The Current State of Validation of Administrative Healthcare Databases in Italy: A Systematic Review

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Abstract: *Background*: Administrative healthcare databases are widely present in Italy. Our aim was to describe the current state of healthcare databases validity in terms of discharge diagnoses (according to the International Classification of Diseases, ICD-9 code) and their output in terms of research.

Methods: A systematic search of electronic databases including Medline and Embase (1995-2013) and of local sources was performed. Inclusion criteria were: healthcare databases in any Italian territory routinely and passively collecting data; medical investigations or procedures at patient level data; the use of a validation process. The quality of studies was evaluated using the STARD criteria. Citations of the included studies were explored using Scopus and Google Scholar.

Results: The search strategy allowed the identification of 16 studies of which 3 were in Italian. Thirteen studies used regional administrative databases from Lombardia, Piemonte, Lazio, Friuli-Venezia Giulia and Veneto. The ICD-9 codes of the following diseases were successfully validated: amyotrophic lateral sclerosis (3 studies in four different regional administrative databases), stroke (3 studies), gastrointestinal bleeding (1 study), thrombocytopenia (1 study), epilepsy (1 study), infection (1 study), chronic obstructive pulmonary disease (1 study), Guillain-Barre syndrome (1 study), and cancer diseases (4 studies). The quality of reporting was variable among the studies. Only 6 administrative databases produced further research related to the validated ICD-9 codes.

Conclusion: Administrative healthcare databases in Italy need an extensive process of validation for multiple diagnostic codes to perform high quality epidemiological and health services research.

Keywords: Healthcare databases, Sensitivity, Specificity, Predictive values, Health administrative data, Diagnostic accuracy, Misclassification bias, Diagnostic accuracy, Health services research, Epidemiology.

BACKGROUND

Administrative healthcare databases are becoming a widely used tool for epidemiological studies, health services research, comparative effectiveness investigations of drugs and devices, post-marketing surveillance, drug prescription patterns, and outcome research [1, 2]. Most of the databases contain electronically recorded diagnostic information that are expressed as codes of the International Classification of Diseases ICD-9 or ICD-10 [3]. To constitute a reliable resource for research, the diagnostic discharge data should be of high quality and closely correspond to the electronic information in the administrative database [4, 5]. There are many administrative databases worldwide in which this process of validation has been successfully performed for many diagnostic codes, making them value tools [1, 6-9].

In Italy, the provision and delivery of almost all health care services are performed by 21 Regional Health Authorities, each of whom maintains large healthcare databases with information on drug prescriptions, medical records from private and public hospitals, vital statistics, and demographic data for all residents identified by a unique national identification code [10]. These databases are often used for drug utilization studies [11], epidemiology [8, 12], health services research [13], and health economics [14], but nothing is known about the current state of the healthcare databases that have validated ICD-9 codes.

Our goal was to systematically identify the number of administrative healthcare databases in Italy that had

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validated diagnostic codes; to describe the type and number of diagnoses validated; and to describe epidemiological, health services research and other forms of research performed with these validated ICD-9 codes.

METHODS

A systematic search of electronic records, from January 1, 1995 to December 31, 2013, in the Medline (*via* Ovid) and Embase (*via* Embase.com) databases, was performed. We used a search strategy developed by Benchimol *et al*. [15], designed to capture studies that use healthcare administrative databases (see Appendix). Italian websites of healthcare services at the national, regional and local levels, as well as reference lists of retrieved articles and hand searches of pertinent Italian journals (*Epidemiologia e Prevenzione* and *Annali di Igiene*) were examined for relevant publications.

To be included, studies needed to satisfy the following criteria: 1) to have routinely used healthcare databases in any Italian territory, routinely and passively collecting data without an *a priori* research question; 2) to have contained a patient-related health outcome, medical investigation or procedure; and 3) to have employed a validation process. Studies using databases that were not truly administrative (e.g. cancer registries, epidemiology surveillance systems, etc.) were excluded. No language restriction was used.

Studies were included if they used databases containing significant clinical information (e.g., pathology/histology results, laboratory or microbiological data, chart notes, etc.), vital statistics (i.e., births and deaths) and disease registries (unless these data were used as the reference standard for validation of the administrative data). Studies using databases that contained data from quality improvement programs, or that validated the performance of comorbidity measures, were excluded unless they also validated the identification of disease components of the measure.

