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ORIGINAL ARTICLE

Generation and validation of algorithms to identify subjects with dementia using administrative data

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Abstract

Objectives To generate and validate algorithms for the identification of individuals with dementia in the community setting, by the interrogation of administrative records, an inexpensive and already available source of data.

Methods We collected and anonymized information on demented individuals 65 years of age or older from ten general practitioners (GPs) in the district of Brianza (Northern Italy) and compared this with the administrative data of the local health protection agency (*Agenzia per la Tutela della Salute*). Indicators of the disease in the administrative database (diagnosis of dementia in the hospital discharge records; use of cholinesterase inhibitors/memantine; neuropsychological tests; brain CT/MRI; outpatient neurological visits) were used separately and in different combinations to generate algorithms for the detection of patients with dementia.

Results When used individually, indicators of dementia showed good specificity, but low sensitivity. By their combination, we generated different algorithms: I-therapy with ChEI/memantine *or* diagnosis of dementia at discharge *or* neuropsychological tests (specificity 97.9%, sensitivity 52.5%); II-therapy with ChEI/memantine *or* diagnosis of dementia at discharge *or* neuropsychological tests *or* brain CT/MRI *or* neurological visit (sensitivity 90.8%, specificity 70.6%); III-therapy with ChEI/memantine *or* diagnosis of dementia at discharge *or* neuropsychological tests *or* brain CT/MRIMRI *and* neurological visit (specificity 89.3%, sensitivity 73.3%).

Conclusions These results show that algorithms obtained from administrative data are not sufficiently accurate in classifying patients with dementia, whichever combination of variables is used for the identification of the disease. Studies in large patient cohorts are needed to develop further strategies for identifying patients with dementia in the community setting.

Keywords Algorithm · Dementia · Administrative data · Sensitivity · Specificity

Introduction

Dementia is a syndrome caused by different disorders affecting the brain, leading to a progressive deterioration of memory and other mental functions and behavioral abnormalities. The ability to be self-sufficient and to perform the everyday-living activities is impaired, giving rise to an ever increasing dependence and need for care. Dementia is a huge public health problem, one of the most common diseases in the elderly and a major cause of disability and mortality, mainly in high-income countries, where the average age of the population is constantly increasing. Alzheimer's disease (AD) is the commonest form of dementia, followed by vascular dementia and other neurodegenerative conditions [1].

The populations of high-income countries, like Italy, are constantly aging, with a consequent exponential increase of

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patients with dementia [2, 3]. The burden of dementia seems to be increasing even faster than previously estimated by studies on smaller datasets [4–6].

The diagnosis of dementia is still mainly based on neuropsychological assessment, while blood and neuroimaging tests are mainly performed to exclude other causes of cognitive impairment. Currently, an appropriate diagnosis of dementia is best obtained by a combination of clinical features, supported by laboratory findings and neuroimaging techniques, both structural and functional. Neuropsychological evaluation can be useful to differentiate AD dementia from other forms of cognitive decline, through the evaluation of different characteristics of memory deficit that predominate in the earliest stages of the disease [7].

Other diagnostic tests include biochemical and functional imaging techniques. However, although CSF levels of amyloid beta (Aβ) and tau proteins can support the suspicious of AD [8], and positron-emission tomography (fluorodeoxyglucose [FDG]-PET and Aβ-PET) and single-photon emission tomography (SPECT) are second-level imaging markers, the value of these tests in current clinical practice is still uncertain. In addition, they are poorly accessible and expensive [9].

Pharmacologic interventions are also used in the attempt to slow the progression of the disease and improve symptoms [10]. Different groups of drugs are prescribed in clinical practice for the control of symptoms of cognitive decline. Two specific classes of treatments have modest and transient effects on cognitive decline, cholinesterase inhibitors (ChEI), and memantine, a non-competitive NMDA receptor antagonist [11].

To date, there are no valid tools for the evaluation of the burden of this condition in the community, necessary for the planning of health interventions and the containment of public expenditures. Administrative records, that include claims for the diagnosis and treatment of all the diseases in well-defined populations, represent an easily accessible and inexpensive source of data [12, 13]. The variables included in the administrative databases could be easily used, when properly combined, to identify patients with certain diseases, such as dementia, differentiating them from healthy individuals or with other clinical conditions. To date, only few studies used administrative data to identify patients through the development of algorithms to ascertain dementia in the community setting [14–19].

