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ABSTRACT

Objective: To evaluate the incidence of cancer in persons with Alzheimer disease (AD) and the incidence of AD dementia in persons with cancer.

Methods: This was a cohort study in Northern Italy on more than 1 million residents. Cancer incidence was derived from the local health authority (ASL-Mi1) tumor registry and AD dementia incidence from registries of drug prescriptions, hospitalizations, and payment exemptions. Expected cases of AD dementia were calculated by applying the age-, sex-, and calendar year–specific incidence rates observed in the whole population to the subgroup constituted of persons with newly diagnosed cancers during the observation period (2004–2009). The same calculations were carried out for cancers in patients with AD dementia. Separate analyses were carried out for the time period preceding or following the index diagnosis for survivors and nonsurvivors until the end of 2009 and for different types and sites of cancer.

Results: The risk of cancer in patients with AD dementia was halved, and the risk of AD dementia in patients with cancer was 35% reduced. This relationship was observed in almost all subgroup analyses, suggesting that some anticipated potential confounding factors did not significantly influence the results.

Conclusions: The occurrence of both cancer and AD dementia increases exponentially with age, but with an inverse relationship; older persons with cancer have a reduced risk of AD dementia and vice versa. As AD dementia and cancer are negative hallmarks of aging and senescence, we suggest that AD dementia, cancer, and senescence could be manifestations of a unique phenomenon related to human aging. ***Neurology*® 2013;81:322–328**

GLOSSARY

AD = Alzheimer disease; **CI** = confidence interval; ***ICD-10*** = *International Classification of Diseases*, 10th revision; **RR** = relative risk.

Alzheimer disease (AD) and cancer increase exponentially with age, but can be regarded as opposite phenomena[1,2]; AD is a consequence of the incapacity of damaged neuronal cells to renovate and repair (neurodegeneration) and cancer of controlling the fundamental process of cell renovation and tissue repair represented by cellular replication.[3]

A lower incidence of AD dementia in people who have cancer, and less cancer in persons with AD dementia, has been reported.[4–6] A similar relationship has been observed between cancer and other neurodegenerative disorders, such as Parkinson disease.[7] Issues of confounding might underlie the observed lower occurrence of cancer in patients with dementia and vice versa.[8] First, both cancer and AD dementia limit life expectancy of affected persons and thus reduce the available lifetime for occurrence of other diseases. Second, the presence of one disease might obscure the diagnosis of other disorders, because any new occurring symptoms in patients with AD dementia or cancer might be interpreted as a consequence of the already diagnosed primary disease. Finally, cognitive decline due to AD neurodegeneration may be falsely interpreted as an undesired chemotherapy side effect in patients with cancer.[9]

Previous studies evaluated populations with limited sample sizes and considered the risk of cancer after a diagnosis of AD dementia and the risk of AD dementia after cancer diagnosis. This study

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From the National Research Council of Italy (M.M., F.A., F.P.), Institute of Biomedical Technologies, Segrate (Milan); Foundation IRCCS "Santa Lucia" (M.M., S.D., C.C., K.P.), Rome; Alzheimer Departmental Unit (C.P.), AO of Garbagnate (Milan); University "Tor Vergata" (C.C.), Rome; and Epidemiology Unit (A.R.), Local Health Authority of Milano 1, Milan, Italy.

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evaluated the risk of co-occurrence of AD dementia and cancer independently from the temporal order of appearance of each disease in a general population in Italy.

METHODS

Standard protocol approvals, registrations, and patient consents. As the study used public registry data, ethical approval and patient consent were not required.

Study population. This was a prospective/retrospective historical cohort study including persons aged 60+ years registered in the computerized Health Information System of the Local Health Authority of Milano 1 (ASL-Mi1) who were diagnosed with cancer (n = 21,451) or AD dementia (n = 2,832) for the first time from January 1, 2004, to December 31, 2009. For each member of the cancer cohort, we defined 2 time periods of exposure to the risk of AD dementia: one preceding the diagnosis of cancer and a second following that diagnosis. The same definition of 2 risk periods was identified for patients with AD dementia. The Health Information System of ASL-Mi1 serves about 1 million inhabitants and included 1) the Pharmaceutical Prescriptions Registry from January 2001 to December 2011 (n = 70,315,961 prescriptions), 2) the Hospital Discharge Registry from January 1996 to March 2011 (n = 3,196,595 admissions), and 3) the Mortality Registry from January 1999 to March 2010 (n = 86,819 deaths) and payment exemptions for special disease conditions (n = 409,099). Cancer cases were identified by the cancer and tumor registry from January 2004 to December 2009.

