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Evolution of the Rate of Antidepressant Prescriptions in Alzheimer's Disease and Related Disorders Between 2010 and 2014: Results from the French National Database on Alzheimer's Disease (BNA)

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Abstract.
Background: Safety warnings from health authorities are currently intended to limit the use of psychotropic agents in dementia-related conditions. Evidence concerning the use of antidepressants in dementia is, however, scarce and contradictory.
Objective: To evaluate antidepressant use among individuals with Alzheimer's disease (AD) and related disorders in the French population between 2010 and 2014.
Method: Antidepressant prescriptions in individuals with AD, mixed dementia (MD), and vascular dementia (VaD) in the French National Alzheimer Database between 2010 and 2014 were analyzed ($N = 199{,}544$).
Results: Multivariate analysis showed an annual significant increase ($p < 0.001$) in the prescription rate of antidepressants from 26% (2010) to 31% (2014), and identified female gender, younger age, higher education, living in long-term facilities, more severe cognitive decline, and presence of vascular signs (VaD and MD) as associated factors for antidepressant prescribing.
Conclusion: The annual increase of antidepressant prescribing among individuals with AD, MD, and VaD in French specialized settings may be partially related to the lack of current valuable medications for dementia-related behavioral symptoms.

Keywords: Alzheimer's disease, antidepressant, dementia, psychotropic medication

INTRODUCTION

Prescription of antidepressants in the elderly population is mostly related to the management of depressive symptoms and of major depressive disorders, as well as for management of several dementia-related behavioral disturbances such as anxiety, irritability, and disinhibition. However, current evidence for antidepressant use in the management of depression in people living with dementia tends to be inconclusive [1]. In dementia, antidepressant use is more frequent among depressed versus non-depressed individuals, but only around 60% of depressed individuals with dementia is treated with antidepressant medications [2]. Additionally, rates of antidepressant use do not significantly differ between

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depressed individuals with and without associated dementia in long-term care facilities [3].

In large cohorts investigating the use of psychotropic medications, antidepressant use in dementia remains important. The percentage of individuals diagnosed with Alzheimer's disease (AD) or receiving at least one prescription of anti-AD symptomatic agents who received antidepressant medications ranged from 46-47% in the south of France (2010) [4] and in the USA (2008) [5], to 53%in Finland (2005–2011) [6]. Lower percentages were found in the UK, where antidepressant average use in individuals with dementia and first-time users of anti-AD symptomatic agents between 1995 and 2011 increased from 10.7% to 26.3% [7].

Rates of antidepressant use among elderly individuals with dementia living in long-term care facilities could be even higher, up to 98% [5, 8], with several geographical discrepancies (around 30% in Switzerland [9] and 65.6% in the USA [5]).

Psychotropic medication use is usually associated with greater severity of dementia and poorer medical status. It has also been longitudinally associated with more rapid cognitive decline. Antidepressants and selective serotonin re-uptake inhibitors (SSRIs) (as well as benzodiazepines and typical antipsychotics) have been associated with a more rapid increase in dementia severity, and SSRIs (as well as conventional and atypical antipsychotics) with a more rapid increase in neuropsychiatric symptoms [10].

Use of antidepressants could also vary according to the type of dementia. It has been previously shown that among elderly individuals with neuropathologically verified-dementia, a history of depression prior to dementia onset was more common and more therapy-resistant in vascular dementia (VaD) than in AD [11]. A recent meta-analysis confirmed that late-life depression is associated with increased likelihood of dementia, but was unable to find a relationship with a specific type of dementia (AD or VaD) [12].

The evolution of antidepressant use in the aging populations (with or without dementia) across years is not clear when considering the existing literature. Furthermore, despite the fact that two recent studies reported a lack of efficacy of several common antidepressants for the management of depression in AD [1, 13], to the best of our knowledge, no recent recommendations for the use of antidepressant in AD and related disorders have been proposed. On the contrary, safety warnings have been issued for other psychotropic medications, such as antipsychotics, leading to specific recommendations for their prescription, with governmental incentives to decrease their use. As antidepressants efficacy for the management of behavioral and psychological symptoms of dementia has been shown to be similar to antipsychotics [14], it is possible that the reduction of antipsychotics could have promoted antidepressant use as alternative pharmacologic treatment.

