ORIGINAL RESEARCH

The Reliability of Hospital and Pharmaceutical Data to Assess Prevalent Cases of Chronic Obstructive Pulmonary Disease

Annunziata Faustini,[1] Cristina Canova,[2] Silvia Cascini,[1] Vincenzo Baldo,[3] Karin Bonora,[4]
Gianfranco De Girolamo,[4] Pierantonio Romor,[5] Loris Zanier,[6] and Lorenzo Simonato[3]

1 Epidemiology Department, Regional Health Service of Lazio, Rome, Italy

2 MRC-HPA Centre for Environment and Health, National Heart and Lung Institute, Imperial College, London, United Kingdom

3 Department of Environmental Medicine and Public Health, School of Medicine, University of Padua, Padua, Italy

4 Department of Public Health, Local Health Authority, Modena, Italy

5 Regional Health Information System management of Friuli Venetia Giulia region, INSIEL SpA, Udine, Italia

6 Epidemiology Department Regional Health Service of Friuli Venetia Giulia, Udine, Italia

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Correspondence to: Annunziata Faustini, Epidemiology Department, Regional Health Service of Lazio, via S. Costanza n 53, 00198, Rome, Italy, phone: 0039/06/83060440, fax 0039/06/83060463, email: faustini@asplazio.it

Abstract

Identifying chronic obstructive disease (COPD) cases is required to estimate COPD prevalence, to enroll COPD cohorts and to estimate air pollution health effects. Administrative health data are frequently used to identify COPD cases, though their validity has not been satisfactorily assessed. This paper aims to assess the contribution of pharmaceutical data in detecting COPD cases and to estimate the reliability of hospital/mortality databases in detecting COPD cases. Prevalent COPD cases among 35-plus-year-olds were estimated in four Italian areas in 2006 from hospital/mortality registries and adding pharmaceutical data. Age-specific and age-standardized prevalence rates were calculated in each area. Internal validity of COPD diagnoses from hospital and mortality databases was assessed. Pharmaceutical database was used to confirm the hospital/mortality COPD cases and to examine the selection and misclassification of hospitalized cases. Possible misclassification between COPD and asthma cases was estimated using hospital data. Prevalent COPD cases were 77,098 from hospital/mortality registries, 172,357 when respiratory prescriptions were added. Prevalence ranged from 4.0%–6.7%. Only 22.7% of pharmaceutical COPD cases were hospitalized or died and only 37.2% of hospital/mortality cases consumed respiratory medicines; this last proportion increased to 64.5% among the older cases with a principal diagnosis. COPD cases with a contemporary asthma diagnosis were 3.1%. We found that pharmaceutical data increases COPD prevalence estimates 2.2–2.5 times. Hospitalization does not necessarily indicate COPD severity, COPD as a principal diagnosis confirmed with medicine prescription more likely represented true cases. Misclassification affects asthma cases to greater extent than COPD cases.

Introduction

Chronic obstructive pulmonary disease (COPD) is a considerable health problem with a worldwide prevalence of 10% (1), the fifth-leading cause of death in developed countries, and among the top 10 causes of disability in several countries (2).

Given this background, COPD prevalence is an important indicator to evaluate the health status of a population, to plan interventions and evaluate their impact. Unfortunately, detecting COPD cases is challenging because the onset of symptoms is often neglected (3) and the diagnosis is rarely supported by spirometry. Moreover, household health surveys to estimate COPD frequency may be affected by important methodological problems in sampling. A meta-analysis (4) reported prevalence estimates ranging

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between 6% in the United States and 16% in Sweden. A multi-centre study using the same survey methods (1), reported estimates ranging between 6% in Germany and 19% in South Africa.

The increasing availability of current health databases, particularly cause mortality registers (CMR) and hospital discharge registers (HDR), is a strong encouragement to use administrative data to estimate COPD prevalence, but also to assess COPD treatment outcomes (5,6) and the air pollution effects (7–10). Although less frequently, even prescription data have been used to estimate COPD prevalence (11) and to enroll COPD cohorts (12). Nevertheless, the validity of the administrative sources has not been satisfactorily assessed. On the other hands, different study designs need different characteristics of validity; estimating prevalence requires high sensitivity, enrolling a cohort requires high specificity and to analyze the effects of air pollution one should avoid misclassifying cases.

The sensitivity and positive predictive value (PPV) of hospital and mortality datasets in detecting COPD cases have been estimated with indirect methods (13–16). Algorithms have been developed to improve the use of administrative data sets; those based on multiple sources and taking a longitudinal approach (which includes subjects who received a COPD diagnosis in the previous years) are suggested to increase the sensitivity of COPD prevalence (16,17). Data from general practitioners and specialists were the most frequent additional sources, contributing up to 76% of the total prevalent COPD cases (18). Data from general practitioners have been used also to test the specificity of COPD hospital and dead cases (19,20).

We carried out a study 1) to estimate the reliability of hospital and pharmaceutical data to assess prevalent cases of COPD and 2) to analyze the possible selection and misclassification of COPD cases from administrative databases.

Methods

COPD cases were obtained from four Italian areas with different sized populations and different administrative profiles: the Friuli-Venetia-Giulia (FVG) region, two health districts: Modena and Rovigo, and the city of Rome. HDR and CMR were used as sources of data for the period 2002–2006; pharmaceutical data for 2005–2007.

A COPD case was defined as a 35-plus-year-old subject discharged from hospital with a principal or secondary diagnosis of COPD or a subject who died from COPD (underlying cause of death) or a subject who used respiratory medicines; the definition further identifies probable and possible COPD cases based on the length of treatment and the number of packages consumed in one year (11). Medicines were identified with codes of the Anatomical Therapeutic Chemical (ATC) classification, where those specific for COPD complied with the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines (21). More details about the algo-

rithm to detect pharmaceutical COPD cases are reported in supplemental material (Appendix 1). Human subjects did not participate in the study since only administrative databases were used with no involvement of individuals, and under the privacy laws enforced in Italy.