All sources were linked at an individual level using fiscal codes as the unique identifier. Pharmaceutical prescriptions were coded according to the Anatomical Therapeutic Chemicals classification.

AD dementia ascertainment. We identified persons who were prescribed an antidementia drug (donepezil, rivastigmine, galantamine, or memantine) or had a hospital discharge or payment exemption for AD dementia for the first time during the study period (2004–2009). In Italy, the Health System reimburses antidementia drugs to patients with AD dementia, but not to persons with other forms of dementia or cognitive impairment. Only physicians working in special hospital units who are expert in dementia (neurologists, geriatricians, and psychiatrists) make the diagnosis and prescribe the drugs.[10] Thus, we rely on the assumption that almost all the persons taking acetylcholinesterase inhibitors or memantine had AD dementia. The date of first AD dementia diagnosis was considered as the date of the first 1) antidementia drug prescription, 2) hospital discharge, or 3) payment exemption for AD dementia.

Ascertainment of cancer. After identifying all cancers in the cohort from January 1, 2004, to January 1, 2011, in the local Cancer Registry, we identified the date of cancer incidence, defined as a new invasive cancer. Cancers were coded according to topography and morphology as epithelial, mesenchymal, blood, nervous, and unspecified, according to the *ICD-10*.

Statistical analysis. To control for possible biases introduced by a systematic underdiagnosis of new diseases and life expectancy reduction in persons with AD dementia or cancer, we carried out 3 stratified analyses. For each cohort member, we defined a retrospective and prospective follow-up, respectively, preceding and following the diagnosis of cancer or AD dementia. The retrospective follow-up period started on January 1, 2004, for persons who were 60+ on that date, or at the completion of this age for those who were younger, and ended at the date of diagnosis of AD dementia or cancer, respectively. The prospective period started with the diagnosis of cancer or AD dementia and ended with death or on December 31, 2009. If an underdiagnosis of other diseases occurs once a diagnosis of AD dementia or cancer is established, then we would expect that lower than expected occurrences would be restricted to the prospective follow-up period only. Separate analyses were carried out for persons surviving or dying during the follow-up. If the occurrence of AD dementia (or cancer) in persons with cancer (or AD dementia) was less than in the general population due to reduced survival or competing causes of death, we expected to find differences between observed and expected cases mainly in nonsurvivors. Separate analyses were also carried out for cancers classified by tissue of origin and by the 5 most frequent cancer sites.

The age-, sex-, and calendar year–specific incidence rates of cancers in the general ASL Mi1 population were calculated from the cancer registry during 2004–2009. The person-years at risk were grouped into 5 ages: 60–64, 65–69, 70–74, 75–79, and 80+ years. Specific incidences were calculated by sex and age. Expected cancers in the AD dementia cohort were calculated by multiplying the appropriate person-years of observation for the age-, sex-, and calendar year–specific incidences of the general ASL-Mi1 population. The expected AD dementia cases in the cancer cohort were calculated similarly, by calculating the incidence of AD dementia in the whole population.

Relative risks (RR) were estimated as observed time-expected occurrences. Statistical significance and 95% confidence interval (95% CI) for the RRs were obtained.[11]

Specific comparisons of expected and observed cancers and AD dementia were carried out for the time periods preceding and following the date of the index diagnosis, for persons surviving or deceased during the follow-up period, for cancers of different tissues of origin, and for the 5 most frequent tumor sites.

RESULTS

Between 2004 and 2009, there were 204,468 residents aged 60+ years living in the area of ASL-Mi1, contributing to a total of 1,225,891.0 person-years at risk of AD dementia or cancer. There were 21,451 (n = 12,225, 57.0% men) newly diagnosed cancer cases and 2,832 (n = 947, 33.4% men) AD dementia cases, giving a crude incidence rate per 10,000 person-years of 175.1 and 22.1, respectively (table 1). The 20 most frequent types of cancers represented nearly 90% of all incident cases. The most frequent was breast cancer (women), followed by prostate, colon, lung, and urinary bladder cancers.

