Comparison between hospital discharge and mortality data for Alzheimer's disease in Italy

Luisa Frova[1], Stefano Marchetti[1], Monica Pace[1], Laura Murianni[2], Alessandra Burgio[1]

[1]Italian National Institute of Statistics, Rome, Italy; [2]Catholic University of Sacred Heart, Rome, Italy

Correspondence to: Laura Murianni, Istituto di Igiene, Catholic University of Sacred Heart, Viale Francesco Vito, 1, 00168 Rome, Italy.

E-mail: laura.murianni@rm.unicatt.it

Abstract

Background: Alzheimer's Disease is the most common manifestation of dementia affecting almost 24 million people worldwide. It afflicts mainly the elderly. The aims of this study are to provide hospitalization and mortality trends for Alzheimer's Disease, to provide first evidence about co-morbidity in Alzheimer's Disease and to describe co-morbidity profiles.

Methods: Two sources of Alzheimer's Disease trends were investigated: the main diagnosis from hospital discharges and the underlying cause of death. Co-morbidity was studied by analysing the multiple diagnoses from hospital discharge files and the multiple causes of death from mortality files.

Results: Trends of Alzheimer's Disease are increasing both for hospitalization and for mortality rates. When all diagnoses and multiple causes are considered the patterns are similar.

When Alzheimer's Disease is reported as the main diagnosis in hospital discharges, the diseases more frequently associated with the disease are other mental disorders, hypertensive diseases, cerebrovascular diseases and other diseases of the circulatory system. The diseases most frequently associated with mortality are ill-defined causes, pneumonia, influenza and other diseases of the respiratory system. Moreover, associations between Alzheimer's Disease and cerebrovascular diseases, and with diseases of the circulatory system, are found in both databases.

Conclusions: Data regarding deaths and hospital discharges show similar patterns for Alzheimer's Disease both for trends and age profiles. Many similarities among the two data sources are also found when analysing co-morbidities. These results highlight the coherence of different data sources and underline the importance of carrying out a systematic analysis of these databases for purpose of improving epidemiological information.

Key words: Alzheimer' s disease, hospitalization discharge, mortality schedule

Introduction

More than 24 million people worldwide and over 6 million people in the European Union are afflicted by dementia [1, 2]. It is predicted that this number will double in the next 20 years along with the ageing of the population.

Dementia prevalence estimates, however, are strikingly different across countries: for example in France and Germany for females aged 90 and older it was estimated to be greater than 50%, meanwhile in Spain it was slightly less than 30% [3].

The highest prevalence of dementia is estimated for Asian-Americans (around 70% in the population aged 90 and over), followed by the North American population (60%) and Europeans (40%) [4].

There are millions of caregivers who care for people with dementia at home to the best of their ability with varying levels of support from the state [2]. In Italy, a substantial amount of costs related to care for these patients are sustained by relatives: the Italian National Health Service provides only a small share of direct costs [5]. Moreover, there is strong evidence that people with dementia have increased delayed discharge from and readmission to hospital, premature admission to home care and a lack of appropriate services due to under-diagnosis [6].

Alzheimer's Disease (AD) is the most widespread form of dementia and has become an important health issue in those countries where the population is ageing: it is a neurodegenerative disease typical of the elderly population. AD has a long duration, affecting patients for an average of 8-10 years, and shows a progressive degeneration ultimately leading to the complete physical incapability and mental deterioration. To face such an emergent, growing health problem in western societies, efforts are required both in terms of health care and social assistance.

The most likely estimation of the prevalence of AD in Italy is around 1.4-1.6% of the population (30-99 years). AD is the most frequent dementia found among the elderly population in Italy: 95% of those affected by AD are more than 65 years old and the crude rate of AD prevalence for those over 65 is estimated to be between 7.2-7.6%. Its incidence in Italy is about 1.6% for men and 3.2% for women aged 65 and over. In 2020 it is estimated that 584,000 new cases of dementia will occur in Italy [7,8].

Nevertheless, there is a lack of information regarding AD in Italy [7,9,10].

The presence of co-morbidities is a typical feature of AD patients, making patient care even more complex. Cognitive disabilities are the most recognized problems associated with AD; moreover AD is increasingly being recognized as an underlying cause of death in many countries [4,9,11,12]. It was shown that AD could reduce life expectancy by 50% in men and 40% in women at age 70 with a remaining decreasing effect on mortality up to the age of 90 [13]. On the other hand, AD as the underlying or contributory cause of death appears to be underreported in death certificates as recorded in administrative databases [14,15]. Underreporting is a relevant issue even for hospital discharge data [16]; in both sources of information underreporting is mainly due to the objective difficulty of reaching a differential diagnosis among the various kinds of dementia.

The aims of this study are to identify AD trends from hospitalization and mortality data, to give first evidence about co-morbidity in AD and to describe co-morbidity profiles of people affected by AD or dying with a diagnosis of AD in Italy.

Methods

AD trends are described by means of age-standardized rates both for the main diagnosis in hospital discharge data and for underlying cause of death.

Co-morbidity was studied by analysing the multiple diagnoses from hospital discharge data and the multiple causes of death data.

Data on hospitalization came from the Italian Ministry of Health and the classification adopted for the diseases was the International Classification of Diseases (ICD) 9th revision, Clinical Modification (CM). Hospital discharge trends refer to events and not to patients; they were analysed for the period 1999-2004.

