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# The Proportional Venn Diagram of Obstructive Lung Disease in the Italian General Population\*

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**Study objectives:** The Venn diagram of obstructive lung disease (OLD) has been recently quantified. We aimed to quantify the proportion of the general population with OLD, and the intersections of physician-diagnosed asthma, chronic bronchitis (CB), and emphysema in two Italian general population samples, in relationship to airflow obstruction (AO) determined through spirometry.

**Design and participants:** We analyzed data from two prospective studies (4,353 patients) carried out in the rural area of Po River delta from 1988 to 1991 and in the urban area of Pisa from 1991 to 1993.

**Results:** Prevalence rates of asthma, CB, and emphysema were 5.3%, 1.5%, and 1.2% in the Po delta, and 6.5%, 2.5%, and 3.6% in Pisa. A double Venn diagram, which was used to quantify the distribution of CB, emphysema, and asthma in relation to the presence/absence of AO, identified 15 categories. Isolated AO was the most frequent category (Po delta, 11.0%; Pisa, 6.7%), followed by asthma only without AO (Po delta, 3.3%; Pisa, 4.3%). The combination of the three OLD conditions was the only category that always showed higher prevalence rates for those with AO (Po delta, 0.20%; Pisa, 0.16%) than for those without AO (Po delta, 0.04%; Pisa, 0.05%). Of those with either OLD or AO, there were 61.4% in Po delta and 38.2% in Pisa with isolated AO, 24.8% and 41.9%, respectively, with an OLD without AO, and 13.8% and 19.9%, respectively, with simultaneous OLD and AO. For both genders, the frequency of isolated asthma decreased with age, while that of isolated AO, CB-emphysema, and the combination of asthma and CB-emphysema increased.

**Conclusion:** About 18% of the Italian general population samples either reported the presence of OLD or showed spirometric signs of AO. We confirmed that the Venn diagram of OLD can be quantified in the general population by extending the mutually exclusive disease categories (including a concomitant diagnosis of asthma, CB, or emphysema) to 15.

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**Key words:** asthma; COPD; epidemiology; morbidity; obstructive lung disease; Venn diagram

**Abbreviations:** AO = airway obstruction; ATS = American Thoracic Society; CB = chronic bronchitis; GOLD = Global Initiative for Chronic Obstructive Pulmonary Disease; NHANES = National Health and Nutrition Examination; OLD = obstructive lung disease; SVC = slow vital capacity

COPD is a very important cause of mortality and morbidity in Europe.<sup>1–3</sup> Asthma is the most common chronic condition in children and can be diagnosed at all ages.<sup>4</sup> Although COPD and asthma are considered to be different entities with respect to pathophysiologic and cellular mechanisms,<sup>5</sup> it is well-recognized that chronic persistent asthma may have features of irreversible airflow obstruction, thus being encompassed within the term *COPD*, as was clearly shown in the nonproportional Venn diagram published in a 1995 American Thoracic Society (ATS) document.<sup>6</sup> Furthermore, much of the data that are available on COPD mortality and morbidity

are based on the combination of chronic bronchitis (CB), emphysema, and asthma (codes 490 to 493 of the *International Classification of Diseases*, 9th revision,<sup>7</sup> or codes J40 to J47 of *International Classification of Diseases*, 10th revision.<sup>8</sup>

According to estimates by Murray and Lopez,<sup>9</sup> if tobacco epidemic trends remain unchanged in the interval from 1990 to 2020, then COPD will jump from sixth to third among the leading causes of death worldwide. The actual prevalence of obstructive lung disease (OLD) within a given population may vary widely depending on the tools used for its identification, from self-reported respiratory symptoms, to

medical diagnosis, to abnormal lung function. Community surveys in countries of both northern and southern Europe<sup>10</sup> have indicated that at least 4 to 6% of the adult population have clinically relevant COPD, and that the prevalence increases sharply with age. However, almost two thirds have only a mild reduction in lung function.