The quality of the included studies was evaluated using a checklist developed by Benchimol *et al*. [15], based on the criteria published by the Standards for Reporting of Diagnostic accuracy (STARD) initiative for the accurate reporting of investigations of diagnostic studies [16].

To evaluate the performance of the validated administrative healthcare databases in terms of epidemiological or health services research and other forms of subsequent research, we identified the citations from the medical literature of the published studies, following the first publication describing the validation of the administrative database. We used the Scopus database (www.scopus.com) and Google Scholar to identify the related citations (March 1, 2014).

Two authors independently screened titles and abstracts for inclusion (MLL, RDF). Disagreement was resolved by consensus. Two authors independently reviewed all the included studies and assessed the quality of reporting (FC, MO). Disagreement was resolved by consensus.

The distribution of various characteristics of the examined studies were reported using descriptive statistics.

RESULTS

The initial electronic search in Medline and Embase returned 12,939 citations. After screening titles and abstracts, we selected 54 reports for more detailed evaluation. In addition, 34 articles were identified from an Internet search, a reference check and a hand search of Italian journals for which full-text versions were obtained for further evaluation (Figure **1**). Overall 88 full-text articles were evaluated, which identified 16 studies that satisfied the inclusion criteria.

Description of Excluded Studies

Seventy-two studies were excluded from the review following full-text eligibility assessment. Most of the studies were not validation studies. However, some studies that did carry out validation, deserve some description: one study that validated ICD-9 codes for rheumatoid arthritis was excluded because it was published only as an abstract [17]; one study, despite attempting to assess misclassification of chronic obstructive pulmonary disease cases (COPD) from administrative databases, it did not use an adequate reference standard to validate COPD ICD-9-CM codes [18]; one study that validated ICD-9 codes for myocardial infarction in a network of three European countries, did not use an administrative database for the Italian data [19, 20], and two studies that considered infectious diseases [21, 22] did not use an adequate reference standard, were excluded from the analysis. The complete list of excluded studies, with reasons for the exclusion, is presented in the Supplemental Material.