The mean age of patients with AD dementia at time of first diagnosis was 78 years, older than for cancer patients (table 1). The AD dementia cohort contributed a total of 15,063.0 person-years of observation, of which more than half was spent before the diagnosis. The cancer cohort contributed 101,317.9 person-years (60,023.0 before the diagnosis). For both cancers and AD dementia, the overall observation time was shorter for persons who did not survive until the end of follow-up.

In 161 cases, cancer and AD dementia were diagnosed in the same persons; AD dementia preceded the diagnosis of cancer in 68 cases (table 2). In cancer patients, 246 cases of AD dementia were expected from the incidence observed in the whole population; the risk of AD dementia occurrence relative to the general population of the same age and sex was significantly reduced (RR 0.65; 95% CI 0.56–0.76). In the AD dementia cohort, 281.2 cancer cases were expected (observed/expected RR 0.57; 95% CI 0.49–0.67). In comparison

Table 1 Incidence rates, age, sex, and person-years of observation before and after the diagnosis and within survivors and nonsurvivors of the 2 cohorts of people with cancers or Alzheimer disease dementia

	Alzheimer dementia cohort (n = 2,832)	Cancer cohort (n = 21,451)
Men/women, n	947/1,885	12,225/9,226
Age, y, mean ± SD	78.1 ± 6.8	72.4 ± 7.8
Person-years		
Total	15,063.0	101,317.9
Before the diagnosis	8,674.5	60,023.0
After the diagnosis	6,388.5	41,294.9
Survivors	9,877.7	55,642.5
Nonsurvivors	5,185.3	45,675.4
IR (95% CI)[a]	22.1 (21.9–22.4)	175.1 (174.4–175.8)
Type of cancer, IR (95% CI)[a]		
Breast (n = 2,586, 12.1%)		21.1 (20.9–21.4)
Prostate (n = 2,298, 10.7%)		18.8 (18.5–19.0)
Colon (n = 2,168, 10.1%)		17.7 (17.5–17.9)
Lung (n = 2,167, 10.1%)		17.7 (17.5–17.9)
Urinary bladder (n = 1,739, 8.1%)		14.2 (14.0–14.4)
Gastric (n = 1,071, 5.0%)		8.7 (8.6–8.9)
Metastases (unspecified primary tumor) (n = 1,023, 4.8%)		8.3 (8.2–8.5)
Rectal (n = 960, 4.5%)		7.8 (7.7–8.0)
Liver (n = 938, 4.4%)		7.7 (7.5–7.8)
Pancreas (n = 646, 3.0%)		5.3 (5.1–5.4)
Kidney (n = 624, 2.9%)		5.1 (5.0–5.2)
Metastases (specified primary tumor) (n = 585, 2.7%)		4.8 (4.7–4.9)
Lymphomas (n = 511, 2.4%)		4.2 (4.1–4.3)
Uterine body (n = 426, 2.0%)		3.5 (3.4–3.6)
Leukemias (n = 382, 1.8%)		3.1 (3.0–3.2)
Multiple myeloma (n = 312, 1.5%)		2.5 (2.5–2.6)
Brain (n = 298, 1.4%)		2.4 (2.3–2.5)
Biliary system (n = 280, 1.3%)		2.3 (2.2–2.4)
Larynx (n = 252, 1.2%)		2.1 (2.0–2.1)
Ovary (n = 242, 1.1%)		2.0 (1.9–2.1)
Other (n = 1,177, 5.5%)		9.6 (8.4–9.7)

Abbreviations: CI = confidence interval; IR = incidence rate.
[a] IR per 10,000 person-years (95% CI).

with the general population of the same age and sex, the risk of AD dementia among persons with cancer was 35% reduced and the risk of cancer in patients with AD dementia nearly halved.

