The French National Alzheimer Database

A fast growing database for researchers and clinicians[1]

The number of patients with dementia grows steadily due to the increasing life expectancy of elderly people. This trend causes a major public health problem and creates a social and economic burden throughout the world. In 2010, it was estimated that 35.6 million people lived with dementia resulting in a total worldwide cost of dementia of US$604 billion [1,2]. The EURODEM study reported an age standardized prevalence of dementia of 6.4% [3]. For France, prevalence rates vary between 9.2% for elderly above 70 years and 17.8% above 75 years of age [4-6]. Recently published projections show that the number of people suffering from Alzheimer dementia in the USA will nearly triple between 2010 and 2050 [7]. The need for valid prevalence figures on dementia and knowledge about related risk factors in the light of this ever increasing number of patients is more than obvious.

Therefore, in 2008 the third French National Plan for "Alzheimer and Related Disorders" 2008-2012 was launched, having the following objectives: to strengthen research on Alzheimer's disease and related disorders, to promote earlier diagnosis and to improve both patient management and support for carers. One specific part of this plan resulted in the creation, in 2009, of the French National Alzheimer Database (BNA), aiming to provide epidemiological data as well as activity indicators for all French memory centres. The information collected in the BNA consists of a limited set of data concerning demographic, diagnostic and clinical details, defined by national consensus [8]. The number of variables is restricted to facilitate and enhance the participation in this national database. Participants are the French memory units (memory centres and the memory resource and research centres) and independent specialists.

The objective of this document is to report the degree of national coverage of the BNA and to describe the demographic and medical characteristics of the patients registered in this national registry during the period 2009-2012. The future applications of the French National Alzheimer Database in terms of research and policy-making possibilities will be discussed.

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Material and Methods

The French National Alzheimer Database (BNA) contains 31 items, amongst others demographic data on the patient, diagnostic details, the type of care carried out during the patient's visit to the centre and clinical measures such as the MMSE (Mini Mental State Examination [9]). Every participating centre or independent specialist has its own online access used to forward data and to query the national database for anonymous data. A detailed description of the BNA has already been published [8].

The BNA was launched end of 2009. Since the implementation of the first Alzheimer Plan in France in 2001, the organisation of testing and follow up for dementia has been based on a nationwide network comprising memory units divided into memory centres (*CM: Consultations Mémoire*) and memory resource and research centres (*CMRR: Centres Mémoire de Ressources et de Recherche*). The CMRRs, located in teaching hospitals, have also teaching and research functions and are responsible for supervising the CMs. This public health service network is supplemented by independent specialists (neurologists, geriatricians and psychiatrists), who also play a role in the diagnosis and follow up of Alzheimer disease patients. The French Ministry of Health (*DGOS: Direction Générale de l'Offre de Soins*) holds a detailed list of all existing memory centres and memory resource and research centres in Metropolitan France and overseas regions. Using this list, the national coverage rate of the different memory units (CM and CMRR) participating in the BNA by the end of 2012 was calculated. The number of independent specialists sending data to the BNA was also determined.

In the BNA every consultation or other medical act is recorded as a separate record. Therefore, one patient can figure more than once in the BNA, depending on the number of medical acts he underwent. The total number of consultations and other medical acts in the BNA is defined by the number of records in the BNA at a certain date, for this study the 31st of December 2012. To determine the total number of patients registered in the BNA, every single patient was only counted once using the unique identification number attributed to each patient. The total number of medical acts per patient by the end of the study period was also studied. To describe the patient's characteristics, the last record of the patient was used for patients with multiple records in the study period. If data on a certain characteristic was missing in the last record, it was retrieved from the previous record if existing.

The BNA differentiates 38 diagnostic groups, based on the ICD-10 classification. In this study the diagnoses were aggregated into 8 subgroups: Alzheimer disease; Related disorders; Mild cognitive impairment (MCI); Depression and other psychiatric disorders; Subjective memory complaint; Other neurological disorders; Other; and Diagnoses pending. If the diagnosis of a patient changed during the study period, the last stated diagnosis was used in this study. Similarly, if a patient had several records containing a MMSE score, the latest score was taken into account. Educational level, coded in 6 categories in the BNA was recoded to no formal education; primary school; secondary school; and post-secondary/tertiary education. Place of living was defined as follows: Living alone; Living with family or family nearby; Hospital; Nursing home; and other. The MMS score was categorised into groups of cognitive impairment: score 0-9 as severe impairment; 10-19 as moderate; 20-26 as mild and 27+ as no impairment.