Our group has already examined the importance of gender, aging, and tobacco smoking in the development of COPD,<sup>11</sup> using data collected in two longitudinal surveys that were carried out in the rural area of the Po River delta (in north Italy) and in the urban area of Pisa between 1980 and 1993. Data on the prevalence rates of CB, emphysema (determined by medical diagnosis), and some respiratory symptoms, stratified by gender and smoking habit, were analyzed. The prevalence rate of CB was found to be lower than that of chronic cough and phlegm, symptoms that the diagnosis of CB is based on.<sup>12</sup> This confirms that the frequency of such disease is underestimated when only medical diagnoses are considered.<sup>13</sup> Furthermore, an underestimation of the prevalence of COPD of 25 to 50% and higher, has been found by several authors.<sup>1,14,15</sup>

Even when the diagnosis is based on an objective tool like spirometry, highly variable prevalence rates are found, also within the same population, when using the different criteria endorsed by different scientific societies. For instance, Viegi et al<sup>16</sup> have shown, in adults  $\geq 25$  years of age (1,727 subjects) who were investigated from 1988 to 1991, that the prevalence rates of airflow obstruction ranged from 11%, using the European Respiratory Society criterion,<sup>1</sup> to 18%, using the "clinical" criterion (later labeled as a criterion for Global Initiative for Chronic Obstructive Pulmonary Disease [GOLD] stage 1 to 4 disease),<sup>17</sup> to 40.4%, using the 1986 ATS criteria.<sup>18</sup> A recent review by Halbert et al<sup>19</sup> reported on 32 sources of COPD prevalence rates, represent-

ing 17 countries and 8 World Health Organization-classified regions. Prevalence estimates were based on spirometry (11 studies), respiratory symptoms (14 studies), patient-reported disease (10 studies), or expert opinion. The reported prevalence ranged from 0.23 to 18.3%. The lowest prevalence rates (0.2 to 2.5%) were based on expert opinion.

Until recently, the nonproportional Venn diagram of OLD produced for the 1995 ATS guidelines had not been quantified. Soriano et al<sup>20</sup> analyzed data from the US National Health and Nutrition Examination (NHANES) III survey (1988 to 1994) and the UK General Practice Research Database for the year 1998. The areas of intersection among the three OLD conditions (*ie*, CB, emphysema, and asthma) produced seven mutually exclusive disease groups. Concomitant diagnosis of asthma, CB, or emphysema was common among OLD patients from the general population, particularly in adults aged  $\geq 50$  years. We aimed to quantify the proportion of the general population with OLD, and the intersections of physician-diagnosed asthma, CB, and emphysema in two Italian general population samples, in relationship with airflow obstruction as determined through spirometry.

## MATERIALS AND METHODS

Data were collected during the second cross-sectional survey of the two prospective studies carried out in the rural area of the Po delta from 1988 to 1991 (2,841 subjects; age range, 8 to 75 years) and in the urban area of Pisa from 1991 to 1993 (2,841 subjects; age range, 8 to 97 years). Both surveys were performed using the same standard protocol already described in previous articles.<sup>11,13,16,21-24</sup> A brief description is reported below.

For each subject, information on respiratory symptoms, diseases, and risk factors were obtained by a standardized interviewer-administered questionnaire, developed by the Italian National Research Council based on that of the US National Heart, Lung, and Blood Institute. The questionnaire contains 67 main questions covering demography, general health status, respiratory symptoms, respiratory diseases, allergy symptoms, family history of respiratory and allergic diseases, tobacco smoking, occupational history, environmental and socioeconomic conditions, and recent infectious episodes. Each interviewer was adequately trained prior to administering the survey. Similar to the NHANES III, subjects were defined as having CB/emphysema and asthma if they answered positively to the questions, "Have you ever been told you have CB (emphysema)?" and "Have you ever had asthma or asthmatic bronchitis?" and also have reported physician confirmation.

Subjects aged  $\leq 75$  years were invited to perform lung function tests according to the ATS protocol<sup>25</sup>: slow vital capacity (SVC); and FVC. At least two trials were repeated to obtain a satisfactory SVC value. The highest SVC value was retained for statistical analyses. Afterward, as many as eight FVC maneuvers were performed to obtain at least three acceptable trials. Among them, the two largest FVC and FEV<sub>1</sub> values should not vary by  $> 5\%$ . The highest FVC and FEV<sub>1</sub> values were selected, regardless of the maneuver.