Similar risk reductions for the occurrence of AD dementia before and after cancer diagnosis were observed; the RR before the diagnosis of cancer was 0.66 (95% CI 0.54–0.81) and after cancer diagnosis was 0.64 (95% CI 0.50–0.81). The risk of cancer in patients with AD dementia was significantly reduced by 20% after the diagnosis of AD dementia (RR 0.79; 95% CI 0.64–0.97) but the reduction was higher in the period preceding AD dementia diagnosis (RR 0.42; 95% CI 0.32–0.53). The RRs of AD dementia and cancer were always lower in survivors than in nonsurvivors. In nonsurvivors from the AD dementia cohort the risk reduction of cancer occurrence was borderline statistically significant (RR 0.86; 95% CI 0.68–1.06, $p = 0.07$). The observed cases of AD dementia in cancers with different tissue of origin were always lower than expected, with the exception of nervous system tumors (3 observed vs 2.6 expected). Only the RR of AD dementia occurrence in tumors of epithelial origin was significantly lower than 1, but the risk reductions for

Table 2 Observed and expected cases and relative risk of occurrence of Alzheimer disease dementia in the cohort of persons with cancer and of cancers in the cohort of persons with AD dementia[a]

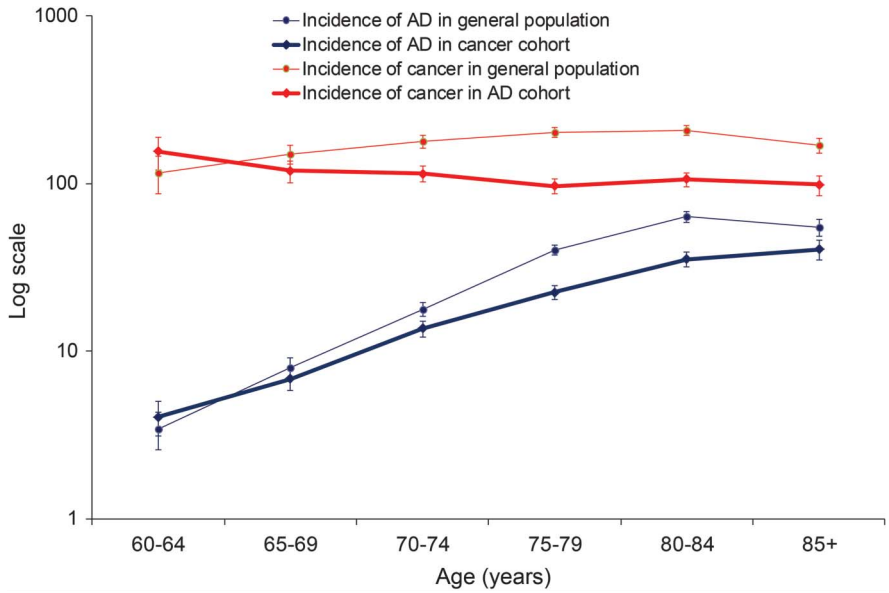
	Cancers in AD dementia cohort		AD dementia in cancer cohort	
	Obs/exp[b]	RR (95% CI)	Obs/exp[b]	RR (95% CI)
Total	161/281.2	0.57 (0.49–0.67)	161/246.0	0.65 (0.56–0.76)
Before the diagnosis	68/163.4	0.42 (0.32–0.53)	93/140.1	0.66 (0.54–0.81)
After the diagnosis	93/117.8	0.79 (0.64–0.97)	68/105.9	0.64 (0.50–0.81)
In survivors	78/184.4	0.42 (0.33–0.53)	78/135.1	0.58 (0.46–0.72)
In nonsurvivors	83/96.8	0.86 (0.68–1.06)	83/110.9	0.75 (0.60–0.93)
Cancer type				
Epithelial	132/219.9	0.60 (0.50–0.71)	132/200.2	0.66 (0.55–0.78)
Mesenchymal	3/5.2	0.58 (0.12–1.70)	3/4.4	0.69 (0.14–2.00)
Blood	9/19.1	0.47 (0.21–0.89)	9/16.3	0.55 (0.25–1.05)
Nervous system	3/4.3	0.70 (0.14–2.05)	3/2.6	1.17 (0.23–3.41)
Unspecified	14/32.8	0.43 (0.23–0.72)	14/22.5	0.62 (0.34–1.04)
Cancer site				
Breast	26/37.0	0.70 (0.46–1.03)	26/38.1	0.68 (0.45–1.00)
Lung	16/26.6	0.60 (0.34–0.98)	16/18.7	0.85 (0.49–1.39)
Bladder	18/22.4	0.81 (0.48–1.27)	18/22.9	0.79 (0.47–1.24)
Prostate	19/20.3	0.94 (0.56–1.46)	19/22.0	0.87 (0.52–1.35)
Colorectal	13/30.0	0.43 (0.23–0.74)	13/29.5	0.44 (0.23–0.75)
Other	69/145.0	0.48 (0.37–0.60)	69/114.8	0.60 (0.47–0.76)