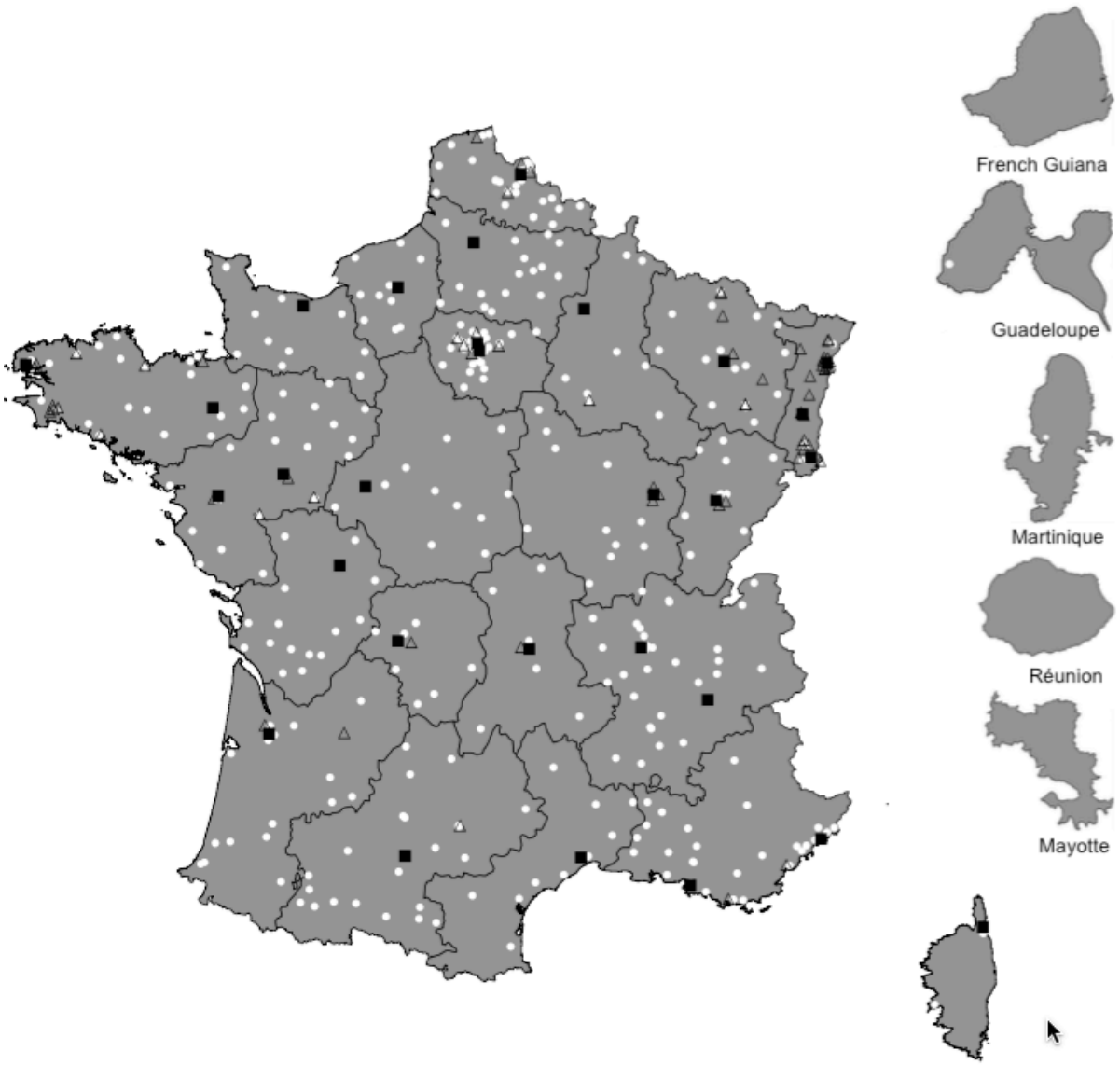
Data extracted from the BNA were processed using SAS Enterprise Guide, version 4.1.

