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Neuropsychological tests for the diagnosis of dementia: results of a survey in Italian memory clinics

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Neuropsychological tests for the diagnosis of dementia: results of a survey in Italian memory clinics

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ABSTRACT

Aim. Providing an overview of the neuropsychological tests used in Italian memory clinics for the assessment of cognitive disorders and dementias.

Methods. Out of all 536 active Centers for Cognitive Disorders and Dementias (CCDDs), 501 were surveyed between February 2014 and August 2015 to verify the characteristics of the centers who performed, as part of the diagnostic process, a comprehensive neuropsychological assessment (NPA), defined as the administration of at least one test for verbal and visual episodic memory, attention, constructional praxis, verbal fluency, and executive functions (Minimum Core Tests - MCT).

Results. A total of 45.7% of Italian CCDDs performed a comprehensive MCT as part of the diagnostic process. The logistic regression model showed that the probability of including at least one psychologist in the team was higher in the CCDDs that reported using a comprehensive NPA (OR=4.547; 95% CI: 2.9192-7.100), that CCDDs in Southern Italy had a lower probability of using an MCT (OR = 0.559; 95% CI: 0.352-0.887), and that the use of an MCT was higher in University/ISRH CCDDs (OR = 10.967; 95% CI: 3.849-31.250).

Conclusion. Almost half of the CCDDs perform a set of MCTs; in the others only few tests or screening procedure are administered. Neuropsychological tests used in Italian CCDDs are comparable to those used in other European countries. Since a comprehensive NPA remains the best way to assess and monitor cognitive deficits over time, it is of extreme importance to raise a debate on the current status of NPAs in clinical practice.

Article summary (strengths and limitations of this study)

- The study provides an overview of the frequency of use and the availability of neuropsychological assessment (NPA) in Italian memory clinics. Collected data refer to a

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large and representative number of Italian CCDDs (501 out of all the 536 active CCDDs were surveyed).

- A definition is proposal of what to consider as comprehensive NPA in the diagnostic process of dementia, and considerations are made on the adequacy of the neuropsychological tests currently available in clinical practice
- the study represents a first attempt to describe how to approach cognitive testing in patients with dementia within the national public health system
- a possible limitation of the study is its being based on data from self-reported questionnaires, administered to health professionals in charge of enrolled CCDDs.

Key words

Neuropsychological test; Memory clinic; Survey research; Dementia; Alzheimer disease, Diagnosis;

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INTRODUCTION

Cognitive testing is consistently considered as extremely relevant in the diagnosis and follow-up of patients with dementia. International guidelines[1-2] specifically address its use in addition to clinical investigation - the so-called incremental validity[3]. A neuropsychological assessment (NPA) needs not only to define the severity of dementia, but also to confirm a diagnostic hypothesis. Once dementia is diagnosed, a simple "omnibus" test (e.g. Mini-Mental State Examination – MMSE; Milan Overall Dementia Assessment - MODA) can provide a deterioration score, which is useful for the clinical monitoring over time[4]

However, when cognitive complaints are subtle and patients still maintains normal daily life activities, preclinical impairments can only be detected through a comprehensive NPA. The choice of a specific tool can vary (for a review, see Ngo and Holroyd-Leduc[5]), but it should always be proven to have strong psychometric properties.

Over the years, great efforts were made to harmonize and uniform the cognitive assessment in dementia. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD) was created in 1986 by the National Institute of Aging (NIA) to standardize the procedures for the evaluation and diagnosis of patients with Alzheimer's disease (AD). They elaborated a neuropsychology battery including tests for verbal fluency and naming, the MMSE, word list recall and recognition, constructional praxis, and recall of constructional praxis. Word list recall, in particular, was found to be the best at distinguishing between patients with AD and healthy controls[6]. Some years later, the AD Center (ADC) program of the NIA conducted a survey to gather data about assessment practices, including those for cognitive domain. The study designed a brief cognitive battery, to be used in ADCs for the assessment of cognitive abilities in elderlies either without dementia, or with MCI or AD[7]. However, as the authors pointed out, it provided a good first evaluation, but it did

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not prove as an appropriate substitute for a comprehensive NPA. Moreover, differently from the CERAD battery, it did not result as an adequate tool to detect subtle impairments[8].

As for Europe, the EFNS (European Federation of Neurological Societies) task force performed a survey on the neuropsychological tests used to detect dementia in 25 countries, with the objective of harmonizing their use across these countries[9]. The survey identified 213 different tools, and not all of them were validated in each country. For example,18-21 countries reported using verbal memory tests, but such tests were validated only in 11-14 of these countries. Such a finding highlighted a crucial issue, that is, the psychometric solidity of the tools and their reliability in clinical practice. It also underlined a difficulty in selecting which tests are to be used in dementia, due to differences in the cultural context, in clinical and research practice, and in health care policies.

More recently, further recommendations were proposed for a comprehensive NPA[10-11], as it may be a good indicator of a future progression from subtle impairments to AD. Based on four international experiences and a review of the literature, irrespective of the suggested variability in cognitive tests, these recommendations pointed out the need of exploring the major cognitive domains – that is, episodic memory, constructional praxis, attention, verbal fluency and executive functions (Table 1).

Table 1 - Neuropsychological assessment for dementia: comparison of test measures recommended by four international experiences and by a review of the literature

CERAD[6]	UDS[a][7]	CIMA-Q battery[10]	Finney *et al*[11]
Boston Naming Test Constructional praxis Mini-Mental State Exam Recall of constructional	Animal list generation Boston naming test Digit symbol Digit span forward & backward	Animal fluency Auditory Verbal Boston naming Digit Symbol Learning Test Line Object	Assessment (MOCA) Boston naming test COWAT Hopkins / California verbal learning test

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praxis Verbal Fluency Word list memory Word list recall Word list recognition	Logical Memory, story A Mini Mental State Exam Trail Making Test (A - B) Vegetable list generation	decision Orientation Rey Trail Making Test (A-B)	Mattis Dementia Rating Scale Mini Mental State Exam Montreal Cognitive Rey-Osterrieth complex Figure Stroop test Trail Making Test (A- B) Wisconsin card sorting test
[a] low sensitivity (73.6%) and specificity (70.8%) for MCI			

The Italian scenario

In 2000, the Italian Ministry of Health (MoH) and the Italian National Institute of Health (INIH, Istituto Superiore di Sanità) implemented the Cronos study[12]. About 500 MCs, also referred to as Alzheimer's Evaluation Units (AEU, Unità Valutative Alzheimer) were established among all Italian Regions, to coordinate the complex process of caring for individuals with conditions leading to dementia[13-14].

These centers were specifically dedicated to the diagnosis and management of Alzheimer's Disease (AD) and other dementias. Two surveys, one in 2002 and the other in 2006, were conducted to identify and characterize the activities carried out by the AEUs, allowing to assess the importance of the role of AEUs in the diagnosis and treatment of people with dementia, along with the wide variations at a regional and local level[13-14].