To our knowledge, there are no studies investigating the validity of administrative databases to identify patients with dementia in a well-defined population in Italy. On this background, the aim of this study was to generate and validate predefined algorithms for the identification of demented patients using administrative data in a large group of patients within the district of Brianza (Northern Italy). This can provide an innovative, rapid, and economic tool to estimate the prevalence of dementia in the community, offering a valuable support for population-based studies.

Material and methods

Patients and databases

Health care in Italy is publicly funded for all residents, irrespective of social class or employment. Citizens are cared for by the GPs as part of the National Health System (NHS). GPs were selected because they represent the local population and are the first contact for any individual with a medical complaint. They can also provide treatments free of charge to those being diagnosed. During the first phase of the study, we contacted 18 GPs in the district of Brianza, who were selected based on previous collaborations with research institutions. Of these, 16 GPs accepted to take part in the study. Since the data collected from the archives of six GPs initially included in this research resulted incomplete, we decided to exclude their contribution.

For the aims of the study, we generated two different databases. The first database included data of patients with dementia, aged 65 years or older, obtained from the medical records of local general practitioners (GPs) of the district of Brianza (Monza and Lecco, Northern Italy). The patients identified in the GPs' records were considered the gold standard for the diagnosis of dementia and were included in the *gold standard database*. To be included in the study, the GPs were requested to have computerized archives with complete information about their affiliates. Through the screening of their records, the GPs identified all demented patients aged 65 years or older. All demented patients were included, regardless of the etiology. The diagnosis of dementia was based on the DSM-V criteria [20], supported by a neurological evaluation and/or by a corrected Mini-Mental State Examination (MMSE) score below 21. If the diagnosis was made by a neurologist, this was included in the GP's archive as a medical report, while if the criterion was MMSE < 21, then, a neurological examination was not required. The following data were collected from the GP's archives for the period 2000 through 2016: date of birth, gender, living status (dead or alive), year of diagnosis of dementia, imaging tests (CT, MRI), other diagnostic tests where available (FDG-PET, SPECT), neurologic and geriatric visits with numbers, neuropsychological tests, visits at a memory clinic, admission to a nursing home, drugs prescribed since the diagnosis (ChEI, memantine, and others). The type of dementia was not recorded because it was not available in all GPs' records.

The *administrative database* was generated using the records of the *Agenzia per la Tutela della Salute* (*ATS*) Brianza, tracing the patients affiliated to the participating GPs, aged 65 years or older, during the period 2000–2016. From these subjects, we collected the following data: name of GP, drugs prescribed (ChEI, memantine singly, or in combination), neuropsychological tests, hospital discharge diagnoses, neurologic outpatient visits, imaging tests (CT, MRI, FDG-PET).

Hospital discharge diagnoses were coded according to the International Classification of Diseases, 9th version (ICD-9) [21], and for the purposes of this study, all diagnoses were considered, from the primary to the seventh. The pharmaceutical prescription records contain the medication name and anatomic therapeutic chemical (ATC) classification code [22], quantity, and dispensation date for all medications dispensed by the retail pharmacies of Local Health Units and reimbursed by the Italian NHS. The test prescription records include all ambulatorial tests prescribed by GPs or specialists and reimbursed by the Italian NHS.

The record linkage of the two databases was performed by the ATS Brianza, blindly to investigators using the fiscal code as key. To preserve anonymity, patients were identified through a unique alpha-numeric code in both databases. The patients' identity remained unknown to all investigators.

All data were managed according to the current Italian law on privacy, and authorization was obtained from the ATS Brianza to obtain and use the administrative data for the purposes of this study.

Algorithms' generation

To identify demented patients in the administrative database, we considered the following variables as possible indicators of dementia: use of cholinesterase inhibitors/memantine; diagnosis of dementia in the hospital discharge records; neuropsychological tests; brain CT/MRI exams; outpatient neurological visits. These variables were analyzed individually, and in different combinations. The three variables considered most specific for the diagnosis of dementia (neuropsychological tests, ICD-9 code for dementia in the hospital discharge records, use of ChEI and/or memantine) were first analyzed separately and then in combination (presence of at least one of the three). To improve diagnostic accuracy, we then added three other variables (brain CT, brain MRI, outpatient neurological visits) in different combinations. For each single variable and combination of variables, individuals in the administrative database were classified as positive (if the single variable or combination of variables was present) or negative (if the single variable or combination of variables was not present). All individuals classified as positive or negative were then compared with the gold standard (patients with dementia were identified in the gold standard database). All positive subjects that were found in the gold standard database were classified as true positives (TP), while those not found in the gold standard database were classified as false positives (FP). All negative subjects that were found in the gold standard database were classified as false negatives (FN), while those not found in the gold standard database were classified as true negatives (TN). Sensitivity (SE), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) were calculated. A ROC analysis was also performed, calculating AUC (area under the ROC Curve) with 95% confidence intervals (CI).

