



A Randomized Controlled Trial on Office Spirometry in Asthma and COPD in Standard General Practice*

Data From Spirometry in Asthma and COPD: a Comparative Evaluation Italian Study†

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Study objectives: To evaluate whether office spirometry by general practitioners (GPs) is feasible and may improve the diagnosis of asthma and COPD.

Methods: A prospective, randomized, comparative trial was planned involving 57 Italian pulmonology centers and 570 GPs who had to enroll consecutive subjects aged 18 to 65 years with symptoms of asthma or COPD without a previous diagnosis. Patients were randomized 1:1 into two groups with an interactive voice responding system: conventional evaluation alone vs conventional evaluation and spirometry. Office spirometry was performed by GPs who were trained by reference specialists using a portable electronic spirometer (Spirobank Office; MIR; Rome, Italy). Diagnosis was confirmed by the reference specialist center in blind fashion.

Results: Seventy-four GPs complied to the trial. Of 333 patients enrolled, 136 nonrandom violators completed the protocol. Per-protocol analysis showed a concordant diagnosis between GPs and specialists in 78.6% of cases in the conventional evaluation-plus-spirometry group vs 69.2% in the conventional evaluation group ($p = 0.35$). In the intention-to-treat analysis, the respective percentages of concordant diagnosis were 57.9 and 56.7 ($p = 0.87$).

Conclusions: Office spirometry by GPs is feasible, but frequent protocol violation and inadequate sample size did not allow us to prove a significant advantage of office spirometry in improving the diagnosis of asthma and COPD in standard general practice as organized at present in Italy, thus reinforcing the need for close cooperation between GPs and specialists in respiratory medicine.

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Key words: asthma; COPD; general practice; office spirometry

Abbreviations: CI = confidence interval; GP = general practitioner; IVRS = interactive voice responding system; OR = odds ratio; PEF = peak expiratory flow

Asthma and COPD are major health problems but are still largely underdiagnosed and undertreated.^{1,2} The role of general practitioners (GPs) is pivotal in the early diagnosis of these diseases, widely recognized as a crucial step in reducing management costs and improving quality of life. Spirometry is the standard method for reaching an accurate diagnosis of asthma and COPD. The use of peak flow meters could be a simple alternative for GPs, but there is no evidence that they can be a reliable tool in the diagnosis of asthma.³ The use of spirometry in general practice has been actively investigated in

recent years with conflicting results in the different settings. According to some authors, spirometry in general practice may reduce the underdiagnosis⁴ or misdiagnosis^{5,6} of chronic respiratory disorders. A consensus statement of the National Lung Health Education Program recommends the development, validation, and implementation of office spirometry in the primary care setting.⁷ An article on the Differential Diagnosis Between Asthma and COPD study⁸ demonstrated that early detection of COPD in general practice is significantly improved by office spirometry. One peculiarity of the different studies

reporting positive results concerning office spirometry is the limited number of GPs involved, and the strict control of the protocol and methodology by specialist personnel. The collaboration in general practice of nonphysicians, such as respiratory nurses and medical undergraduates, seems to render the use of office spirometry more feasible and useful in the diagnosis of COPD.⁹ On a larger scale, a study of 33 GPs in Japan and > 1,000 patients showed a good impact of office spirometry in COPD diagnosis.¹⁰

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Technical issues and present levels of standardization, however, do not guarantee as yet the full reliability of office spirometry, despite the easy-to-use and affordable sophisticated devices available today.¹¹ In countries where efforts to implement office spirometry have been made on a large scale, wide regional variations have been reported in the frequency of utilization and appropriateness.^{12,13} Thiadens et al¹⁴ demonstrated that approximately one half of subjects with a history of persistent cough are affected by asthma or COPD, and most cases can be identified only with history and objective examination. It is quite obvious that since local health policies, organizations, and resources influence the practice of GPs, the applicability on a large scale of the different protocols described in the literature requires trials for implementation at the local level. The aim of this study was to assess in a very large number of general practices in Italy, the feasibility of office spirometry on a day-by-day basis and, as a primary end point, to verify whether conventional evaluation (history and physical examination) followed by spirometry may be better than conven-

tional evaluation alone in identifying patients with different chronic obstructive airways disorders.