Abbreviations: AD = Alzheimer disease; CI = confidence interval; RR = relative risk.
[a] Expectations are calculated with reference to the general population of the same sex, age, and calendar year of follow-up.
[b] Observed vs expected values.

blood tumors and other nonepithelial, mesenchymal, nervous, or blood cancers were borderline significant. The observed cancers of different tissues of origin in patients with AD dementia were always lower than those expected; the risk reductions were statistically significant for tumors of epithelial, and other nonepithelial, mesenchymal, blood, or nervous tissue origin. The observed cases of AD dementia in the 5 most frequent cancer sites were always lower than those expected. However, the RR was significantly reduced only in persons with colorectal cancers or with tumors of other nonepithelial, mesenchymal, blood, or nervous origin. The observed occurrence of the 5 most frequent sites of cancer in patients with AD dementia was lower than expected, but the cases of prostate cancer observed were almost equal to those expected. The risk of occurrence was significantly reduced for lung and colorectal cancer and for other tumors of nonepithelial, mesenchymal, blood, or nervous origin.

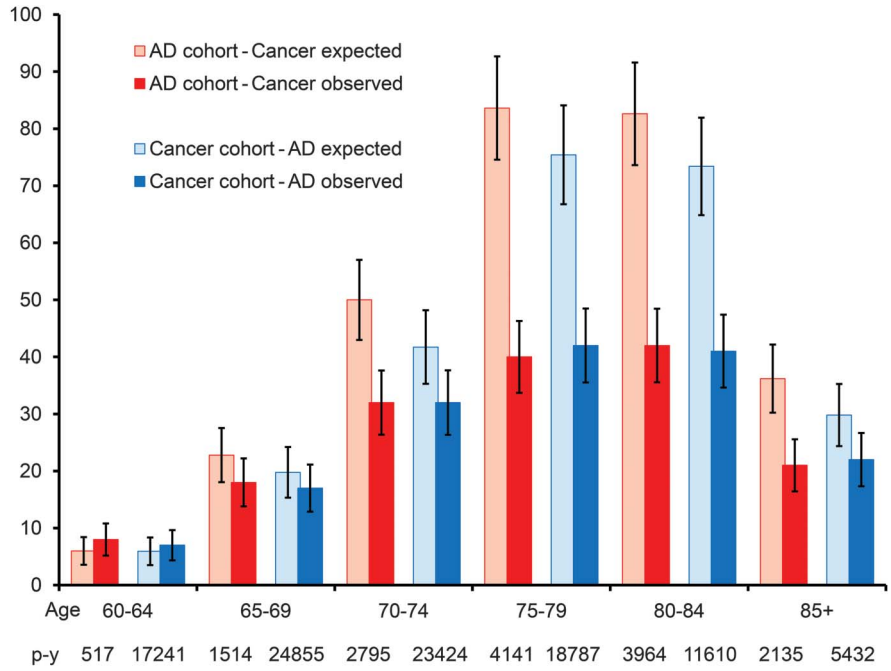
Figures 1 and 2 report the AD dementia and cancer age-specific incidences observed in the 2 cohorts and the general population, as well as the age-specific observed and expected cases of AD dementia or cancer. At 64–69 years, the observed cancers were somewhat higher than expected, but starting from age 70, the expected cases were always higher than those observed. In the cancer cohort, the RR of AD dementia were lower than 1 starting from age 65–69 and decreased further at age 70–74, remaining substantially stable until age 85+. The same was true for cancer in the

Figure 1 Age-specific incidence rates of cancers and Alzheimer disease dementia



Age-specific incidence rates of cancers in the general population and in the cohort of persons with Alzheimer disease (AD) dementia, and age-specific incidence rates of AD dementia in the general population and in the cohort of persons with cancers, ×10,000 person-years.

Figure 2 Age-specific observed and expected cases of Alzheimer disease dementia and cancer



Age-specific observed and expected cases of Alzheimer disease (AD) dementia in the cohort of persons with cancers, and age-specific observed and expected cases of cancer in the cohort of persons with AD dementia.

AD dementia cohort, but at the oldest age class the risk reduction was lower and no longer statistically significant (table 3).