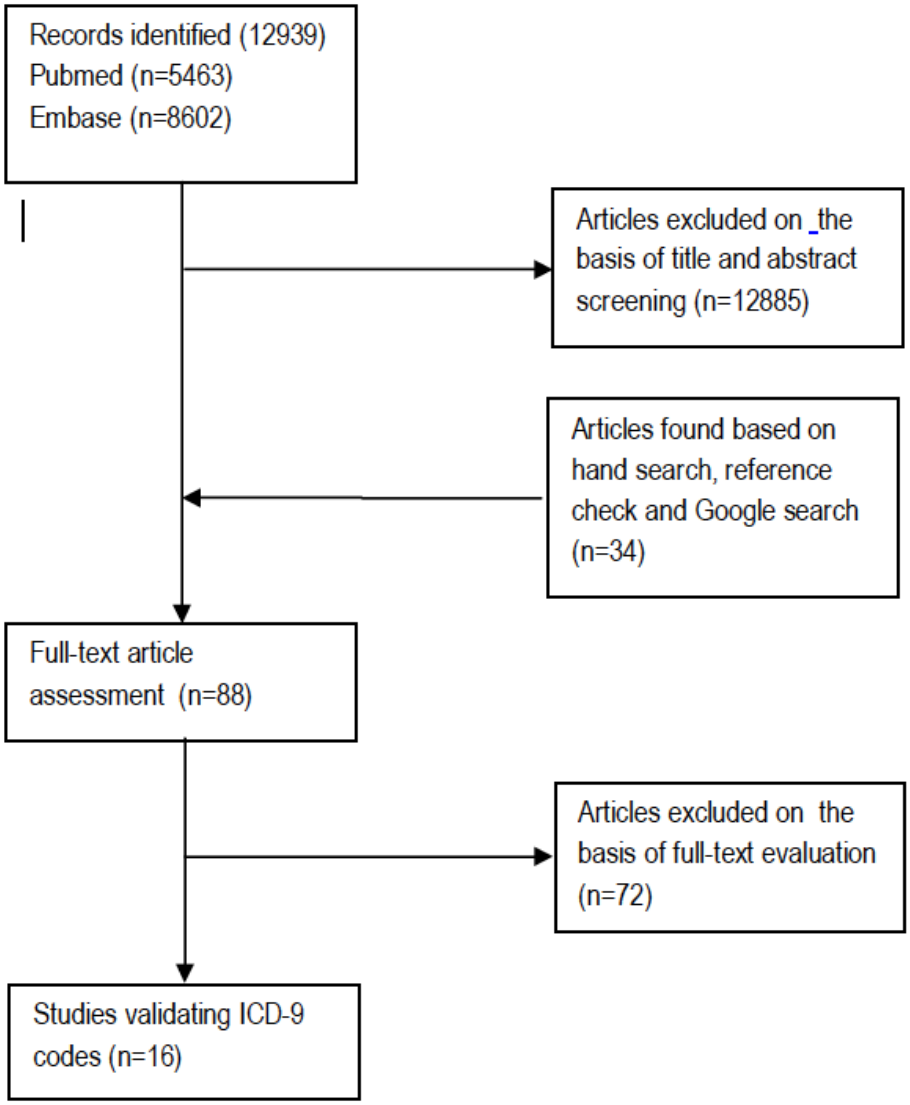

Figure 1: Study screening process.

Description of Included Studies

The 16 studies that were included in this systematic review were all published as full-text articles between 1999 to 2013. Three studies were published in Italian [23-25]. The coverage of the data was at regional level (9 studies [22, 24, 26-32]), provincial level (1 study [33]), district level (2 studies [23, 34]), and hospital level (4 studies [25, 35-37]). Five studies used ICD-9-CM codes for validation [25, 30, 31, 34, 35] and the remaining studies used the older version of ICD-9. Nine studies had as a primary aim to assess the validity of hospital discharge diagnoses. The basic characteristics of the studies are presented in Table **1**.

Validated Disease Codes

The following codes were considered for validation: stroke related codes (3 studies: 1 performed at the regional level (Veneto) [32] and 2 at the hospital level (Novara [36] and Lugo di Romagna [37]); amyotrophic lateral sclerosis related codes (3 studies at the regional level in Lombardia [33], Piemonte and Valle d'Aosta [29], and Friuli-Venezia Giulia [30]); gastrointestinal bleeding related codes (1 study performed at the regional level Friuli-Venezia Giulia [28]); thrombocytopenia related codes (1 study performed at the hospital level [35]); epilepsy related codes (1 study performed at the district of Lecco [34]); COPD related codes (1 study performed at the hospital level [25]). Two studies that evaluated lymphoid malignancies in the district of Reggio Emilia [23] and infections in all rehabilitation units in Lombardia [22] did not list the number of the ICD-9 codes. The remaining studies evaluated codes of different malignancies that are described in Table **1**.