MATERIALS AND METHODS

Study Design and Participants

This prospective, randomized, controlled, comparative trial involving 57 Italian reference specialist centers and 570 GPs (10 for each specialist center, randomly selected) homogeneously distributed throughout the country was designed to evaluate whether office spirometry by GPs may improve diagnostic accuracy in asthma and COPD. A preliminary phase consisted of two meetings of the 57 specialist centers to agree on the conduct of the study, including materials such as the questionnaires for patients and GPs, and the educational plan for primary physicians. Specialists agreed to refer to international Global Initiative for Chronic Obstructive Lung Disease and Global Initiative for Asthma guidelines.^{1,2}

A run-in phase from May to October 2002 was planned in which each specialist center held two educational meetings of 4 h each with GPs centered on international guidelines on asthma and COPD and spirometry, including practical sessions with the instrument selected for the study (Table 1). A simple questionnaire concluded the run-in period to evaluate the opinion of each GP on the feasibility and usefulness of office spirometry and to identify doctors willing to participate in the randomized comparative trial. Reasons for not participating were not formally requested. As an alternative to the randomized study, the GPs were also invited to continue for a period of 9 months with the application of office spirometry as part of a parallel observational study on the simple feasibility and self-rated usefulness of the test. The only incentives permitted legally for all doctors participating in the study were as follows: donation of the spirometer for research purposes by the nonprofit scientific association supporting the study, and acquisition of continuous medical education credits for the educational sessions.

Approval of the study by an ethics committee was left to the responsibility of each of the participating specialist centers. Each patient was requested to give informed consent to the processing of personal data.

Patients

The enrollment of patients started on November 1, 2002, and was concluded on July 31, 2003, 9 months later. Consecutive subjects aged from 18 to 65 years and with symptoms suggestive of asthma or COPD (cough, dyspnea, wheezing, chest tightness) without a previous diagnosis were considered. An upper age limit was initially chosen to avoid an excessive bias toward a diagnosis of COPD, since this was not a case finding study but a feasibility and differential diagnosis study.

The study population was randomized 1:1 into two groups (by means of an interactive voice responding system [IVRS]): conventional evaluation without spirometry vs conventional evaluation with spirometry. The size of randomization-balanced blocks was 10 patients within study. Conventional evaluation included case history supported by a questionnaire (for items, see below) and physical examination. Random violation was defined as absence of IVRS code or IVRS treatment code different from actual treatment. Exclusion criteria were a previous diagnosis of asthma or COPD; history of cardiac failure; neuromuscular or autoimmune disorders; present cancer; interstitial lung disease; thoracic surgery in the previous 6 months; present infectious disorders; or respiratory infection in the month before entering the study.

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Table 1—List of Contents of the Educational Meetings Held by Pulmonary Specialists for GPs

Pathophysiology of the respiratory system
Role of spirometry in respiratory medicine
Obstructive lung disorders: natural history, clinical features, and differential diagnosis of asthma and COPD
Discussion of three clinical cases (asthma, COPD, and mixed pattern)
Standard requirements for respiratory function tests according to international guidelines
How to perform spirometry (including reversibility tests): practical indications
The instruction of patients
Interpretation of spirometry results in different clinical situations
Algorithm for the interpretation of spirometry
Practical tests on the interpretation of spirometry: 12 clinical cases (interactive)
Continuing medical education questionnaires for self-evaluation
Practical session fully devoted to the field demonstration on how to use the portable spirometer adopted for the study plus direct testing of the personal device by GPs

The GPs filled in a form with medical record of the patients (history, risk factors, objective finding, spirometric data according to randomization, diagnosis, and therapy). Risk factors included familiarity; allergy; tobacco smoking; occupational exposure to gas; fumes and inorganic/organic dusts; otorhinolaryngologic comorbidities (rhinitis, rhinorrhea, postnasal drip, polyposis, sinusitis); and gastroenterologic comorbidities (gastroesophageal reflux, hiatal hernia, pyrosis, dyspepsia, epigastric pain). A copy of each form was sent to a coordinating data center.

The patient was then referred to the specialist with only part of the documentation (excluding diagnosis and therapy to which the specialist was blind) in order to have a final diagnosis that was sent to the data center in charge of comparing the diagnosis at the two levels (standard practice vs specialist) and defining the degree of concordance. All pulmonary specialists involved in the study were hospital based or employed in services with full equipment for respiratory function testing. The specialists' diagnosis was taken as a "gold standard." The calculation of sample size defined that at least 650 new cases had to be competitively enrolled by GPs to test the null hypothesis (= equivalence of the two diagnostic procedures).