Prevalent cases in 2006 were counted as residents who were hospitalized in 2002–2006 (the first hospitalization was chosen as index) and were still alive on 1st January 2006, according to the longitudinal approach (16,17), plus those who died from COPD in 2006 and were never hospitalized in 2002–2006, and those who took respiratory medicines starting in 2006, were not hospitalized in 2002–2006 and did not die from COPD in 2006. Subjects' ages as given in discharge records in 2002–2005 period were updated to the same day and month of 2006.

Two algorithms were developed to estimate prevalence; the first included only hospitalizations and deaths (HDR-CMR), the second added pharmaceutical data (HDR-CMR-DRUG). The two algorithms are reported in detail in supplemental material (Appendix 2), together with the codes of International Classification of Diseases, 9th revision (ICD-9) and the ATC codes. Crude and age standardized rates were estimated as the percentage cases in the resident population as of the 30th of June, 2006, with 95% confidence intervals (95% CI), in each area. The 2006 Italian population was used to standardize rates.

Box 1		COPD pharmaceutical cases		
		YES	NO	
COPD hospital or dead cases	YES	a	c	a+c
	NO*	b	??	
		a+b		

a = subject who were discharged or dead with COPD and took medicines following discharge or preceding death, according to pharmaceutical COPD case definition
c = COPD hospital or dead cases who did not take medicines
b = COPD pharmaceutical cases who had no COPD hospital diagnosis nor died from COPD

* included those not hospitalised in 2002-2006 or discharged with diagnosis other than COPD, respiratory failure or congestive heart failure.

To estimate the magnitude of misclassification of the COPD cases when the administrative diagnoses were used, we assumed that having been prescribed respiratory medicines along with a hospital diagnosis of COPD was more likely to represent true COPD than a diagnosis or a prescription alone. Then we estimated the proportion of the pharmaceutical COPD cases who were discharged with a COPD diagnosis in the 5-year period or who died from COPD in 2006 (a/a+b) (sensitivity) and the proportion of hospitalized or died COPD cases who took respiratory medicines (a/a+c) (box 1) (PPV).

The year of treatment follow-up for hospital cases started after discharge for those hospitalized in 2006 or at the time the first pharmaceutical prescription was filled in 2006 for those hospitalized in previous years; for those who died, the year that preceded death was used to assess their treatment.

These analyses were carried out on different age groups (35–64 year-olds, 65–84 year-olds and 85-plus-year-olds), using different definitions of hospital COPD cases (both principal and secondary COPD diagnoses, a principal diagnosis of COPD or a secondary diagnosis combined with a principal diagnosis of respiratory failure (ICD-9 Codes = 518.8, 518.5, 786.0) or congestive heart failure (ICD-9 Codes = 428.0)), and excluding COPD cases who also received an asthma diagnosis (ICD-9 Code = 493) in any hospitalization between 2002 and 2006. We did not carry out sensitivity analysis for the less specific codes of COPD (ICD-9 Codes = 490, 494, 496) since they represented 4.6%. The analyses were done in each area separately, then pooled estimates were obtained with a random meta-analysis and the heterogeneity across the areas was estimated.

Box 2

a = subjects who were discharged or died from COPD and took medicines following discharge or preceding death according to pharmaceutical definition of probable COPD

c = subjects who were discharged or died from COPD who took medicines according to pharmaceutical definitions of possible COPD

b = probable COPD pharmaceutical cases who had no hospital diagnosis nor died from COPD

d = possible COPD pharmaceutical cases who had no hospital diagnosis nor died from COPD

To test the hypothesis that the most severe cases of COPD would be selected when hospital and mortality data were used, we assumed that having been prescribed respiratory medicines according to probable case definition along with a hospital COPD diagnosis, was more likely to be a severe COPD case than having been prescribed according to possible case definition or not being hospitalized. We restricted the analysis to the pharmaceutical COPD cases classified according to treatment regimens. Then we estimated the proportion of those who took respiratory medicines according to the probable COPD case definition, who were discharged with COPD or who died from COPD (a/a+b) (sensitivity), the proportion of hospitalized or dead COPD cases

who took medicines according to the probable COPD case definition (a/a+c) (PPV). In this case, we could add the proportion of those taking respiratory medicines according to the possible COPD case definition who were not hospitalized or did not receive hospital diagnoses of COPD, respiratory failure or heart failure in the 5-year period (d/c+d) (specificity) (box 2).

To estimate the magnitude of misclassification between COPD and asthma, we detected the 35-plus-year-olds who were hospitalized for asthma in 2002–2006. Then, we estimated three proportions: the prevalent COPD cases who had an asthma diagnosis in any hospitalization during 2002-2006, the COPD cases identified from pharmaceutical data only who had a hospital diagnosis of asthma and the asthmatics who never received a COPD diagnosis but could have been identified as prevalent COPD cases according to their medicine intake.

Results

All 76,701 35-plus-year-old subjects who were hospitalized in the 5-year period with a COPD diagnosis were included as COPD prevalent cases in 2006. COPD was registered as the principal diagnosis for 26% of these cases; this proportion grew to 34% adding, in turn, cases with respiratory failure or heart failure as the principal diagnosis and COPD as the secondary. Subjects who died from COPD in 2006 and had not been hospitalized, contributed 397 more prevalent cases. Pharmaceutical data identified 95,259 additional cases. There were a total of 77,098 prevalent cases of COPD in 2006 according to the HDR-CMR algorithm and 172,357 using the HDR-CMR-DRUG algorithm (Table 1).