Results

During the studied period 2009-2012, the participation rate of the French memory units and independent specialists increased steadily. By the end of 2012, of the 427 memory units initially described in France [8], 357 units (83.6%) submitted data to the BNA (28/28 CMRRs and 329/399 CMs). The total number of independent specialists contributing data to the BNA on a voluntary basis increased from 33 in 2010 [8] to 65 by the end of 2012.

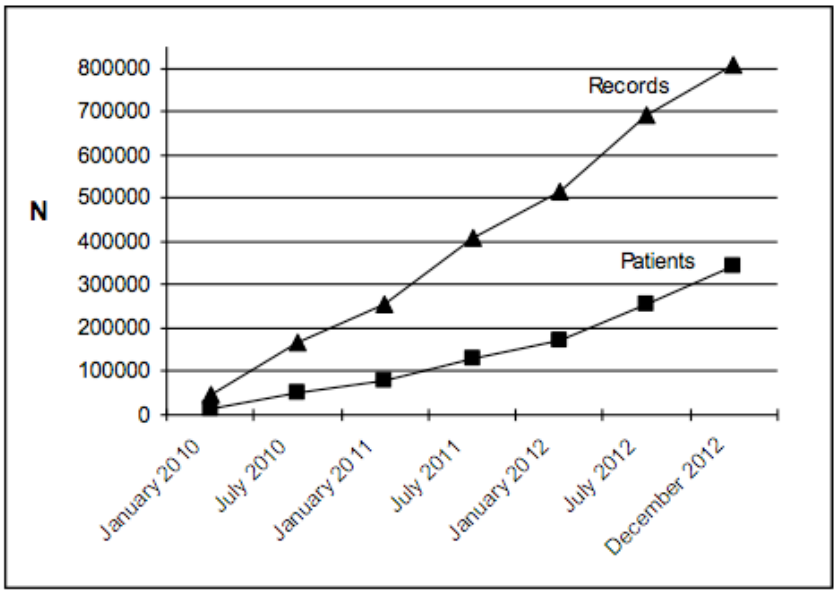
Figure 1 shows the geographical distribution of all the participating CMRRs, CMs and independent specialists in France including the French overseas departments. In Metropolitan France certain regions have a high concentration of memory units and independent specialists (e.g. Paris region and northern France) whereas in other regions the distribution is sparser (regions in the middle of France). Only two overseas regions have memory consults so far.

Figure 1. Geographical distribution of the participating memory units (■ = memory resource and research centres; O = memory centres) and independent specialists (∆) in France and overseas regions by the end of 2012



The number of registered patients in the BNA increased significantly, from 12,455 patients on January, 1st, 2010 to 341,498 patients on December, 31st, 2012

Figure 2. Number of patients and number of consultations and other medical acts registered in the French National Alzheimer Database during the period 2009-2012



Since January 2012, the increase in the number of registered patients is even more pronounced than before. In parallel the number of registered medical records (medical acts such as consultations, neurological examinations etc.) included in the BNA also steeply increased, reaching over 800,000 acts by the end of 2012. Due to the inclusion of both new patients and all medical acts performed per patient over time, the slope of the total number of records rises even steeper than the number of patients. In 2010, most patients had only one record included in the BNA (62%) and patients with a follow-up of more than 2 records represented only 14% of the total population. By the end of 2012, patients with more than 2 records represented 30% and the number of patients having 4 or more records had increased from 5% to 17% (table 1).

Table 1 presents the patients' characteristics of all patients registered in the BNA by the end of 2012. Overall, patients had a mean age of 76.4 years, women being on average older than men (77.5 years *vs* 74.5 years). The mean age for Alzheimer patients is 81.9 years old, for patients with related disorders it is 79.3 years and for patients with mild cognitive impairment the mean age is 75.1 years. Table 1 also shows the distribution of the educational level and the place of living of all patients registered in the BNA. Most of the patients live at home together with their family or family geographically close. The mean MMSE score of the patients registered in the BNA is 20.9 (20.5 for women and 21.6 for men). Sixty three percent of the patients have a pharmacologic treatment and 24% of the patients undergo psychosocial interventions such as psychotherapy. Around 30% of the patients are registered by the CMRR.