The aim of the present study was to investigate the evolution of antidepressant use among individuals diagnosed with AD, mixed dementia (MD), and VaD in specialized settings between 2010 and 2014, using inputs from the French National database on Alzheimer's disease (BNA), in regard to the decrease of antipsychotics. The secondary aims were to investigate demographic and clinical factors associated with the use of antidepressants in dementia, and to compare the use of antidepressants between dementia with (VaD and MD) or without (AD) associated vascular signs.

MATERIALS AND METHODS

French Alzheimer national database

The BNA is part of the French strategy to fight against dementia [15, 16]. The aim of this database is to provide information about the medical activity of the French memory centers in order to 1) adapt the healthcare provision, and 2) generate epidemiologic knowledge on the diseases and the medical practices. Information collected in the BNA consists of a limited set of data concerning demographic, diagnostic, and clinical data selected by a national consensus group. The number of variables was restricted to facilitate and enhance care providers to participate in this national database. Participants are all the 456 French memory units [memory centers ($n = 399$) and resource and research memory centers (regional level, $n = 57$)] and independent neurologists ($n = 61$) who expressed the willingness to participate.

In the BNA, each time a patient consults a center, a record is generated and transferred to the database. Therefore, one patient can figure more than once in the BNA, depending on the number of medical acts he/she underwent.

Information we used for this study are: gender, age, living conditions, education, type of center, referring modalities, location of the patient, Mini-Mental Score Examination (MMSE) [17], date of consultation, diagnosis, and treatments. The BNA differentiates 38 diagnostic groups, based on ICD-10

classification. The code related to AD is F00.1, to MD is F00.2, and F01.9 is used for VaD. For treatments, the BNA records the presence of a prescription for 6 groups of psychotropic drugs classified as follow: antidepressant, anxiolytic, hypnotic, antipsychotic, cholinesterase inhibitors (ChEIs), and N-Methyl-D-aspartate receptor antagonist (NMDA). No data is available on drug generics or brand names, nor on dosage.

Please refer to [18] for a more detailed description of the BNA.

Subjects selection

We performed an extraction from the database with data from 1 January 2010 to 31 December 2014. Individuals who received one of the three diagnoses of interest (AD, MD, and VaD) at least once during the study timeframe were included in the analysis.

Individuals receiving prescriptions of anti-AD agents without an associated AD diagnosis were not considered for the analysis.

A single patient could have different entries in different years of study, corresponding to different consultations. To describe the whole population included in the study, we selected the first diagnosis attributed to the patient within the study period. To describe the population according to the year of consultation we adopted the same rule, so if an individual had two or more different diagnoses between 2010 and 2014, the first one was systematically considered. Similarly, if patients were assigned with different scores at the MMSE tests during the study period, the first MMSE done in the period for the analysis was systematically considered for the descriptive analysis. For the multivariate analyses, all MMSE scores were considered.

Concerning treatments, a patient was considered as "under treatment" if at least one prescription appeared each year during the study period.

Statistical analysis

The proposed design is a repeated cross sectional study.

Descriptive analyses were conducted using percentages for categorical variables, and mean and standard deviation for quantitative ones. If needed, quantitative variables were categorized.

To analyze factors associated with antidepressant prescribing, we performed regression analyses including baseline data (age, gender, education, type of center, sent by, location of the patient, diagnosis) and follow-up data (MMSE, neuroleptic, hypnotic, anxiolytic, NMDA antagonists, ChEIs, lifestyle). To take into account possible repeated measures (as a same patient can have several consultations over the period, and thus several data entries), we used generalized estimating equations models (GEE).

All variables significantly associated with antidepressant prescribing in a univariate GEE model ($p < 0.05$) were included in the multivariate GEE models. Only variables still significantly associated with the outcome variable with a p-value <0.05 were kept in the final model. We also tested all second order interactions concerning the variable "year of consultation" and significant interactions were included in the final model. Adjusted odds ratios are presented with a 95% confidence interval.

All tests were performed bilaterally. Statistics were done with SAS Enterprise Guide software, version 5.1 (SAS Inc., Cary, NC).

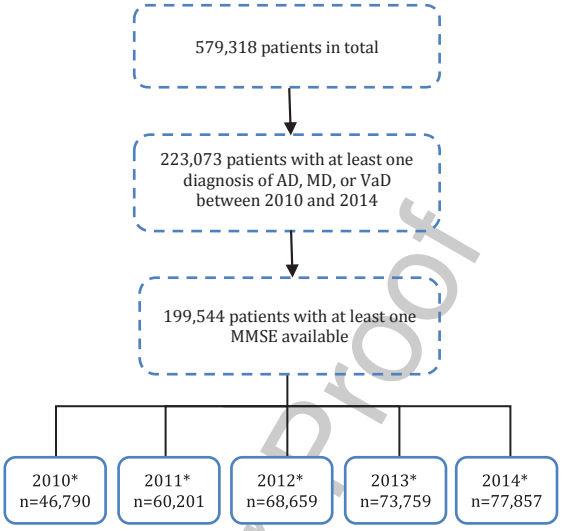

Fig. 1. Selection of the participants included in the study. *number of individuals (with a diagnosis of AD, MD, or VaD and at least one MMSE available) each year. A same individual could have more than one consultation each year.

