. Any variations within agreed ranges are investigated and submitted to each participating GP. Physicians who fail to meet standard quality criteria are not considered for epidemiological studies.<sup>20</sup>

For this study, 400 GPs with a list of patient population of 617,280 individuals at the end of December 2006, were selected to be representatives of the whole Italian population and also because they ensured the required data quality.

### Ascertainment of COPD and drug prescription

Cases of COPD were identified on the basis of the ICD-9 code (491, 492, 496). All drugs prescribed were abstracted and codified according to the R03 therapeutic pharmacological subgroup (drugs for obstructive airway diseases) of the Anatomical Therapeutic Chemical Classification.

## Results

### Population characteristics

The total sample included 15,229 (2.47% of the entire population) subjects suffering from COPD that were recorded by participant physicians during the period 1997–2006. The main features of the study sample are described in Tables 1 and 2. The age-specific prevalence of COPD increased, widening the difference, especially in the elderly both in males and females. However, it should be pointed out that COPD was also diagnosed in 690 patients aged between 0 and 40 years. Of our patients, 25.5% were smokers and 47.4% ex-smokers, but smoking history was missed in 27.1%, and this is surprisingly for patients who were diagnosed with COPD.

### COPD assessment

Chest radiograph was the most common diagnostic test performed. In fact, 10,310 (67.7%) of all COPD patients had a spirometry at least once in a period of 10 years (1997 to 2006), while in the same period only 4854 (31.9%) had a spirometry because of COPD and other 1272 for a reason other than COPD, 4554 (29.9%) were referred to a pulmonary disease specialist because of COPD and other 1275 for a different reason, and 0.94% had a visit to an allergologist. From 1997 to 2006, 1137 (7.5%) of the examined COPD population, especially the oldest ones, were hospitalized at least once for the disease, although 5566 of all patients with COPD were hospitalized for diseases other than COPD (Table 3).

### Use of drugs

Overall, in 2006, 10,936 (71.1%) patients received at least one drug for their disease. In particular, salmeterol/

**Table 1** COPD patient characteristics.

Variable	N
Total	15,229
Male sex	9294
Female sex	5935
Age categories (years)	
0–49	1567
50–69	4977
70+	8685
Smoking status	
Former smoker	3886
Current smoker	7211
Data not available	4132
Body mass index (kg/m <sup>2</sup> )	
18<	123
18–24	3192
25–29	4237
30>	3006
Data not available	4671

**Table 2** Most frequently used diagnostic procedures to assess COPD.

Diagnostic procedure	N
Spirometry	
because of COPD	4854
for a different reason	1272
Chest X-ray	
because of COPD	6030
for a different reason	4274
Referral to a pulmonary disease specialist	
because of COPD	4554
for a different reason	1275
Referral to an allergologist	
because of COPD	143
for a different reason	527

fluticasone was prescribed 6441 times, tiotropium 4962, theophylline 3142, beclomethasone 2853, salbutamol 2256, formoterol 2191, salbutamol/beclomethasone 2129, oxitropium 1802 and formoterol/budesonide 1741 times (Table 4). It should be noted that on the whole there were 5718 prescriptions for inhaled corticosteroids (beclomethasone, fluticasone, budesonide, and flunisolide) in monotherapy, in addition to 10,331 prescriptions of an inhaled corticosteroid in association with a  $\beta_2$ -agonist, and 516 prescriptions for montelukast, whereas there were 8074 prescriptions for long-acting bronchodilators in monotherapy and 5132 prescriptions for short-acting bronchodilators. In regard to the groups of drugs administered, a greater proportion of long-acting  $\beta_2$ -agonists, in

**Table 3** Hospital admission and emergency room visits.

	N
<i>Hospital admission</i>	
Because of COPD	1137
age categories (years)	
0–59	109
60–79	603
80+	425
For a different reason	5566
age categories (years)	
0–59	860
60–79	3105
80+	1601
<i>Emergency room visits</i>	
because of COPD	89
age categories (years)	
0–59	7
60–79	55
80+	26
For a different reason	934
age categories (years)	
0–59	162
60–79	515
80+	258

**Table 4** Prescription of the most-used active agents of the R03 group in 2006.

Active agent	Prescriptions (N)
Salmeterol/fluticasone	6441
Tiotropium	4962
Theophylline	3142
Beclomethasone	2853
Salbutamol	2256
Formoterol	2191
Salbutamol/beclomethasone	2129
Oxitropium	1802
Formoterol/budesonide	1741
Fluticasone	1185
Budesonide	1113
Salmeterol	921
Ipratropium bromide	870
Doxofylline	864
Flunisolide	567
Montelukast	516
Bamifylline	507
Fenoterol	204
Fenoterol/ipratropium	168

monotherapy or in combination with an inhaled corticosteroid, were used compared with long-duration anticholinergics.

