Morbidity and mortality of Alzheimer disease in Italy

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Background

Alzheimer disease (AD) is a neurodegenerative disease typical of the elderly population. It is the most spread kind of dementia and has become an important health issue in those countries where the population is ageing.
AD has a long duration, affecting the 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, spreading health problem in western societies efforts are required, both in terms of health care and social assistance.
The most likely estimation of prevalence of AD in Italy is of 1.4-1.6% (30-99 years). The 95% of those affected by AD is more than 65 years old and the crude rate of prevalence of AD over 65 year is estimated to be between 7.2-7.6%. Incidence is appraised to be in Italy about 1.6% for men and 3.2% for women aged 65 and over. Nevertheless there is a lack of information regarding AD in Italy (Di Carlo A, *et al*., 2002; Dementia in Europe, yearbook 2006; Ravaglia G, *et al*., 2005).
Presence of co-morbidities is a typical feature of AD patients, making the patient care even more complex.
Aims of this study are to provide trends of AD for hospitalization and mortality, to provide the first evidence about co-morbidity of AD and to describe co-morbidity profiles of people affected by AD in Italy.

Data and Methods

AD trends are described by the standardized rates both for the main diagnosis from hospital discharges and the underlying cause of death.
Co-morbidity has been studied by analysing the multiple diagnoses from hospital discharge file and by the multiple causes of death from mortality file.
Data on hospitalization come from the Italian Ministry of Health and the classification adopted for the diseases is the ICD9CM. Hospital discharge trends refer to events and not to patients and have been analysed for the period 1999-2004.
Data on mortality come from the Vital Statistics Death Registry run by the Italian National Institute of Statistics (Istat); the classifications adopted are ICD9 until 2002 and ICD10 for 2003. Mortality trends refer to the period 1985-2003. Starting from 1995 mortality data, Istat adopted the automated coding system (Frova L, *et al*., 2004) based on the MMDS (Mortality Medical Data System) package developed by the National Centre for Health Statistics in USA.
Co-morbidity analysis has been carried out on 2003 data for both topics. For hospital discharges the maximum number of secondary diagnosis that can be reported in the form is five, while for mortality statistics there is not an upper limit to the number of diseases, but in practice the mean number of multiple causes is about four and only a couple of death certificates has a maximum of 16 diseases (Israel RH, *et al*., 1986).
Twenty-seven groups of diseases have been 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 evidences from several clinical and epidemiological studies. Five of these groups refer to neoplasm, five to diseases of the nervous system, four to the circulatory system, two to the respiratory system. Four groups have been 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 have been considered too. External causes are coded using two codes for mortality: one for the injury description and one for the external cause of death; while hospital discharges are not coded by the supplementary classification of external causes of

injury and poisoning (E800-E999). Records for the analysis have been selected by searching for the AD code in at least one of the diagnoses or one of the multiple causes of death.

Table 1 – Selected groups for the co-morbidity analysis for Alzheimer disease by the ICD9CM and ICD10 classifications.

	GROUPS OF CAUSES	Hospital discharges Icd 9 CM	Mortality Icd10
1	Infectious diseases	001-139	A00-B99
2	Malignant neoplasm of the digestive system including peritoneum and retroperithoneum	150-159	C15-C26, C45.1, C48
3	Malignant neoplasm of the respiratory system including mesothelioma of pleura	160-165	C30-C39, C45.0
4	Malignant neoplasm of bone, connective and mesothelial tissue, breast and ill-defined primary sites	170-175	C40-C44, C49-C50, C76
5	Malignant neoplasm of genito-urinary organs	179-189	C51-C68
6	Other neoplasm	140-149, 176, 190-208, 210-239	C00-C14, C27-C29, C45.2-C45.9, C46-C47, C69-C75, C77-D48
7	Diabetes mellitus	250	E10-E14
8	Blood diseases	280-289	D50-D76
9	Alzheimer diseases	331.0	G30
10	Other diseases of the nervous system	320-330, 331.1-331.9, 333-389	G00-G12, G23-G25, G31-G44, G47-G98
11	Senile and pre-senile dementia (ICD9); Vascular and unspecified dementia (ICD10)	290	F01, F03
12	Other mental and behavioural disorders	291-319	F04-F99
13	Hypertensive diseases	401-405	I10-I15
14	Ischaemic diseases	410-414	I20-I25
15	Cerebrovascular diseases	430-438	G45, I60-I69
16	Cardiac arrest	427.5	I46
17	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
18	Pneumonia and influenza	480-487	J10-J18
19	Other diseases of the respiratory system	460-479, 488-519	J00-J09, J20-J98
20	Diseases of the digestive system	520-579	K00-K93
21	Skin Ulcers	707	L89, L97, L98.4
22	Senility without psychosis	797	R54
23	External causes	E800-E999	V01-Y89
24	Parkinson disease	332	G20-G21
25	Respiratory collapse and coma	780.0, 785.5, 799.1	R09.2, R40, R57
26	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
27	Other causes	All other causes	All other causes
40	Not coded causes		U00