DISCUSSION In agreement with previous studies,[4–6] we observed that the occurrence of cancers in patients with AD dementia and of AD dementia in persons with cancer are both reduced. The lower than expected incidence of AD dementia and cancer became statistically significant only in individuals aged 70+, suggesting that the low risk of co-occurrence between the 2 disorders might be characteristic of older ages. The strength of RR for the relationship between AD dementia and cancer was the same size when considering separately the risk before and after diagnosis of the index disease and when considering persons surviving or not surviving for the entire observation period.

The lower risk of AD dementia in patients with cancer, and vice versa, was generally observed also when considering different cancer sites or cancers with different tissues of origin. However, due to the small number of observed and expected cases, some of the risk reductions were not statistically significant. The only exception was for AD dementia in tumors originating in the nervous system, where the expected cases were somewhat lower than those observed (2.6 vs 3). Two of these persons had a diagnosis of AD dementia within 2 months prior to the diagnosis of

Table 3 Age-specific risks, relative to the general population, of occurrence of cancer in the cohort of patients with AD dementia and of AD dementia in the cohort of persons with cancer

	Cancer in AD dementia cohort			AD dementia in cancer cohort		
Age, y	Person-years	Obs/Exp[a]	RR (95% CI)	Person-years	Obs/Exp[a]	RR (95% CI)
60–64	516.7	8/6.0	1.34 (0.58–2.63)	17,240.7	7/5.9	1.18 (0.47–2.43)
65–69	1,514.0	18/22.8	0.79 (0.47–1.25)	24,855.3	17/19.8	0.86 (0.50–1.38)
70–74	2,795.3	32/50.0	0.64 (0.44–0.90)	23,424.2	32/41.7	0.77 (0.52–1.08)
75–79	4,141.0	40/83.6	0.48 (0.34–0.65)	18,786.7	42/75.4	0.56 (0.40–0.75)
80–84	3,964.4	42/82.6	0.51 (0.37–0.69)	11,609.6	41/73.4	0.56 (0.40–0.76)
85+	2,135.4	21/36.2	0.58 (0.36–0.89)	5,432.4	22/29.8	0.74 (0.46–1.12)
Total	15,066.8	161/281.2	0.57 (0.49–0.67)	101,349.0	161/246.0	0.65 (0.56–0.76)

Abbreviations: AD = Alzheimer disease; CI = confidence interval; RR = relative risk.
[a] Observed vs expected values.

brain tumor, suggesting that the presence of cognitive impairment caused by a brain tumor was initially misinterpreted as due to a primary neurodegenerative dementia. A contradictory result was the finding of a risk of AD dementia occurrence in persons with prostate cancer that was almost equal to that of the general population. This may be due to chance variability due to the many subgroup analyses carried out.

A strength of this study was the control for anticipated confounding factors.[8] We analyzed 2 follow-up periods: one retrospective preceding the diagnosis of the index disease and the other following that diagnosis. Results were similar for the 2 periods, suggesting that the lower risk of AD dementia in patients with cancer, and vice versa, is not due to underdiagnosis of new diseases once AD dementia or cancer is diagnosed. We found similar results in survivors and nonsurvivors, suggesting that our results are not influenced by the reduced life expectancy of persons with AD dementia or cancer. Another strength was that we analyzed different types/sites of cancer. We found substantially similar results for and within the different cancer types, suggesting that the lower risk of AD dementia in patients with cancer, and vice versa, is not confounded by some conditions or characteristics specific to one or more types of cancers (particularly of diagnosis and treatment).