Data on mortality came from the Vital Statistics Death Registry run by the Italian National Institute of Statistics (Istat), the classifications adopted were ICD 9th revision until 2002 and ICD 10th revision for 2003. Mortality trends refer to the period 1985-2003.

Since deaths occurred in 1995, Istat has adopted the automated coding system [17] based on the MMDS (Mortality Medical Data System) package developed by the US National Centre for Health Statistics [18].

Co-morbidity analysis was carried out for the year 2003 for both databases. Concerning hospital discharges, five was the maximum number of secondary diagnosis that could be reported in the form, while for mortality statistics an upper limit to the number of diseases was not set, but in practice the mean number of multiple causes was about four and only a couple of death certificates had a maximum of 16 diseases [17].

Twenty-seven groups of diseases were selected in order to describe co-morbidity profiles of people affected by AD (Table 1). The criteria followed for the selection were based on the evidence from several clinical and epidemiological studies [9,19, 20]. Five of these groups referred to neoplasm, five to diseases of the nervous system, four to the circulatory system and two to the respiratory system. Furthermore four groups were selected to refer to ill-defined diseases or to mechanisms of death because these are very often reported on death certificates referring to the aged decedents. External causes, infectious diseases, skin ulcers and diabetes were also considered. External causes were coded using two codes for mortality: one for the injury description and one for the external cause of death, while hospital discharges were not coded by the supplementary classification of external causes of injury and poisoning (E800-E999). Records for the analysis were selected by searching for the AD code in at least one of the diagnoses or one of the multiple causes of death.

The ICD 10 revision allowed us to include all AD mentions in multiple cause of death statistics, even if not accurate terms were reported (such as dementia in Alzheimer).

Results

Trends

AD trends are increasing both for hospitalization and mortality rates. These trends probably reflect changes in the availability of improved diagnostic procedures, and changes in the attitudes of physicians about attributing AD as a cause of death, as well as an actual increase of the incidence of the disease [15].

The hospitalization rate for women was significantly higher than for men: 94 and 77

Table 1. Selected Groups for the co-morbidity analysis for Alzheimer disease by the (ICD9CM and ICD10 classifications), Italy, 2003.

GROUPS	Hospital discharges Icd 9 CM	Mortality Icd10
Infectious diseases	001-139	A00-B99
Malignant neoplasm of the digestive system including peritoneum and retroperitoneum	150-159	C15-C26, C45.1, C48
Malignant neoplasm of the respiratory system including mesothelioma of pleura	160-165	C30-C39, C45.0
Malignant neoplasm of bone, connective and mesothelial tissue, breast and ill-defined primary sites	170-175	C40-C44, C49-C50, C76
Malignant neoplasm of genito-urinary organs	179-189	C51-C68
Other neoplasms	140-149, 176, 190-208, 210-239	C00-C14, C27-C29, C45.2-C45.9, C46-C47, C69-C75, C77-D48
Diabetes mellitus	250	E10-E14
Blood diseases	280-289	D50-D76
Alzheimer disease	331.0	G30
Parkinson disease	332	G20-G21
Other diseases of the nervous system	320-330, 331.1-331.9, 333-389	G00-G12, G23-G25, G31-G44, G47-G98
Senile and pre-senile dementia (ICD9); Vascular and unspecified dementia (ICD10)	290	F01, F03
Other mental and behavioural disorders	291-319	F04-F99
Hypertensive diseases	401-405	I10-I15
Ischemic diseases	410-414	I20-I25
Cerebrovascular diseases	430-438	G45, I60-I69
Cardiac arrest	427.5	I46
Other diseases of the circulatory system	390-398, 415-417, 420-427.4, 427.6-429, 440-448, 451-459	I00-I09, I26-I45, I46.0-I46.1, I47-I51
Pneumonia and influenza	480-487	J10-J18
Other diseases of the respiratory system	460-479, 488-519	J00-J09, J20-J98
Diseases of the digestive system	520-579	K00-K93
Skin Ulcers	707	L89, L97, L98.4
Senility without psychosis	797	R54
Injury and Poisoning or External causes	800-999	V01-Y89
Respiratory collapse and coma	780.0, 785.5, 799.1	R09.2, R40, R57
Other ill-defined causes	780.1-785.4, 785.6-799.0, 799.2-799.9	R00.0-R09.1, R09.3-R39.9, R41-R56, R58-R99
Other causes	All other causes	All other causes
Not coded causes		U00

per one hundred thousand respectively in 2004 (Figure 1). It is important to remember that hospital discharge data refer to events and not to patients. This can explain the higher rates for women probably due to an older age structure and to higher re-hospitalizations rates.

As concerned hospitalization trends, a rapid increase was observed in the first three years followed by a smoother increase in the last three years.

Figure 2 shows trends in AD rates for main and secondary diagnoses. Both rates increased from 1999; however since 2001 the increase was observed for the secondary diagnoses only. This could be attributed to an increase of hospital readmissions for diseases related to AD or to a reduction of AD underreporting as secondary diagnosis.

Mortality rates were similar in both sexes (about 3 per one hundred thousand in 1985 and 60 per one hundred thousand in 2003), as shown in Figure 1. The implementation of ICD10 in 2003 caused a peak in mortality in this year: the sharp increase in AD rate was mainly due to changes in the selection criteria for underlying cause of death. The effect of the introduction of the ICD10 has been estimated by means of a bridge coding study on Italian data showing a comparability ratio of 1.18 [21, 22]. Considering a reduction of 18 % in the rate, then the value is coherent with the previous trend.