Results

Data collection

A total of 185 subjects with dementia, aged 65+ years, were reported by the ten participating GPs for the period 2000–2016. Since the hospital discharge records were not available at the *ATS* Brianza for the period 2000–2005, we excluded 14 patients who died, migrated, or were diagnosed with dementia before January 1, 2006. This reduced to 171, the number of demented cases identified. Moreover, since the information on the outpatient visits was complete only for the period 2012–2016, 51 additional patients were excluded having died or migrated or having a diagnosis of dementia prior to January 1, 2012. The final gold standard cohort used for the validation of the algorithms included 120 subjects with dementia (Fig. 1).

The administrative records of the *ATS* Brianza included a total of 17,885 affiliates of the ten participating GPs. Only patients aged 65+ years followed during the period 2012–2016 were included, leaving a total of 4882 subjects (Fig. 1).

Table 1 illustrates the general characteristics of the 120 subjects with dementia identified in the GPs' records. The number of these demented individuals tended to increase with age, peaking between 81 and 85 years of age (36.7%). At the time of the study, 14.2% of patients were deceased, 20.8% had contacts with the memory clinic, and 21.7% resided in nursing homes. Treatment with ChEIs was present in 30.0% of patients, memantine in 16.7%, neuroleptics in 44.2%, and other drugs active on the central nervous system in 38.3%. Geriatric and neurological visits were carried out in 71.7% and 48.3% of patients, respectively. The majority of patients underwent brain CT scan (79.2%), while only 30.0% had brain MRI. Neuropsychological assessment was available in 64.2% of subjects and other tests (FDG-PET, SPECT) in 6.7%.

Variables and algorithms for dementia

The sensitivity, specificity, PPV, and NPV of the variables selected from the administrative database and tested individually and in various combinations are reported in Table 2. The three variables considered to be the most specific for the diagnosis of dementia (pharmacological therapy with ChEI and/or memantine, diagnosis of dementia in the hospital discharge records, and neuropsychological assessment) showed a good specificity (99.5%, 98.8%, and 99.4%), but had a low sensitivity (30.0%, 18.3%, and 17.5%).

In order to increase sensitivity, we generated different algorithms. A first algorithm, defined by having at least one of