One limitation is that case ascertainment relied on administrative data that were not primarily collected for scientific purposes. The methods of ascertainment for both diseases are likely to have high specificity, but might lack sensitivity. AD dementia cases were ascertained by means of drug prescriptions, hospitalization, and payment exemptions, but not all persons with AD dementia experience one of these exposures. Most patients with AD dementia are never hospitalized specifically for their dementing illness; more frequently they require hospital care for inter-occurring disorders directly or indirectly related to, or independent from, dementia and often have a high risk of mortality due to these adverse events.[12] Accordingly, we identified about 75% of persons with AD dementia via the drug prescription registries. Prevalence studies show that a percentage of patients with AD dementia are not treated with antidementia drugs. This would lead to a number of false-negative cases in our study. Our incidence estimates are almost equal to those for AD dementia of moderate severity from ad hoc European epidemiologic studies,[3] suggesting that our figures possibly underrepresent milder AD dementia cases with symptoms not severe enough to facilitate the diagnosis or not needing treatment. It is difficult to predict how this underascertainment might bias the results, but we do not hypothesize that there would be a higher cancer occurrence in patients with AD dementia who were not prescribed antidementia drugs or those with a milder disease form. Conversely, it is highly unlikely that there are many false-positive AD dementia cases in our study because in Italy, acetylcholinesterase inhibitors and memantine are prescribed only for persons with mild to moderate AD dementia. These prescriptions are only made by physicians who are expert in dementia disorders, working in certified special units.[10] National guidelines recommend acetylcholinesterase inhibitor treatment for all patients with newly diagnosed AD dementia. Thus, very few false-positive AD dementia cases were included in our cohort.

Tumor cases were ascertained through hospital discharge forms that are the main source of information of the tumor registry, but not all persons with cancers require hospitalization. In Italy, most patients with cancer have at least one episode of hospitalization, with the exception of skin cancers. Indeed, skin cancers, which are frequent in older persons, accounted for less than 1% of cancers in our population. The potential for bias of this lack of sensitivity in our method of cancer ascertainment is difficult to estimate. However, we verified the number of AD dementia cases with respect to expectancy for many different cancer types and made separate analyses for the 5 most frequent cancer sites and for tumors with different tissue origins, and the results were similar to those found in the entire cohort, suggesting that the reduced occurrence of AD dementia is general to any type of cancer and indirectly excludes the possibility that this result might be contradicted by skin cancers.

A limitation of using large-scale registry data is that it is not possible to investigate the role of certain risk factors for cancer or AD dementia, particularly lifestyle factors. For example, it could be hypothesized that a risk factor for one disease (e.g., smoking as a risk factor for cancer) might be less common in people who later develop AD dementia. Although we were unable to directly examine lifestyle factors, we conducted supplementary analysis to investigate whether there was a difference in AD dementia risk in the cancer cohort after stratifying for smoking-related cancers vs cancers that are unrelated to smoking. The RR of AD dementia were similar in the stratified groups (data not shown), suggesting that smoking is unlikely to play a confounding role. Further, we were unable to extend the analysis to compare the risks of other related disorders such as cerebrovascular disease. Our sample included only AD dementia and cancer cohorts. An interesting target for future research may be to examine whether the reduced risk of cancer seen in persons with AD dementia is also seen for other disorders such as cerebrovascular disease. This might help clarify whether the opposing risks observed in our study are specific to AD dementia and cancer.

Aging and senescence are marked by the increased occurrence of many human diseases, particularly by an exponential age-related increase of cancer and neurodegenerative disorders, particularly AD dementia. Therefore, the finding of a lower risk of AD dementia in

patients with cancer, and vice versa, in the elderly might appear counterintuitive. However, cancer and AD dementia might have opposite biological mechanisms. The initiating event of the transformation from normal to cancerous cells is DNA damage, and some control mechanisms called "caretakers" can prevent or repair this damage, while other mechanisms, called "gatekeepers," are capable of eliminating cancerous cells.[13] Among gatekeepers, cellular senescence is a process contrasting the replication of normal and cancer cells that can be activated also by oncogenes intuitively as a form of defense against the uncontrolled replication of cancer cells. Evidence shows a process of inefficient cellular mitotic cycling in neurons of patients with AD dementia that is accompanied by an efficient process of cellular senescence ending with apoptotic death.[14–16] This inefficient capacity of cellular reproduction and efficient tendency to senescence and apoptosis of AD dementia is somewhat specular to cancer and might be the biological explanation for the observed reduced incidence of AD dementia in patients with cancer, and vice versa. However, further studies are needed, particularly on the complex relationships of cancer and AD dementia with aging and senescence.

AD dementia and cancer can be viewed as opposite faces of senescence, and interpreting these diseases within the unitary context of senescence processes, particularly if our results are confirmed in future epidemiologic and laboratory studies, might represent a valuable opportunity for knowledge and human health.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception and design, or analysis and interpretation of data, as well as drafting the article or revising it critically for important intellectual content. All authors have seen and approved the final version to be published. Everyone who fulfills the criteria for authorship has been included as an author.

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DISCLOSURE

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