Table 1: Characteristics of Included Studies

Study ID	Study aim	Source	Enrollment period	Reference standard	Type of disease: ICD-9 code validated	Measure of accuracy used
Baldi 2008	To develop algorithm to identify incidence cancer cases	Piemonte region	2000-2001	Regional Cancer Registry	Breast cancer: 174.0-174.9; 233.0; Colon cancer: 153.0-153.9, 154.0-154.1, 154.8; lung cancer: 162.0-162.9.	SE; PPV
Beghi 2001	To assess the validity of the hospital discharge for ALS epidemiology	6 provinces (Lombardia region)	1994–1995	Medical chart review	Motor neuron-disease: 335.2	SE, SP, PPV
Bogliun 2002	To assess the validity of hospital discharge diagnoses as a tracer of the Guillain-Barrè syndrome	Lombardia region	1996	Regional Guillain-Barrè syndrome registry / medical chart review	Acute infectious or post-infectious polyneuritis ICD-9 357.0	SE, PPV
Calzari 2006	To evaluate their accuracy for the diagnosis of lymphoid malignancies	Reggio Emilia district	1997-2001	Hospital discharge data, death certificates, pathologic records	Hodgkin's and non-Hodgkin lymphoma, multiple myeloma, acute and chronic lymphatic leukemia, Waldenstrom's disease. ICD-9 codes not listed	SE
Cattaruzzi 1999	To assess the accuracy of ICD-9 codes for gastrointestinal bleeding.	Friuli-Venezia Giulia region	January 1991 - June 1995	Medical chart review	Upper Gastrointestinal Bleeding: ICD-9 (site- and lesion-specific codes) 531 to 534; (non-specific codes) 578.0, 578.1, 578.9)	PPV
Chiò 2002	To assess the validity of ALS discharge diagnoses	Piemonte and Valle d'Aosta regions	1995-1996	Validated disease register	Amyotrophic lateral sclerosis: ICD-9 335.2.	SE, PPV
Fano 2012	To assess the outcome "thirty days mortality after admission for reacutized COPD" before and after a reabstract study.	Grassi Hospital (Lazio region)	2006-2007	Medical chart review	COPD (primary diagnosis): ICD-9-CM codes: 490, 491, 492, 494 o 496; Acute respiratory failure (secondary diagnosis): ICD-9-CM 518.81, 518.82, 518.83, 518.84.	Descriptive
Franchi 2013	To correlate clinical data and administrative data on epilepsy	District of Lecco (Lombardia region)	2000-2008	General practitioner record	Epilepsy: ICD-9-CM code: 345.x; myoclonus: 333.2; convulsions: 780.3; neonatal seizures: 779.0; spasms, other abnormal involuntary movements: 781.0.	SE, SP, PPV, NPV, AUC

(Table 1). Continued.

Study ID	Study aim	Source	Enrollment period	Reference standard	Type of disease: ICD-9 code validated	Measure of accuracy used
Galdarossa 2012	To assess the epidemiology of thrombocytopenia	Padova Hospital	2004-2008	Medical chart review	Thrombocytopenia: ICD-9-CM 287.30, 31, 32, 33, 39	SE, SP, PPV, NPV
Leone 2004	To evaluate the accuracy of stroke-related ICD-9 codes	Novara Hospital	1998	Medical chart review	Stroke and TIA: ICD-9: 430, 431, 434, 435 and 436	SE, PPV
Palange 2004	To estimate pleural mesothelioma incidence in the Lazio region	Lazio region	1997-2000	Medical chart review	Pleural mesothelioma ICD-9:163.0-9	Descriptive
Pisa 2009	To evaluate the accuracy of hospital discharge data as a source of ALS cases.	Friuli-Venezia Giulia region	2005-2006	Medical chart review	Amyotrophic Lateral Sclerosis: ICD9-CM 335.20	SE, SP, PPV NPV
Rinaldi 2003	To assess the accuracy of ICD-9 codes in identifying ischemic stroke	General Hospital of Lugo di Romagna	26 April-13 December 1999	Clinical assessment and medical review	Acute ischemic stroke: ICD-9 434, 436	SE, PPV
Schifano 2006	To identify Indicators of breast cancer severity and appropriateness of surgery	Lazio region	1997-1998	Medical chart review	Breast cancer: ICD-9-CM 174.0-174.9; 233.0.	SE, SP, PPV
Spolaore 2005	To assess the accuracy of hospital discharge diagnoses	Veneto region	1999	Medical chart review	Stroke: ICD-9: 342, 430 to 434, and 436 to 438	PPV
Tinelli 2002	To describe the frequency and type of infections acquired by patients hospitalized in rehabilitation units	131 rehabilitation units (Lombardia region)	2005-2006	Medical chart review	ICD-9 related to infections not listed	SE, PPV

SE = Sensitivity; SP=Specificity; PPV= positive predictive value; NPV= negative predictive value; AUC= Area under the curve; ALS=Amyotrophic lateral sclerosis; NSAID= Non-steroidal anti-inflammatory drug; CI= Confidence interval; TIA=Transient ischemic attack; COPD=Chronic obstructive pulmonary disease; ICD-9= International Classification of Disease.