Age specific rates: comparison of years 1999 and 2003

In Figure 3a and Figure 3b, hospital discharge and mortality age profiles are shown for 1999 and 2003 for men and women. Profiles by age and period are very similar in the two databases and can better explain trends. The increase of rates between 1999 and 2003 is mainly due to the increase of rates in those aged 80 years and over. The highest increase is observed in men over 90 years of age: more than a two hundred per cent increase both for hospital discharges (217%) and mortality (247%) is observed. For women, the highest increase was seen between 85-89 years (+164% for hospitalization and +181% for mortality). Highest hospitalization rates were seen at 80-84 years for both sexes. For mortality, the peak shifted to next age-class (85-89 years). The decline seen for the oldest ages may be due to the underreporting of AD in these age groups.

Co-morbidity

About 27 thousand cases of hospitalization and 11 thousand cases for mortality were found by searching for the AD code in the hospital discharge database as the main or secondary diagnosis and in the multiple cause of death file (Table 2). Women represent about the 65% of the total in both populations.

The mean number of diseases or conditions reported is 3.3 for hospital discharges and 4.1 for mortality. Out of the total records, about 39% of

Figure 1. AD standardized hospital discharge and mortality rates: main diagnosis and underlying cause of death. 1985-2004.

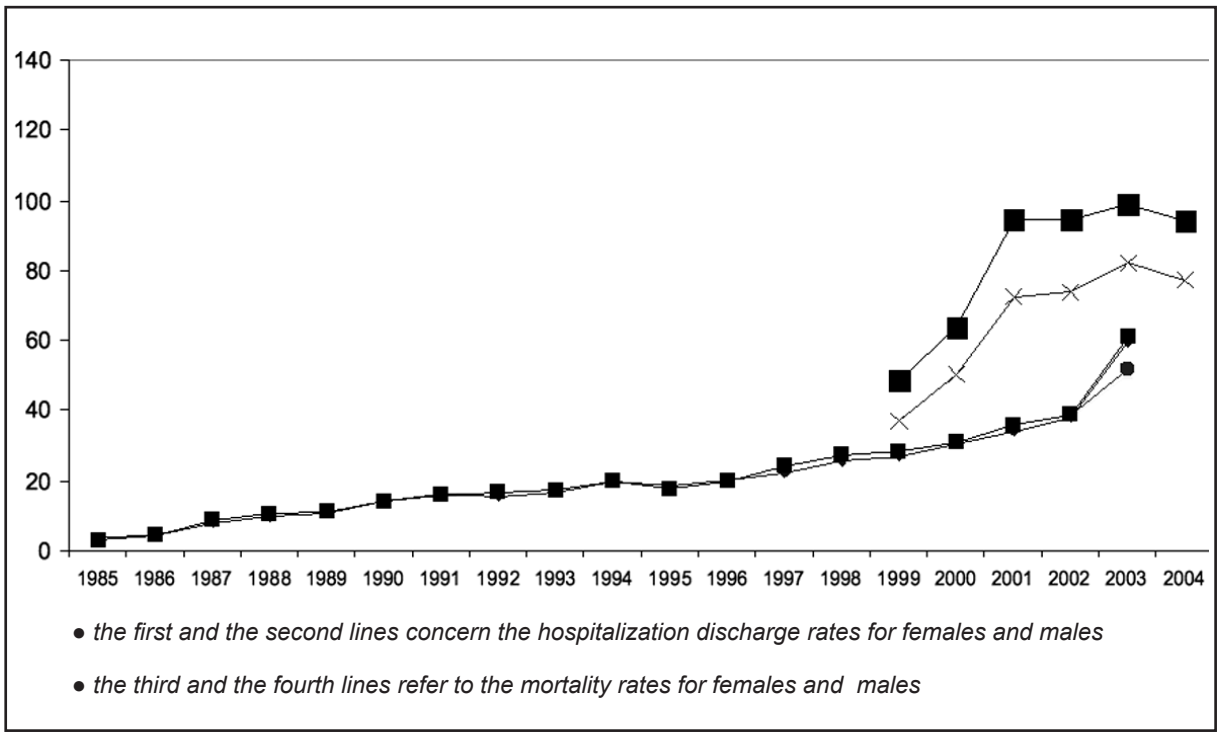
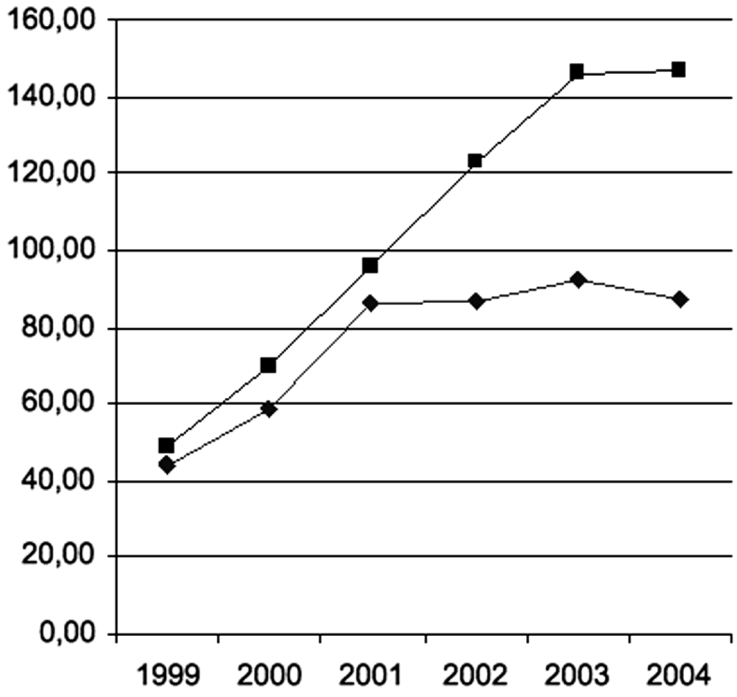
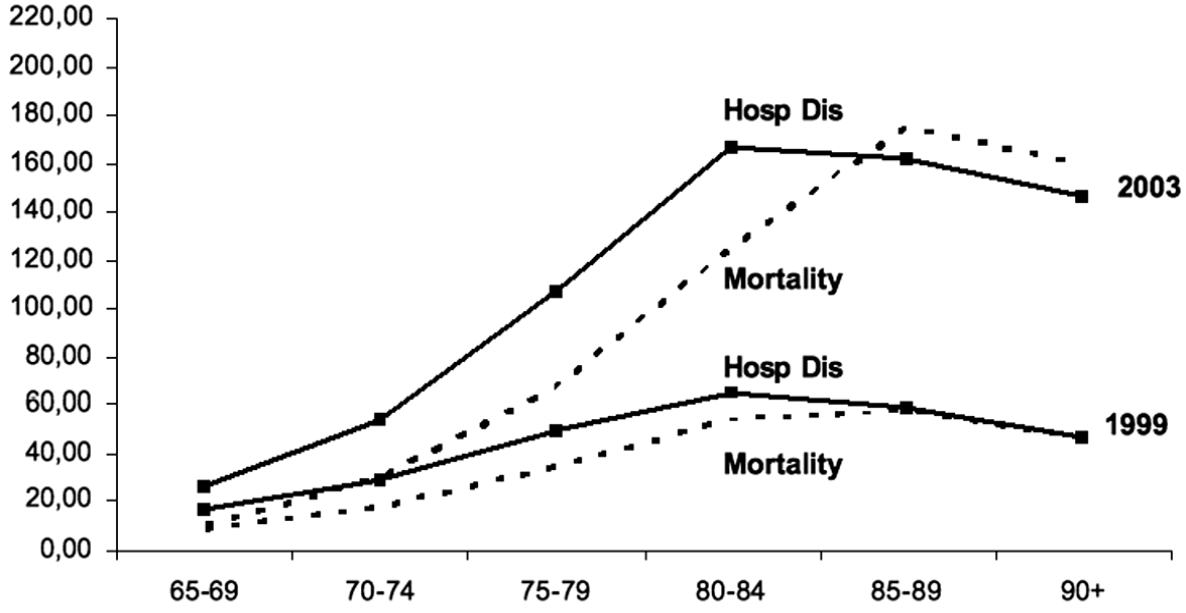