The two estimates of COPD prevalence had similarities, in all areas; age-standardized rates increased adding the pharmaceutical data; the values obtained using the HDR-CMR-DRUG algorithm ranged between 4.03% of the residents in the FVG region and 6.71% of the residents in Rome, with estimates that are between 2.5 and 2.2 times higher than the HDR-CMR algorithm, respectively (Table 2). In each area, COPD prevalence increased proportionally with age and males showed higher values than females at any age (Figure 1).

According to the HDR-CMR-DRUG algorithm, the COPD cases were 33% in 35–64 year-old, 55% in 65–84 and 11% in 85-plus-year-olds (Table 1). Deaths increased from 0.02% in 35–64 year-olds to 0.2% and 1.1% in the older groups, respectively; hospitalizations increased from 23% to 53% and 69%, respectively, whereas pharmaceutical-identified cases decreased from 77% to 47% and 30%, respectively, in the older groups.

The proportion of pharmaceutical COPD cases who were hospitalized or died from COPD, was low (22.7%; 95% CI = 19.9% – 25.9%) (Table 3). Even the proportion of COPD cases who took medicines after hospital discharge or before death was low (37.2%; 95% CI = 29.4%-47.1%) (Table 4). The 65-84 year-olds showed the highest values of predictive value, whichever COPD hospital case
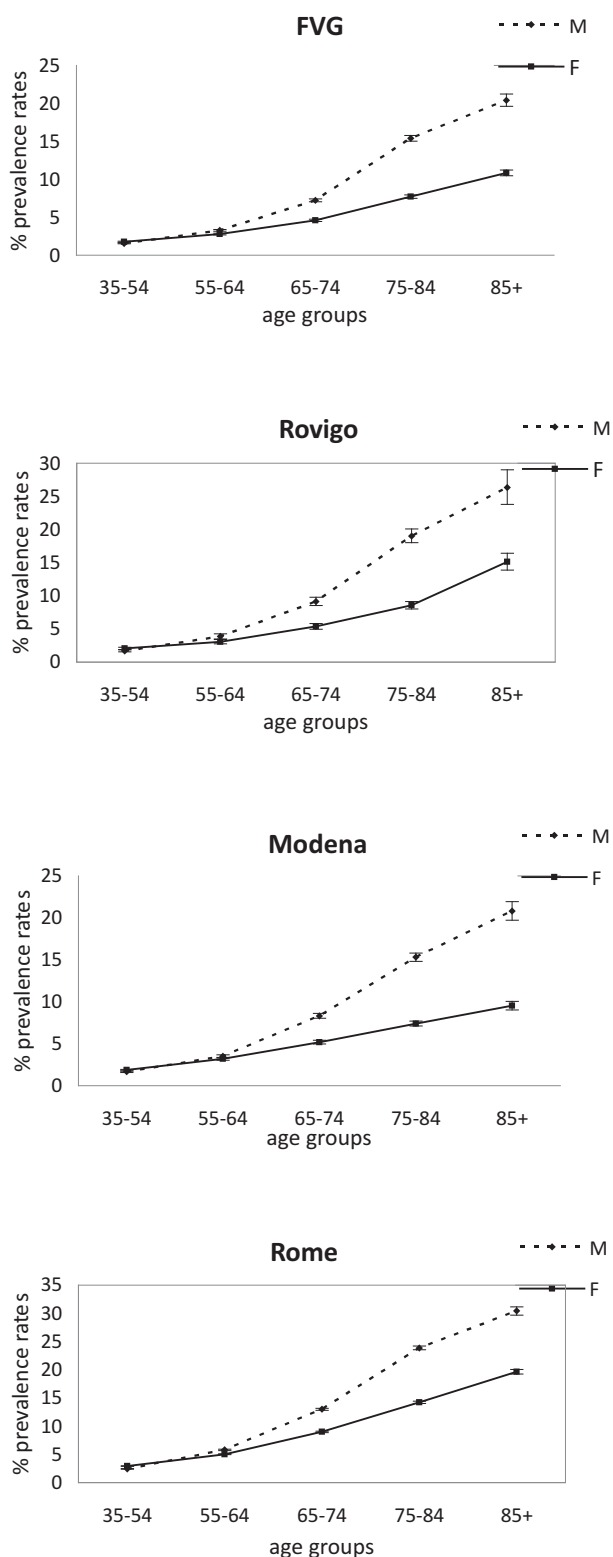
Figure 1. Age specific prevalence rates, for men and females, using the algorithm that includes pharmaceutical data - four Italian areas, 2006.

definition had been used (Table 4). Sensitivity decreased but predictive value increased when hospital cases were selected by principal diagnoses, in all age groups (Tables 3 and 4). Excluding COPD cases who had received an asthma diagnosis slightly reduced both sensitivity and predictive value. A high heterogeneity of sensitivity was observed across cities, for any COPD case definition in subjects over 85.

When the analyses were restricted to those who took medicines to compare probable and possible COPD cases, the proportion of the pharmaceutical COPD cases who were hospitalized or died from COPD was still low: 24.2% (95% CI = 21.4% – 27.0%) (Table 5). In contrast, the proportion of COPD hospitalized or dead cases who took medicines coherently with a reliable definition of pharmaceutical case (probable cases), reached 96.5% (95% CI = 95.7% - 97.2 0%) (Table 5); likewise, the proportion of those not hospitalized or dead subjects who took medicines coherently with a less-definite definition of COPD case (possible cases), reached 91.3% (95% CI = 89.4% – 93.3%) (Table 5). Sensitivity increased with age, PPV was similar in all age groups, but specificity decreased at older ages.

Among prevalent COPD cases identified by algorithm including pharmaceutical data, 3.1% received a hospital diagnosis of asthma. The COPD cases who had also an asthma diagnosis were slightly younger (average age 66.2 years) than those without asthma (average 68.7 years). Among prevalent COPD from pharmaceutical data only, 2.6% had an asthma diagnosis in the period 2002-2006. In contrast, among 4981 subjects who received a hospital diagnosis of asthma but no COPD diagnosis, 47.6% could have been classified as COPD according to their medicine intake.