Table 1. Patients' characteristics of all patients (N=341,498) registered in the French National Alzheimer Database (BNA) by the end of 2012

	TOTAL				FEMALES				MALES			
	N	**%**	**Mean**	**SD**	**N**	**%**	**Mean**	**SD**	**N**	**%**	**Mean**	**SD**
Total population	341,498	100			215,113	63.0			126,385	37.0		
Mean age (yrs)			76.4	12.9			77.5	12.4			74.5	13.4
Educational level												
No formal education	24,562	7.2			16,423	7.6			8,139	6.4		
Primary school	141,739	41.5			97,550	45.4			44,189	35.0		
Secondary school	98,354	28.8			57,985	27.0			40,369	31.9		
Post-secondary/tertiary education	37,128	10.9			17,921	8.3			19,207	15.2		
unknown	39,715	11.6			25,234	11.7			14,481	11.5		
Place of living*												
Living alone	32,034	9.4			24,491	11.4			7,543	6.0		
Living with family or family nearby	240,967	70.5			142,121	66.1			98,846	78.2		
Nursing home	34,108	10.0			25,656	11.9			8,452	6.7		
Hospital	8,598	2.5			5,155	2.4			3,443	2.7		
Other	25,791	7.6			17,690	8.2			8,101	6.4		
MMSE score†			20.9	6.9			20.5	6.9			21.6	6.7
Pharmacologic treatment												
Yes	223,670	62.5			144,671	67.3			78,999	62.5		
No	117,828	34.5			70,442	32.7			47,386	37.5		
Psychosocial intervention (e.g. psychotherapy, physio-therapy, speech therapy)												
Yes	82,357	24.1			54,406	25.3			27,951	22.1		
No	259,141	75.9			160,707	74.7			98,434	77.9		
Type of centre												
CMRR	100,955	29.5			60,787	28.3			40,168	31.8		
CM	231,769	67.9			149,130	69.3			82,639	65.4		
Independent specialist	8,774	2.6			5,196	2.4			3,578	2.8		
Number of medical acts per patient												
1	164,659	48.2			103,201	48.0			61,458	48.6		
2	73,910	21.6			47,097	21.9			26,813	21.2		
3	44,284	13.0			28,145	13.1			16,139	12.8		
4 or more	58,645	17.2			36,670	17.0			21,975	17.4		

Table 2 shows the distribution of the diagnostic categories defined for the patients registered in the BNA. Out of a total of 341,498 patients, Alzheimer's disease (AD) accounted for 26.4% of all diagnoses, related disorders for 21.7% and Mild Cognitive Impairment (MCI) for 8.7%. The category "diagnoses pending" represents also a large category (20.3%). Gender differences are observed in the diagnostic distribution, for example AD is diagnosed in 30% of the women and 21% of the men.

Table 2. Diagnoses of patients recorded by the end of 2012 in the French National Alzheimer Database (BNA), by gender

			Females		**Males**	
Diagnostic category*	**N**	**%**	**N**	**%**	**N**	**%**
Alzheimer disease	90,176	26.4	63,638	29.6	26,538	21.0
Related disorders	73,982	21.7	42,030	19.5	31,952	25.3
Mild cognitive impairment (MCI)	29,571	8.7	17,470	8.1	12,101	9.6
Depression and other psychiatric disorders	32,817	9.6	22,499	10.5	10,318	8.1
Subjective memory complaint	27,951	8.2	17,631	8.2	10,320	8.2
Other neurological disorders	16,859	4.9	7,978	3.7	8,881	7.0
Other	787	0.2	526	0.2	261	0.2
Diagnoses pending	69,355	20.3	43,341	20.2	26,014	20.6

In Table 3 the distribution of the last registered MMSE scores is presented by diagnostic category. Within the group of Alzheimer patients, 57% has severe or moderate cognitive impairment. The mean MMSE score is 16.4 for AD patients, 18.5 for related disorders and 25.6 for MCI. The number of registered patients without MMSE is significant.

Table 3. Cognitive impairment based on the MMSE score for patients registered in the BNA by diagnostic category

	Cognitive impairment*				
Diagnostic category	**severe** (%)	**moderate** (%)	**mild** (%)	**no impairm.** (%)	**unknown (%)**
Alzheimer disease	12.8	44.0	28.5	2.9	11.8
Related disorders	7.8	36.1	32.7	8.5	14.9
MCI	0.3	4.5	42.2	42.7	10.3
Depression and other psychiatric disorders	1.1	8.5	31.8	43.9	14.7
Subjective memory complaint	0.5	3.4	22.5	59.6	14.0
Other neurological disorders	1.4	9.6	27.6	32.6	28.8
Other	1.4	11.7	38.4	35.3	13.2
Diagnoses pending	2.5	19.9	34.4	22.9	20.3

Table 4 shows that the place of living is related to the diagnosis of the patient. The majority of patients registered in the BNA still live at home, the major part surrounded by their family. However, for the group of Alzheimer patients 8% (n=7191) still live at home alone. For the related disorders this percentage is 6.7%. 15% of both Alzheimer patients and patients with related disorders registered in the BNA are institutionalised in a nursing home.