Quality of the Studies

The quality of reporting is summarized in Table **2.** Except for 2 studies that used registries [26, 29] and 1 that used general practitioner record [34], all the studies used medical chart reviews as the reference standard; two studies, in addition to the assessment of medical chart reviews, used clinical assessment [37] or disease registry [27]. Only 9 studies described the characteristics of the assessors examining the reference standard; 3 of these studies reported the blinding of the evaluator. None of these 9 studies reported whether there was more than one assessor or reported the agreement between assessors.

In terms of the estimates of accuracy, only 3 studies reported at least 4 estimates of diagnostic accuracy. The most common statistics used to estimate diagnostic accuracy were sensitivity (n=12), positive predictive value (PPV) (n=12), and specificity (n=6). While two studies used PPV only, two studies did not report any diagnostic estimate despite the possibility to indirectly construct a cross-tabulation [24, 34]; and ten studies did not report the confidence interval for the diagnostic estimate.

Productivity of Validated Administrative Databases

The administrative database of Lombardia contained validated ICD-9 codes for four diseases of which two, Guillain-Barrè syndrome and amyotrophic lateral sclerosis, were rare diseases. Despite the number of citations related to the codes of these rare diseases, only one study that evaluated the incidence of amyotrophic lateral sclerosis in Lombardia was considered to have used the validated ICD-9 codes.

The administrative database of Piemonte included validated ICD-9 codes for stroke, amyotrophic lateral sclerosis and tumors of the breast, the colon and the lungs. Overall, there were 67 citations identified, of which 5 had indicated using the validated codes for research.

Table 2: Quality of Reporting of Included Studies Based on a Modified STARD Guidelines

TITLE, KEYWORDS, ABSTRACT	Yes	No	Unclear	Not applicable
Identify article as study of assessing diagnostic accuracy	12 (75%)	4 (25%)	0 (0%)	0 (0%)
Identify article as study of administrative data	11 (69%)	4 (25%)	1 (6%)	0 (0%)
INTRODUCTION				
State disease identification & validation one of goals of study	14 (88%)	2 (13%)	0 (0%)	0 (0%)
METHODS				
Participants in validation cohort:				
Describe validation cohort *(Cohort of patients to which reference standard was applied)*	16 (100%)	0 (0%)	0 (0%)	0 (0%)
· Age	7 (44%)	7 (44%)	2 (13%)	0 (0%)
· Disease	13 (81%)	1 (6%)	2 (13%)	0 (0%)
· Severity	2 (13%)	9 (56%)	3 (19%)	2 (13%)
· Location/Jurisdiction	16 (100%)	0 (0%)	0 (0%)	0 (0%)
Describe recruitment procedure of validation cohort:				
· Inclusion criteria	15 (94%)	0 (0%)	1 (6%)	0 (0%)
· Exclusion criteria	3 (19%)	4 (25%)	9 (56%)	0 (0%)
Describe patient sampling *(random, consecutive, all, etc.)*	16 (100%)	0 (0%)	0 (0%)	0 (0%)
Describe data collection				
· Who identified patients and did selection adhere to patient recruitment criteria	7 (44%)	0 (0%)	9 (56%)	0 (0%)
· Who collected data	4 (25%)	0 (0%)	12 (75%)	0 (0%)
· A priori data collection form	3 (19%)	2 (13%)	11 (69%)	0 (0%)
· Disease classification	9 (56%)	0 (0%)	7 (44%)	0 (0%)
· Split sample *(i.e. re-validation using a separate cohort)*	2 (13%)	5 (31%)	9 (56%)	0 (0%)
Test Methods:				
Describe number, training and expertise of persons reading reference standard	9 (56%)	1 (6%)	6 (38%)	0 (0%)
If >1 person reading reference standard, quote measure of consistency (e.g. kappa)	0 (0%)	8 (50%)	5 (31%)	3 (19%)
Blinding of interpreters of reference standard to results of classification by administrative data *(e.g. Chart abstractor blinded to how that chart was coded)*	3 (19%)	1 (6%)	12 (75%)	0 (0%)
Statistical Methods:				
Describe methods of calculating/comparing diagnostic accuracy	10 (63%)	4 (25%)	2 (13%)	0 (0%)
RESULTS:				
Participants:				
Report when study done, start/end dates of enrollment	14 (88%)	0 (0%)	2 (13%)	0 (0%)
Describe number of people who satisfied inclusion/exclusion criteria	15 (94%)	0 (0%)	0 (0%)	1 (6%)
Study flow diagram	5 (31%)	11 (69%)	0 (0%)	0 (0%)
Test results:				
Report distribution of disease severity	2 (13%)	5 (31%)	5 (31%)	4 (25%)
Report cross-tabulation of index tests by results of reference standard	10 (63%)	6 (38%)	0 (0%)	0 (0%)
Estimates:				
Report at least 4 estimates of diagnostic accuracy	3 (19%)	13 (81%)	0 (0%)	0 (0%)

(Table 2). Continued.