Up to 98% of subjects consumed respiratory medicines from the ATC groups, which were recommended for COPD. All probable COPD cases used beta-2-agonists, 36.4% took anticholinergics, 18.2% xantines and at least 61.5% glucocorticoids (Table 6). It is noteworthy that 12% of probable COPD cases took leukotriene receptor antagonists, though they are recommended to asthmatics (Table 6).

Discussion

We found that adding pharmaceutical data to hospital and mortality data, contributed 55% additional COPD prevalent cases. Few cases among those treated required hospitalization in the previous years, the highest values were observed in 85-plus-year-olds; few cases among those discharged or who died from COPD, took respiratory medicines, the highest values were observed in 65–84 year-olds when principal diagnoses were used to define cases. The COPD prevalent cases who had an asthma diagnosis were 3.1%.

Using both a longitudinal approach and adding pharmaceutical data contributed to higher estimates of COPD prevalence. The former leads to estimates that are three times higher than the cross-sectional approach and the latter doubled the prevalence as estimated using HDR-CMR algorithm. As there is a lack of external validation for the algorithms that included all the available health data (hospitalizations, deaths and medicines), the previous

Table 1. Study population, according to different algorithms, four areas, 2006

	HDR-CMR algorithm						
Areas	**Total**	**35-64**		**65-84**		**85+ year-olds**	
	N	**N**	**%**	**N**	**%**	**N**	**%**
FVG region	14488	1888	13.0	9230	63.7	3370	23.3
Modena district	8269	1334	16.1	5353	64.7	1582	19.1
Rovigo district	2607	362	13.9	1683	64.6	562	21.6
Rome city	51734	9520	18.4	34148	66.0	8066	15.6
Total	**77098**	**13104**	**17.0**	**50414**	**65.4**	**13580**	**17.6**
	HDR-CMR-DRUG algorithm						
Areas	**Total**	**35-64**		**65-84**		**85+ year-olds**	
	N	**N**	**%**	**N**	**%**	**N**	**%**
FVG region	34629	11094	32.0	18643	53.8	4892	14.1
Modena district	18667	6278	33.6	10105	54.1	2284	12.2
Rovigo district	5781	1756	30.4	3257	56.3	768	13.3
Rome city	113280	38281	33.8	63480	56.0	11519	10.2
Total	**172357**	**57409**	**33.3**	**95485**	**55.4**	**19463**	**11.3**
	pharmaceutical COPD cases						
Areas	**Total**	**35-64**		**65-84**		**85+ year-olds**	
	N	**N**	**%**	**N**	**%**	**N**	**%**
FVG region	26211	9886	37.7	13677	52.2	2648	10.1
Modena district	13750	5364	39.0	7164	52.1	1222	8.9
Rovigo district	4205	1499	35.6	2344	55.7	362	8.6
Rome city	76326	30914	40.5	40201	52.7	5211	6.8
Total	**120492**	**47663**	**39.6**	**63386**	**52.6**	**9443**	**7.8**
	probable COPD cases						
Areas	**Total**	**35-64**		**65-84**		**85+ year-olds**	
	N	**N**	**%**	**N**	**%**	**N**	**%**
FVG region	24072	8809	36.6	12801	53.2	2462	10.2
Modena district	12373	4657	37.6	6592	53.3	1124	9.1
Rovigo district	3887	1345	34.6	2205	56.7	337	8.7
Rome city	68281	26582	38.9	36922	54.1	4777	7.0
Total	**108613**	**41393**	**38.1**	**58520**	**53.9**	**8700**	**8.0**
	possible COPD cases						
Areas	**Total**	**35-64**		**65-84**		**85+ year-olds**	
	N	**N**	**%**	**N**	**%**	**N**	**%**
FVG region	2139	1077	50.4	876	41.0	186	8.7
Modena district	1377	707	51.3	572	41.5	98	7.1
Rovigo district	318	154	48.4	139	43.7	25	7.9
Rome city	8045	4332	53.8	3279	40.8	434	5.4
Total	**11879**	**6270**	**52.8**	**4866**	**41.0**	**743**	**6.3**