RESULTS

Between 2010 and 2014, 223,073 individuals with a diagnosis of AD, MD, or VaD consulted one of the BNA centers. Among them, 199,544 individuals were considered for the final analysis as they had over the 2010–2014 period at least one global cognitive evaluation using the MMSE (mean of 1.7 consultations; see Fig. 1).

Demographic characteristics of the study population are presented in Table 1.

For the three diagnostic subgroups, the majority of individuals with dementia were living in the community (more than 80%), within a 50-kilometer area from the memory clinic (more than 90%), were mainly addressed by the GP (more than 55%), and had a primary or lower education level (more than 50%).

Among all diagnostic subgroups ($n = 199,544$), 60,913 individuals (30.3%) received at least one antidepressant prescription between 2010 and 2014 [30.5% for AD ($n = 39,720$), 31.3% for MD ($n = 14,794$), 29.4% for VaD ($n = 6,399$)]. Antidepressant prescribing frequencies were 29.5% for community-living individuals (29.6% for AD, 30.0% for MD, and 27.8% for VaD) and 35.8% for individuals from long-term care facilities (35.2% for AD, 36.8% for MD, and 36.2% for VaD), respectively (See Supplementary Data).

Prevalence of antidepressant use had an average frequency of 25–30% per year between 2010 and 2014, with a slight tendency to increase from 2010 to 2014 (Table 2).

Considering individuals that received at least one antidepressant prescription per year, more than 50% were prescribed antidepressants every year as a single psychotropic medication. An association of antidepressant and anxiolytic was found for around 20% of patients each year. All others types of psychotropic associations were around or lower than 5%. The association between antidepressant and anti-dementia agents (NMDA antagonists and ChEIs) was between 20% and 30% for NMDA antagonists, and between 45% and 60% for ChEIs, with a decrease from 2010 to 2013 followed by an increase as of 2014.

Table 3 shows the estimated odds ratios for the multivariate GEE models for antidepressant prescription. After multivariate adjustment, we found a significant increased use of antidepressants each year, from 2010 to 2014, a significant increased level of prescriptions for females versus males, as well as for individuals with secondary and superior educational levels, for patients from long-term care facilities versus community-living individuals, and a decreased use when age was higher. Antidepressant prescribing from neurologists in private practice was significantly lower compared to classical memory consultations and regional reference memory centers. Use of any other type of psychotropic drugs or anti-dementia agents was an associated factor of antidepressant prescribing. In addition, the use of antidepressants was significantly more important for MD and VaD compared to AD. Interactions between years and gender, years and level of education, and years and age at baseline were significant and added to the final models (data not shown).

DISCUSSION

Our main results showed a prescription rate of antidepressant use among individuals diagnosed with AD, MD or VaD in France at around 25–30%, with a significant increase in antidepressant use from 2010 to 2014.

Prevalence of antidepressant use

Our results regarding prevalence of antidepressant use are consistent with most previous studies on people with dementia that included several diagnostic categories, as we did [19], while studies including only people with AD found rates of antidepressant use slightly higher: 34.8% in Arbus (686 AD subjects from the REAL.fr cohort) [2], 39% in Tartaglia (3,638 AD subjects (mean age = 76)) [20].

Previous studies found that several factors are associated with increased rates of psychotropic medications, including gender (female), oldest age, low income or low education level, 'not married' status or low linking social capital [21], a history of psychiatric disease [3], longer AD duration, and a more severe AD stage [20]. Regarding antidepressants specifically, the aforementioned factors remained globally similar, also including an association between antidepressant use and higher vascular risk factors [20].

In agreement with these studies, we did find an increased antidepressant use for females versus males, and for more cognitively impaired individuals (lower MMSE score). However, contrary to previous reports, we found that older individuals and individuals with lower education levels received significantly fewer antidepressants over the 5-year study period. Antidepressant use increased for individuals living in long-term care facilities, possibly due to the increased risk of associated behavioral and psychological symptoms in this population [22, 23].