Figure 2. Standardized hospital discharge rates (per 100,000) for AD by diagnosis (main and secondary). 1999-2004.



● *the first line is "all primary diagnosis"; the second line is "all secondary diagnosis"*

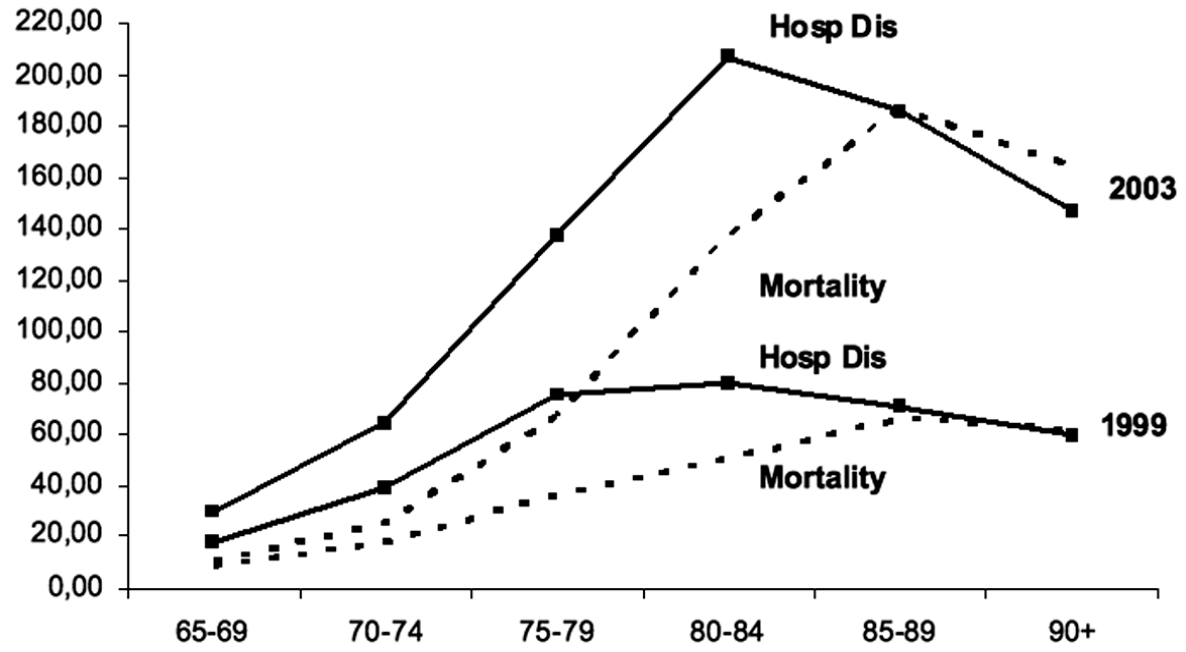
Figure 3a. AD age-specific hospital discharge and mortality rates. Males (1999, 2003).