## Discussion

To the best of our knowledge, this is the first study that reports the diagnostic accuracy of COPD registers and evaluates guideline adherence in the management of stable COPD in primary care in Italy. Our data clearly indicate that there has been no practical implementation of COPD guidelines by Italian GPs, although we believe that the behaviour of our physicians cannot be judged truly wrong.

First of all, we must highlight that the majority of our findings match perfectly with what has been observed worldwide.<sup>6–14</sup> COPD guidelines in some practice settings have progressed from passively diffused documents published in professional journals to more active implementation. Despite these efforts, physician and organizational practice patterns continue to resist change and are reluctant to rapidly adopt guideline recommendations, because of multiple barriers that are only beginning to be understood.<sup>5</sup> The three-part mission of COPD guidelines includes systematic development, dissemination, and implementation. However, until recently, most COPD guideline developers have created hard-to-adopt, non-explicit recommendations using informal consensus methods or expert opinion. Most have only disseminated their guidelines through publication in subspecialty journals rather than reaching frontline physicians through multiple media and forums. And most guideline developers have not created effective implementation strategies. Consequently, little evidence has shown that COPD guidelines have affected health care processes or improved respiratory health.<sup>21</sup>

Other barriers should also be considered. It has been suggested that many GPs are not fully aware of the importance of symptoms and risk factors for COPD.<sup>22</sup> Moreover, only few GPs use spirometric criteria to define COPD,<sup>7</sup> although multiple international guidelines that have addressed the diagnosis of COPD<sup>1–3</sup> recognize spirometry as the “gold standard” for confirming the presence of irreversible airflow limitation. Nonetheless, we must honestly report that many now recommend that spirometry to detect COPD be used only for current or former smokers seen in medical care settings who have a high probability of COPD, as determined by a questionnaire that includes age, body mass index (obesity indicating a lower risk of COPD), pack-years of smoking, dyspnea on exertion, wheeze, and a history of allergies (indicating a lower risk of COPD).<sup>23,24</sup>

In our COPD population, spirometry was performed for only one third of the cases. This finding fits perfectly with the results of the National Committee for Quality Assurance (NCQA) study<sup>25</sup> that suggested that approximately 32% of a broad range of patients with a new COPD diagnosis had undergone spirometry within the previous 2 years to 6 months following diagnosis. In addition, spirometric testing appeared to decrease with increasing age.

It is difficult to explain the reluctance of GPs to refer their patients with suspected diagnosis of COPD with spirometry. A study, which investigated the degree of use of spirometry to establish the diagnosis of COPD in Italy by using a standardised questionnaire that has been self-administered to a sample of 2425 Italian GPs,<sup>26</sup> reported that 30% of GPs do not use spirometry to establish the diagnosis of COPD. The main reasons given for the failure to use spirometry were that spirometry is not necessary for the diagnosis of COPD or there are logistical limitations to the access of the patients to lung function laboratories. An US survey,<sup>27</sup> which sought to identify management problems that constrain the ability of primary care physicians to better diagnose and manage COPD, documented that physicians do not believe that they have time to adequately assess the disease using spirometry; specifically, they feel that they have little or no chance to affect patients' smoking-cessation rates because of the rigid and compact schedule required of the modern medical practice. Another Italian study, which evaluated whether office spirometry by GPs is feasible and may improve the diagnosis of asthma and COPD,<sup>28</sup> documented that a conventional evaluation of patients with symptoms of chronic airways obstruction including a detailed questionnaire and physical examination is not inferior to a conventional evaluation plus office spirometry, although a type II error cannot be excluded, since the enrolment of participating patients reached only about half of the goal determined by *a priori* sample size calculations. Moreover, the study showed that where the general practice is organized as in Italy (on an individual basis without nursing or technical assistance), office spirometry is feasible; but even when automated simple and reliable devices are available along with technical instruction at the start, regular application tends to decrease progressively within a few months if there are no reinforcing recalls or retraining, despite a favourable rating on usefulness. Yet the GPs should be aware that there is documentation that incorporation of spirometry testing into family medicine practices leads to spirometry testing

with acceptable levels of technical quality and concordant interpretation and is followed by management changes for almost half of the patients.<sup>29</sup>