Consistent with previous findings, the presence of vascular signs increased the likelihood for people with dementia to receive antidepressants, despite crude rates of antidepressant use for people with MD/VaD were globally similar to those for people with AD (data not shown). Unfortunately, the BNA does not provide information regarding the

Table 1
Demographic characteristics according the diagnosis – BNA ($N = 199,544$)

	All ($N = 199,544$)		AD ($n = 130,437$)		MD ($n = 47,318$)		VaD ($n = 21,789$)	
	n	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Age at first consultation with the diagnosis								
≤75 years	29,204	(14.6)	20,777	(15.9)	4,712	(10.0)	3,715	(17.1)
76–80	39,853	(20.0)	26,450	(20.3)	8,980	(19.0)	4,423	(20.3)
81–85	61,469	(30.8)	39,860	(30.6)	15,264	(32.3)	6,345	(29.1)
>85	69,018	(34.6)	43,350	(33.2)	18,362	(38.8)	7,306	(33.5)
Gender								
Female	133,096	(66.7)	91,533	(70.2)	29,490	(62.3)	12,073	(55.4)
Male	66,448	(33.3)	38,904	(29.8)	17,828	(37.7)	9,716	(44.6)
Education								
No education / primary	116,697	(58.5)	74,415	(57.1)	29,276	(61.9)	13,006	(59.7)
Secondary 1st cycle	31,619	(15.9)	20,470	(15.7)	7,456	(15.8)	3,693	(17.0)
Secondary 2nd cycle	16,543	(8.3)	11,494	(8.8)	3,353	(7.1)	1,696	(7.8)
Superior	14,355	(7.2)	9,952	(7.6)	2,932	(6.2)	1,471	(6.8)
Unknown	20,330	(10.2)	14,106	(10.8)	4,301	(9.1)	1,923	(8.8)
Type of center								
Memory clinic	150,409	(75.4)	96,378	(73.9)	37,249	(78.7)	16,782	(77.0)
Regional specialized memory clinic	43,943	(22.0)	30,137	(23.1)	9,127	(19.3)	4,679	(21.5)
Private practice neurologist	5,192	(2.6)	3,922	(3.0)	942	(2.0)	328	(1.5)
Initially referred by								
GP	131,584	(65.9)	89,440	(68.6)	30,140	(63.7)	12,004	(55.1)
Neurologist	9,564	(4.8)	6,636	(5.1)	1,703	(3.6)	1,225	(5.6)
Other specialist	22,239	(11.1)	13,016	(10.0)	5,996	(12.7)	3,227	(14.8)
Direct	8,500	(4.3)	6,078	(4.7)	1,733	(3.7)	689	(3.2)
Others	27,657	(13.9)	15,267	(11.7)	7,746	(16.4)	4,644	(21.3)
Lifestyle at baseline								
Community-living	167,319	(83.9)	111,046	(85.1)	38,589	(81.6)	17,684	(81.2)
Long-term care facility	32,225	(16.2)	19,391	(14.9)	8,729	(18.5)	4,105	(18.8)
Location of the patient at baseline								
Within 50 Km from the memory clinic	184,406	(92.4)	119,775	(91.8)	44,337	(93.7)	20,294	(93.1)
>50 Km from the memory clinic	15,238	(7.6)	10,662	(8.2)	2,981	(6.3)	1,495	(6.9)
MMSE at first record								
0–10	24,761	(12.4)	17,968	(13.8)	5,156	(10.9)	1,637	(7.5)
11–20	103,348	(51.8)	67,439	(51.7)	26,169	(55.3)	9,740	(44.7)
21–30	71,435	(35.8)	45,030	(34.5)	15,993	(33.8)	10,412	(47.8)

AD, Alzheimer's disease; MD, mixed dementia; VaD, vascular dementia; GP, general practitioner.

mood status of people with dementia, and thus does not allow investigation of the potential relationship between depressive symptoms and increased risk of antidepressant prescribing for individuals with vascular signs.

Between 2010 and 2014, MMSE scores at the first record in the BNA tended to slightly increase (data not shown). This trend was similar for all diagnostic subgroups despite AD patients being more cognitively impaired at baseline compared to those patients with MD and VaD.

Concerning co-prescriptions, antidepressant medications were frequently associated with other psychotropic drugs, and more specifically with anxiolytic medications [24]. In the Swedish registry investigating newly diagnosed individuals with mild AD, 2.6% concurrently used ≥3 psychotropic medications [25]. Our results are in this line with these previous studies, showing an overall 20% frequency of the antidepressant-anxiolytic association. In the BNA, associations of 3 or more psychotropic medications were lower than 5%.