The 2002 survey showed a wide variability between AEUs, both in the type of cognitive tests, and their use. About 50% of AEUs declared to perform a NPA, but such a percentage was probably over-estimated due to an unclear definition of "*what*" a NPA should actually be. The ADAS-cog

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(Alzheimer's Disease Assessment Scale – cognitive subscale), for example, resulted as the more frequently used instrument, despite it being proven as useful for the monitoring, but not for the diagnosis. On the other hand, a test for episodic memory, attention and/or language was employed only in 5.6 (18.4%) of cases. The study highlighted two main issues: i) a higher probability of misdiagnosis in AEUs that do not use a NPA, and ii) a need to improve the psychometric properties of some tools. To the same purpose, Bianchi & Dai Prà[15] fully reviewed twenty years of Italian normative studies (1987 to 2007), and provided new standards to choose the best tools to be used in clinical practice. Authors suggested to use short batteries to test patients in the advanced stages of the disease, while they recommend to administer patients in preclinical stages a core assessment of episodic memory.

In 2014, the Italian "National Dementia Plan" (NDP), among other actions, renamed the existing memory clinics (AEUs) as "Centers for Cognitive Disorders and Dementias" (CCDD, Centri per i Disturbi Cognitivi e le Demenze), maintaining their central role in the network of health care and social care services, and recognizing the need to reorganize services for dementia in integrated care pathways[16]. Along with taking part in the development of the NDP, the INIH was also entrusted, within the 2013 program of research actions of the National Centre for Disease Prevention and Control (NCDPC), funded by the Ministry of Health (MoH), with the management of the national project: "Survey of the social and health services dedicated to dementias and creation of a specific website: Observatory for dementias".

As part of this project a new survey was conducted in 2015[17], whose methodology and methodological issues will be presented in a currently submitted paper (unpublished observation).

The aim of the present survey was to gather information about the NPA tools that are currently being used in clinical practice in the Italian CCDDs. Information on the presence and distribution of CCDDs all over the country, on the tools used for the diagnosis of dementia, and on the type of

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healthcare professionals included in the staff of the CCDDs, with a particular focus on psychologists, have been also collected and reported to raise a debate on the current status of NPAs in clinical practice.

MATERIALS AND METHODS

Surveyed services

A total of 536 CCDDs, already known and available structures, were surveyed from February 2014 to August 2015 at a national level. The methodology used to carry out the survey of all health and social services, either completely or partially refunded by the National Health Services, that are currently available in Italy for people with dementia, will be reported in an currently submitted paper (unpublished observation).

Survey questionnaire

A standardized form, designed to identify structure, process, and outcome indicators, was used to gather information on the type of NPA tools, and the clinical scales, tests and batteries used in CCDDs, for the diagnosis and assessment of dementias.

All tests, batteries, and clinical scales already validated in the Italian population were identified based on compendia of cognitive testing[18-19] and the recommendations issued by the Italian Neuropsychological Society[20] (Table 2). Identified tools were included in a list to be added in the survey questionnaire with the aim of collecting data on the neuropsychological tests currently used in Italian CCDDs for the diagnosis of dementias.

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Table 2 - Most frequently used neuropsychological tests, batteries and clinical scales in Italy

	Italian normative studies [Referencies]
Test or battery	
Digit-span	Orsini et al, 1987[21]
Corsi spatial span	Orsini et al, 1987[21]
Babcock' short-tale	Carlesimo et al, 2002[22]
Rey 15-word	Carlesimo et al, 1996[23]
Rey Complex Figure (RCF)	Carlesimo et al, 2002[22]
Attentional Matrices	Spinnler & Tognoni, 1987[24]
Stroop test	Caffarra et al, 2002[25]
Trail Making Test (TMT)	Giovagnoli et al, 1996[26]
Frontal Assessment Battery (FAB)	Appollonio et al, 2005[27]
Modified Wisconsin Card Sorting Test (MCST)	Caffarra et al, 2004[28]
Phonemic word fluency test (FAS)	Carlesimo et al, 1996[23]
Semantic word fluency test	Novelli et al, 1986[29]
Visual naming	Sartori et al, 1988[30]
Aachener Aphasia naming test (AAT)	Luzzatti et al, 1996[31]
Clock' drawing	Mondini et al, 2003[32]
Drawings copy	Carlesimo et al, 2002[22]
Oral-facial apraxia	Spinnler & Tognoni, 1987[24]
Ideomotor apraxia	Spinnler & Tognoni, 1987[24]
Coloured Progressive Matrices (CPM)	Carlesimo et al, 1996[23]
Standard Progressive Matrices (SPM)	Caffarra et al, 2003[33]
Mini-Mental State Examination	Measso et al, 1993[34]
Milan Overall Dementia Assessment (MODA)	Brazzelli et al, 1994[35]
Mental Deterioration Battery (MDB)	Carlesimo et al, 1996[23]
Alzheimer's Disease Assessment Scale (ADAS)	Fioravanti et al, 1994[36]
Clinical and Behavioral Scales	
Activities of Daily Living (ADL)	Katz ,1963[37]
Instrumental Activities of Daily Living (IADL)	Lawton & Brody, 1969[38]
Geriatric Depression Scale (GDS)	Yesavage et al, 1983[39]
Frontal Behavioral Inventory (FBI)	Alberici et al, 2007[40]
Insight Scale	Ott et al, 1996[41]
Neuropsychiatric Inventory (NPI)	Cummings et al, 1994[42]

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Information on the presence of a psychologist in the staff, on the type of service (being it part of a hospital, territorial, or university structure, or an Institute for Scientific Research and Healthcare (ISRH, Istituto di Ricovero e Cura a Carattere Scientifico), and on the overall percentage of patients that are annually assisted and receive a comprehensive neuropsychological assessment was also included.

Completed forms, administered to health professionals in charge of enrolled CCDDs, were collected through a specifically designed online platform, and data were exported for statistical analyses.

Proposed Minimum core tests

Neuropsychological tests were grouped according to cognitive and functional domains, based on compendia of cognitive testing[18-19] and the recommendations from the Italian Neuropsychological Society[20]: i) Screening test, ii) Batteries for global assessment, iii) tests for Memory, Attention, Executive functions, Constructional Abilities, iv) Emotional status and Behavior. As for Language, Naming tests were categorized separately from Semantic Fluency tests, due to their validation studies being of low quality.

According to the above mentioned recommendations[18-20], we defined a *Minimum Core Tests* (MCT) as an appropriate comprehensive NPA within the diagnostic process. Our definition of MCT required the inclusion in the NPA for the diagnosis of dementia of at least one test for both verbal and visual episodic memory, one test for attention, one test for constructional praxis, one test for verbal fluency, and one test for the executive functions.

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Statistical analysis

A Chi-square test was used for analyzing categorical variables. A regression logistic model was elaborated to assess the association between the use of a minimum core of neuropsychological tests and the geographical distribution and type of CCDDs. ORs and their 95% Confidence Intervals (CIs) were calculated within the model. P-values lower than 0.05 (5%) were considered as statistically significant. Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS- Version 23.0).

RESULTS

A total of 501 (93.5%) centers returned the completed forms: 219 (43.7%) from Northern Italy, 87 (17.4%) from Central Italy, and 195 (38.9%) from Southern Italy and the islands. The geographical distribution and type of CCDDs are reported in table 3.