Chest radiograph was the most common diagnostic test performed. In fact, 67.7% of our COPD patients had a chest X-ray at least once in a period of 10 years. This figure indicates that Italian GPs overutilize chest X-ray, but it is difficult to affirm that this diagnostic behaviour is really wrong. In any case, this finding is in agreement with the conduct of Spanish GPs,<sup>30</sup> although it contrasts with the behaviour of GPs in other countries. For instance, in 2005 few British GPs thought that a chest radiograph was essential.<sup>31</sup> In fact, an abnormal chest X-ray is rarely diagnostic in COPD unless obvious bulbous disease is present, although guidelines highlight that it is valuable in excluding alternative diagnoses and establishing the presence of significant comorbidities, such as cardiac failure.<sup>1,3</sup> Nonetheless, chest radiography is a valuable, inexpensive means of diagnosing moderate-to-severe emphysema. Correct recognition of emphysema on chest radiography would be equally valuable in patients who do not have or are not known to have COPD.<sup>32</sup> This is quite likely to occur in clinical practice because chest radiographs are often taken for reasons other than a chronic respiratory illness. If the chest radiograph of one such patient meets the criteria for emphysema, it is likely that the disease is present and the patient should be tested for airflow obstruction. Should the patient be a smoker, the diagnosis of emphysema would be a particularly strong indication for giving up smoking since the lungs of such patients are overtly damaged by inhaled smoke.

One third of the COPD patients were referred to a pulmonary disease specialist because of COPD. This does not seem to be inappropriate behaviour. NICE guidelines<sup>2</sup> highlight that a specialist opinion may be helpful at any stage of the disease. Referral may be to establish the diagnosis, to exclude other pathology, to reassure the patient, to reinforce the need to stop smoking, to optimise treatment, or to assess the need for the more complex and expensive therapies appropriate to severe COPD. However, International Primary Care Respiratory Group Guidelines<sup>28</sup> are more conservative. They recommend that referral to a specialist should be considered only if therapy appropriate to the stage of the patient's disease does not control symptoms. The problem is that, historically, assessment of COPD severity is based on the patient's level of symptoms, but also, and mainly, on the severity of the spirometric abnormality,<sup>1–3</sup> and, as stressed before, in our COPD population, spirometry was performed for only one third of the cases. Consequently, the stage of the disease was unknown in many patients.

All guidelines highlight that smoking cessation is the single most effective and cost-effective way to reduce exposure to COPD risk factors.<sup>1–3</sup> Although almost half of the examined patients were current smokers, the HSD did not offer any information on attempts to help people to stop smoking. This is an important lack of information because there is strong evidence that GPs are an important source of smoking cessation advice.<sup>33</sup> In any case, we must stress that a survey has documented that Italian GPs do not often take action against smoking likely because the percentage of current smokers among them is high and,

moreover, many of them believe that their patients will not accept their advice.<sup>34</sup>

The current GOLD guidelines<sup>3</sup> recommend that an inhaled corticosteroids be added to bronchodilator therapy only for COPD patients at stages III (severe) and IV (very severe), who are those with an FEV<sub>1</sub>/FVC ratio < 0.70 and an FEV<sub>1</sub> < 50% of predicted still having exacerbations. Nonetheless, over-treatment with inhaled corticosteroids was apparent in our patients. The lack of spirometric data for many patients does not allow us to verify whether those who received inhaled corticosteroids met the guideline criteria. In any case, over-treatment with inhaled corticosteroids concurs with the work by Decramer et al.,<sup>6</sup> who revealed that 49% of GPs prescribed inhaled corticosteroids to all of their COPD patients. Also Jones et al.<sup>35</sup> have recently reported an evident over-treatment with inhaled corticosteroids in primary care. Over-treatment suggests a waste of resources and puts patients at risk of adverse effects.<sup>36</sup> Nonetheless, we wish to highlight that, although historically, the severity of COPD has been classified according to FEV<sub>1</sub>, which may not correlate directly with symptoms, a symptomatic approach to therapy using clinical stages may be more useful. Consequently, physicians should individualize treatment and try an additional type of drug if the patient symptomatically needs to try something else, and yet stop the additional drug if it does not seem to help.<sup>37</sup> Plausibly, this is what has been done by our GPs, most likely on empirical basis.