Italian estimates of COPD prevalence and the relationship observed between gender and age groups make us confident in our results. It is possible however that true COPD cases were underestimated due to under-diagnosis and therefore under-treatment (22). An average COPD prevalence of about 13% has been estimated in seven Italian surveys (2,4) carried out between 1999 and 2003. These studies included all severity GOLD stages, and a large meta-analysis (4) showed that including GOLD first stage cases doubled the prevalence based on GOLD second stage cases. Moreover, one of the aforementioned surveys estimated a 3.6% COPD prevalence for moderate/
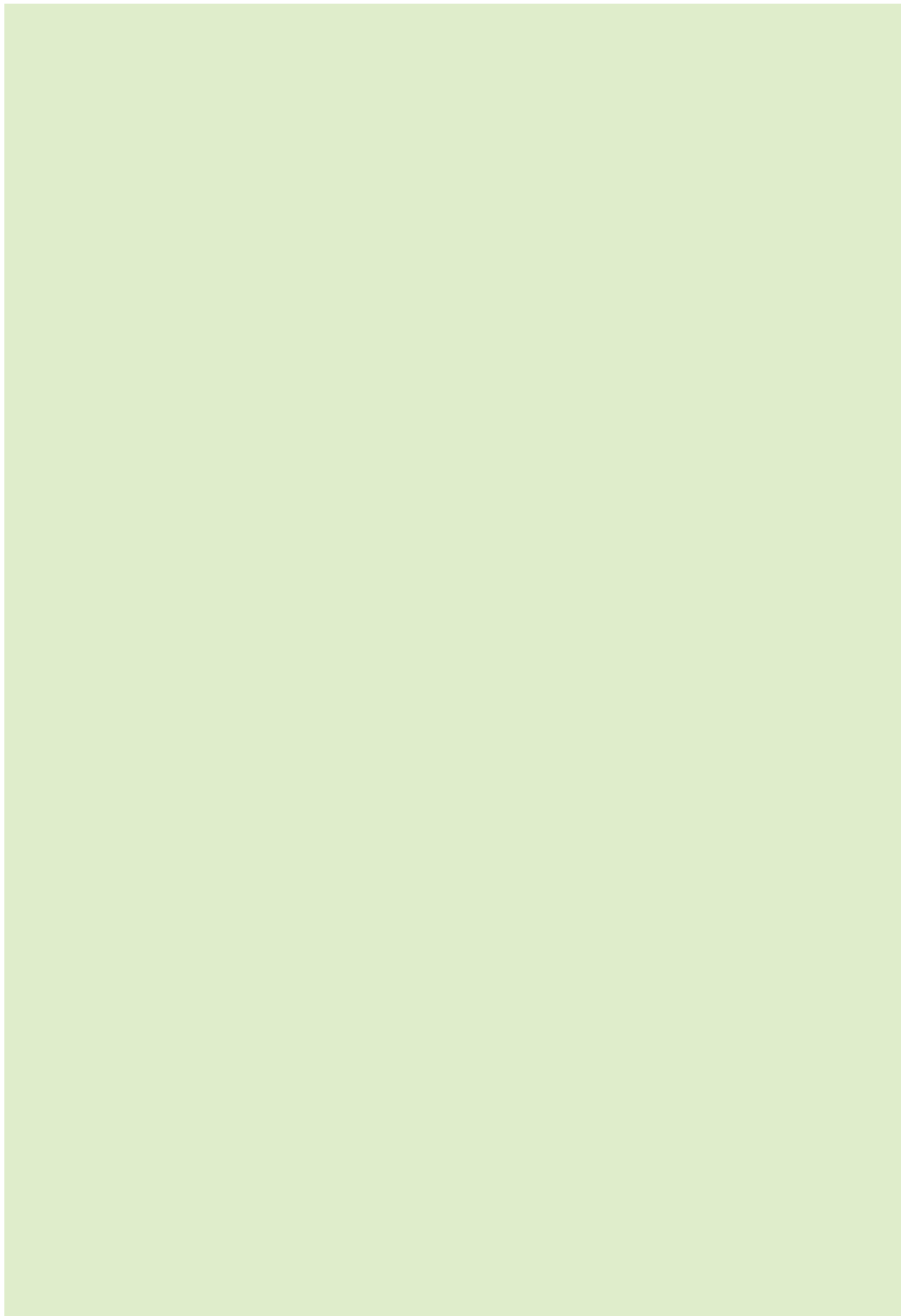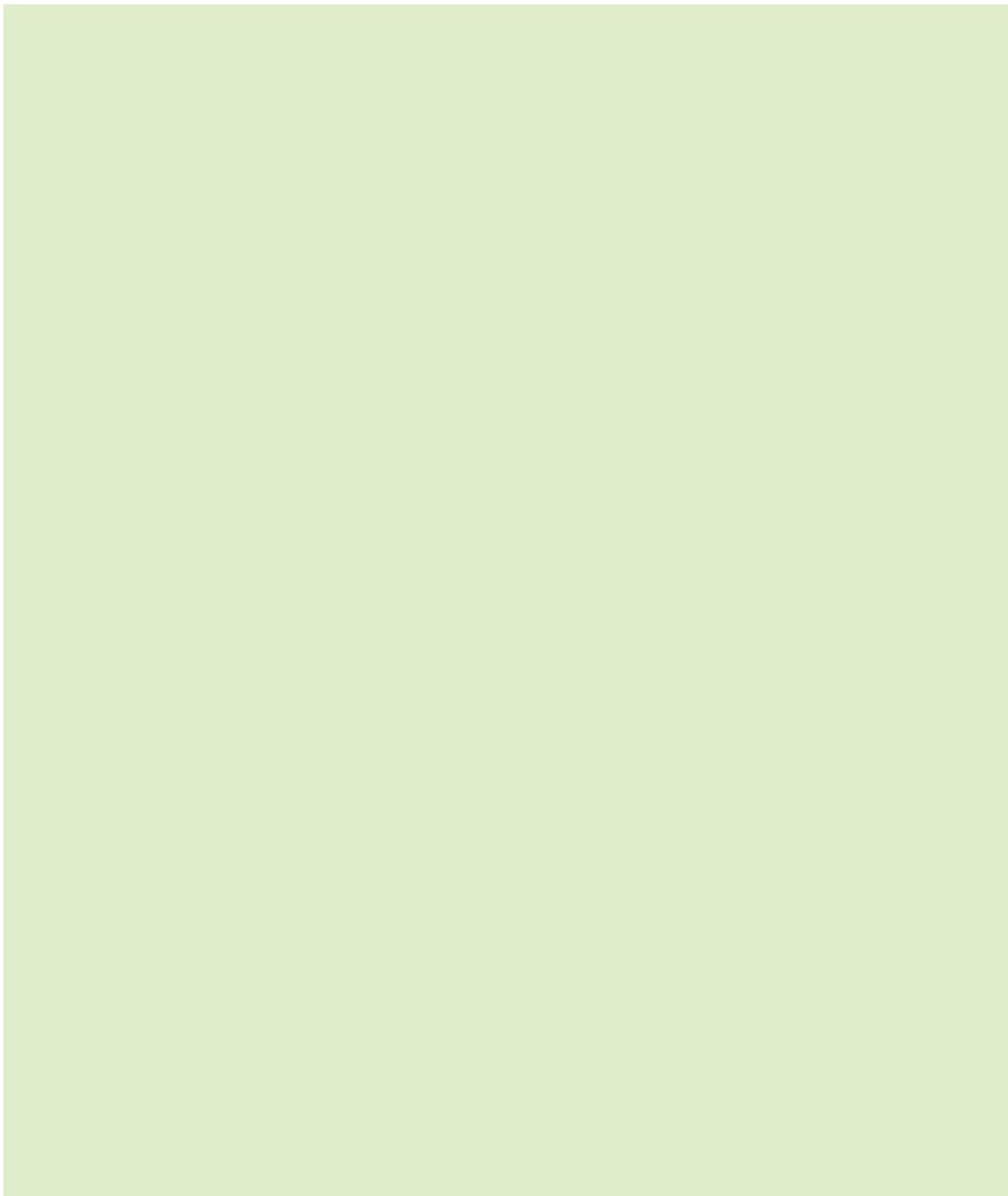
severe cases (23). In spite of large variations in estimates, many countries have data coherent with characteristics we found for COPD, like increases with age and more frequent occurrence in males (1,24). Results from a recent 10-European-country cohort (25) also confirm higher incidence of COPD in males than in females and a clear age-trend for COPD cases according to the GOLD definition. An increasing trend in females has been reported in some countries in more recent years (26). Nevertheless, the caution in using pharmaceutical data to estimate COPD prevalence in previous studies is the result of significant challenges, such as the difficulties in differentiating COPD treatment from asthma treatment, finding a temporal defi