Table 3 - Distribution of the Centers for Cognitive Disorders and Dementias included in the survey according to their type and geographical distribution

Type of CCDD	Geographical distribution			
	Northern Italy N (%)	Central Italy N (%)	Southern Italy N (%)	Total N (%)
Hospital	148 (67.6)	43 (49.4)	75 (38.5)	266 (53.1)
Territorial Services	53 (24.2)	31 (35.6)	112 (57.4)	196 (39.1)
University/ISRH	18 (8.2)	13 (14.9)	8 (4.1)	39 (7.8)
Total	219 (43.7)	87 (17.4)	195 (38.9)	501 (100)

CCDD – Center for Cognitive Disorders and Dementias

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Table 4 shows data on the use of NP tools in Italian CCDDs. Data collected within the current survey (2015) were compared with those collected within the 2002 survey.

Overall, a significant change in the use of neuropsychological tests was observed as compared to the 2002 survey ($\chi^2 = 36712.88$; $p < 0.0001$) (table 4).

Table 4 - Comparison between the Neuropsychological tests in use in Italian CCDDs in the current survey (2015) and those that were in use during the 2002 survey

	Tests in use during the 2002 survey[13-14]	**Tests in use during the 2015 survey**
Domains-Functions /Test	%	%
Memory		
Rey 15-words	11	65
Babcock' short-tale	11.2	69.6
RCF recall	-	52.2
Corsi spatial span	12	46.4
Digit-span	4.8	52.8
Visual memory	1.3	-
Language		
AAT	1.5	17.8
Visual naming	-	17
Semantic word fluency test	15.3	61.2
Token test	13.3	-
Constructional abilities		
Drawings copy	-	52.4
RCF – copy	5.6	55.4
Clock' drawing	9.7	83.6
Attention		
Stroop test	2.3	33.2
TMT-A	1.3	51.6
Attentional Matrices	18.4	54.4
Executive functions		
SPM	6.1	41.4
CPM	1.3	33.2
MCST	0.3	24.2
TMT-B	1.3	51.6
FAS	17.1	61.8

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Clinical and Behavioral Scales		
ADAS-cog	24	2.4
MDB	-	22.6
MODA	23.5	29.8
WAIS-R	3.1	-
MoCA	-	6.6

RCF: Rey Complex Figure; AAT: Aachener Aphasia naming test; TMT: Trail Making Test; SPM: Standard Progressive Matrices; CPM: Coloured Progressive Matrices; MCST: Modified Wisconsin Card Sorting Test; FAS: Phonemic word fluency test; ADAS-cog: Alzheimer's Disease Assessment Scale- cognitive subscale; MDB: Mental Deterioration Battery; MODA: Milan Overall Dementia Assessment; WAIS-R: Wechsler Adult Intelligence Scale-Revised; MoCA: Montreal Cognitive Assessment

A total of 229 (45.7%) of the included CCDDs reported using a comprehensive NPA for the diagnosis of dementia, meeting the criteria for the MCT (table 5).

Of the 229 CCDDs that reported using an MCT, 81.7% included a psychologist in the team (table 5). The majority of services using an MCT were reported in Northern Italy (55.5%) and were hospital services (60.3%), while the lower frequency was reported in Southern Italy and the Islands (25.3%) (table 5).

Table 5 - Geographical distribution, type of structure, and presence of at least a psychologist in the Center for Cognitive Disorders and Dementias using and not using a Minimum core set of neuropsychological tests.

	Use of a Minimum core set of neuropsychological tests		
	Yes (n= 229) (%)	**No (n=272) (%)**	**p value**
Geographical distribution of CCDDs			
Northern Italy	127 (55.5%)	92 (33.8%)	
Central Italy	44 (19.2%)	43 (15.8%)	0.001
Southern Italy and Islands	58 (25.3%)	137 (50.4%)	
Type of CCDD			
Territorial Services	57 (24.9%)	139 (51.1%)	
Hospital	138 (60.3%)	128 (47.1%)	0.001

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University/ISRH	34 (14.8%)	5 (1.8%)	
Psychologist (at least one)	187 (81.7%)	119 (43.8%)	0.001

CCDD: Center for Cognitive Disorders and Dementias

ISRH: Institute for Scientific Research and Healthcare

The logistic regression model showed that the probability of including at least one psychologist in the team was higher in the CCDDs that reported using a comprehensive NPA (OR=4.547; 95% CI: 2.9192-7.100), that CCDDs in Southern Italy had a lower probability of using an MCT (OR = 0.559; 95% CI: 0.352-0.887), and that the probability of using an MCT was higher in University/ISRH CCDDs (OR = 10.967; 95% CI: 3.849-31.250) (Table 6).

Table 6 - Regression logistic model on the use of a minimum core of neuropsychological tests in Centers for Cognitive Disorders and Dementias

	OR	95% CI		p value
		Lower	Upper	
Psychologist (at least one)				
Not	1.00			
Yes	4.55	2.91	7.10	0.001
Geographical distribution of CCDDs				
Northern Italy	1.00			
Central Italy	1.13	0.63	2.02	0.685
Southern Italy - Islands	0.56	0.35	0.89	0.014
Type of CCDD				
Territorial Services	1.00			
Hospital	1.96	1.28	3.02	0.002
University/IRCSS	10.97	3.85	31.25	0.001

CCDD: Center for Cognitive Disorders and Dementias

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DISCUSSION AND CONCLUSION

The present survey provides an overview of use and availability of NPA in Italian CCDDs. Previous reports also gathered information on the tools used to assess and diagnose dementia, but they either included a limited number of centers[43], or involved only representatives of national neurological associations[9]. Our study, instead, focused on healthcare centers directly dealing with dementia, thus it represents a first attempt to describe how to approach cognitive testing in patients with this condition within the public national health system.

The first relevant finding was a considerable difference both in the type of tools adopted and in their use between the 2002 survey and the present one. Some of the tools were less frequently used due to either their low sensitivity (e.g. Visual Memory), or their inadequacy in identifying dementia (WAIS-r). Some other tools, having been introduced in clinical practice as a consequence of their diffusion as an outcome measure in clinical trials on cholinesterase inhibitors, now are considerably less widespread (e.g. ADAS-cog).

On the other hand, the use of some key tools for the early diagnosis of dementia, such as tests for episodic memory, phonemic and semantic fluency, executive functions, and constructional abilities, sensibly increased.

This might be explained by a progressive increase in the number of available cognitive tests between the year 1987, when the Study of Standardization by Spinnler & Tognoni[24] was published, and the year 2000, when the AEUs were created. During these 13 years, about 49 studies were carried out, and 64 during the next decade. This caused a progressive shifting from "historical" tests (e.g. the WAIS scales) to new tests, that better complied with the demographical changes of the population, and this trend is still ongoing (see Barletta-Rodolfi et al[20]).

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When comparing results from this survey with data from other European countries[9], no substantial differences were found in the type of tests used. All cognitive domains resulted to be assessed in a quite homogeneous way, despite a degree of variability in some tools (e.g. in language and verbal memory). Tests aimed at assessing abstract thinking (e.g. Raven's Progressive Matrices) resulted as widely used in Italy while they seemed to be not as frequently used in other European countries. All tests used in Italian structures were validated on the Italian population, thus resulted as having good psychometric properties.