Results

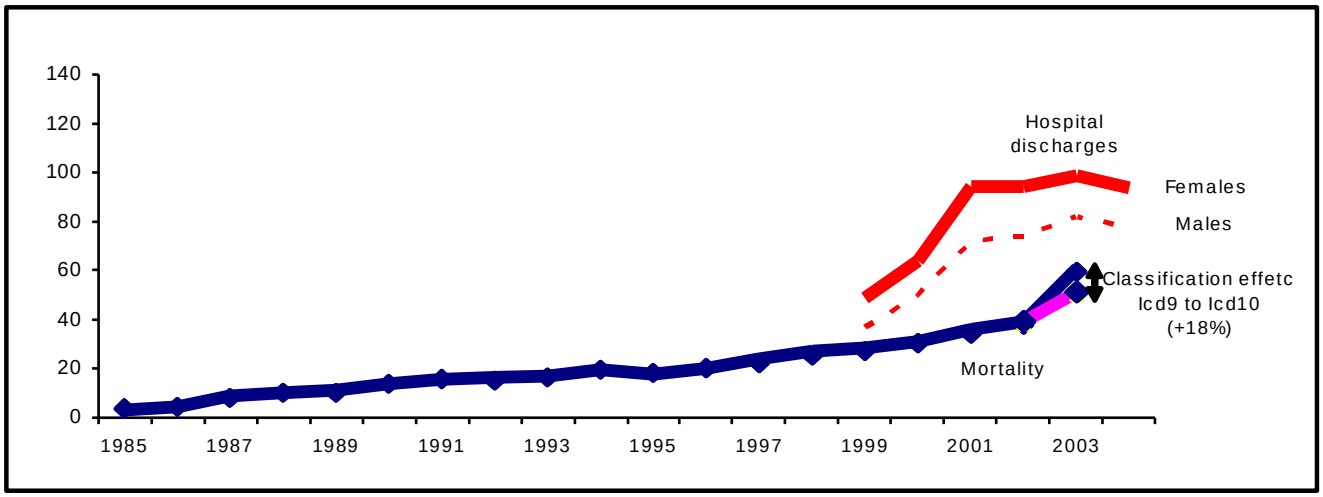
Trends of AD are increasing both for hospitalization and mortality rates. The trends likely reflect changes in the availability of improved diagnostics procedures, modifications in attitudes of physicians about attributing AD as a cause of death (Hoyert DL, Rosenberg HM., 1999) as well as an actual increase of the incidence of the disease.

The hospitalization rate for females is significantly higher than that of men (94 per one hundred thousand and 77 respectively in 2004). A rapid increase is observed in the first three years followed by a smoothed increase in the last three years: in this case too the effect should be due to a better quality in the completion of the discharge form since this difference disappears when the rate is calculated using all the diagnosis. 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.

Mortality rates have comparable values in both sexes (about 3 per one hundred thousand in 1985 and 60 in 2003), as shown in Figure 1. The implementation of ICD10 caused a peak in mortality in