TITLE, KEYWORDS, ABSTRACT	Yes	No	Unclear	Not applicable
Diagnostic Accuracy Measures Reported:				
· Sensitivity	12 (75%)	4 (25%)	0 (0%)	0 (0%)
· Specificity	6 (38%)	10 (63%)	0 (0%)	0 (0%)
· PPV	12 (75%)	4 (25%)	0 (0%)	0 (0%)
· NPV	3 (19%)	13 (81%)	0 (0%)	0 (0%)
· Likelihood ratios	0 (0%)	16 (100%)	0 (0%)	0 (0%)
· Kappa	0 (0%)	16 (100%)	0 (0%)	0 (0%)
· Area under the ROC curve / c-statistic	2 (13%)	14 (88%)	0 (0%)	0 (0%)
· Accuracy/agreement	0 (0%)	16 (100%)	0 (0%)	0 (0%)
Report accuracy for subgroups *(e.g. age, geography, different sex, etc.)*	1 (6%)	15 (94%)	0 (0%)	0 (0%)
If PPV/NPV reported, ratio of cases/controls of validation cohort approximate prevalence of condition in the population	1 (6%)	1 (6%)	0 (0%)	14 (88%)
Report 95% confidence intervals for each diagnostic measure	6 (38%)	10 (63%)	0 (0%)	0 (0%)
DISCUSSION:				
Discuss the applicability of the validation findings	13 (81%)	2 (13%)	1 (6%)	0 (0%)

PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operating characteristic; CI, confidence interval.

The administrative database of Lazio comprised validated ICD-9 codes for COPD, breast cancer, mesothelioma and received 13 citations using the validated codes.

The administrative database of Friuli Venezia-Giulia included validated ICD-9 codes for gastrointestinal bleeding and amyotrophic lateral sclerosis. The study that documented the validation of the rare disease, amyotrophic lateral sclerosis, was published in 2009 and did not receive any citation [30]. Conversely, the study that validated the codes for gastrointestinal bleeding received at least 75 citations of which 2 employed the validated ICD-9 codes [38, 39].

The only publication that had validated stroke related diseases, from the administrative databases of Veneto, received 35 citations none of which was pertinent to the validated database. The remaining databases did not receive any citations. Table **3** shows the ICD-9 codes that were validated, with the related diagnostic accuracy estimates, the number of citations from Scopus and Google Scholar and the subsequent research based on the validated disease codes.

DISCUSSION

As the use of administrative healthcare databases grows, validation is increasingly recognized as an important component of research [2, 15, 40-42]. In this comprehensive systematic review, we identified 16 studies that performed the process of validation of diagnostic codes for healthcare administrative databases in Italy. Despite their widespread presence, only 5 regional administrative databases were effectively validated and only for ICD-9 codes of a limited number of diseases. In addition, we were able to assess the practical use of the databases for research by using the Scopus and Google Scholar databases to identify published articles that had cited the validated databases.

In general, some researchers were more oriented towards validation of rare diseases in administrative databases [27, 29, 30, 33]. For example, the validation of the codes for amyotrophic lateral sclerosis was performed in almost all the northern regions of Italy including Lombardia, Piemonte, Valle d'Aosta and Friuli-Venezia Giulia. The validation process produced some research in epidemiology and organizational assessments [43-45]. Baldi *et al*. [26] validated cancer related ICD-9 codes, using Piemonte's regional database, and performed subsequent studies that evaluated the determinants of patterns of healthcare and survival in lung and breast cancer [46-48]. After validating the codes for breast cancer severity, Rossi *et al*. used the Lazio regional administrative database to assess the efficacy of breast cancer screening programs [49, 50].