Table 4. Place of living (%) for the patients registered in the BNA by diagnostic category

	Place of living*				
Diagnostic category	**Living alone**	**Living with family or family nearby**	**Nursing home**	**Hospital**	**Other**
Alzheimer disease	8.0	68.6	15.3	1.3	6.8
Related disorders	6.7	68.2	15.4	2.9	6.8
MCI	10.0	80.4	3.0	0.8	5.8
Depression and other psychiatric disorders	13.2	70.2	5.7	3.5	7.4
Subjective memory complaint	13.1	75.7	2.0	1.3	7.9
Other neurological disorders	7.7	76.0	3.7	3.3	9.3
Other	11.6	66.7	7.4	5.3	9.0
Diagnoses pending	10.9	68.3	7.1	4.2	9.5

Comments

By the end of 2012, all 28 specialised French memory resource and research centres (CMRR) participated in the BNA and a majority of the other memory centres (CM), resulting in a national participation rate of all memory units of 84%. This represents an increase in participation since 2010, year in which the reported participation rate was 75% [8]. The number of participating independent specialists also increased during the same period, but remains small. In order to increase the participation incentive, the government established an official Memory Consultation Label by the end of 2011. One of the criteria to obtain this official label is the mandatory participation in the French National Alzheimer database. Another stimulus has been given beginning of 2013 by the French Court of Auditors recommending that participation should be compulsory for all memory units.

The number of patients registered in the BNA underwent an impressive increase since the end of 2009, reaching almost 350,000 patients by the end of 2012. This increase in newly registered patients is even more important since January 2012, after implementing the above mentioned official Memory Consultation Label.

By the end of 2012, the number of registered medical acts in the BNA for this group of patients exceeded 800,000 records. Apart from the ever increasing number of medical acts due to newly registered patients in the BNA, there is also a significant increase in the number of patients having more than one record registered. The BNA is designed to enable longitudinal, prospective research on patients. With time, more and more patients will have several records in the BNA enabling follow-up

and longitudinal analyses. By the end of 2012, 17% of the patients had already 4 or more records in the database, representing a group of more than 58,000 patients.

This document illustrates some of the research possibilities using the BNA. The place of living is interesting when studying the social burden for families or the economic burden for the society [2]. Our data show that the majority of patients consulting for AD, related disorders or other neurological problems live together with their family or with their family geographically close, emphasizing the huge impact on the informal caregivers.

The patients' characteristics observed in the BNA population correspond to the ones described in the literature, confirming the validity of the registered data. The database contains more women than men (63% vs 37%) and more women were diagnosed AD than men (30% vs 21%). This reflects first of all a known difference in survival between men and women, women dying at an older age than men and therefore having more time to develop dementia. This finding is, however, even more emphasized by the fact that even after taking into account age differences, women are known to have a higher prevalence of AD than men [4,12,13]. Gender differences are also described in the diagnostic workup to assess AD and in the disease evolution [14,15], both items that can also be studied using longitudinal BNA data.

The recording of educational level in the BNA is a great asset of this database. It allows research to take this variable into account as the literature describes a relationship between education and the prevalence of dementia and in particular AD [12,13,16].

The BNA includes a wide variety of diagnoses including the main categories AD, related disorders, MCI but also subjective memory complaints and depression. This enables research on different patient groups. One in five patients has his diagnosis still pending. This represents an important group of patients in the BNA and future efforts should be undertaken to reduce this category, for example by sending reminders to the caregivers if the diagnosis is not specified after a defined period.