GPs involved in the parallel observational part of the study were given the same exclusion criteria as for the comparative trial, but inclusion criteria were enlarged to also allow patients with a known diagnosis of asthma or COPD on follow-up and there were no upper age limitations. GPs were requested to enroll at least 10 patients. For each patient, they had to fill in a simple form registering age, sex, smoking habits, diagnosis, time for instruction of patient and spirometry performance, and referral to specialist; at the end of the study, a questionnaire was administered to GPs to rate the usefulness of spirometry.

Spirometry

Office spirometry was performed by GPs using a portable multifunction spirometer (Spirobank Office; MIR; Rome, Italy). Each of these spirometers is calibrated before being sold and does not need further regular calibration unless major damage occurs. GPs were previously trained on spirometry by reference specialists using the same type of device. No technical or interpretation problems were reported by specialists. Spirometry supplies were given free.

The parameters registered, absolute values and percentage of predicted, were as follows: FVC, FEV₁, percentage of predicted FEV₁, peak expiratory flow (PEF), and forced expiratory flow at 25 to 75% of FVC. Predicted values were those approved by the European Respiratory Society. Spirometry was considered normal for FEV₁/FVC ratio ≥ 0.7 and FVC $\geq 80\%$ of predicted. Patterns of abnormality were defined as follows: airway obstruction (FEV₁/FVC ratio < 0.7 ; FVC $\geq 80\%$ of predicted), mixed (FEV₁/FVC ratio < 0.7 ; FVC $< 80\%$ of predicted), and restrictive pattern (FEV₁/FVC ≥ 0.7 ; FVC $< 80\%$ of predicted).

The Spirobank Office spirometer has a quality check for reliability and reproducibility of spirometric curves (according to American Thoracic Society criteria), allowing to accept or refuse a test, and provided an automated interpretation of spirometry. The Spirobank Office spirometer adopts the following reproducibility criteria: PEF reproducible if Δ PEF is $< 10\%$; FVC reproducible if Δ FVC is $< 5\%$ or < 200 mL; and FEV₁ reproducible if Δ FEV₁ is $< 5\%$ or < 100 mL. After the second test, a "–" sign on the display means "not reproducible" and a "+" sign means that the test is reproducible.

Reversibility tests with bronchodilators or corticosteroids were fully described in the educational sessions, but it was not obligatory for GPs to perform these tests themselves. They could, if preferred, refer the patient to the specialist for the test. There was no direct control of spirometry by GPs by the reference specialists.

Data Management and Statistics

An information technology manager and a data manager were available in the data center. The IVRS system allowed a day-by-day updating of the enrollment process; at regular intervals, IVRS telephone calls were matched with data forms actually received. The data received were recorded in a computer database and checked for completeness and clinical compatibility. In the case of missing or unreliable data, a request was sent to the researcher (GP or specialist) to verify data.

Descriptive statistical analysis included mean and SD or median and range for continuous data; and absolute and relative frequency for categorical data. The homogeneity in the distribution of the frequency of new diagnosis in the two procedures under comparison was evaluated with the χ^2 test; the odds ratio (OR) between the respective frequencies of the two procedures was calculated with 95% confidence intervals (CIs). To determine the predictive power of historical and objective data in the medical records on the diagnosis of asthma or COPD, ORs and 95% CIs were calculated according to a logistic regression model adjusting for all variables in the model and applied on the global population of patients and on those patients with concordant diagnosis between GPs and specialists.

RESULTS

The vast majority of GPs attended the educational meetings (95% attended both sessions, and 99% attended at least one). No GP coworkers attended, since most Italian GPs work individually without staff support. Approximately 13% of GPs had postgraduate training in respiratory medicine, but none had ever used a spirometer regularly in their activity as GP.

Eighty-eight percent of GPs had from 1,000 to 1,500 patients registered at their practice; the re-

remaining 12% had < 1,000 patients. Each GP estimated that on average approximately 40 to 50 patients with COPD were registered in their practice. According to a conservative estimate, Italian GPs with 1,000 to 1,500 patients receive on average 25 to 30 patients per day, 5 days a week, in their office.