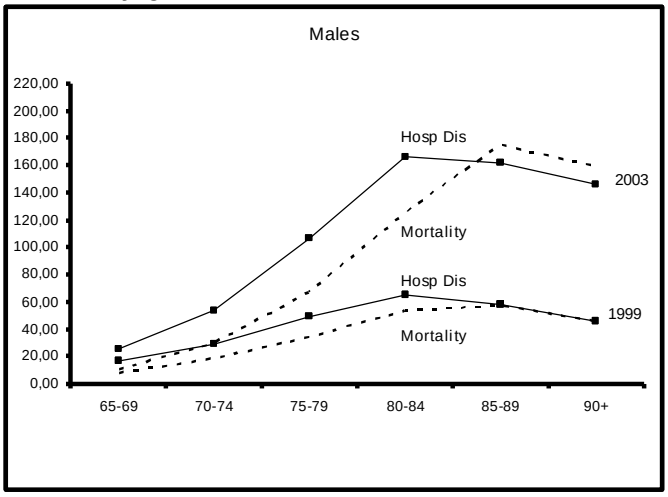
2003; the sharp increase of AD rate was mainly due to changes in the selection rules for underlying cause of death. The effect of the introduction of the ICD10 has been estimated being 18% (Anderson RN, Rosenberg HM, 2003). Then considering a 18% reduction of the rate, the value is coherent with the past trend .

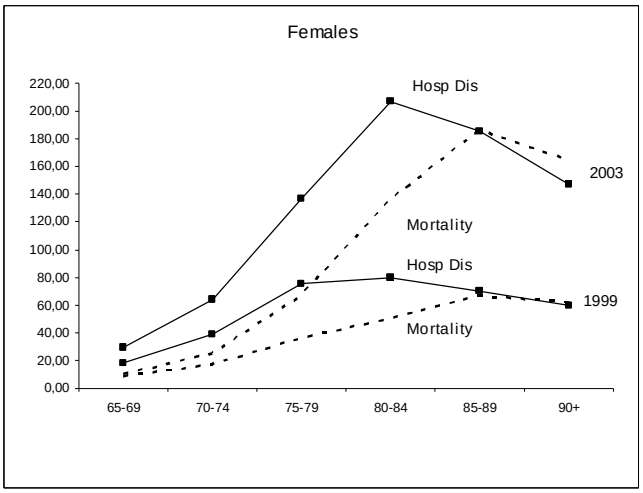
Figure 1 - Standardized hospital discharge and mortality rates (per 100,000) for Alzheimer disease by gender. Years 1985 – 2003.



In Figure 2 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 data sources and can better explain the temporal trends. The increase of rates between 1999 and 2003 is mainly due to the increase of rates at 80 years and over. The relative increase is highest for 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 relative increase is at 85-89 years (+164% for hospitalization and +181% for mortality).
Highest hospitalization rates are at 80-84 years for both sexes. While, for mortality, the peak is shifted to next age-class (85-89 years). The decline at the oldest ages may be due to undereporting of AD at these ages.

Figure 2 - Age-specific hospital discharge and mortality rates (per 100,000) for Alzheimer disease by gender. Years 1999 and 2003.





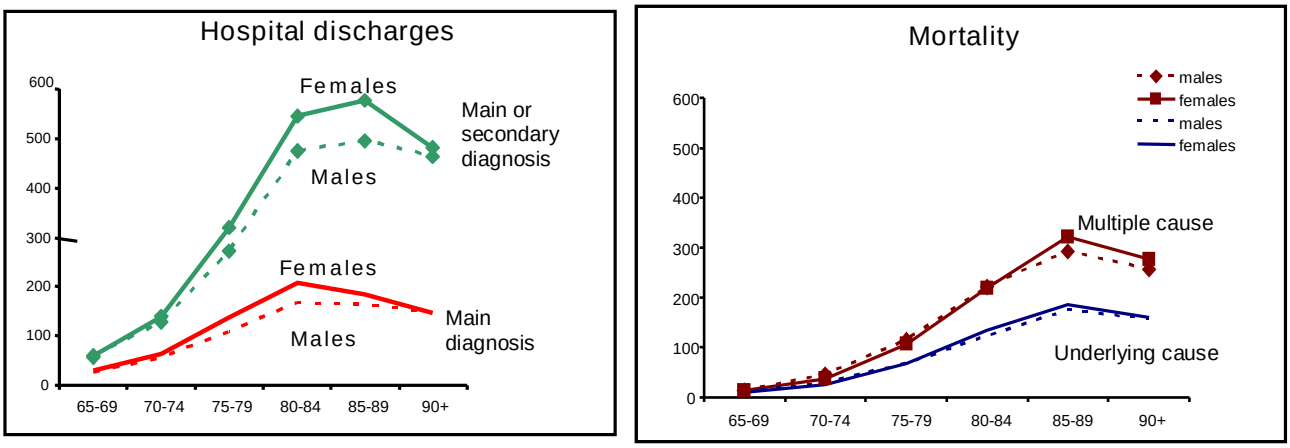
About 27 thousand cases for hospitalization and 11 thousand cases for mortality were found by searching for the AD code in the hospital discharge data base as main or secondary diagnosis and in the multiple cause of death file (Table 2).
Women represent about the 65% of the total in both populations.
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 the 39% of the hospital discharges have AD as main diagnosis, while for deaths is selected as the underlying cause in 60% of cases. When AD is the main diagnosis or underlying cause, the mean 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 mean number of diseases raises to 3.6 for hospitalization and to 4.8 for mortality.