Another relevant finding was that the majority of CCDDs administering an MCT had at least a psychologists in the team. About 46% of the centers offered an MCT, with significant differences between centers in Northern Italy and centers in Central and Southern Italy. Centers in Northern Italy seemed to show the best characteristics, while the centers in Central and Southern Italy seemed to have similar organizational characteristics. The importance of having a professional specifically trained to administer NPA tools has been highlighted since 1985, when the American Psychological Association (APA) defined and detailed the required standards for neuropsychological examiners[44]. Italy included these requirements within the expertise of professional psychologists (l. 56/89; D.M. 24/7/2006). However, uncertainties still exist on *who can do what*, thus the administration of neuropsychological (NP) tests should require supervised clinical training, and the scores from any NP test should be interpreted taking into consideration both neuroanatomical findings and results from cognitive and clinical psychology.

However, results from the present survey also showed that in more than half of the included CCDDs the screening procedures were mainly based on the administration of single, or at best few, rough cognitive (e.g. MMSE) and functional (e.g. ADL, IADL) tests. This lack of expertise brings back the issue of *what is an NPA and what is it thought to be*.

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The knowledge on the clinical manifestations of AD has considerably increased since 1984, when the NINCDS-ADRDA criteria were established for the diagnosis of probable AD[45].

NINCDS-ADRDA criteria were then revised by the NIA[46], to meet the need to clearly discriminate between AD and either other conditions leading to dementia (e.g. Frontotemporal Dementia, Primary Progressive Aphasia), and non-amnestic forms of AD.

Core clinical criteria for a diagnosis of all-cause dementia require the presence of cognitive or behavioral symptoms involving at least two cognitive domains among memory, judgment, visuospatial abilities, language and behavior. The new criteria, instead, to define a diagnosis of probable AD, require an either amnestic or non-amnestic significant initial cognitive deficit, and, in case of a non-amnestic AD, concomitant linguistic, visuospatial and executive dysfunctions.

Therefore, the NPA needs not only to quantify the deficit, but also to define its pattern, considering that each cognitive function have its neural network involving different brain areas[47].

However, short cognitive tests have become increasingly widespread in clinical practice, in particular in countries where healthcare policies are defined based on their cost-effectiveness, that is, on the costs of tools and instruments, the time needed to administer them, and the costs related to misdiagnoses (false positives and/or false negatives).

This kind of tests are currently being promoted by some international programs to optimize the cognitive screening in primary care[48-49], where a high prevalence of undiagnosed cases had been found[4]. However, the CCDDs, which were designed as secondary/tertiary referral units, should use them as part of the clinical examination, rather than adopt them as diagnostic tools, considering their intrinsic limitations (for a review, see Brown, 2016[50]).

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A comprehensive NPA, anyhow, still remains the best way to evaluate, quantify, and monitor cognitive deficits over time[47], and it should be the minimum requirement for the diagnosis of dementia.

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Conflict of interest: Authors have no conflict of interest to declare

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Use of neuropsychological tests for the diagnosis of dementia: a survey of Italian memory clinics

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ABSTRACT

Aim. Providing an overview of the neuropsychological tests used in Italian memory clinics (defined as Centers for Cognitive Disorders and Dementias – CCDD in Italy) for the diagnosis of cognitive disorders and dementias.

Methods. A total of 501 CCDDs, out of all 536 active CCDDs, were surveyed between February 2014 and August 2015 to verify the characteristics of the centers who performed a comprehensive neuropsychological assessment (NPA), defined as the administration of at least one test for verbal and visual episodic memory, attention, constructional praxis, verbal fluency, and executive functions (Minimum Core Tests - MCT), as part of the diagnostic process.

Results. A total of 45.7% of Italian CCDDs performed a comprehensive MCT as part of the diagnostic process. The logistic regression model showed that the probability of including at least one psychologist in the team was higher in the CCDDs that reported using a comprehensive NPA (OR=4.55; 95% CI: 2.92-7.1), that CCDDs in Southern Italy had a lower probability of using an MCT (OR = 0.56; 95% CI: 0.35-0.89), and that the use of an MCT was higher in University/ISRH CCDDs (OR = 10.97; 95% CI: 3.85-31.25).

Conclusion. Almost half of the CCDDs administered a set of MCTs; while the remaining centers only performed few tests or screening procedures. The neuropsychological tests used in Italian CCDDs were comparable to those used in other European countries. Performing a comprehensive NPA remains the best way to assess and monitor cognitive deficits over time, thus further debate on the current status of NPAs in clinical practice is needed.

Article summary (strengths and limitations of this study)

- The study provides an overview of the frequency of use and the availability of neuropsychological assessment (NPA) in Italian memory clinics (defined as Centers for

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Cognitive Disorders and Dementias – CCDD in Italy). Collected data refer to a large and representative number of Italian CCDDs (501 out of all the 536 active CCDDs were surveyed).

- a limitation of the study is its being based on data from self-reported questionnaires, administered to health professionals in charge of enrolled CCDDs which could potentially over-estimate the actual scenario.

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Key words

Neuropsychological test; Memory clinic; Survey research; Dementia; Alzheimer disease, Diagnosis;

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INTRODUCTION

Cognitive testing is consistently considered as extremely relevant in the diagnosis and follow-up of patients with dementia. International guidelines [1-2] specifically address its use in addition to clinical investigation - the so-called incremental validity [3]. A neuropsychological assessment (NPA) is aimed at defining the severity of dementia, but also at confirming a diagnostic hypothesis. Once dementia is diagnosed, a simple "omnibus" test (e.g. Mini-Mental State Examination – MMSE; Milan Overall Dementia Assessment - MODA) can provide a deterioration score, which is useful for the clinical monitoring over time [4]. However, in case of patients with subtle cognitive complaints but maintaining normal daily life activities, possible preclinical impairments can only be detected through a comprehensive NPA. The specific tool to be chosen in each case can vary (for a review, see Ngo and Holroyd-Leduc [5]), but it should always be proven to have strong psychometric properties.

Several attempts were made, over the years, to harmonize and uniform cognitive assessment in dementia. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD) was created in 1986 by the National Institute of Aging (NIA) to standardize the procedures for the evaluation and diagnosis of patients with Alzheimer's disease (AD). The neuropsychological battery proposed by CERAD includes tests for verbal fluency and naming, the MMSE, word list recall and recognition, constructional praxis, and recall of constructional praxis. The Word list recall test, in particular, was found to be the best in distinguishing between patients with AD and healthy controls [6]. In 2009, the AD Center (ADC) program of the NIA carried out a survey to gather data on assessment practices, including tools for the evaluation of the cognitive domain. The study designed a brief cognitive battery, to be used in ADCs [7]. However, as the authors pointed out, the battery resulted as appropriate for a first evaluation, but it did not prove as an adequate substitute for a comprehensive NPA. Moreover, it did not result as an adequate tool to detect subtle impairments as compared with the CERAD battery [8].