Antidepressant medications have been shown to be prescribed in dementia for different causes, from disturbing behaviors to depressive symptoms (around 25%) and major depressive disorders (around 50%) [3]. Reasons leading to antidepressant use, however, were not available in the BNA, that does not provide any information regarding associated disturbing behaviors and cannot report two associated diagnoses for a same patient (i.e,. dementia and associated depressive syndrome).

Evolution of antidepressant use between 2010 and 2014

Interestingly, we did observe an overall slight increase of antidepressant medications over the last

Table 2
Frequency of antidepressant prescription and psychotropic associations across years from 2010 to 2014. ChEIs = cholinesterase inhibitors

			2010	2011	2012	2013	2014
*At least one antidepressant prescription***							
	No	*n*	34,656	42,692	48,144	51,737	53,242
		%	74.1	70.9	70.1	70.1	68.4
	Yes	*n*	12,134	17,509	20,515	22,022	24,615
		%	25.9	29.1	29.9	29.9	31.6
	total		46,790	60,201	68,659	73,759	77,857
Psychotropic associations among patients receiving at least one antidepressant prescription							
Antidepressant only		*n*	7,041	9,939	11,570	12,406	13,491
		%	58.0	56.8	56.4	56.3	54.8
Antidepressant + hypnotic		*n*	670	1,010	1,211	1,257	1,361
		%	5.5	5.8	5.9	5.7	5.5
Antidepressant + hypnotic + antipsychotic		*n*	134	208	193	214	228
		%	1.1	1.2	0.9	1.0	0.9
Antidepressant + antipsychotic		*n*	641	976	1,072	1,144	1,285
		%	5.3	5.6	5.2	5.2	5.22
Antidepressant + anxiolytic		*n*	2,496	3,527	4,327	4,732	5,471
		%	20.6	20.1	21.1	21.5	22.2
Antidepressant + anxiolytic + hypnotic		*n*	525	808	948	969	1,141
		%	4.3	4.6	4.6	4.4	4.6
Antidepressant + anxiolytic + antipsychotic		*n*	463	769	898	982	1,227
		%	3.8	4.4	4.4	4.5	5.0
Antidepressant + anxiolytic + hypnotic + antipsychotic		*n*	164	272	296	318	411
		%	1.4	1.6	1.4	1.4	1.7
	total		12,134	17,509	20,515	22,022	24,615
Anti-dementia agents among patients receiving at least one antidepressant prescription							
Antidepressant + NMDA antagonist	No	*n*	8,430	12,895	15,982	17,279	17,842
		%	69.5	73.7	77.9	78.5	72.5
	Yes	*n*	3,704	4,614	4,533	4,743	6,773
		%	30.5	26.3	22.1	21.5	27.5
	total		12,134	17,509	20,515	22,022	24,615
Antidepressant + ChEIs	No	*n*	4,450	6,939	9,297	11,710	11,991
		%	36.7	39.6	45.3	53.2	48.7
	Yes	*n*	7,684	10,570	11,218	10,312	12,624
		%	63.3	60.4	54.7	46.8	51.3
	total		12,134	17,509	20,515	22,022	24,615
Antidepressant + ChEIs + NMDA antagonist	No	*n*	10,180	15,180	18,521	20,386	21,833
		%	83.9	86.7	90.3	92.6	88.7
	Yes	*n*	1,954	2,329	1,994	1,636	2,782
		%	16.1	13.3	9.7	7.4	11.3
	total		12,134	17,509	20,515	22,022	24,615

** $p < 0.001$.

5-year among elderly individuals diagnosed with AD, MD, or VaD in the BNA. Several hypotheses could be advanced to explain the increased prescription rate of antidepressants from 2010 to 2014.

A first possibility, as advanced in the introduction, is that the increase in the antidepressant use reflected changes over the time in prescribing habits. Use of anti-AD symptomatic agents (ChEIs and NMDA antagonists) has decreased in France after the publication, in 2012, of several warnings against this type of pharmacologic treatments (lack of efficacy and risk of adverse events) [26]. Safety warnings for antipsychotics in dementia likely led also to a decrease in antipsychotic prescribing [27]. Both anti-AD agents and antipsychotics could contribute to the management of behavioral and psychological symptoms in dementia, and their decreased use could have promoted antidepressant use as alternative pharmacologic treatment.