A chronic pharmacologic treatment is taken by 63% of the registered patients. This percentage was even higher for female patients. In the literature, percentages of 16% to 22% have recently been reported specifically for antipsychotic use among persons with AD or related disorders [17-19]. Specific analyses on drug use are possible using the BNA as eight different drug categories are distinguished in the register, e.g. acetylcholinesterase inhibitors, NMDA receptor antagonists, neuroleptics, anxiolytics etc. Drug use in patients with mild cognitive impairment was studied using the BNA data [20]. The relationship between treatment use and place of living was also determined as there are reported differences in drug use between patients still living at home and patients living in nursing homes [21]. Similar analyses can be performed studying the use of psychosocial interventions such as psychotherapy.

The mean MMSE score for all patients registered in the BNA is 21, all diagnostic categories combined. For AD patients it is 16.4, for patients with related disorders it is 18.5 and for MCI patients it is 25.6. In their French prospective population based cohort, Ramaroson et al. reported that 59% of their demented patients (80% of which had AD and all aged 75 years and over) had severe or moderate cognitive impairment [5]. For the AD population registered in the BNA, that is younger than the above mentioned cohort, this percentage is 57%. At the moment, two research studies are ongoing both examining the MMSE scores registered in the BNA. The first is determining the relationship between

the MMSE score and the patient's demographic characteristics. As the BNA is designed to provide follow-up data on a patient's level, the other research is focussing on the evolution of the patient's MMSE score over time.

For the moment, it remains difficult to try to interpret the reported diagnostic group percentages as French prevalence figures for the different diseases. First of all, the participation rate of the memory units is not yet 100% and the independent specialists start participating. Therefore, the BNA does not cover all patients and all parts of France yet. In the literature geographical differences (between countries but also regional differences within a country) have been described in reported dementia prevalences [13,22]. Second, there might be differential reporting as the participation rate depends on the type of centre and caregiver. Variations in diagnosis between different kinds of caregivers have been described [22]. Thirdly, there is still a large group of patients in the BNA for whom the diagnosis is still pending (20%) and this is not negligible when trying to calculate prevalence data. Another aspect, are the patients living in nursing homes and homes for elderly. These homes do not participate in the BNA and it is known that the major part of their residents never consult a memory unit or independent specialist, a trend that is only accentuated with increasing age of the patients. For the moment, only 10% of the registered patients in the BNA are referred by the nursing home where they live. A last factor concerns the not negligible proportion of demented patients that remain undiagnosed in the general population or patients that only consult a general practitioner. Taking all these factors in consideration, we conclude that for the moment the BNA does not cover the entire population of patients with dementia and therefore one should be extremely cautious trying to extract valid French prevalence figures from it yet.

Before data enter the BNA, inconsistency checks are performed on different levels. For example, records with missing values in compulsory variables are rejected and invalid dates are also not accepted and should be corrected before entering the BNA. Another new item of the ongoing quality control procedure of the BNA is the feedback giving to all participating centres by means of a six-monthly report. This report describes for each specific centre or independent specialist, the number of newly included patients from the beginning of their participation and in the last six month period and provides feedback on detected incoherencies. For example, patients diagnosed as MCI with a MMSE score below 10 or patients with a missing MMSE score since more than 6 months are listed. Recently a new computer application has been launched facilitating free Web based data entry to the BNA and incorporating even more internal inconsistency checks. All these aspects help to improve the quality of the registered data.

The French National Alzheimer Database provides both for policy makers and for participating centres ongoing information on amongst others Alzheimer disease. Analyses of the data can be used to prepare activity reports but can also lead to research hypotheses and improvements in patient care. Using the BNA, correlations can be explored between Alzheimer Disease, other related disorders or the MMSE score on the one side and demographic, social or medical variables on the other side. Although the BNA provides a minimum dataset in comparison with other datasets containing biological, histological or a multitude of clinical data, its advantage is of course its size and statistical

power. More and more epidemiologic and clinical research is going on using the data resulting from the BNA.

In their articles Prince et al. [1] and Misiak et al. [10] both conclude that all countries need to commission nationally representative surveys that are repeated regularly to monitor trends in dementia. They also emphasize the necessity to evaluate these trends with regard to demographic factors such as age, gender and educational level. This confirms the relevance and importance of continuing the current French National Alzheimer database. In view of the ever growing impact of Alzheimer disease and related disorders due to the aging population and taking into account the huge burden it places on people with the disease, their caregivers and the society, the monitoring of this trend and related factors is getting more than ever important. The French National Alzheimer database will play a major role in this, the coming years.

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