● *the first and the second lines refer respectively to the hospitalization discharge rates for males and the mortality rates for males in 2003*

● *the third and the fourth lines refer respectively to the hospitalization discharge rates for males and the mortality rates for males in 1999*

Figure 3b. AD age-specific hospital discharge and mortality rates. Females (1999, 2003).



- *the first and the second lines refer respectively to the hospitalization discharge rates for females and the mortality rates for females in 2003*
- *the third and the fourth lines refer respectively to the hospitalization discharge rates for females and the mortality rates for females in 1999*

Table 2. Descriptive indicators of co-morbidity for Alzheimer's Disease - Year 2003.

Alzheimer disease	Number of cases	Average number of reported conditions	Percentage
		Hospital discharges	
Main diagnosis	10,363	2.7	39.0%
Secondary diagnosis	16,378	3.6	61.0%
Total	26,741	3.3	100.0%
		Mortality	
Underlying cause	6,657	3.6	60.4%
Not underlying cause	4,364	4.8	39.6%
Multiple cause (total)	11,021	4.1	100.0%

hospital discharges had AD as the main diagnosis, while for deaths 60% of cases had AD as the underlying cause.

When AD is the main diagnosis or the underlying cause, the average number of diseases reduces to 2.7 and 3.6 respectively.

When AD is not the main diagnosis or the underlying cause, the co-morbidity profile is more complex and the average number of diseases rises to 3.6 for hospitalization and to 4.8 for mortality.

Co-morbidity - age specific rates in 2003

Figure 4 shows specific age hospitalization and mortality rates, for AD as the main diagnosis and underlying cause. Moreover, all the AD mentions have been included in Figures 4 and 5.

Age patterns are similar for hospitalization

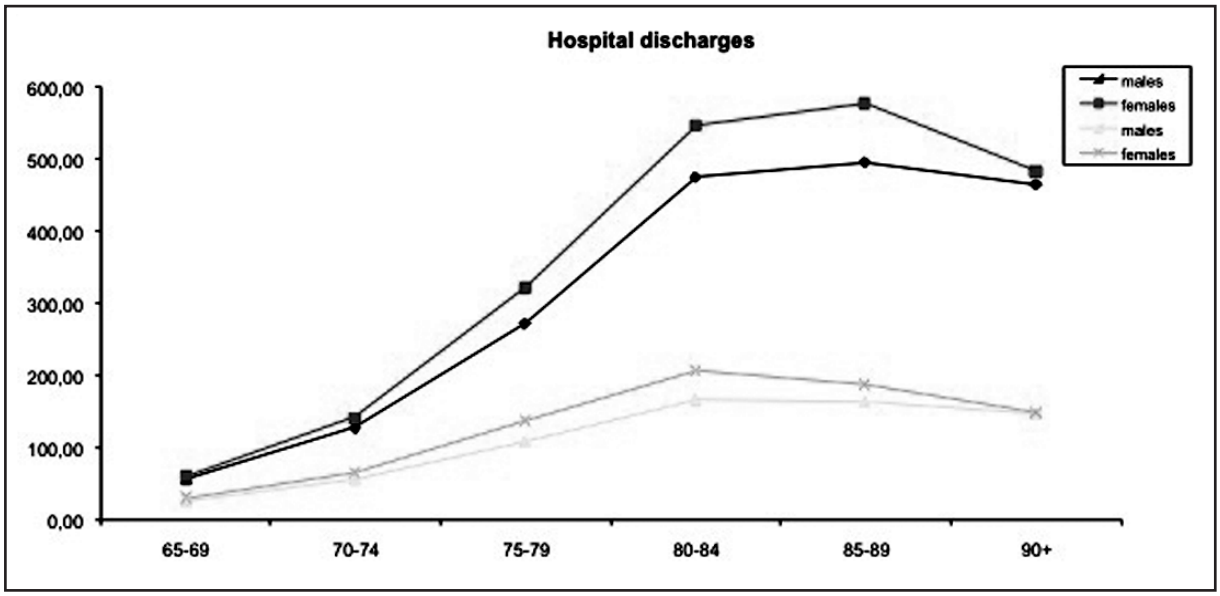
Figure 4. Age-specific hospital discharge and mortality rates (per 100,000) for Alzheimer disease by gender and co-morbidity - Year 2003.

Rates per 100.000

Hospital discharges				
	Main or secondary diagnosis		Main diagnosis	
Age	males	females	males	females
65-69	56,70	60,22	25,92	29,63
70-74	127,72	139,22	53,67	64,00
75-79	272,29	320,25	106,32	137,07
80-84	473,63	544,23	166,47	206,79
85-89	494,71	576,93	161,52	185,68
90+	463,12	480,94	145,70	146,81

Mortality				
	Multiple cause		Underlying cause	
Age	males	females	males	females
65-69	14,09	14,64	10,26	10,41
70-74	45,35	38,02	29,43	25,03
75-79	114,29	105,84	66,34	66,12
80-84	221,90	218,58	122,93	134,40
85-89	293,03	321,52	173,43	184,67
90+	256,71	276,95	156,11	160,22

Figure 4. AD age-specific hospital discharge rates by gender and co-morbidity (2003).



and mortality also when multiple causes and all diagnoses are considered.