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As for Europe, the EFNS (European Federation of Neurological Societies) task force performed a survey on the neuropsychological tests used to detect dementia in 25 countries, with the objective of harmonizing their use across these countries [9]. The survey identified 213 different tools, pointing out that not all of them were validated in each country. Specifically, 18-21 countries reported using verbal memory tests, but only the tests used in 11-14 of these countries were validated. These findings highlighted the critical issue of the psychometric solidity of the tools used in clinical practice, and their reliability. It also underlined a difficulty in selecting which tests are to be used for the assessment and diagnosis of dementia, due to differences in the cultural context, in clinical and research practice, and in health care policies.

Further recommendations were recently proposed for a comprehensive NPA [10-11], as it may work as a good predictor of progression from subtle impairments to AD.,–These recommendations pointed out the need of exploring the major cognitive domains – episodic memory, constructional praxis, attention, verbal fluency and executive functions (Table 1).

Table 1 - Recommendations for Neuropsychological assessment for dementia:

CERAD[6]	UDS[a][7]	CIMA-Q battery[10]	Finney *et al*[11]
Boston Naming Test Constructional praxis Mini-Mental State Exam Recall of constructional praxis Verbal Fluency Word list memory Word list recall Word list recognition	Animal list generation Boston naming test Digit symbol Digit span forward & backward Logical Memory, story A Mini Mental State Exam Trail Making Test (A - B) Vegetable list generation	Animal fluency Auditory Verbal Boston naming Digit Symbol Learning Test Line Object decision Orientation Rey Trail Making Test (A-B)	Assessment (MOCA) Boston naming test COWAT Hopkins / California verbal learning test Mattis Dementia Rating Scale Mini Mental State Exam Montreal Cognitive Rey-Osterrieth complex Figure Stroop test Trail Making Test (A- B) Wisconsin card sorting test
[a] low sensitivity (73.6%) and specificity (70.8%) for MCI			

The Italian scenario

Italy is structured in 18 regions and 2 self-administered provinces, and its NHS is organized at national, regional, and local level. At a national level, the Ministry of Health, supported by several

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specialized agencies, establishes the basic principles and objectives of the health system, defines the core health services to be guaranteed across the country, and distributes to each region its quote of national funds. Regions are substantial self-administered in defining of the structure of their local health systems, and are responsible for organizing and delivering health care. At a local level, public and community health services, and primary care is directly delivered by local health authorities (Aziende Sanitarie Locali), while secondary and specialized care is either directly delivered by ASLs or accessible through public hospitals or accredited private structures.

The diagnosis, treatment and support of people with dementia within the Italian NHS is currently managed by different health and social health services. Memory clinics are defined, within the Italian NHS, as Centers for Cognitive Disorders and Dementias (CCDD) and can be based in public, territorial, outpatient services, hospitals or University hospitals, or Institute for Scientific Research and Healthcare (ISRH). The team of healthcare professionals involved in these centers includes neurologists, geriatricians and psychiatrists, and financial support is provided by the NHS. CCDDs are specifically dedicated to the assessment, diagnosis and management of dementias, and are entitled to prescribe specific pharmacological treatments for Alzheimer Disease (i.e. donepezil, rivastigmine, galantamine, memantine) and/or behavioral and psychological symptoms of dementia (i.e. antipsychotic drugs) based on the diagnosis and the treatment plan. In 2000, a first survey of all Italian CCDDs was performed within the Cronos study, a project implemented by the Italian Ministry of Health and the Italian National Institute of Health, that identified about 500 memory clinics in Italy.[12]

Two more surveys, one performed in 2002 and the second in 2006, aimed at identifying and characterizing the activities carried out by memory clinics. Their objective was to acknowledge the importance of the role of memory clinics in the diagnosis and treatment of people with dementia, but also to assess the wide variability in their distribution and characteristics at a regional and local level [13-14].

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The 2002 survey showed a wide variability between memory clinics, both in the type of cognitive tests adopted, and their use. About 50% of memory clinics declared to perform a NPA, but such a percentage was probably over-estimated due to an unclear definition of "*what*" a NPA should actually be. The ADAS-cog (Alzheimer's Disease Assessment Scale – cognitive subscale) resulted to be the most frequently used tool, despite it being proven as useful for the monitoring, but not for the diagnosis of dementia. On the other hand, only 5.6-18% of the structures reported using a test for episodic memory, attention and/or language. The study highlighted two main issues: i) a higher probability of misdiagnosis in the memory clinics that did not use a NPA, and ii) a need to improve the psychometric properties of some of the adopted tools. In 2008, Bianchi & Dai Prà [15] published a review of all Italian normative studies published from 1987 to 2007, and provided new standards to choose the best tools to be used in clinical practice. The results of the review support the use of short batteries to test patients with advanced dementia, and to administer a core assessment of episodic memory to subjects in the preclinical stages of the disease.

The Italian "National Dementia Plan" (NDP), in 2014, redefined the existing memory clinics renaming them as "Centers for Cognitive Disorders and Dementias" (CCDD), but maintaining their central role in the network of health care and social care services, and recognizing the need to reorganize services for dementia in integrated care pathways [16]. The INIH actively participated in the development of the NDP, and was also entrusted, within the 2013 program of research actions of the National Centre for Disease Prevention and Control (NCDPC), funded by the ~~il~~MoH, with the management of the national project: "Survey of the social and health services dedicated to dementias and creation of a specific website: Observatory for dementias".

A new survey was conducted in 2015[17], as part of this project. The methodology and methodological issues of the survey are reported in a dedicate publication [17]

This study had the objective of describing the use of neuropsychological tests for the diagnosis of cognitive disorders and dementia within the Italian CCDDs, and to investigate the possible

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relationship between the use of these tests and the presence or absence of a psychologist in the multidisciplinary teams working in CCDDs.

MATERIALS AND METHODS

Surveyed services

A total of 536 CCDDs were surveyed from February 2014 to August 2015 at a national level. The methodology used to carry out the survey of all health and social services currently available in Italy for people with dementia is reported in a dedicated paper [17]. A list of all CCDDs was obtained contacting designed representatives from each region, as these structures are heterogeneously distributed across the territory [17].

The survey was included in action 1.2 of the objective 1 of the Italian national plan of dementia [16]. No ethical approval or informed consent was used as all respondents were public institutions and all questions were about services' activities.

Survey questionnaire

A standardized form, designed to identify structure, process, and outcome indicators, was used to gather information on the type of NPA tools, and the clinical scales, tests and batteries used in CCDDs, for the diagnosis and assessment of dementias.

Information on the presence of a psychologist in the staff, on the type of service (e.g. part of a hospital, territorial, or university structure, or an ISRH), on the overall percentage of patients

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assisted per year, and on the proportion of patients who receive a comprehensive neuropsychological assessment was also included.

The questionnaire was administered to all health professionals in charge of enrolled CCDDs. The completed forms were collected through a specifically designed online platform, and data were exported for statistical analyses (see supplementary data).

Minimum core tests

Neuropsychological tests were classified according to the cognitive and functional domains they investigated. Based on compendia of cognitive testing[18-19] and the recommendations from the Italian Neuropsychological Society [20], the following categories were defined: i) screening test, ii) batteries for global assessment, iii) tests for memory, attention, executive functions, constructional abilities, iv) emotional status and behavior. Naming tests were categorized separately from semantic fluency tests, due to their validation studies being of low quality.