nition that corresponds to a chronic treatment and having an exhaustive validation of the pharmaceutical data.

Sensitivity and predictive values of HDR-CMR algorithm were very low. The sensitivity increased with age, confirming that exacerbations and complications of COPD are likely to be more frequent in older subjects (27). Nevertheless, sensitivity never exceeded 40%; thus indicating that data from hospital and mortality registers underestimate prevalent COPD cases.

Comparing hospital case definitions showed that principal diagnoses of COPD, respiratory failure or congestive heart failure detected fewer COPD cases but they were more likely to be true cases, as a higher percentage

of these cases also took respiratory medicines. In other words, a COPD case definition based on the principal diagnoses further underestimated prevalence but improved the reliability of hospital COPD cases making them suitable for enrolment in a COPD cohort, as has been suggested for other chronic diseases (28).

Our conclusions are conditioned by the validation criterion we used; the Bayesian latent class analysis could represent a possible alternative to validate COPD cases using pharmaceutical data, since it would be able to assess the validity of multiple sources and adjust for the imperfect sensitivity and specificity of each source, in the absence of a real gold standard (29–31).

Hospitalized COPD cases showed a low reliability. Now, if it is reasonable to expect that only 22.7% of COPD cases

among those treated had required hospitalization in a 5-year period, it is surprising that only 37.2% of discharged or dead COPD cases took respiratory medicines. Although this proportion increased using principal diagnoses, it never exceeded 65%. Similar results have been reported previously in Canada (13), where up to 47% of clinically diagnosed COPD patients were not prescribed beta-2 agonist inhalants. These results are difficult to interpret as they clearly reject the hypothesis that hospital-diagnosed COPD cases are the most reliable; rather, they suggest a possible negative misclassification of hospital cases.

When we assessed the severity of COPD cases among those who took medicines, the hypothesis that hospitalized COPD cases were the most severe (32) was confirmed, since they were prescribed as probable cases