Highest rates are seen for people aged 85-89 years, except when AD is the main diagnosis in hospital discharge: actually in this case the highest rate is in the age-class 80-84 years for both sexes.

The ratio between hospitalization rates for all diagnoses and main diagnosis is equal to 2.6 and it increases with age from 2.2 to 3.3 at 90 years and over. The same ratio calculated for mortality is lower (1.6) but still increasing with age from 1.4 to 1.7.

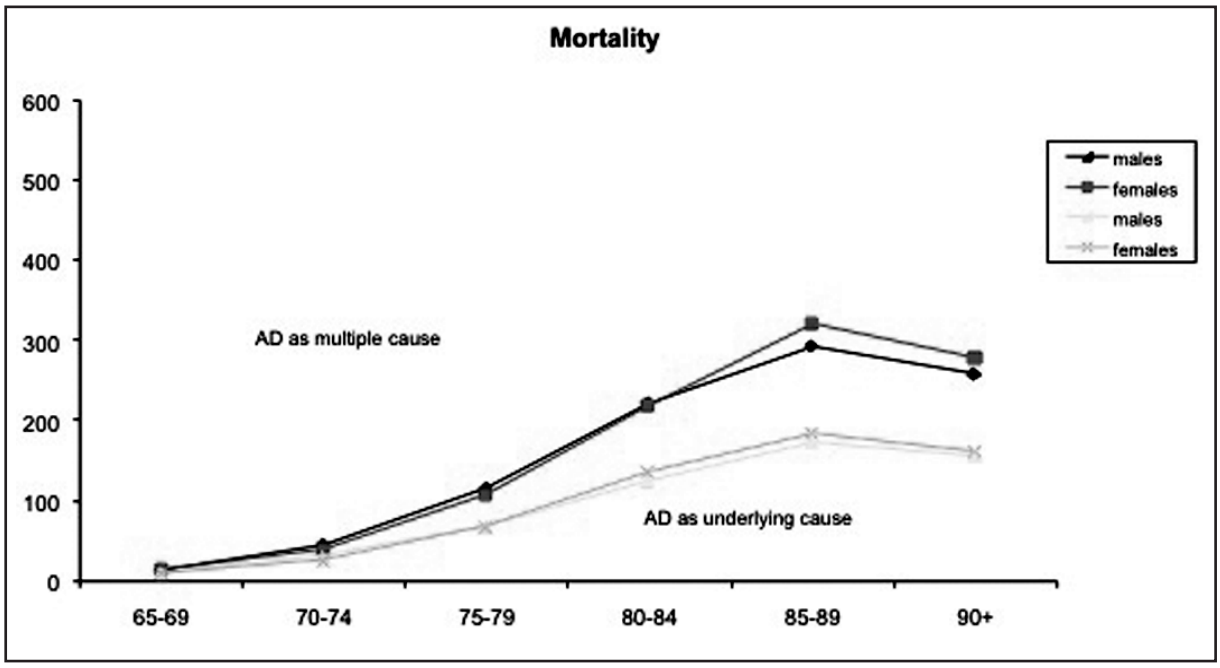
This is mainly due to competing risks among different diseases, that become more and more important at older ages. The number of diseases affecting people increases with age and consequently the probability that AD is reported as the main diagnosis or underlying cause of death at older ages decreases.

Co-morbidity in AD – analysis of associations

When AD is reported as the main diagnosis in hospital discharges, the diseases more frequently associated with it are the same in males and females and are prevalently other mental disorders, hypertensive diseases, cerebrovascular diseases and other diseases of the circulatory system (Table 3).

As above, differences by gender are not observed for mortality, but the associated diseases are different with respect to hospitalization: ill defined causes, such as cardiac arrest, respiratory

Figure 5. AD age-specific mortality rates by gender and co-morbidity (2003).



collapse and other ill-defined causes and senility are frequently associated with AD. Other significant effects are found for pneumonia and influenza as well as other diseases of the respiratory system.

Only cerebrovascular diseases and other diseases of the circulatory system are associated with AD both in mortality and in hospital discharges files.

When AD is a secondary diagnosis, about 50% of hospital discharge forms contained codes related to diseases of the circulatory system (ischemic, cerebrovascular or others) both for males and females. However, the co-morbidity profile differs between gender: diseases of the respiratory system (including pneumonia and influenza) are more frequent for men, while hypertensive diseases and external causes are more frequent for women.

As concerns mortality, when AD was a not the underlying cause of death, more than 50% of certificates contained codes related to the diseases of the circulatory system. The co-morbidity profile between gender is the same of that described for hospitalization.

An exception regards ill-defined diseases (cardiac arrest, respiratory collapse and other ill-defined causes) that are frequently reported in the death certificates as terminal causes of death.

Discussion

Data on deaths and hospital discharges show similar patterns for Alzheimer disease both for trends and age profiles: AD rates are increasing in Italy, above all among very old people. This is probably due to the improvement of diagnostic methods, to a more widespread reporting attitude of physicians about AD and to an actual increase in the incidence and prevalence rates [15,23].

Many similarities among the two data sources are found when analysing co-morbidities also.

Diseases associated to AD are in most cases those also common to the elderly not affected by AD. These are diseases of the circulatory and of the respiratory systems. The main differences are found for pneumonia (more frequent in mortality) and for injuries (more frequent for females in hospitalization).