A second possibility is that the increase in antidepressant use over the time could be partially explained by the progressive inclusion in the BNA of less severe stages of people with dementia, likely having early behavioral disturbances such as depressive symptoms. This is confirmed by the evolution of the MMSE score at the first record: indeed we did observe a better cognitive status at first record between 2010 and 2014. The severity of behavioral and psychological

Table 3
Determinants of antidepressant prescription using GEE estimation – BNA ($N = 199,544$)

		multivariate GEE	
		Adjusted Odds ratio [CI 95%]	*p*-value
Years			
2010	1		
2011	1.19	[1.13; 1.26]	<0.001
2012	1.32	[1.24; 1.41]	<0.001
2013	1.42	[1.32; 1.52]	<0.001
2014	1.59	[1.49; 1.70]	<0.001
MMSE			
0–10	1.06	[1.03; 1.09]	<0.001
11–20	1.04	[1.02; 1.05]	<0.001
21–30	1		
Age at the time of the diagnosis			
≤75 years	1		
76–80	0.90	[0.84; 0.96]	0.001
81–85	0.82	[0.77; 0.87]	<0.001
>85	0.79	[0.75; 0.84]	<0.001
Gender			
Female	1.48	[1.41; 1.54]	<0.001
Male	1		
Education			
No education / primary	1		
Secondary 1st cycle	1.05	[0.99; 1.11]	0.093
Secondary 2nd cycle	1.21	[1.12; 1.30]	<0.001
Superior	1.15	[1.06; 1.25]	0.001
Unknown	0.90	[0.84; 0.97]	0.004
Type of centre			
Memory clinic	1		
Regional reference memory clinic	1.13	[1.10; 1.16]	<0.001
Private practice neurologist	0.45	[0.42; 0.48]	<0.001
Neuroleptic			
No	1		
Yes	1.56	[1.50; 1.61]	<0.001
Hypnotic			
No	1		
Yes	1.82	[1.76; 1.89]	<0.001
Anxiolytic			
No	1		
Yes	2.70	[2.63; 2.78]	<0.001
NMDA antagonist			
No	1		
Yes	1.20	[1.18; 1.22]	<0.001
ChEIs			
No	1		
Yes	1.33	[1.30; 1.35]	<0.001
Lifestyle			
Community-living	1		
Long-term care facility	1.25	[1.22; 1.28]	<0.001
Diagnosis			
AD	1		
MD	1.11	[1.08; 1.13]	<0.001
VaD	1.17	[1.13; 1.21]	<0.001
*Years * Gender* [1]			0.006
*Years * Level of education* [1]			0.025
*Years * Age at baseline* [1]			0.006

[1] significant interactions entered in the model.

symptoms tend to increase with the severity of the dementia [28]. However depressive symptoms are often early symptoms in the dementia process, and their prevalence remain steady during the evolution of the disease [28]. This interpretation cannot be tested directly because the BNA does not provide any specific information on the severity of depressive symptoms and their evolution over time.

Limitations of the present study

The BNA represents an interesting epidemiologic tool as it grants access to a large number of individuals in the field of dementia, and allows follow-up analyses of the study population, as we did in the present study. Despite the fact that the size and the follow-up for the dementia population make the BNA a quite unique database, several limitations should be noted.

First, data are entered into the BNA by different physicians; although they all follow standard criteria for diagnosis, there is no external verification that those criteria were met, and this may eventually decrease the reliability of the diagnostic code assigned to patients. Second, individuals included in the BNA are not fully representative of the total French population with AD and associated disorders; indeed, the BNA includes the great majority of people with AD and associated disorders that is referred by specialized centers (French memory units), but one part of the population with dementia is under GP supervision only (GPs do not have currently access to the BNA), and another part of the population is referred by specialists (geriatricians, neurologists, psychiatrists) from private practice that are not using the BNA database. Finally, available information on antidepressant medications in the BNA does not provide a highly complete set of information: for instance the type of antidepressant (tricyclic antidepressants, SSRIs, others), the daily dose, the antidepressant commercial name, and the reasons leading to antidepressant prescribing are not available. Additionally, the history of depression and the severity of associated behavioral and psychological symptoms are not provided in the BNA.

Future studies employing different databases would be important to verify whether the observed trend of increased antidepressant prescribing over time does extend to non-French populations with dementia, and whether similar results can be obtained with a patient population not referred to specialized memory centers.

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SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: http://dx.doi.org/10.3233/JAD-160238.

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