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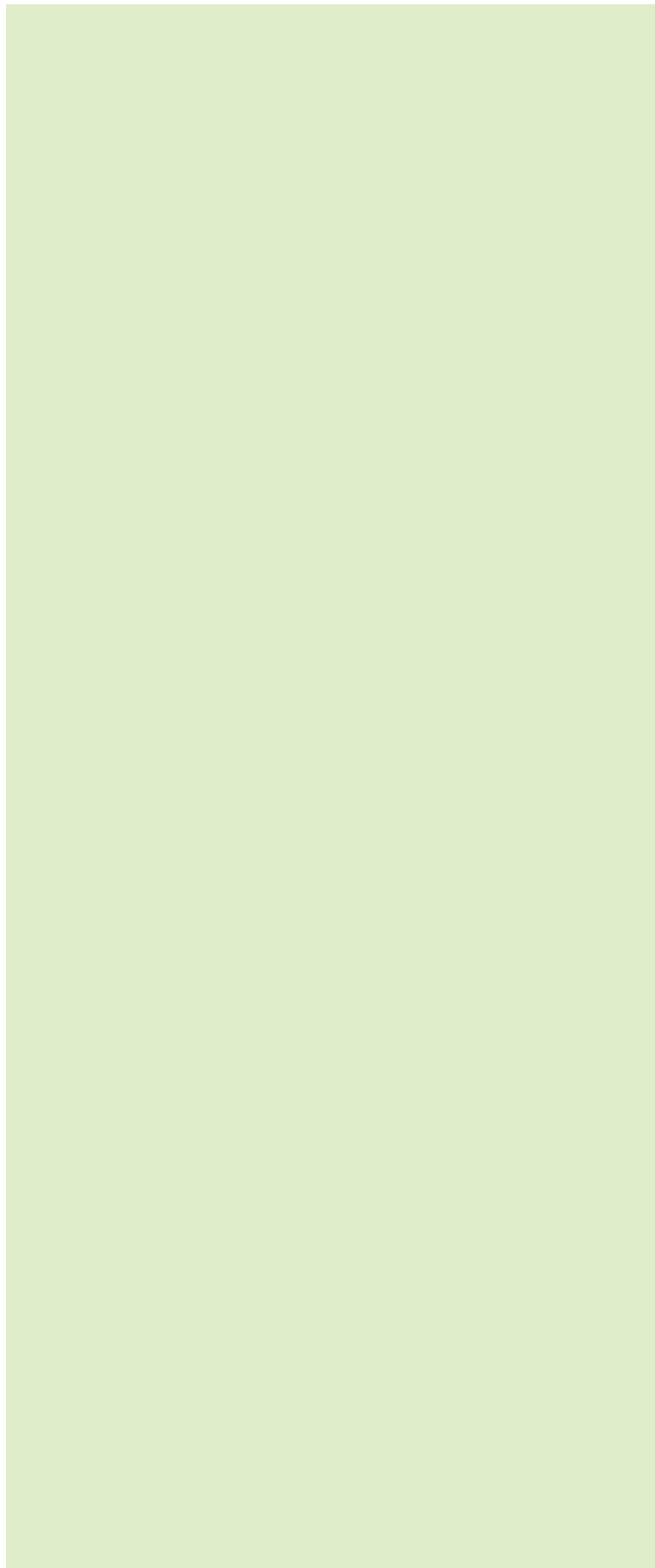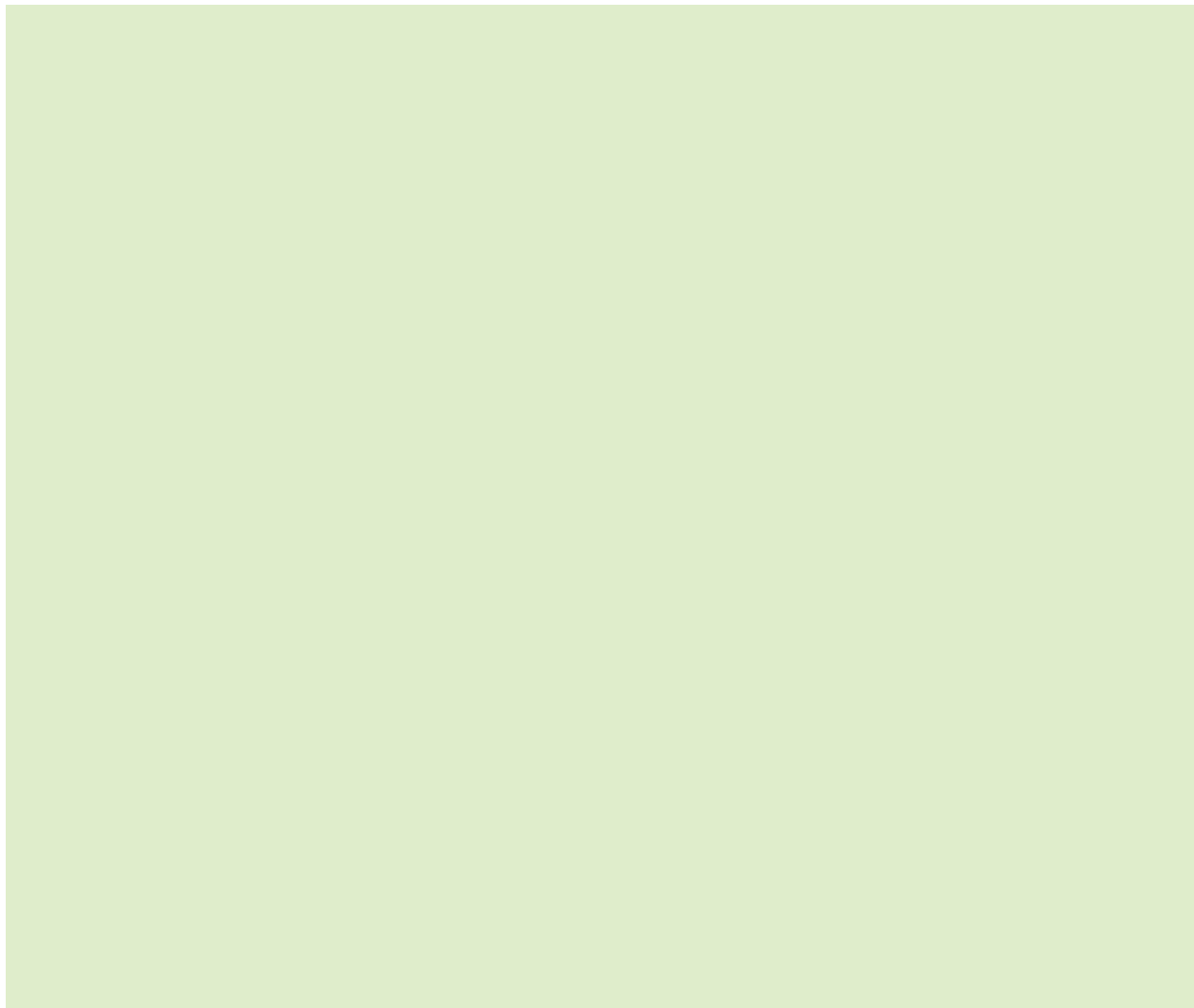
much more frequently (96.5%) than as possible cases, and up to 92.6% of possible cases were not hospitalized or died. It is worthy to note that a very recent study (33) which validated hospital and pharmacy COPD cases with spirometry results, reported validity estimates (36% the sensitivity, 92% the specificity and 81% the PPV) very similar to those observed here.

On the other hand, if we wanted a more reliable definition of COPD, to be enrolled into a cohort we should add to the previous criteria of a principal diagnosis and advanced age (65–84), meeting the criteria for a probable pharmaceutical case.