The mean \pm SD number of spirometries in the run-in was 19 ± 19 per GP (range, 0 to 120 per GP). After the run-in period, a total of 429 of the 570 GPs (75%) replied to a questionnaire rating the feasibility and usefulness of spirometry as high in 85%, moderate in 14.5%, and nihil only in 0.5% of cases. Nevertheless, only 104 primary physicians (18%) agreed to enter the randomized trial, while 236 GPs (41.4%) agreed to take part in the observational part of the study. The main reasons for not participating in the randomized trial were, in order of decreasing importance, lack of time, lack of confidence with research trials, and lack of compensation.

In the 9-month study period, 333 patients (mean age, 49.0 ± 15.0 years; 172 female and 159 male patients; data missing for 2 patients) were enrolled. The enrollment did not always respect the 65-year age limit, but this was considered a minor protocol violation and all data were processed independently of an upper age limit. As for smoking habits, 172 subjects were nonsmokers (51.7%), 101 were smokers (30.3%), 43 were ex-smokers (12.9%), and 17 were missing data (5.1%). The prevalence of smoking or a former smoking habit was lowest in asthma patients (19.6% and 11.2%, respectively) and highest in the COPD group (46.4% and 19.6%, respectively). Surprisingly, the percentage of nonsmokers (34%) was higher than expected for COPD.

Each GP enrolled a median of three patients, with a range of 1 to 5 patients in the first group and 1 to 20 patients in the spirometry group. Eighty-three patients entered the conventional evaluation, and 250 patients entered the conventional-plus-spirometry group. There were 149 patients who resulted as random violators. The primary causes of the frequent randomization errors were, at a similar frequency, that the GPs did not call the IVRS phone number and performed spirometry on most of the patients with respiratory symptoms, or that they called and then disregarded the patient assignment. Of the 184 nonrandom violators, 65 patients were allocated in the conventional evaluation and 119 patients were in the conventional-plus-spirometry group. Two hundred twenty-four patients completed the evaluation process. In 44 of these cases, the GP did not specify any diagnosis. Figure 1 shows the flow diagram of the actual evaluation of the case series.

The average time for each visit was 14 ± 5.2 min; the mean time required to instruct patients for spirometry was 5.6 ± 3.1 min; the performance of

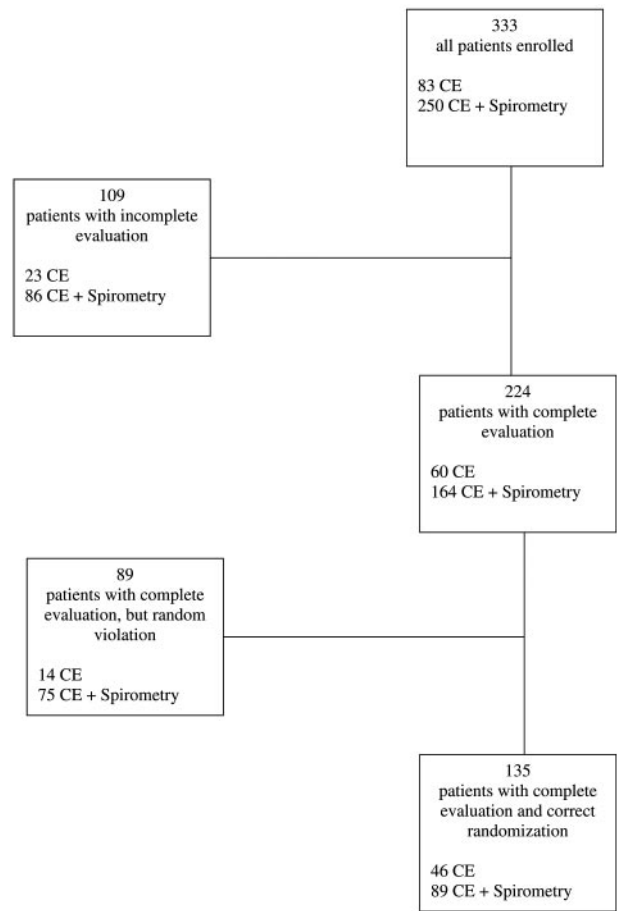


FIGURE 1. Flow diagram showing the number of patients enrolled, randomized, and completing the trial. CE = conventional evaluation.

spirometry took on average 6.4 ± 3.5 min. Mean FEV_1 was $83.7 \pm 20.9\%$ of predicted, and mean FVC was $91.9 \pm 20.4\%$ of predicted. No bronchodilator tests were reported by GPs. Spirometry findings in the normal range were 61.8%; patterns of abnormality were 16.4% for airway obstruction, 12.0% for mixed pattern, and 9.8% for a low FVC without obstruction.