Also consumption of long-acting bronchodilators was relatively low, mainly if we think about the recommendations in the guidelines.<sup>1-3</sup> This was an inexplicable prescriptive behaviour considering that bronchodilators are the cornerstone of COPD therapy. A volume of published evidence sustains the role of long-acting bronchodilators in the treatment of stable COPD. These agents not only induce prolonged bronchodilation, but also translate this action into other health-outcome measures that relate to quality of life, such as the severity of dyspnea, exercise capacity, and exacerbations.<sup>38</sup> In any case, it has been reported that practices in primary care varied substantially in prescribing long-acting bronchodilators. The proportion of patients prescribed with long-acting  $\beta_2$ -agonists ranged between 23% and 56% in different practices, and between 9% and 25% for long-acting anticholinergics in the Devon (UK) primary care audit.<sup>35</sup> Moreover, a US survey centered on COPD case vignettes documented that physicians in primary care settings seemed unclear about the appropriate role of long-acting bronchodilators.<sup>12</sup> Only 35% of them chose a long-acting bronchodilator when a short-acting agent had failed. A third of physicians also chose a combination short-acting bronchodilator. It must be mentioned that in regard to the groups of drugs administered, a greater proportion of long-acting  $\beta_2$ -agonists, in monotherapy or in combination with an inhaled corticosteroid, were used compared to long-duration anticholinergics. This finding concurs with Miravittles et al.<sup>39</sup> who reported that the prescription of long-acting  $\beta_2$ -agonists was more frequent than tiotropium in a group of Spanish GPs.

Consumption of leukotriene receptor antagonists was low, but greater than was to be expected in view of the fact that their effectiveness in the treatment of COPD is very limited.<sup>40</sup> Also the prescription of methyl-xanthines

(theophylline, doxofylline, and bamifylline) was greater than was to be expected. In fact, theophylline, which used to be part of the mainstay of treatment for COPD, has been relegated to third-line therapy in COPD guidelines because of the frequency of side effects and relative low efficacy.<sup>1,3,41</sup> Nonetheless, we do not believe that the use of methyl-xanthines is a major violation of guidelines. Theophylline is inexpensive and still has its role. In fact, it tends to be added to these inhaled bronchodilators in more severe patients and has been shown to give additional clinical improvement when added to a long-acting  $\beta_2$ -agonist.<sup>42,43</sup>

It must be highlighted that the Italian College of General Practitioners (SIMG) carried out a study to investigate the degree of control of physician-diagnosed asthma and COPD in Italy between April 2002 and May 2002 using data from questionnaires filled in by the GPs.<sup>44</sup> In most COPD patients (66.2%), the level of severity was defined according to symptom frequency together with the level of airflow obstruction measured by spirometry. However in 24.9% of cases the physician used only the symptom frequency as a measure of severity and, furthermore, in 8.9% of cases the physician used only the level of airflow obstruction as measured by spirometry. Considering only the patients with a diagnosis of moderate-to-severe COPD ( $n = 4985$ ), only 2425 (48.6%) were treated with long-acting inhaled  $\beta_2$ -agonists together with inhaled corticosteroids according to the GOLD guidelines. Around half (50.3%) of all patients had at least one specialist visit in the 12 months before their entry into the study. The percentage of patients with at least one severe exacerbation (defined as hospitalization or emergency room visit or intensive care unit in the 12 months before their entry into the study) were, respectively, 17.5% (hospitalizations), 12.5% (emergency room visits) and 1.2% (intensive care unit admissions).

It appears that, after four years, Italian GPs have reduced the use of spirometry for diagnosis of COPD, diminished the number of consults with a pulmonary disease specialist because of COPD, and started to use tiotropium. In addition, fewer patients have been hospitalized. Apparently, these findings, apart from the reduced use of spirometry, indicate an improved approach to the treatment of COPD GPs. The problem in trusting this conclusion is that responses given to questions included in a questionnaire do not always represent the actual conduct of the interviewed doctor, whereas the use of a population-based general practice database allows to study a real life clinical setting. Consequently, we believe that what we have described in the present study offers a more realistic picture of the behaviour of Italian GPs in relation to patients suffering from COPD, also considering that comparative analyses have demonstrated the validity of the information gathered in the HSD.<sup>45</sup>

In conclusion, our results contribute to outline the pattern of COPD management by Italian GPs. Above all, our data indicate that management of stable COPD in primary care in Italy does often not correspond to guidelines. In particular, it appears that GPs usually prescribe treatment without the use of spirometry, and/or without taking into account the severity of airway obstruction. This finding fits with what has been documented in other countries,<sup>6-14</sup> and

points out the need to generate recommendations that could be truly accepted by all and not only by academics and specialists.

### Conflict of interest statement

None of the authors had financial or personal relationships with other people or organizations that could inappropriately influence this work.

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