In the Po delta, a computerized pneumotachograph (Pulmo-

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nary system 47804S; Hewlett-Packard; Waltham, MA) was used for the acquisition of lung function data, whereas, a water-sealed spirometer (Baires; Biomedin; Padova, Italy [the instrument utilized by the centers participating in the European Community Respiratory Health Survey])<sup>26</sup> was used in Pisa. The current analyses refer only to data derived from subjects who had acceptable FVC test results (total, 4,353 subjects; Po delta, 2,463 subjects; Pisa, 1,890 subjects). The definition of airway obstruction (AO) was made according to the GOLD criterion for stage 1 to 4 disease (*ie*, FEV<sub>1</sub>/FVC ratio < 70%) without considering percent predicted FEV<sub>1</sub> values.<sup>17</sup>

A double Venn diagram (Fig 1) has been used to quantify the distribution of CB, emphysema, and asthma in relation to the presence/absence of AO. The first diagram (diagram A) refers to the presence of AO. The second diagram (diagram B) refers to the absence of AO. In turn, each diagram is split into other parts (eight parts for diagram A; seven parts for diagram B). For the sake of completeness, it is appropriate to note that there was a 16th part that was not depicted, which included the remainder of the population (*ie*, the subjects with neither AO nor respiratory diseases). Statistical analyses were performed using a statistical software package (SPSS, version 9.0 + update 10.0; SPSS; Chicago, IL).<sup>27</sup>

RESULTS

The characteristics of study populations are reported in Table 1. The Po delta sample was larger than the Pisa sample, with men and women being equally distributed in both samples (women in the Po delta, 50.8%; women in Pisa, 49.6%). The mean age for subjects from the Po delta was 36.3 years, and about 6 years older in Pisa (*ie*, 42.1 years; *p* < 0.001). Smoking habit was significantly different between

Table 1—General Characteristics of the Samples Participating in the Second Surveys, by Area of Residence

| Characteristics | Po River Delta | Pisa  | p Value* |
|-----------------|----------------|-------|----------|
| Subjects        | 2,463          | 1,890 |          |
| Women, %        | 50.8           | 49.6  | NS       |
| Age, yr         |                |       |          |
| Mean            | 36.3           | 42.1  | 0.000    |
| SD              | 16.5           | 17.5  |          |
| Minimum–max     | 8–75           | 8–75  |          |
| Smoking, %      |                |       |          |
| Smokers         | 30.8           | 26.8  | 0.003    |
| Ex-smokers      | 25.3           | 29.0  |          |
| Never-smokers   | 43.9           | 44.2  |          |

\*By  $\chi^2$  test for categoric variables or analyses of variance for continuous variables.

the two populations (*p* = 0.003). There was a higher prevalence of current smokers and a lower prevalence of ex-smokers in the Po delta (30.8% and 25.3%, respectively) than in Pisa (26.8% and 29.0%, respectively).

Prevalence rates of OLD were statistically different between the two samples (Table 2). In both populations, asthma (Po delta, 5.26%; Pisa, 6.50%) showed the highest prevalence. In the Po delta, the prevalence of CB (1.53%) was slightly more frequent than that of emphysema (1.17%), and the reverse was true in Pisa (2.49% vs 3.60%, respectively). When considering the relative distribution of subjects within the OLD group, the asthma-only group