A diagnosis of asthma was made by the GP in 107 patients (32.1%; mean patient age, 42.1 ± 14.6 years; 56.1% female); COPD in 97 patients (29.1%; mean patient age, 59.0 ± 10.3 years; 38.1% female); both asthma and COPD in 8 patients (2.4%; mean patient age, 58.6 ± 14.3 years; 62.5% female); other respiratory disease in 24 patients (7.21%; mean patient age, 47.3 ± 15.1 years; 66.7% female); and no diagnosis in 97 patients (29.1%; mean patient age, 45.8 ± 14.2 years; 55.7% female). The mean spirometric values in the asthma group were FEV_1 of $87.8 \pm 18.8\%$ and FVC of $96.5 \pm 17.6\%$ of predicted. A FEV_1/FVC ratio < 0.7 was present in 21.0% of patients receiving a diagnosis of asthma.

In patients receiving a diagnosis of COPD by GPs, mean FEV₁ (70.5 ± 19.4% of predicted) and FVC (81.7 ± 22.0% of predicted) were significantly lower than in asthma patients; surprisingly, 30.1% had normal spirometry results. Median time lapse between GP visit and specialist consultation was 10.5 days (mean, 23 days; SD, 34 days; 95% CI, 18.4 to 27.5; data available for 214 patients). To verify the primary end point, the diagnosis registered by the GPs was compared with that made by the reference specialist.

Owing to the presence of random violators and missing diagnosis, an intention-to-treat and a per-protocol analysis along with a power calculation was carried out on the case series at different levels as shown in Table 2. The results show that in any case (all patients, all patients except those with missing diagnosis, only nonrandom violators, only nonrandom violators except those with missing diagnosis), the level of agreement between GPs and specialists did not change significantly whether or not spirometry was used in the GP's office. The frequency of diagnosis is reported in Table 3, based on the 224 patients who completed the study.

The analysis of the different items in patient records showed that history data in some way supported diagnosis in 16.4% of patients with regard to occupational exposure; 37.8% with regard to familiarity for asthma, COPD, or allergy; and 13.3% and 10.2% with regard to previous diagnosis of seasonal

or perennial allergy, respectively. Allergy was more frequently registered in asthma patients than in other groups, as expected (21.5% had seasonal and 13.1% had perennial allergy). The frequency of the different risk factors was not significantly different between the two arms of the randomized study. The comparison of respiratory symptoms showed a noteworthy difference between asthma and COPD only for expectoration and chest tightness (Table 4). As for comorbidities relevant to lung chronic obstructive disorders, the most prevalent were rhinitis (24.9% of all patients, 40.2% of asthma patients, 4.1% of COPD patients), sinusitis (9.8%, no significant difference between asthma and COPD), and gastroesophageal reflux (15.1% of patients, 17.5% with COPD vs 8.4% with asthma).

Physical examination of the thorax was normal in 33.8% of patients. Wheezes, ronchi, rales, and crackles were reported in 46.2%, 18.7%, 6.2%, and 6.2% of cases, respectively, without significant differences between the two intervention arms. Normal findings were more common in asthma (33.6%) than in COPD (11.3%) patients.

In the global patient population, significant ORs ($p = 0.02$ at least) for diagnostic positive predictive power were found for age ≥ 65 years (OR, 5.65; CI, 2.1 to 15.2), smoking (OR, 5.0; CI, 2.4 to 10.4), and dyspnea (OR, 2.3; CI, 1.1 to 4.6) in the case of COPD. In the differentiation of asthma from COPD, only wheezing (OR, 2.9; CI, 1.6 to 5.4) and allergy

Table 2—Diagnostic Agreement or Disagreement Between GPs and Pulmonary Specialists*

Diagnosis	Diagnostic Methods, No. (%)		Total, No.
	Conventional Plus Spirometry	Conventional	
All patients with complete evaluation†			
In agreement	95 (58)	34 (57)	129
Not in agreement	69 (42)	26 (43)	95
Total	164	60	224
All patients except those (n = 44) with missing diagnosis‡			
In agreement	95 (68)	34 (83)	129
Not in agreement	44 (32)	7 (17)	51
>Total	139	41	180
Only nonrandom violators§			
In agreement	54 (61)	22 (48)	76
Not in agreement	35 (39)	24 (52)	59
Total	89	46	135
Only nonrandom violators except those with missing diagnosis			
In agreement	54 (69)	22 (79)	76
Not in agreement	24 (31)	6 (21)	30
Total	78	28	106

*Primary end point was comparison of diagnosis (agreement or disagreement) between GPs and Specialists in Pulmonary Medicine Who Were Blind to the GPs' Diagnosis. The power figures are the probability of statistical tests to underline a difference when the difference exists.