Table 2 – Descriptive indicators of co-morbidity in AD - Year 2003.

AD	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	4,364	4.8	39.6%
Multiple cause (total)	11,021	4.1	100.0%

Figure 3 shows specific age hospitalization and mortality rates, both considering AD as main diagnosis and underlying cause and including all cases of hospitalization and death with AD mentioned.

Figure 3 - Age-specific hospital discharge and mortality rates (per 100,000) for Alzheimer disease by gender and co-morbidity - Year 2003.



Age patterns are similar for hospitalization and mortality also when multiple causes and all diagnoses are considered.
Highest rates are for people aged 85-89 years, except when AD is the main diagnosis in hospital discharge: in this case in fact, the highest rate is in the age-class 80-84 for both sexes.

The ratio between 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) and it increases with age too (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.

When AD is reported as main diagnosis in hospital discharges, the diseases more frequently associated are the same in males and females and are 'other mental disorders', hypertensive diseases, cerebrovascular diseases and other diseases of the circulatory system (Table 3).
Also for mortality, no differences by gender are observed, but the diseases associated are different from those of hospitalization: ill defined causes, such as cardiac arrest, respiratory collapse and other ill-defined causes and senility are highly frequent. Pneumonia and influenza and other diseases of the respiratory system have significant values too. Only cerebrovascular diseases and other diseases of the circulatory system are in common with hospital discharges.

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.
Infectuous diseases	2.1	5.9	4.1	7.2	2.3	5.5	3.4	6.8
Mal neoplasm digestive system	0.1	1.9	0.5	3.7	0.1	1.7	0.4	3.5
Mal neoplasm respiratory system	0.3	1.3	0.6	3.5	0.0	0.4	0.0	0.7
Mal neopl. bone, connective and breast	0.0	0.6	0.1	0.4	0.2	1.1	1.0	2.8
Mal neoplasm genito-urinary	1.0	3.2	1.4	5.4	0.1	0.7	0.2	1.0
Other neoplasm	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
Parkinson disease	3.6	4.1	2.4	3.9	2.4	2.8	1.4	2.8
Alzheimer Disease	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Other diseases nervous system	6.0	5.2	3.1	3.5	5.6	6.5	3.5	3.5
Senile and pre-senile dementia	2.6	1.7	2.4	1.8	2.7	1.3	2.9	1.5
Other mental 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
Ischaemic 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 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 respiratory system	10.0	25.2	27.3	40.4	5.7	14.9	19.4	27.7
Diseases 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	0.0	0.0	8.5	4.7	0.0	0.0	13.5	6.3
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

When AD is a secondary diagnosis, about 50% of hospital discharge forms contains codes related to the 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 is a not the underlying cause of death more than 50% of certificates contains 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.
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Discussion and conclusions

Data on deaths and on 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 the diagnosis, to a more spread attitude of physicians about reporting AD and to an actual increase of incidence and prevalence rates (Hoyert DL, Rosenberg HM., 1999; Wall MM *et al*., 2005).
Many similarities among the two data sources are found also when analysing co-morbidities since patterns are very similar.
Diseases associated to AD are in most cases those common to the elderly. These are the diseases of the circulatory and of the respiratory systems. Main differences refer to pneumonia (more frequent in mortality) and injuries (more frequent for females in hospitalization).
The decrease of rates for the last age class (90+) is probably due to the under reporting of AD for very old people more than depending from a reduction of incidence. The co-morbidity profile of these people becomes very complex and it is possible that AD is not reported in the certificates, while other diseases more relevant for causing death or for requiring high specialised treatments in hospital are coded.

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