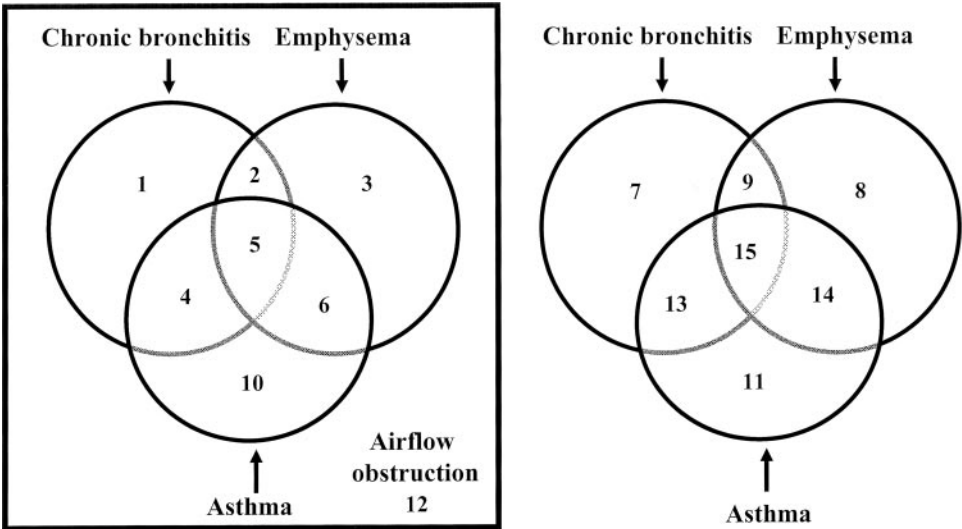


FIGURE 1. Model of the modified Venn diagram. *Left*: with airflow obstruction. *Right*: without airflow obstruction. 1 = AO + chronic bronchitis; 2 = AO + chronic bronchitis + emphysema; 3 = AO + emphysema; 4 = AO + chronic bronchitis + asthma; 5 = AO + chronic bronchitis + emphysema + asthma; 6 = AO + emphysema + asthma; 7 = no AO + chronic bronchitis; 8 = no AO + emphysema; 9 = no AO + chronic bronchitis + emphysema; 10 = AO + asthma; 11 = no AO + asthma; 12 = isolated AO; 13 = no AO + chronic bronchitis + asthma; 14 = no AO + emphysema + asthma; 15 = no AO + chronic bronchitis + emphysema + asthma.

**Table 2—Prevalence Rates of CB, Emphysema, and Asthma in the Two Italian General Population Samples**

| Disease                    | Po River<br>Delta, %<br>(n = 2,463) | Pisa, %<br>(n = 1,890) | p Value* |
|----------------------------|-------------------------------------|------------------------|----------|
| OLD                        | 6.9                                 | 10.9                   | 0.000    |
| Asthma only                | 4.54                                | 5.82                   |          |
| Asthma + CB                | 0.28                                | 0.21                   |          |
| Asthma + emphysema         | 0.20                                | 0.26                   |          |
| CB only                    | 0.89                                | 1.22                   |          |
| CB + emphysema             | 0.12                                | 0.85                   |          |
| Emphysema only             | 0.61                                | 2.28                   |          |
| CB + emphysema<br>+ asthma | 0.24                                | 0.21                   |          |

\*By  $\chi^2$  test.

accounted for 66.0% in the Po delta and 53.6% in Pisa, the CB-only group accounted for 12.9% and 11.2%, respectively, and the emphysema-only group accounted for 8.9% and 21.0%, respectively. In the Po delta, 0.8% had more than one OLD condition, and 0.2% had all three conditions simultaneously. In Pisa, 1.5% had more than one OLD condition, and 0.2% had all three conditions simultaneously. When considering the conventional distinction between COPD (CB and/or emphysema) and asthma, it was observed in the Po delta and Pisa that 30.8% and

13.5%, respectively, of COPD patients also had asthma, while 13.7% and 10.5%, respectively, of asthma patients also had COPD. The proportional Venn diagram (Fig 2) shows that the areas of intersection among the three OLD conditions were different in the two populations.

When spirometric results were taken into account, a double proportional Venn diagram was depicted in order to allocate all 15 categories in the two surveys (Fig 3-4). Isolated AO was the most frequent category (Po delta, 10.96%; Pisa, 6.72%). Asthma only without AO was the second most frequent category (Po delta, 3.25%; Pisa, 4.34%). These figures were much higher than those for asthma only with AO (Po delta, 1.30%; Pisa, 1.48%). In the Po delta, the prevalence rates of CB only (with AO, 0.28%; without AO, 0.61%) were slightly higher than those of emphysema only (with AO, 0.24%; without AO, 0.37%). Conversely, in Pisa the prevalence rates of emphysema only (with AO, 0.63%; without AO, 1.64%) were slightly higher than those of CB only (with AO, 0.48%; without AO, 0.74%). The combination of the three OLD conditions was the only category that always showed higher prevalence rates for those with AO (Po delta, 0.20%; Pisa, 0.16%) than for those without (Po delta, 0.04%; and Pisa, 0.05%).