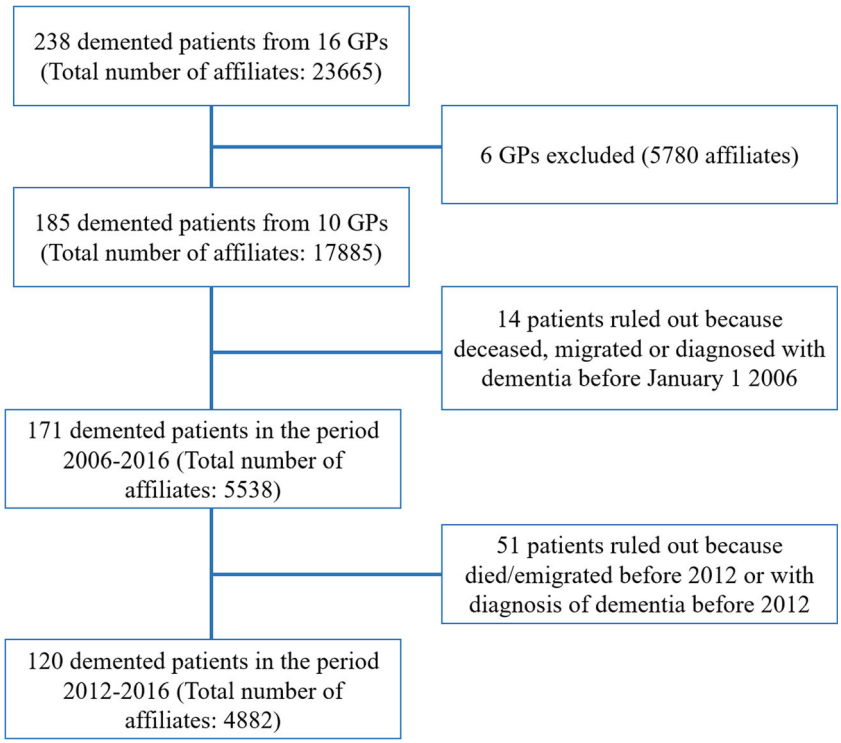

Fig. 1 The flowchart of patients' recruitment

the three variables, resulted in a sensitivity of 52.5% and a specificity of 97.9%. The AUC for the first algorithm was 0.75 (95% CI 0.71–0.80). To further improve sensitivity, we generated a second algorithm by including in the analysis the presence of brain CT/MRI *or* one or more outpatient neurological visits. This contributed to the increase of sensitivity to 90.8%, but reduced specificity to 70.6%. This algorithm had an AUC of 0.81 (95% CI 0.78–0.84). Finally, we tested a third algorithm including the presence of a brain CT/MRI *and* at least one outpatient neurological visit in combination. This algorithm resulted in a sensitivity of 73.3% and a specificity of 89.3% (Table 2), with an AUC of 0.81 (0.77–0.85).

Discussion

In this study, we tested different variables and algorithms for the identification of demented patients by examining retrospective administrative data. The aim of this work was to provide a useful and inexpensive tool to calculate the prevalence of dementia in the general population. These aspects are important especially in high-income countries, where the population is constantly aging.

Different variables of interest, selected among the most specific for the diagnosis of dementia, were tested individually, however resulting in a very low sensitivity. We thus tested different algorithms, in order to improve case ascertainment. The first algorithm, consisting in the presence of at least one variable among hospital discharge diagnosis, neuropsychological assessment, or an *ad hoc* treatment, revealed a high specificity, but a low sensitivity. In general, hospital discharge and use of neuropsychological tests alone are not strictly necessary to confirm the diagnosis of dementia. Furthermore, most demented patients belong to the "oldest old" (see Table 1) and are often assisted by their relatives or other caregivers, frequently without undergoing specific diagnostic investigations for dementia. It is also commonly known that the use of ChEI varies with the age of patients, but with patterns that do not correspond to the prevalence of the disease [23]. This could be explained by the increasing belief of physicians that the risk/benefit ratio of these drugs is high in the oldest old. However, when at least one among hospital discharge, neuropsychological testing, and *ad hoc* treatment was present, we found a specificity of 97.9%, still satisfactory, while the sensitivity increased to 52.5%. Nonetheless, about half of our demented subjects were lost, confirming that these variables alone are insufficient to detect people with dementia in the administrative records. For this reason, we tested a second algorithm including, in addition to at least one of the three most specific diagnostic variables, the assessment of neuroimaging tests (brain CT/MRI scans) *or* outpatient neurological visits. These additional variables improved sensitivity, but reduced specificity, leading to a significant overestimation of the prevalence of the disease. In fact, these variables (neurological visits, brain CT/MRI scans) are non-specific to track demented patients, since they can

Table 1 General characteristics of the 120 patients used as gold standard of the study

Variable	Total number	%
Age at diagnosis		
< 65	0	0.0
65–70	3	2.5
71–75	15	12.5
76–80	30	25.0
81–85	44	36.7
> 85	28	23.3
Gender		
F	79	65.8
M	41	34.2
Deceased	17	14.2
Access to nursing home	26	21.7
Access to memory clinic	25	20.8
Drugs		
Memantine	20	16.7
ChEI	36	30.0
Neuroleptics	53	44.2
Others (SNC)	46	38.3
Geriatric examination (min. 1)	86	71.7
Neurological visit (min. 1)	58	48.3
Brain CT scan	95	79.2
Brain MRI	36	30.0
Neuropsychological assessment	77	64.2
Other tests (FDG-PET, SPECT)	8	6.7
Total	120	100`

be carried out for many other neurological conditions. A third algorithm, resulting from the addition of neurologic visits *and* brain CT/MRI to the three variables initially considered (ChEI/memantine, diagnosis of dementia at hospital discharge, neuropsychological assessment), significantly improved specificity but reduced sensitivity. These results show that, by using the third algorithm, the overestimation of the frequency of the disease is reduced, but at the expense of sensitivity, as about one fourth of patients with dementia was missed.