To verify the use of a comprehensive NPA in the diagnosis of cognitive disorders and dementia, we identified a Minimum Core Tests (MCT). We defined as MCT an essential set of tests for the evaluation of the main cognitive functions., including at least one test for each of the following cognitive domains: both verbal and visual episodic memory, attention, constructional praxis, verbal fluency, and executive functions. A set of test meeting these requirements, in fact, according to the compendia and the recommendations from the INS[18-19], would allow a CCDD to detect both the presence of subtle cognitive impairments and different patterns of dementia.

All tests, batteries, and clinical scales that are currently validated in the Italian population were listed and included in the survey questionnaire with the objective of collecting data on the neuropsychological tests routinely used in Italian CCDDs for the diagnosis of dementias **(Table 2).**

Table 2 - Most frequently used neuropsychological tests, batteries and clinical scales in Italy

	Italian normative studies

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Test or battery	
Digit-span	Orsini et al, 1987[21]
Corsi spatial span	Orsini et al, 1987[21]
Babcock' short-tale	Carlesimo et al, 2002[22]
Rey 15-word	Carlesimo et al, 1996[23]
Rey Complex Figure (RCF)	Carlesimo et al, 2002[22]
Attentional Matrices	Spinnler & Tognoni, 1987[24]
Stroop test	Caffarra et al, 2002[25]
Trail Making Test (TMT)	Giovagnoli et al, 1996[26]
Frontal Assessment Battery (FAB)	Appollonio et al, 2005[27]
Modified Wisconsin Card Sorting Test (MCST)	Caffarra et al, 2004[28]
Phonemic word fluency test (FAS)	Carlesimo et al, 1996[23]
Semantic word fluency test	Novelli et al, 1986[29]
Visual naming	Sartori et al, 1988[30]
Aachener Aphasia naming test (AAT)	Luzzatti et al, 1996[31]
Clock' drawing	Mondini et al, 2003[32]
Drawings copy	Carlesimo et al, 2002[22]
Oral-facial apraxia	Spinnler & Tognoni, 1987[24]
Ideomotor apraxia	Spinnler & Tognoni, 1987[24]
Coloured Progressive Matrices (CPM)	Carlesimo et al, 1996[23]
Standard Progressive Matrices (SPM)	Caffarra et al, 2003[33]
Mini-Mental State Examination	Measso et al, 1993[34]
Milan Overall Dementia Assessment (MODA)	Brazzelli et al, 1994[35]
Mental Deterioration Battery (MDB)	Carlesimo et al, 1996[23]
Alzheimer's Disease Assessment Scale (ADAS)	Fioravanti et al, 1994[36]
Clinical and Behavioral Scales	
Activities of Daily Living (ADL)	Katz ,1963[37]
Instrumental Activities of Daily Living (IADL)	Lawton & Brody, 1969[38]
Geriatric Depression Scale (GDS)	Yesavage et al, 1983[39]
Frontal Behavioral Inventory (FBI)	Alberici et al, 2007[40]
Insight Scale	Ott et al, 1996[41]
Neuropsychiatric Inventory (NPI)	Cummings et al, 1994[42]

Statistical analysis

The frequency of the use of neuropsychological tests for the diagnosis of dementia was calculated and reported as percentages. A chi square test was used to compare the number of services reporting the use of MCT.

A regression logistic model was also designed to assess the association between the use of a minimum core of neuropsychological tests, the geographical distribution and type of CCDDs, and

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the presence of at least one psychologist in the staff. ORs and their 95% Confidence Intervals (CIs) were calculated within the model. P-values lower than 0.05 (5%) were considered as statistically significant. All statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS- Version 23.0).

RESULTS

A total of 501 (93.5%) centers returned the completed forms: 219 (43.7%) from Northern Italy, 87 (17.4%) from Central Italy, and 195 (38.9%) from Southern Italy and the islands. The response rate resulted similar across the different areas. The geographical distribution and type of CCDDs are reported in table 3.

Table 3 – Distribution of the Centers for Cognitive Disorders and Dementias included in the survey according to type and geographical distribution

Type of CCDD	Geographical distribution			
	Northern Italy N (%)	Central Italy N (%)	Southern Italy N (%)	Total N (%)
Hospital	148 (67.6)	43 (49.4)	75 (38.5)	266 (53.1)
Territorial Services	53 (24.2)	31 (35.6)	112 (57.4)	196 (39.1)
University/ISRH	18 (8.2)	13 (14.9)	8 (4.1)	39 (7.8)
Total	219 (43.7)	87 (17.4)	195 (38.9)	501 (100)

CCDD – Center for Cognitive Disorders and Dementias

Table 4 reports data on the use of NP tools in Italian CCDDs. The results from the present survey (2015) were also compared with the results from the 2002 survey.

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Table 4 - Comparison between the Neuropsychological tests used in Italian CCDDs based on the results from two different surveys

	Tests in use during the 2002 survey[13-14]	Tests in use during the current survey
Domains-Functions /Test	%	%
Memory		
Rey 15-words	11	65
Babcock' short-tale	11.2	69.6
RCF recall	-	52.2
Corsi spatial span	12	46.4
Digit-span	4.8	52.8
Visual memory	1.3	-
Language		
AAT	1.5	17.8
Visual naming	-	17
Semantic word fluency test	15.3	61.2
Token test	13.3	-
Constructional abilities		
Drawings copy	-	52.4
RCF – copy	5.6	55.4
Clock' drawing	9.7	83.6
Attention		
Stroop test	2.3	33.2
TMT-A	1.3	51.6
Attentional Matrices	18.4	54.4
Executive functions		
SPM	6.1	41.4
CPM	1.3	33.2
MCST	0.3	24.2
TMT-B	1.3	51.6
FAS	17.1	61.8
Clinical and Behavioral Scales		
ADAS-cog	24	2.4
MDB	-	22.6
MODA	23.5	29.8
WAIS-R	3.1	-
MoCA	-	6.6

RCF: Rey Complex Figure; AAT: Aachener Aphasia naming test; TMT: Trail Making Test; SPM: Standard Progressive Matrices; CPM: Coloured Progressive Matrices; MCST: Modified Wisconsin Card Sorting Test; FAS: Phonemic word fluency test; ADAS-cog: Alzheimer's Disease Assessment Scale- cognitive subscale; MDB: Mental Deterioration Battery; MODA: Milan Overall Dementia Assessment; WAIS-R: Wechsler Adult Intelligence Scale-Revised; MoCA: Montreal Cognitive Assessment

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A total of 229 (45.7%) of the included CCDDs reported using a comprehensive NPA for the diagnosis of dementia, meeting the criteria for the MCT (table 5).

Of the 229 CCDDs that reported using an MCT, 81.7% included a psychologist in the team (table 5). The majority of services that used an MCT were based in Northern Italy (55.5%) and were hospital services (60.3%), while the lower frequency of services using an MCT was reported in Southern Italy and the Islands (25.3%) (table 5).