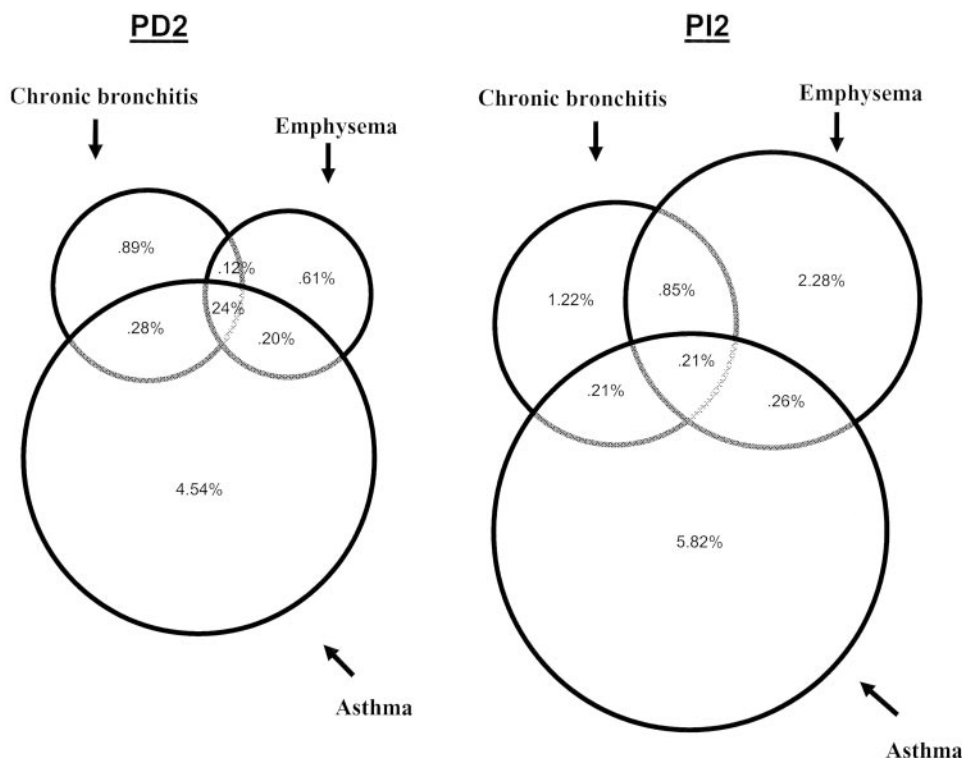


FIGURE 2. Proportional distribution of OLD within the modified Venn diagram. Left: Po delta (PD2) sample. Right: Pisa (PI2) sample.

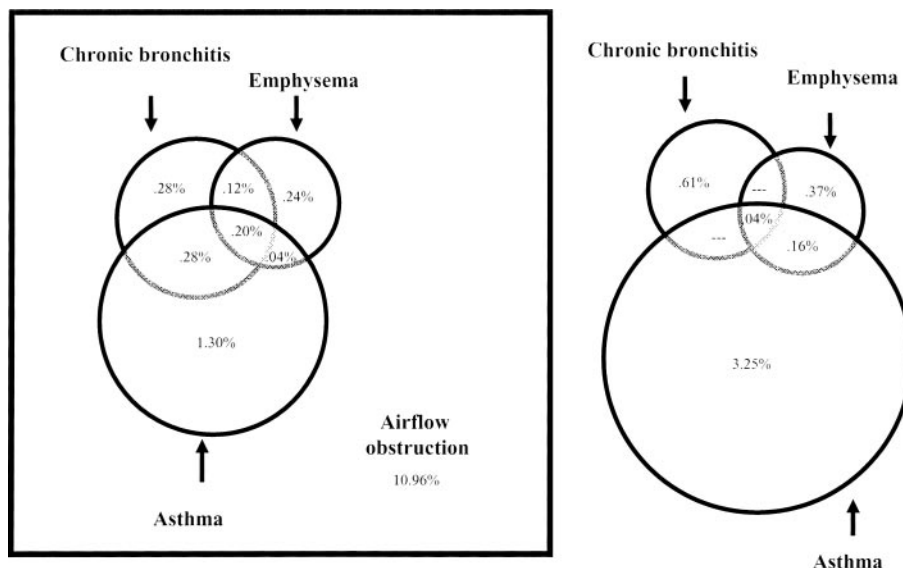


FIGURE 3. Distribution of OLD, with airflow obstruction (*left*) and without airflow obstruction (*right*), in the Po delta sample.

A total of 17.85% of the Po delta population and 17.58% of the Pisa population showed either OLD or AO. Of these subjects, 61.4% in the Po delta and 38.2% in Pisa showed isolated AO, 24.8% in the Po delta and 41.9% in Pisa showed an OLD without AO, and 13.8% in the Po delta and 19.9% in Pisa showed simultaneous OLD and AO.

When the assessment of AO was made within the OLD diagnostic categories, the proportions varied

among participants with asthma only, who showed a lower percentage (Po delta, 28.6%; Pisa, 25.4%), participants with CB only (Po delta, 31.5%; Pisa, 39.3%), or participants with emphysema only (Po delta, 39.3%; Pisa, 27.8%). Participants with all three OLD categories showed the highest proportions of AO (Po delta, 83.3%; Pisa, 76.2%).