The results of this study show that the accuracy of the diagnosis of dementia from administrative records is low, whichever combination of variables is used to trace the disease. These limitations are not only due to the lack of information on the indication to the use of selected diagnostic tests (like neuroimaging), but also due to the fact that the disease can be diagnosed in the absence of hospital admission and because the risk/benefit ratio of the available treatments is low.

Other studies tested the validity of administrative records with suboptimal results, although better than ours. In a US cohort comparing 24,521 subjects with dementia and 95,464 controls, a moderate diagnostic accuracy was found among individuals aged < 65 years but poor discriminatory ability among older adults (≥ 65 years) [24]. In a Spanish study testing a population registry of dementia including 986 cases and 327 controls as validation samples, the calculated sensitivity was 80.2% and the specificity was 99.9% [25]. In a retrospective Canadian study on chart abstraction to validate population-based administrative records, the highest performing algorithm was "one hospitalization code *or* (three physician claims codes at least 30 days apart in a two year period) *or* a prescription filled for an AD-RD specific medication" with sensitivity 79.3%, specificity 99.1%, positive predictive value 80.4%, and negative predictive value 99.0% [16].

The study presents strengths and limitations. The first strength is represented by the large sample that makes our measures robust. The second strength is the use of a population-based sample for the validation of the diagnosis. Notably, all these data were already available at the

Table 2 Accuracy of single variables and combinations of variables (algorithms) in classifying patients with dementias

Single variables	TP	FP	TN	FN	SE (%)	SP (%)	PPV (%)	NPV (%)	Accuracy (%)
Therapy with ChEI/memantine	36	24	4738	84	30.0	99.5	60.0	98.3	97.8
Diagnosis of dementia at discharge	22	56	4706	98	18.3	98.8	28.2	98.0	96.8
Neuropsychological assessment	21	30	4732	99	17.5	99.4	41.2	98.0	97.4
Algorithms									
First—therapy with ChEI/memantine *or* diagnosis of dementia at discharge *or* neuropsychological tests	63	99	4663	57	52.5	97.9	38.9	98.8	96.8
Second—therapy with ChEI/memantine *or* diagnosis of dementia at discharge *or* neuropsychological tests *or* brain CT/MRI *or* neurological visit	109	1400	3362	11	90.8	70.6	7.2	99.7	71.1
Third—therapy with ChEI/memantine *or* diagnosis of dementia at discharge *or* neuropsychological tests *or* brain CT/MRIMRI *and* neurological visit	88	509	4253	32	73.3	89.3	14.7	99.3	88.9

TP, true positives; *FP*, false positives; *TN*, true negatives; *FN*, false negatives; *ChEI*, cholinesterase inhibitors; *CT*, computerized tomography; *MRI*, magnetic resonance imaging

time of the study, leading to a rapid and inexpensive collection of the data necessary for the completion of the study. The first limitation is the reliance on a neurological consultation or the MMSE score for the diagnosis of dementia. None of our patients was reassessed for the purposes of the study. We cannot thus exclude that some of the false positives could have dementia that was not recorded in the GPs' archives. There were 56 subjects who received a diagnosis of dementia upon hospital discharge and 24 subjects who were treated with ChEI and/or memantine, making the diagnosis very likely in all these subjects. Limiting factors include the possible transfer of patients from one GP to another. According to the Italian Health System, the medical records do not follow the patient when moving from one GP to another, with the possibility that the receiving GP could lose part of patient's medical history. Moreover, since the GPs participating in the study are only a fraction of those active in the study area, we cannot exclude that some patients with dementia might have been transferred to other (non-participant) GPs. However, even assuming that discharge diagnoses and treatments were missed by the GPs, the sensitivity and/or specificity values were still suboptimal (first algorithm 70.8%, 99.5%; second algorithm 94.4%, 71.7%; third algorithm 83.6%, 90.7%). Last, the validation referred to the diagnosis of dementia with no specification of disease subtypes.

Conclusions

In summary, the most important achievement of this study is the poor validity of different algorithms for the identification of patients with dementia using administrative data. In the present form, administrative data appear inadequate for the identification of patients with dementia in the community. Future studies on large patient cohorts are needed to develop further strategies for identifying patients with dementia in a community setting.

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Compliance with ethical standards

Ethical statements All the data included in this research were managed according to the current Italian law on privacy and authorization was obtained from the ATS Brianza to obtain and use the administrative data for the purposes of this study.

No experiments on animals have been conducted for the present study.

Conflict of interest The authors declare that they have no conflicts of interest.

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