For frequent diseases such as stroke, researchers were able to validate the codes in three databases (2 of

Table 3: Administrative Databases with Results of Validated ICD-9 Codes and Relevant Citations

Administrative database	Study ID	Overall results	N of citations Scopus/GS*[1]	Relevant citations
Lombardia *(regional)*	Amyotrophic lateral sclerosis [34]	ICD-9 335.2: *SE* 91.6%; *SP* 99.9%; *PPV* 65.4%	22/20	Beghi 2007 [41]: Incidence of ALS in Lombardy.
	Guillainn-Barrè syndrome [28]	ICD-9 357.0: *SE* 90.6%; *PPV* 54.8%	19/18	-
	Epilepsy [35]	ICD-9-CM 345.x: *SE* 85.9%, (95%CI 76.0 - 92.2); *SP* 99.8%, 95% CI 99.7% - 99.8%	0/0	-
	Infection [23]	ICD-9 not listed. *SE* 45% (range 39% to 62%) ; *PPV* 89%	-/2	-
Piemonte *(regional)*	Amyotrophic lateral sclerosis [30]	ICD-9 335.2: *SE* 78.9%; *PPV* 38.8%.	21/27	Logroscino 2010 [42]: Incidence of amyotrophic lateral sclerosis in Europe. Chiò 2006 [43]: Tertiary centres and ALS outcomes.
	Breast, colon and lung cancer [27]	*SE*: Lung cancer 80.8%, breast cancer 76.7%, colorectal cancer 72.4%; *PPV*: lung cancer 78.7%, breast cancer 92.6%, colorectal cancer 87.9%.	17/26	Sacerdote 2012 [44]: Factors and disparities in the management of care. Pagano 2010 [45]: Sociodemographic determinants and survival in lung cancer. Rosato 2009 [46]: Patients'role and hospital characteristics in the initial treatment of early breast cancer.
	Stroke [37]	ICD-9 430–438:*SE* 77%	12/14	-
Lazio *(regional)*	Mesothelioma [25]	Descriptive	-/5	Romeo 2013 Mesothelioma incidence and exposure to asbestos in Lazio region [47].
	COPD [26]	Descriptive: The majority (94%) of reviewed cases were confirmed as being cases of COPD.	0/0	.-
	Breast cancer [32]	*Unclear*	6/8	Rossi 2006 [48]: Effect of screening programmes on the treatment of benign breast neoplasms. Rossi 2008 [49]: Screening programs compared to regularly offered health care services.
Friuli-Venezia Giulia *(regional)*	Gatrointestinal bleed [29]	*PPV*: 97% for ICD-9 531, 532; 84% for 534, and 80% for 533, and 59% for nonspecific codes.	68/75	Castellsague 2013 [39]: Gastrointestinal bleeding in nimesulide users. Sturkenboom 2002 [40]: Gastrointestinal disorders following NSAID treatment.
	Amyotrophic lateral sclerosis [31]	ICD-9 335.20: *SE*: 93% (95%CI: 82–99), *SP* 99% (95%CI: 97–99), *PPV* 87% (95%CI: 75–95), *NPV* 99% (95%CI: 98–99).	9/10	-
Veneto *(regional)*	Stroke [33]	*PPV*: ICD-9 342: 36%; 430: 76%; 431: 78%;432: 54%; 433: 9%; 434: 77%; 436: 61%; 437: 14%; 438: 9%.	23/35	-
Reggio Emilia *(district)*	Lymphoid malignancies [24]	Descriptive	-/1	-

(Table 3). Continued.