The proportions of mutually exclusive disease groups also were displayed as horizontal stacked

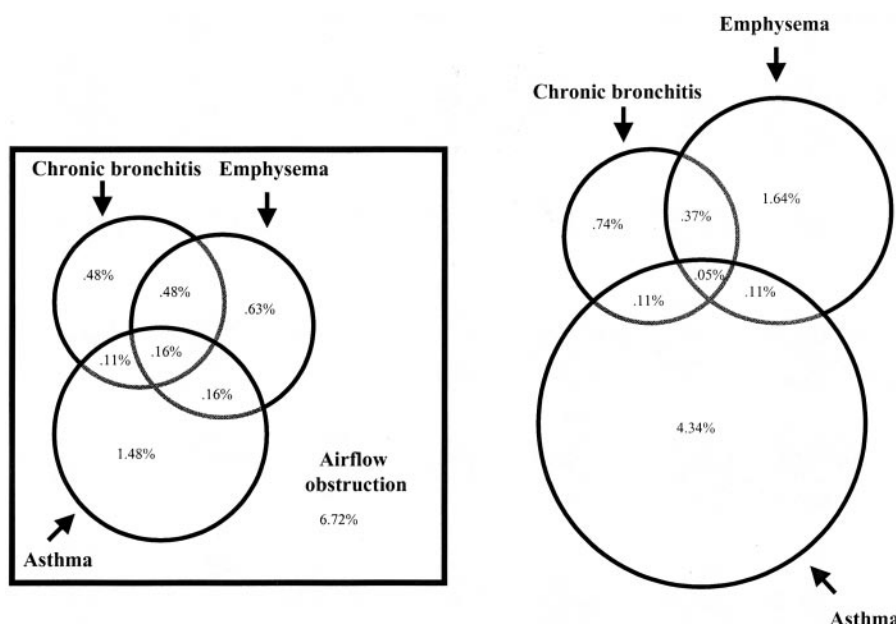


FIGURE 4. Distribution of OLD, with airflow obstruction (*left*) and without airflow obstruction (*right*), in the Pisa sample.

bars, for comparison by gender and age, after pooling the data from the two population samples (Fig 5). For the sake of clarity and simplicity, we grouped CB and emphysema together as CB-emphysema, thus reducing the number of disease groups from 15 to 7. Only people > 20 years of age were analyzed, since CB and emphysema were virtually nonexistent in younger subjects. In both genders, regardless of the presence of obstruction, isolated asthma decreased with age, while the incidence of isolated CB-emphysema and the combination of asthma and CB-emphysema increased. The incidence of isolated AO increased with age as well.

In particular, among these 711 subjects with either OLD or AO, the relative size of the asthma-only group (regardless of the presence of obstruction) decreased with age in men and women (20 to 44 years of age, 41.7% and 52.5%, respectively; 45 to 64 years of age, 11.2% and 24.8%, respectively; and  $\geq 65$  years of age, 5.6% and 14%, respectively). Within the asthma-only group, the proportion of those subjects with AO increased with age in women (20.9%, 28.6%, and 33.3%, respectively), while it increased up to 64 years and then decreased in men (21.8%, 68%, and 60%, respectively). The relative size of the CB-emphysema group (regardless of the presence of obstruction) increased with age in men

and women (20 to 44 years of age, 6.1% and 7.3%, respectively; 45 to 64 years of age, 26.8% and 9.9%, respectively;  $\geq 65$  years of age, 27% and 21%, respectively). Within the CB-emphysema group, the proportion of those with AO increased with age in men (12.5%, 38.3%, and 62.5%, respectively), while it increased up to 64 years and then decreased in women (16.7%, 28.6%, and 22.2%, respectively). Finally, the frequency of the simultaneous presence of all three OLD conditions increased with age in men (3.0%, 3.1%, and 6.7%, respectively), while it increased up to 64 years and then decreased in women (1.2%, 7%, and 4.7%, respectively). Within this group, the proportion of those with AO ranged from 50% (in men 20 to 44 years of age and in women 45 to 64 years of age) to 100% (in younger and older women). The relative size of isolated AO increased from 49.2% in men 20 to 44 years of age, to 58.9% in men 45 to 64 years of age, to 60.7% in men  $\geq 65$  years of age. The values for women in the same age groups were 39%, 58.2%, and 60.5%, respectively.