There are other implications from these results about the use of current health datasets. Younger cases were less frequently detected by the hospital/mortality dataset than the older ones, but they were similarly related to medicine consumption; one possible interpretation is that COPD exacerbations are less likely in young people, another is more adequate home treatment in younger than in older people. Younger cases had the highest specificity for treatments, thus the few cases hospitalized are likely to be reliable and severe. This pattern is more evident when principal diagnoses of COPD or its compli-

cations were analyzed, making the reliability of younger COPD patients identified by a secondary diagnosis very low. Moreover, the youngest pharmaceutical cases may suffer from lower reliability, since they increased four-fold (instead of two-fold in the older groups). In contrast, the 85-plus-year-old COPD cases who take respiratory medicines were more likely to be hospitalized or die from COPD in the study period, but those who were hospitalized or died were the least likely to take medicines after discharge or before death, and there were fewer possible cases who were never hospitalized or died; these results did not change with the principal or secondary diagnosis. Thus, the low specificity and predictive value of the oldest cases are more likely to be due to the validation criteria (based on medicines consumption) than to the poor reliability of hospital diagnoses. Good treatment compliance as well as appropriate prescriptions are more difficult in oldest patients (34) but in turn, this may contribute to increasing hospitalizations. In conclusion, pharmacological COPD case definitions are less adequate to validate older COPD cases.

Only 3.1% of prevalent COPD and only 2.6% of those identified by medicines only had a diagnosis of asthma,

suggesting a low misclassification between COPD and asthma in 35-plus-old subjects. These estimates cannot be conclusive since they were obtained from hospital cases of asthma, who account for almost 3% of the prevalent asthma in young adults in Italy (35). Estimating COPD-asthma misclassification would have to take into account asthmatics in the general population. Previous studies selected older COPD patients (45-plus-year-olds or 50-plus-year-olds) (11,12) to reduce the COPD-asthma misclassification; however not decreasing the asthmatic proportions in 65-year-old-or-older COPD cases in this study and observing an important consumption of leukotriene receptor antagonists among the definite pharmaceutical cases suggest that the hospital cases included different phenotypes of COPD, particularly patients with overlap syndrome asthma-COPD (36) or those for whom long-standing asthma concurred to an irreversible airways obstruction (27). We cannot exclude a misclassification due to frank diagnostic errors between COPD and adult asthma, since we had no data on reversible airways obstruction, bronchial responsiveness, smoking history or airway inflammation (36, 37).

Although we recognize some limits of our analysis, the consistency of the reliability of the estimates among areas that differ so much in population size and health care management, makes us confident in the generalizability of our findings.

Conclusions

The use of hospitalization or mortality data in detecting COPD cases is perhaps too conservative a method. The use of pharmaceutical data in identifying COPD cases should be optimized in order to obtain a more reliable COPD prevalence estimate.

Acknowledgments

Declaration of Interest

All the authors declare that they have no competing interests.

Appendix 2

Algorithm HDR-CMR

Data Sources and COPD prevalent case definition

Register	Selection criteria	Prevalent case definition
Hospital discharge	Having COPD listed as principal or secondary diagnosis (ICD-9 CM 490 - 492, 494, 496) and being at least 35 years-old at discharge	Having COPD diagnosis at discharge in 2006 or in the previous four years if alive on 1st January 2006 (the first hospitalisation was selected) or
Mortality	Having COPD listed as underlying death cause (ICD-9 490 - 492, 494, 496); and being at least 35 years-old at death	Having died from COPD in 2006 if not hospitalised due to COPD in the period 2002–2006

Algorithm HDR-CMR-DRUG

Data Sources and COPD prevalent case definition

| Register	Selection criteria	Prevalent case definition
Hospital discharge	Having COPD listed as principal or secondary diagnosis (ICD-9 CM 490 - 492, 494, 496) and being at least 35 years-old at discharge	Having been discharged with COPD diagnosis in 2006 or in the previous four years if alive on 1st January 2006 (the first hospitalisation was selected) or
Mortality	Having COPD listed as underlying death cause (ICD-9 490 - 492, 494, 496); and being at least 35s year-old at death	Having died with COPD in 2006 if not hospitalised due to COPD in the period 2002–2006 or
Pharmaceutical prescription	Consuming respiratory medicines (ATC R03)	Having consumed COPD medicines in the year following the first pharmaceutical registration in 2006,[1] not having died from COPD in 2006 and never having been hospitalised in 2002–2006.

[1]5 packages of any respiratory medicine in at least 4 months (probable COPD cases), or 3–10 packages in 2–3 months or 3–4 packages in 4–6 months of the same medicine mono-therapy (possible COPD cases).

Appendix 1
Pharmaceutical definition of COPD case

Consumption of respiratory medicines R03

35+year olds

Consumption of at least 5 packages of any R03 in one year

Probable COPD cases : consumption of 5 packages in at least 4 months

Possible COPD cases: consumption of 3-10 packages in 2-3 months or 3-4 packages in 4-6 months

+

Possible COPD cases in mono-therapy (one ATC)

COPD cases
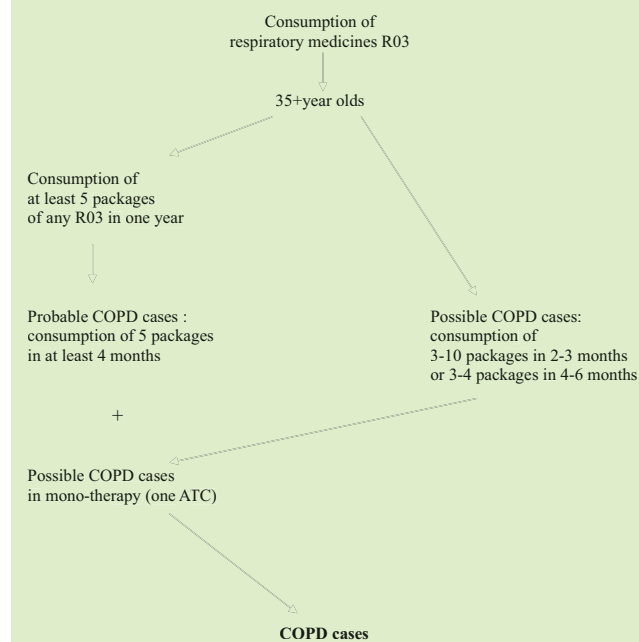
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