The decrease of rates for the upper age class (90+) is probably due to the underreporting of AD for very old people more than on an actual reduction of incidence [9]. The co-morbidity profile of these people becomes very complex and it is possible that AD is not reported in medical certificates, while other diseases more relevant for immediately causing the death or for requiring high specialized treatments in hospital are certified.

These results underline the importance of having a systematic analysis of datasets for improving the information about clinical pathways for AD and on co-morbidities. This study is an example of the "dialogue" between different sources of data which confirm the case-history of people affected by chronic diseases, in particular by AD, that are not well enough known. We should know more in order to tackle these diseases from a clinical and organizational point of view. The analysis of health data for co-morbidity studies is particularly

Table 3. Presence of diseases in AD cases by type of diagnosis and type of multiple cause (percentage distribution). Year 2003.

	Males				Females			
	Hospital discharge diagnoses		Multiple causes of death		Hospital discharge diagnoses		Multiple causes of death	
Diseases	Main	Secondary	U.C.	Not U.C.	Main	Secondary	U.C.	Not U.C.
Infectious diseases	2.1	5.9	4.1	7.2	2.3	5.5	3.4	6.8
Malignant neoplasm of the digestive system including peritoneum and retroperitoneum	0.1	1.9	0.5	3.7	0.1	1.7	0.4	3.5
Malignant neoplasm of the respiratory system including mesothelioma of pleura	0.3	1.3	0.6	3.5	0.0	0.4	0.0	0.7
Malignant neoplasm of bone, connective and mesothelial tissue, breast and ill-defined primary sites	0.0	0.6	0.1	0.4	0.2	1.1	1.0	2.8
Malignant neoplasm of genito-urinary organs	1.0	3.2	1.4	5.4	0.1	0.7	0.2	1.0
Other neoplasms	1.3	4.2	1.7	10.8	1.5	3.7	1.0	7.8
Diabetes mellitus	9.1	10.5	5.7	11.4	9.3	12.3	6.0	13.0
Blood diseases	3.5	6.1	1.6	3.1	3.9	8.8	2.0	3.3
Alzheimer Disease	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Parkinson disease	3.6	4.1	2.4	3.9	2.4	2.8	1.4	2.8
Other diseases of the nervous system	6.0	5.2	3.1	3.5	5.6	6.5	3.5	3.5
Senile and pre-senile dementia (ICD9); Vascular and unspecified dementia (ICD10)	2.6	1.7	2.4	1.8	2.7	1.3	2.9	1.5
Other mental and behavioral disorders	13.7	6.3	0.6	0.4	14.8	6.8	0.8	0.6
Hypertensive diseases	15.9	13.7	5.6	12.2	20.9	17.7	7.5	17.4
Ischemic diseases	8.3	12.0	8.4	21.9	5.8	9.5	7.0	22.4
Cerebrovascular diseases	12.3	12.9	12.2	16.5	11.8	13.3	11.9	18.2
Cardiac arrest	1.1	3.7	33.5	28.0	0.7	2.4	31.8	28.8
Other diseases of the circulatory system	13.3	21.9	19.9	37.3	11.1	21.2	20.8	43.7
Pneumonia and influenza	3.0	17.4	17.5	20.4	1.6	10.4	12.0	13.7
Other diseases of the respiratory system	10.0	25.2	27.3	40.4	5.7	14.9	19.4	27.7
Diseases of the digestive system	6.2	14.9	3.9	8.6	6.3	14.7	2.9	9.3
Skin Ulcers	2.3	4.7	4.9	3.3	2.6	5.3	7.3	4.5
Senility without psychosis	0.0	0.0	8.5	4.7	0.0	0.0	13.5	6.3
Injury and Poisoning or External causes	3.2	10.4	1.8	5.9	4.0	18.1	2.4	7.8
Respiratory collapse and coma	1.5	4.2	25.0	26.0	1.6	4.2	24.7	24.4
Other ill-defined causes	8.7	12.6	29.8	18.7	7.6	11.9	30.8	16.8
Other causes	26.6	38.6	17.1	19.6	30.1	35.9	13.5	20.5

important for this kind of pathology.

Moreover, AD and other dementia are major factors for functional and cognitive disabilities, whereas other severe chronic conditions lead more frequently to death. Therefore, the co-morbidity analysis is helpful for better understanding the disease pattern of people affected by AD in order to arrange suitable care and to address public, social and health care services. The importance of hospitalizations and mortality co-morbidity data for people suffering from AD is then useful not only for clinics but even for policy-decision makers.

In order to define clinical pathways for elderly AD sufferers, it would be very interesting to consider data aside from hospital discharge and mortality data, above all because "emergency wards of hospitals are not suitable places for such care" [11]. For instance the analysis of primary care and other outpatient care data (like residential care or home care) would contribute to a better understanding of the medical and social complexity of AD and provide elements to improve the health care of patients [24].

Further studies are needed, also, on factors associated with high rates of hospitalization in dementia patients including aspects of ambulatory management that may be improved [25].The risk of an avoidable inpatient admission or a preventable complication in an inpatient setting increases dramatically with the number of chronic conditions. Better primary care, especially coordination of care, could reduce avoidable hospitalization rates, especially for individuals with multiple chronic conditions.

Little is known about how chronic conditions cluster. Understanding how conditions impact on the burden of disease, and on the costs and quality of care received, is crucial for improving the care of patients with multiple chronic conditions.

References

1) Ferri C, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. Lancet 2006;366:2112-7.