## DISCUSSION

In Italy, about 18% of people from two large general population samples have signs of AO or report at least one of the three OLD conditions. Furthermore, asthma, CB, and emphysema largely coexist, especially in the elderly. This indicates that general practitioners tend to group the diagnoses of asthma and COPD together. In addition, our proportional Venn diagrams describe the prevalence rates of OLD and AO in the general population through 15 mutually exclusive groups. This different presentation should be considered as a positive replication in an independent database of the concept generated by Soriano et al.<sup>20</sup>

The strengths of our research are the large study sample sizes, the standard protocols, which already had passed the scrutiny of independent reviewers,<sup>11,13,16</sup> and the analyses in two representative populations living in rural and in urban geographic areas. Furthermore, we have provided prevalence rates of AO following the GOLD criteria for stage 1 to 4 disease (*ie*,  $FEV_1/FVC$  ratio < 0.70).<sup>28</sup> Our rates fall into the upper range of COPD prevalence rates recently reported by Halbert et al,<sup>19</sup> confirming that the World Health Organization projections on COPD burden based on expert opinion<sup>9</sup> have probably been underestimated.

The overlap of the three OLD conditions has already been demonstrated by Mannino et al<sup>29</sup> on the NHANES III surveys in the United States. Subsequently, such data were used by Soriano et al<sup>20</sup>

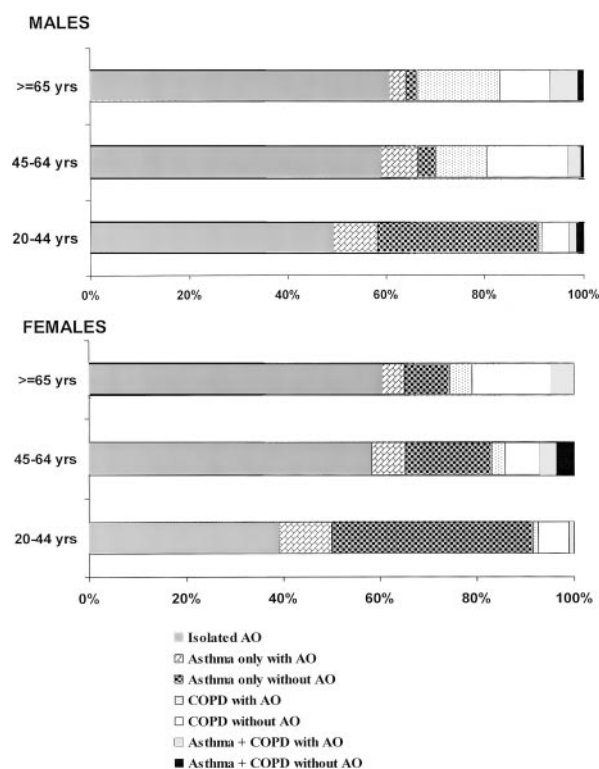


FIGURE 5. Proportions of seven mutually exclusive groups (AO, asthma, and COPD) by gender and age in the whole population.

to derive the first proportional Venn diagram of OLD with seven mutually exclusive disease groups. Interestingly, the Italian data are more similar to those of the NHANES III surveys (*ie*, a population survey with questionnaire and spirometry findings) than to those of the UK General Practice Research Database (*ie*, an archive based on records of family practitioners, without spirometry findings).

The validity of our results is enhanced by the higher proportions of AO among subjects reporting diagnostic labels of COPD, compared to those in NHANES III. Standard interviewer-administered questionnaires and spirometry protocols were used in the United States and Italy. In the United States,<sup>20,29</sup> a more specific criterion was used (GOLD stage IB [*ie*, FEV<sub>1</sub>/FVC ratio < 0.7 and FEV<sub>1</sub> < 80% predicted]), whereas in Italy a more sensitive criterion (*ie*, GOLD criterion for stage 1 to 4 disease, without considering FEV<sub>1</sub> percent predicted) was used. Indeed, we believe that it is more informative to provide sensitive data to estimate the burden of COPD in the population, in view of the underutilization of spirometry.