Table 5 - Geographical distribution, type of structure, and presence of at least a psychologist in the CCDDs that used and did not use a Minimum core set of neuropsychological tests.

	Use of a Minimum core set of neuropsychological tests		
	Yes (n= 229) (%)	**No (n=272) (%)**	**p value**
Geographical distribution of CCDDs			
Northern Italy	127 (55.5%)	92 (33.8%)	
Central Italy	44 (19.2%)	43 (15.8%)	0.001
Southern Italy and Islands	58 (25.3%)	137 (50.4%)	
Type of CCDD			
Territorial Services	57 (24.9%)	139 (51.1%)	
Hospital	138 (60.3%)	128 (47.1%)	0.001
University/ISRH	34 (14.8%)	5 (1.8%)	
Psychologist (at least one)	187 (81.7%)	119 (43.8%)	0.001

CCDD: Center for Cognitive Disorders and Dementias

ISRH: Institute for Scientific Research and Healthcare

The logistic regression model showed that the probability of including at least one psychologist in the team was higher in the CCDDs that reported using a comprehensive NPA (OR=4.55; 95% CI: 2.92-7.1). The model also showed that CCDDs in Southern Italy had a lower probability of using an MCT (OR = 0.56; 95% CI: 0.35-0.89), and that the probability of using an MCT was higher in University/ISRH CCDDs (OR = 10.97; 95% CI: 3.85-31.25) (Table 6).

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Table 6 - Logistic regression model showing the association between the use of a minimum core of neuropsychological tests in CCDDs and their geographical distribution and type, and the presence of at least one psychologist in the staff.

	OR	95% CI		p value
		Lower	Upper	
Psychologist (at least one)				
Not	1.00			
Yes	4.55	2.91	7.10	0.001
Geographical distribution of CCDDs				
Northern Italy	1.00			
Central Italy	1.13	0.63	2.02	0.685
Southern Italy - Islands	0.56	0.35	0.89	0.014
Type of CCDD				
Territorial Services	1.00			
Hospital	1.96	1.28	3.02	0.002
University/IRCSS	10.97	3.85	31.25	0.001

CCDD: Center for Cognitive Disorders and Dementias

DISCUSSION AND CONCLUSION

The present survey provides an overview of the use and the availability of NPA in Italian CCDDs. Some previous studies gathered information on the tools used to assess and diagnose dementia, but they either included a limited number of centers [43], or involved only representatives of national neurological associations [9]. Our study specifically focused on healthcare centers that directly manage people with dementia with the objective of describing the approach to cognitive testing in patients with dementia within the public national health system.

The first, relevant finding was a considerable difference between the 2002 survey and this survey in both in the type of tools adopted and their use. Some of the tools were used much more sporadically due to either their low sensitivity (e.g. Visual Memory), or their inadequacy in identifying dementia (WAIS-r). Some other tools, instead, are now considerably less widespread (e.g. ADAS-cog) as they were introduced in clinical practice due to their diffusion as an outcome measure in clinical trials on cholinesterase inhibitors. On the other hand, a considerable increase was observed in the

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use of some key tools for the early diagnosis of dementia, such as tests for episodic memory, phonemic and semantic fluency, executive functions, and constructional abilities.

This might be explained by a progressive increase in the number of available cognitive tests between the year 1987, when the Study of Standardization by Spinnler & Tognoni [24] was published, and the year 2000, when the AEUs were created. About 49 studies were carried out during these 13 years, and 64 in the following 10 years. This caused a progressive shifting from "historical" tests (e.g. the WAIS scales) to new tests specifically designed to target the demographical changes of the population, and the trend is still ongoing (see Barletta-Rodolfi et al [20]).

When comparing results from this survey with data from other European countries [9], no substantial differences were observed in the type of tests used. All cognitive domains resulted to be assessed in a quite homogeneous way, despite a degree of variability in some tools (e.g. in language and verbal memory). However, two specificities emerged. First, the tests aimed at assessing abstract thinking (e.g. Raven's Progressive Matrices) resulted as widely used in Italy, while their use seemed to be much less frequent in other European countries. Second, all tests used in Italian structures were validated on the Italian population, and thus resulted as having good psychometric properties.

Results from the survey showed also that the majority of CCDDs administering an MCT included at least a psychologist in the team. About 46% of the centers offered an MCT, with significant differences between the centers in Northern Italy and the centers in Central and Southern Italy. The CCDDs in Northern Italy seemed to have a better profile, while the CCDDs in Central and Southern Italy seemed to have similar organizational characteristics. The importance of including an operator specifically trained to administer NPA tools was first highlighted in 1985, when the American Psychological Association (APA) defined and detailed the required standards for neuropsychological examiners [44]. Italy included these requirements within the expertise of

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professional psychologists (l. 56/89; D.M. 24/7/2006). However, uncertainties still exist on *who can do what*. Moreover, any health professional who administer NP tests should be specifically trained, and a constant interaction between neuroanatomical specialties and cognitive and clinical psychology should be maintained when interpreting the results from any type of NP test.

Results from the present survey also showed that more than half of the included CCDDs based their screening procedures mainly on the administration of rough cognitive (e.g. MMSE) and functional (e.g. ADL, IADL) scales, or a small set tests. This lack of expertise raises the issue of *what is an NPA and what is it thought to be*.

The knowledge on the clinical manifestations of AD considerably increased starting from 1984, when the NINCDS-ADRDA criteria for the diagnosis of probable AD were established [45].

The NINCDS-ADRDA criteria were then revised by the NIA [46], due to the need to clearly discriminate AD from either other conditions leading to dementia (e.g. Frontotemporal Dementia, Primary Progressive Aphasia), or non-amnestic forms of AD. The core clinical criteria for a diagnosis of all-cause dementia require the presence of cognitive or behavioral symptoms involving at least two cognitive domains among memory, judgment, visuospatial abilities, language and behavior. The new criteria to define a diagnosis of probable AD, also require an either amnestic or non-amnestic significant initial cognitive deficit, and, in case of a non-amnestic AD, concomitant linguistic, visuospatial and executive dysfunctions.

Therefore, the NPA needs to quantify the deficit, but also to define a pattern of scores that can provide a diagnostic clue on the possible etiology, considering that cognitive functions depend on neural network involving different brain areas [47].

A recent review highlighted that mild cognitive impairments may be undetected by simple mental status examination and brief screening tests[48, 49]. Short cognitive tests, however, are still widespread in clinical practice, in particular in countries where healthcare policies are defined based

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on their cost-effectiveness, and specifically, on the costs of tools and instruments, the time needed to administer them, and the costs related to misdiagnoses (false positives and/or false negatives).

This kind of tests are currently being promoted by some international programs to optimize the cognitive screening in primary care [50-51], where the prevalence of undiagnosed cases is high [4]. However, CCDDs, that are designed as second-/third-level referral units, should use this type of tests as part of the clinical examination and in the monitoring over time of already diagnosed patients, rather than adopt them as diagnostic tools, considering their intrinsic limitations (for a review, see Brown, 2016 [52]). A comprehensive NPA thus, is currently the best way to assess and quantify cognitive deficits [47], and should be the minimum requirement for the diagnosis of dementia.