†OR, 1.05; 95% CI, 0.58 to 1.01; power, 2%; χ^2 p value, 0.8658.

‡OR, 0.44; 95% CI, 0.18 to 1.08; power, 35%; χ^2 p value, 0.0686.

§OR, 1.68; 95% CI, 0.82 to 3.45; power, 23%; χ^2 p value, 0.1537.

||OR, 0.61; 95% CI, 0.22 to 1.71; power, 9%; χ^2 p value, 0.3466.

Table 3—Frequency of Diagnosis by GPs and Pulmonary Specialists*

Diagnosis by GPs	Diagnosis by Pulmonary Specialists						
	Asthma	COPD	Asthma Plus COPD	Asthma Plus Other†	COPD Plus Other†	Other†	None
Asthma	51‡	12	3	13	1	9	1
COPD	10	40‡	0	0	6	4	1
Asthma plus COPD	1	3	1‡	1	0	0	0
Asthma plus other	1	0	0	0‡	0	0	0
COPD plus other	0	2	0	0	1‡	1	0
Other	3	6	0	4	0	4‡	0
No diagnosis	14	16	4	1	0	9	1‡

*Data are presented as No. Primary end point was the frequency of diagnosis by GPs and pulmonary specialist in the subgroup of 224 patients completing the study.

†Other = diagnosis other than asthma or COPD. The main groups of specialist diagnosis other than asthma or COPD included inflammatory or allergic upper airway disorders (34.6% of other diagnosis), acute bronchitis (27.3%), gastroesophageal reflux (9.1%), cardiovascular disorders (7.3%), obesity (5.5%), and obstructive sleep apnea syndrome (3.6%).

‡Concordant diagnosis.

(OR, 3.2; CI, 1.6 to 6.6) made a significant positive contribution ($p = 0.001$ at least).

Considering only patients with concordant diagnosis between GP and specialist, age ≥ 65 years, smoking, and occupational exposure oriented toward COPD with ORs of 11.6 (CI, 1.2 to 113.0), 16.6 (CI, 3.7 to 74.8), and 10.1 (CI, 1.4 to 72.3), respectively ($p = 0.03$ at least). Allergy and wheezing oriented toward asthma with ORs of 13.0 (CI, 1.7 to 99.2) and 8.7 (CI, 1.9 to 38.7), respectively ($p = 0.01$ at least).

Those 236 GPs who after run-in continued to use the spirometer for purposes of the observational study enrolled 2,055 patients (mean, 8.7 ± 2.6 patients per GP; median, 10; range, 1 to 19; 54% male; mean age, 51.4 years [range, 7 to 95 years]; 31% smokers; 16% former smokers of whom 45% without a known diagnosis [3% missing data]). Of the 52% with a known diagnosis, 34.4% had COPD and 37.5% had asthma. Median time for instruction of patients was 5 min (range, 1 to 60 min), and time for performance was 6 min (range, 1 to 50 min). The enrollment trend is shown in Figure 2. After 5 months, when 74% of patients had been recruited,

the rate of enrollment began to decrease sharply and reached a minimal number of 16 patients (0.8% of total) in the last month of the study.

The final questionnaire on the usefulness of office spirometry gave the following results: 57.1% very useful, 15% moderately useful, 0.3% useless, and 27.6% no reply. As compared to the same questionnaire administered immediately after the run-in phase (see above), there was a sharp decrease in the number of “very useful” responses, with an abstinence rate of 27.6% not registered in the earlier questionnaire.