2) Alzheimer Europe. Dementia in Europe Yearbook 2008. Avaialble from: http://ec.europa.eu/health/ph_information/reporting/docs/2008_dementiayearbook_en.pdf. [Accessed on march 2011].

3) Moise P, Schwarzinger M, Myung-Yong Um and the Dementia Experts' Group. OECD Health Working Papers n. 13. Dementia care in 9 Oecd countries: a comparative analysis. DELSA/ELSA/WD/HEA(2004) 4. 28 July 2004.

4) Fratiglioni L, De Ronchi D, Agüero-Torres H. World-wide Prevalence and Incidence of Dementia. Drugs Aging 1999;15:365-75.

5) Gambina G, Broggio E, Martini MC, Merzari L, Gaburro G, Ferrari G. Analisi del costo sociale delle persone affette da malattia di Alzheimer assistite a domicilio. [Social cost analysis of home care Alzheimer's patients]. Convegno Nazionale Associazione Italiana di Economia Sanitaria: "Le frontiere della sanità tra decentramento istituzionale e sperimentazioni gestionali". Facoltà di Economia, Università di Bologna 25-27 settembre 2002. Available from: www.aiesweb.it/media/pdf/co0003/016.pdf. [Accessed on march 2011].

6) The House of Commons Committee of Public Accounts. Improving services for people with dementia, HC228, January 2008.

7) Ravaglia G, Forti P, Maioli F, Martelli M, Servadei L, Brunetti N, Dal Monte E, Bianchin M, Mariani E. Incidence and etiology of dementia in a large elderly Italian population. Neurology. 2005;64:1525-30.

8) Scafato E, Gandin C, Farchi G, et al. for IPREA Working Group. Italian project on epidemiology of Alzheimer's disease (I.PR.E.A.): study design and methodology of cross-sectional survey. Aging Clin Exper Res 2005;17(1):29-34.

9) Di Carlo A, Baldereschi M, Amaducci L, et al. for the ILSA Working Group. Incidence of Dementia, Alzheimer's disease and Vascular Dementia in Italy. The ILSA Study. J Am Geriatrics Soc 2002;50:41-8.

10) Frova L, Marchetti S, Pace M, Burgio A. Morbidity and mortality of Alzheimer disease in Italy. Presented at the "European Population Conference 2008", European Association for Population Studies (EAPS) Barcelona, 9-12 July 2008. Available from: http://epc2008.princeton.edu/download.aspx?submissionId=80616. [Accessed on march 2011].

11) Helmer C, Joly P, Letenneur L, Commenges D, Dartigues JF. Mortality with dementia: results from a French prospective community- based cohort. Am J Epidemiol 201;154(7):642-8.

12) Wolfson C, Wolfson DB, Asgharian M, et al. A reevaluation of the duration of survival after the onset of dementia. New Engl J Med 2001;344(15):1111-6.

13) Dodge HH, Shen C, Pandav R, DeKosky ST, Ganguli M. Functional transitions and active life expectancy associated with Alzheimer disease. Arch Neurol 2003;60(2):253-9.

14) Ewbank DC. Deaths attributable to Alzheimer's disease in the United States. Am J Public Health 1999;89(1):90-2.

15) Hoyert DL, Rosenberg HM. Mortality from Alzheimer's disease: An update". National Vital statistics reports. 1999;47(20). Hyattsville, Maryland: National Center for Health Statistics, 1999.

16) Greco A, Cascavilla L, Paris F, et al. Undercoding of Alzheimer's disease and related dementias in hospitalized elderly patients in Italy". Am J Alzheimers Dis Other Demen 2005;20(3):167-70.

17) Frova L, Marchetti S, Pace M (eds). Applying Acs to Causes

of Death Statistics in Italy - Some Clues on Implementation, Bridge Coding and Further Steps. Istat, Essays n. 13/2004.

18) Center for Disease Control and Prevention. National Centre for Health Statistics. USA . National Vital Statistics System. Datasets and Related Documentation for Mortality Data. Available from: http://www.cdc.gov/nchs/nvss/mortality_methods.htm. [Accessed on march 2011].

19) Witthaus E, Ott A, Barendregt JJ, Breteler M, Bonneux L. Burden of mortality and morbidity from dementia. Alzheimer Dis Assoc Disord 1999;13(3):176-81.

20) Fu C, Chute DJ, Farag ES, Garakian J, Cummings JL, Vinters HV. Comorbidity in dementia: an autopsy study. Arch Pathol Lab Med 2004;128(1):32-8.

21) Istat. Cause di morte Anno 2003. Available from: http://www.istat.it/dati/dataset/20080111_00/. [Accessed on march 2011].

22) Anderson RN, Rosenberg HM. Disease classification: measuring the effect of the Tenth Revision of the International Classification of Diseases on cause-of-death data in the United States". Stat Med 2003;22(9):1551-70.

23) Israel RA, Rosenberg HM, Curtin LR. Analytical potential for multiple-cause-of-death data. Am J Epid 1986;124:161-79.

24) Schubert CC, Boustani M, Callahan CM, Perkins AJ, Carney CP, Fox C, Unverzagt F, Hui S, Hendrie HC. Comorbidity profile of dementia patients in primary care: are they sicker? J Am Geriatr Soc 2006;54(1):104-9.

25) Bynum JP, Rabins PV, Weller W, Niefeld M, Anderson GF, Wu AW. The relationship between a dementia diagnosis, chronic illness, medicare expenditures, and hospital use. J Am Geriatr Soc 2004;52(2):187-94.