Administrative database	Study ID	Overall results	N of citations Scopus/GS*[1]	Relevant citations
Padova *(hospital)*	Thrombocitopenia [36]	ICD-9-CM 287.31: *SE*:80% (95%CI 0.51–0.94); *SP*: 88% (95%CI 0.67–0.96) *PPV*:80% (95%CI 0.56–0.97); *NPV*:88.4% (95%CI 0.68–0.96%)	1/2	-
Lugo di Romagna *(hospital)*	Stroke [38]	ICD-9 434: *SE 82%, PPV* 71%; ICD-9 436: *SE* 76% *PPV 76%*	15-22	-

[1]GS=Google Scholar; SE = Sensitivity; SP=Specificity; PPV= positive predictive value; NPV= negative predictive value; AUC= Area under the curve; ALS= Amyotrophic lateral sclerosis; NSAID= Non-steroidal anti-inflammatory drug; CI= Confidence interval; TIA=Transient ischemic attack; COPD=Chronic obstructive pulmonary disease; ICD-9= International Classification of Disease.

which were large regional databases, Table **3**), but they did not produce further research. The database from Friuli-Venezia Giulia, containing the validated ICD-9 codes for gastrointestinal bleeding, was used to evaluate the association between nimesulide and other non-steroidal anti-inflammatory drugs and gastrointestinal bleeding [28, 38, 39].

STRENGTH AND LIMITATIONS

We used the search strategy developed by Benchimol *et al*. [15], because, unlike other search strategies of administrative data [51], it was more oriented to identifying validation studies with very high sensitivity and low specificity, generating a large number of abstracts to evaluate. Despite this aspect, Benchimol's search strategy may not have captured all the relevant records, either because some abstracts may have not used relevant keywords or because Italian was used. To overcome this limitation, we searched the Internet, the Italian Regional and Local Health Unit websites, relevant regional health reports and relevant Italian journals, which led to identifying 6 articles. Another limitation might have been the use of Scopus or Google Scholar to search for study citations as a secondary indicator of research productivity of validated administrative databases. First, this approach is not a reliable tool, especially when the validation study was recently published, as it requires considerable time to publish the results of research using databases. Second, the accessibility of these databases can differ, which may have influenced the indicators of research productivity of the databases, even for the 8 codes validated at least 10 years ago. However, further investigation is necessary to explore the issue of accessibility of databases.

SIGNIFICANCE AND CONCLUSION

Healthcare databases in Italy experienced a rapid growth as a consequence of the introduction of the Diagnosis-Related Group (DRG) system in 1995. This system was initially used for reimbursement purposes, and subsequently, for the measurement of healthcare performance [10]. Discharge abstract data included the ICD-9 codes (which was replaced by the ICD-9-CM codes) and a number of procedures. Individual health and drug use data are collected using a unique lifetime fiscal code, similar to social security numbers in the US, which is provided to all residents. The use of a unique code allows linking diverse data, including pharmaceutical and immunization records and outpatient clinical diagnoses, and permits collecting information even when the patient receives health assistance from different regions.

Debates on the use of administrative databases routinely occur [12] and algorithms have been proposed to assess the disease status of large populations in Italy [52, 53]. In general, Italian administrative databases have the potential to address important questions in post-marketing surveillance [8, 54], epidemiology [12], quality performance and health services research [55]. In its annual review of drug utilization, the Italian Medicines Agency (AIFA), reported a list of 103 peer-reviewed publications of drug utilization studies performed in Italy [56]. Although most of these studies were focused on drug utilization and compliance, pharmacoeconomics and healthcare performance, this indicated that databases were widely used.

In conclusion, administrative databases in Italy are a valuable source of patient healthcare information that can be employed for a variety of studies with a

potentially high impact on public health policy and health care spending, but these databases require an extensive process of validation of multiple diagnostic codes.

ABBREVIATIONS

ICD = International Classification of Diseases

STARD = Standards for Reporting of Diagnostic accuracy

COPD = chronic obstructive pulmonary disease cases

AIFA = Agenzia Italiana del Farmaco (Italian Medicines Agency)

DRG = Diagnosis-Related Group

COMPETING INTERESTS

The authors declare that they have no competing interests

AUTHORS' CONTRIBUTIONS

IA and AM conceived the paper; IA, AM, LF, RC, PG, PC drafted the manuscript; IA, MO, PG, FC, MLL, RC, LF participated in the design of the study; MLL, RD FC, MO acquired the data; IA, PE, RDF, GG, AM, MM analysed and interpretation the data; IA, AM, MO,PG, FC, PE, MM, MLL, GG revised critically the manuscript for important intellectual content. All authors read and approved the final manuscript.

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SUPPLEMENTAL MATERIAL

The supplemental material can be downloaded from the journal website along with the article.

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