DISCUSSION

Subjects with chronic respiratory disorders frequently have delayed access to diagnostic evaluation and treatment, in many cases because patients themselves minimize their symptoms and do not consult their GP.⁴ An ongoing debate in respiratory medicine focuses on whether the performance of spirom-

Table 4—History of Respiratory Symptoms at Enrollment*

Symptoms	Global Population	Labeled as COPD	Labeled as Asthma
Cough	76	81.4	74.8
Expectoration	37.3	63.9	22.4
Dyspnea	46.7	49.5	45.8
Wheezing	44	43.3	49.5
Chest tightness	27.1	20.6	32.7

*Data are presented as % of patients. Shown are the rates of respiratory symptoms at enrollment according to history; the sum is $> 100\%$ for the coexistence of more than one symptom in one patient.

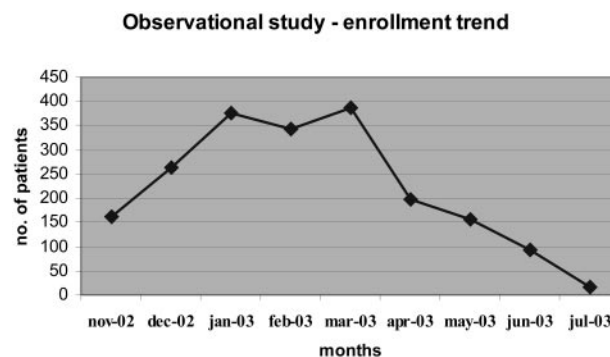


FIGURE 2. Enrollment trend (number of patients per month) during the 9 months of the observational study.

etry by the GP may help in identifying asthma or COPD patients earlier, offering them a correct treatment even though specialist assessment is not readily available. The aim of our study was to verify on a large scale whether the performance of spirometry in the GP's office is feasible and constitutes a better mode for reaching a correct diagnosis of asthma or COPD than a conventional evaluation (including a thorough case history and physical examination) alone.

The type of agreement with GPs and the resources allowed for this study did not allow to carry out a case-finding study; therefore, only patients with one or more respiratory symptoms were included in the study, although it is well known that adult current or former smokers who do not report any respiratory symptoms (at least on a questionnaire) still have a 15 to 30% risk of COPD (depending on age and gender).⁷ Concerning the feasibility of office spirometry, a first point to underline was that, notwithstanding most GPs participating in the study agreed on the usefulness of spirometry in their practice, only half of them accepted to use it regularly for the observational part of the study, and only a limited number agreed to take part in the comparative trial. The main reasons for not participating were lack of time, lack of confidence with research trials, and lack of compensation. Even the most cooperative GPs had an enrollment rate far lower than expected. As a consequence, the randomized trial was underpowered (as shown by the low-power figures in Table 2), introducing the risk of a type II statistical error. The rate of enrollment by each GP in the observational study was better than that in the randomized trial, probably because of less methodologic limitations.

The final judgement of GPs about the usefulness of office spirometry was not as enthusiastic as the one immediately after the run-in period, in agreement with our finding of a clear fading effect, in the long term, with regard to the use of office spirometry, as shown by the enrollment curve. If office spirometry really had been useful as stated in the questionnaires, we would have expected at least a steady intermediate-level application of the test and not a sharp progressive decrease to abolition in the last months of the study.

This means that on a large scale, the application of office spirometry without periodic reinforcing sessions is subject to limitations in quantitative terms, aside from the problem of quality control and assurance¹⁵⁻¹⁷ that in our case relied solely on the automated built-in control of the spirometer. A close interaction with and strict technical support by specialist centers would be the optimal way to provide quality spirometry in general practice at present, although the epidemiologic challenge of asthma and

COPD is already pushing toward a widespread development of pulmonary function testing in the nonspecialist setting.¹⁷

In 44 patients with complete evaluation, the GPs did not reach a definite diagnosis, leaving the task to the specialist. In all patients with a diagnosis from both the GP and pulmonary specialist, the agreement between GP and the specialist ranged from 49 to 83% of cases according to the different subanalyses, with no significant differences found between the two intervention subgroups. Therefore, the findings of the study are substantially inconclusive: spirometric testing did not seem to reinforce a clinical suspicion obtained with conventional evaluation. This would be in agreement with Thiadens et al,¹⁴ who also found that most cases of asthma and COPD can be identified only with history and objective examination. However, a number of possible negative biases in our study—some systemic, others strictly relevant to the study—must be underlined.