The external validity of our study is enhanced by the fact that in our populations the asthma-only group also comprised the largest proportion of OLD patients, and it decreased with increasing age, as in the study by Soriano et al.<sup>20</sup> It is important to point out that our data, like those in NHANES III, were collected before or immediately after the publication of the Global Initiative for Asthma guidelines on asthma,<sup>30</sup> whereas the UK General Practice Research Database provided data that were collected several years after. Thus, it would be helpful to perform similar epidemiologic studies in order to assess the possible influence of the updated GOLD guidelines on COPD diagnosis,<sup>28</sup> and of the updated Global Initiative for Asthma guidelines on asthma diagnosis.<sup>31</sup>

The fact that the concomitant diagnosis of asthma, CB, and emphysema is common among OLD patients from the general population, particularly in adults aged  $\geq 50$  years, also has been demonstrated by researchers who have not attempted to develop a proportional Venn diagram.<sup>32</sup> An interesting study on the early detection of COPD or asthma in a random sample from the general population aged 25 to 70 years has been carried out in 10 general practices located in the eastern part of the Netherlands within the framework of the Detection, Intervention, and Monitoring Program of COPD and Asthma program.<sup>33</sup> A total of 19.4% of the general population showed mild objective signs of COPD or asthma. Recently, it has been demonstrated in a cohort of 1,052 subjects with  $\alpha_1$ -antitrypsin deficiency,

that asthma was present in 21% of the cohort and attacks of wheezing were reported in 66%.

The differences in airway inflammation in patients with fixed airflow obstruction due to asthma or COPD are known.<sup>5</sup> However, there is overwhelming epidemiologic evidence that family practitioners perceive chronic persistent asthma as a form of irreversible airflow obstruction, thus encompassing it within the term *COPD*. This situation may be driven by the underutilization of spirometry as a diagnostic tool and by the feeling that the drugs to be used either in asthma or in COPD are not yet very different. Even many environmental risk factors, such as smoking,<sup>3,4</sup> air pollution,<sup>35</sup> and occupational exposures,<sup>36</sup> are common to both asthma and COPD.

One limitation of our study is the use of two different instruments for lung function determination, a pneumotachograph in the Po delta and a spirometer in Pisa. Although the two instruments followed the 1987 ATS guidelines on the standardization of spirometry,<sup>25</sup> there are some differences<sup>23</sup> that may explain the higher proportions of AO in the Po delta than in Pisa. In fact, compared to the pneumotachograph, the spirometer<sup>37–39</sup> may likely “cut” the FVC maneuver yielding a lower FVC value. Therefore, the spirometer also may overestimate the FEV<sub>1</sub>/FVC ratio, consequently detecting fewer AO subjects, especially those at an early stage of disease. Our data may be another argument for performing new research that is aimed at reaching a standardized and epidemiologically consistent criterion for AO. In further support, Vestbo and Lange<sup>40</sup> have questioned the ability of the GOLD criteria to provide information of prognostic value in COPD patients. Hardie and colleagues<sup>41</sup> have criticized the applicability of the GOLD criteria to the whole population, regardless of age.

Despite the different proportions of subjects with isolated AO, the prevalence rates of OLD and AO combined were very similar in the two Italian populations (*ie*, around 18%). This confirms an elevated social burden from respiratory diseases, as has previously been demonstrated in Europe.<sup>42–45</sup> Our findings also argue for the extensive use of spirometry in both clinical practice and at a general practitioner level. A promising approach in the early detection of COPD in a high-risk population using spirometric screening has come from a Polish study<sup>46</sup> of 11,027 smokers  $\geq 40$  years of age with a smoking history of  $\geq 10$  pack-years. Spirometric signs of AO were found in 24.3% of the screened subjects. In addition, after a minimal antismoking intervention, smokers with abnormal lung function had an approximately doubled quitting rate after 1 year than those with normal spirometry findings.<sup>47</sup> In the Detection, Intervention, and Monitoring Program of COPD and

Asthma study cited above,<sup>33</sup> the average costs per detected case varied from (in US dollars) \$953 (scenario 1) to \$469 (scenario 3). Thus, the detection of COPD or asthma at an early stage by means of a two-stage protocol seems to be feasible at relatively little expense in comparison with those of other mass screening programs.

In conclusion, about 18% of the general population have reported having OLD or have shown spirometric signs of AO. We confirm that the Venn diagram of OLD can be quantified in the general population by extending the mutually exclusive disease categories (including concomitant diagnosis of asthma, CB, or emphysema) to 15. Spirometry should be extensively used in clinical practice to try to overcome the underestimation of the worldwide burden of COPD. Further research is needed to better characterize subjects with different OLD combinations in order to implement better preventative and therapeutic strategies.

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# **The Proportional Venn Diagram of Obstructive Lung Disease in the Italian General Population\***

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