Among systemic biases, objective difficulties in GPs' daily professional activities (mainly lack of time) caused a reduced enrollment by approximately one half of the number planned; as a matter of fact, the spirometry procedure is highly cooperation dependent and requires time for the instruction of patients and for correct performance (at least three maneuvers were recommended). In contrast to the structure of general practice in other countries (the Netherlands or United Kingdom), in Italy GPs work in most cases individually and without technical or nursing support, which can make the difference^{8,9} when patients require deeper investigation and have no prompt access to specialist care. Another important issue is that as yet no fee is granted for spirometry by the national health service in Italy.

Among biases specific for the study, the randomization procedure proved to be complicated and was not applied or was inappropriately applied in a large portion of patients. The quality control of the spirometry relied on the automatic control of the instrument, and neither a regular check nor a direct technical support by the reference centers was envisaged, if not requested by the GP. The underuse of bronchodilator tests certainly influenced the diagnostic accuracy by GPs. Incorrect labeling of patients with respiratory complaints of chronic bronchitis as COPD despite a FEV₁/FVC ratio > 0.7 probably contributed to diagnostic misclassification; the inclusion of stage 0 in Global Initiative for Chronic Obstructive Lung Disease guidelines may have contributed to such a classification error. The finding of 34% of nonsmokers among COPD patients is higher than expected, but this was probably due to misclassification of former smokers as nonsmokers. The use of anamnestic questionnaires with a very detailed

series of information probably helped in addressing the clinical reasoning toward a more confident diagnosis. There is evidence in the literature¹⁸ that the systematic use of a simple questionnaire on smoking and symptoms of COPD is very helpful in case finding. We have no comparison data on whether evaluation of patients by GPs in a "native" setting without a standard questionnaire would have yielded a lower probability of case finding and correct diagnosis of COPD or asthma.

The main symptoms at the moment of the enrollment visit were cough in the majority of patients, followed by dyspnea, wheezing, and chest tightness. According to logistic regression analysis, the peculiar characteristics of asthmatic patients were as follows: young age, allergy, wheezing, and absence of tobacco smoking. On the contrary, smoker subjects with dyspnea, age ≥ 65 years, history of occupational exposure, and no allergy had the highest probability to receive a diagnosis of COPD. However, GPs should be enabled to diagnose early mild or mild-to-moderate asthma or COPD, when the use of questionnaires is insensitive and the possibility of access to spirometry may be even more important than in advanced cases.⁸

It is interesting to observe that some of the limitations emerging in our research were also reported in studies of similar or larger extension than ours on the field application (*ie*, outside a definite research protocol) of office spirometry conducted in other countries. In Ontario, economic incentives proved to influence the use of office spirometry increasing the number of GPs involved but not the volume of activity of each GP; notwithstanding, wide regional variations were found in spirometry utilization with a small number of GPs performing a very high number of studies without any quality and appropriateness control and, conversely, several areas with insufficient access to spirometry.¹²

In the United Kingdom, an audit study was carried out in 1999 on 95 general practices in North Staffordshire. One half of the practices declared that spirometry should be available in the practice, but only 18 practices possessed a spirometer and 8 of them never used it. Lack of formal training was one of the main limitations registered. Open access to hospital spirometry services was an alternative solution preferred by GPs in North Staffordshire.¹³ This audit study was conducted in a period when office spirometry by GPs was underfinanced by the UK National Health Service. Very recent work on 72% of general practices in South Wales (of which 82% had a spirometer) concluded that despite incentives (recommendation by guidelines and the general medical services contract in the United Kingdom) to perform spirometry in general practice, lack of adequate

training in use and interpretation determined a wide variability of confidence and reliability levels in COPD diagnosis. As a matter of fact, spirometry was performed more often if GPs were confident in use and interpretation, and frequency of use was related to greater training periods. Spirometric confirmation of COPD varied widely (0 to 100%; median, 37%).¹⁹ Indeed, different studies^{8,11,15} confirm the importance of training, repeat performance, and quality control by experienced personnel.

In conclusion, our randomized trial shows 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, but objective limitations must be stressed, in particular that the study was underpowered to show a difference between the two groups of patients, with a potential type II statistical error. Moreover, the study shows 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 favorable rating on usefulness. Therefore, at present, a closer interaction between GPs and specialists with an easy referral of subjects with respiratory symptoms and asymptomatic smokers ≥ 45 years old⁷ to specialist facilities is the best option for reducing the rate of underdiagnosis and undertreatment of chronic obstructive disorders. At the same time, studies to identify and resolve the factors preventing field implementation of office spirometry are greatly needed.

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APPENDIX

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