The main strength of this survey is the inclusion of structures based on the whole national territory. This study can be of support in understanding the functioning of Italian CCDDs and the type of NP tools used in clinical practice to assess people with cognitive complaints.

This is an extremely relevant issue, considering also that potentially disease-modifying treatments are currently under development, that will require more sensitive neuropsychological measures for the early identification of cognitive disorders and dementia.

The main limitation of this survey is its being based on self-administered questionnaires, thus potentially over-estimating the scenario. The misuse of NP tests could prevent an homogeneity in the evaluation criteria, and the comparability of data from different CCDDs.

The number and type of tests used in the diagnostic process of dementia should follow recommendations from the Italian Neuropsychological Society included in the National Guidelines, thus closing the gap between cognitive neurosciences and public health.

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This supplementary data include a translation of some items related to the investigation on neuropsychological tools used in clinical practice for the diagnosis of dementia. Information on these tools are included in the survey questionnaire that was designed to collect data, in a standardized form, on Italian memory clinics. The full survey questionnaire is available in Italian upon request. Moreover, an overall description of the methodology used in this survey is available in a dedicated paper (Di Pucchio a et al, 2017).

The survey questionnaires included five sections, and all questions were specifically formulated to collect information on:
1. Location and registry service;
2. Access to the service;
3. Organizational aspects of the services;
4. Treatments and services provision;
5. Data on activities and patient numbers.

A group of researchers, including specialists in dementia, epidemiologists, and members of target services, participated in the development of the survey questionnaires and ensured the validity of included questions (content validity).

Table 1 shows a description of the topics included in the survey questionnaire for Italian memory clinics.

Table 1 – Section/Domain and topics included in the survey questionnaire for memory clinics

Section/Domain and Topics
Location and registry service
Detailed information on service's location, name, phone number and address; type of services provided; type of funding and methods of reimbursement
Access to service
Operating days and hours per week
Ways to access the service (e.g. phone reservation; wording for medical prescription*)
Organizational aspects of the services
Staff profile and composition
Waiting time to access the service
Procedures and service documentation *(Availability of structured procedures for data collection on the activity; Availability of documentation on integrated care pathways)*
Treatments and services
Provided services *(i.e. Pharmacological and non-pharmacological interventions; Non-pharmacological interventions provided to caregivers)*
Referral to other health professionals and access to care coordination
Neuropsychological tools used in the assessment and diagnosis of dementia
Data on activities and number of patients
Number of patients with and without a diagnosis of dementia during the last year
Patients assessed per month
Patients referred for a first assessment per month
Number of patients in charge visited per year (at least one time per year)

Note: The full survey questionnaire is available in Italian upon request

In the "Treatments and services" section of the survey questionnaire, we included a question on the neuropsychological tools used in the assessment and diagnosis of dementia. We asked referents of the memory clinics to select from a predefined list (table 2) all neuropsychological tests, batteries and clinical

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scales routinely used within their memory clinic for the assessment and diagnosis of dementias. Further test could also be added if not included in the list.

Table 2 – List of Neuropsychological tests, batteries and clinical scales included in the survey questionnaire for memory clinics.

Aachener Aphasie Test (AAT)
Activities of Daily Living (ADL)
Alzheimer's Disease Assessment Scale (ADAS)
Attention Matrices
Babcock' short tale
Clock drawing
Coloured Progressive Matrices (CPM)
Corsi spatial span
Digit Span
Drawings copy
Frontal Assessment Battery (FAB)
Frontal Behavioral Inventory (FBI)
Geriatric Depression Scale (GDS)
Ideomotor Apraxia
Insight Scale
Instrumental Activities of Daily Living (IADL)
Mental Deterioration Battery (MDB)
Milan Overall Dementia Assessment (MODA)
Mini-Mental State Examination (MMSE)
Modified Wisconsin Card Sorting Test (MCST)
Neuropsychiatric Inventory (NPI)
Oral-facial apraxia
Phonemic word fluency test (FAS)
Rey 15 words
Rey- Complex Figure (RCF)
Semantic word fluency test
Standard Progressive Matrices (SPM)
Stroop Trail Making Test (TMT)
Visual naming

A web-platform system, the "Dementia Observatory web-platform system", was developed to manage the large amount of data from a very high number of services. This system allowed to create and manage a database with data storage and retrieval functions.
The survey questionnaire was self-administered, completed in an electronic form by the clinical representative of each service. The questionnaire included both closed questions with pre-coded options, and open questions. For the majority of questions answers were required.

Some questions were also included to automatically check for already entered data, to avoid inconsistent answers.

All participants were invited to participate to the survey via email. An introductory cover letter was also sent to explain the objectives of the survey, specifying that the survey was carried out by the Italian NIH and that

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responding was required by the Ministry of Health. The cover letter included a link to access the online questionnaire. The contact name and address of the principal investigator, along with details on how and why the respondent was selected, and any potential benefits or harm resulting from the study were also provided.

To increase the number and accuracy of the responses to the survey different strategies were used, such as:
• keeping in contact with participants through follow-up emails after the initial message, and through telephone support;
• checking and correcting incorrect telephone and/or e-mail contacts;
• directly supporting respondents in completing the survey, when requested;
• contacting respondents who were initially unable to participate, but did not refuse to participate.

Data collected through the web-platform system were then exported in different formats for statistical analysis (SPSS ver. 20, IBM, USA). Null responses generated by typing errors or "impossible" responses to survey questions (i.e. to the question "how many days is the unit open?": outliers were considered numbers equal and/or lower than zero or higher than 7) were removed from calculations if not corrected within a given reference time.

The response rate of contacted services was used to describe the success of the survey, and considered as a primary measure of the quality of the survey.

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Questions to consider when preparing a report of findings from postal surveys (Table 4). *IN Burns KE, Duffett M, Kho ME, Meade MO, Adhikari NK, Sinuff T, Cook DJ; ACCADEMY Group. A guide for the design and conduct of self-administered surveys of clinicians. CMAJ. 2008 Jul 29;179(3):245-52.*

Section	Question	
Abstract		Page*
	Is the objective clearly stated?	Page 2
	Is the design of the study stated?	Page 2
	Is the study setting well described?	Page 2
	Is the survey population described?	Page 2
	Is the response rate reported?	Page 2
	Are the outcome measures identified?	Page 2
	Are the main results clearly reported?	Page 2
	Are the conclusions appropriate?	Page 2
Introduction		
	Is the problem clearly stated?	Page 4, 5
	Is the pertinent literature cited and critically appraised?	Page 5, 6
	Is the relevance of the research question explained?	Page 6, 7
	Is the objective clearly stated?	Page 7,8
Methods		
	Is the study design appropriate to the objective?	Page 8
	Is the setting clearly described?	Page 8
	Are the methods described clearly enough to permit other researchers to duplicate the study?	Page 8, 9,10, 11
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	Is the questionnaire described adequately?	Page 8
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	Do the results address the objective?	Page 11,12, 13,
	Are all respondents accounted for?	Page 11
	Are the results clearly and logically presented?	Page 11,12, 13,
	Are the tables and figures appropriate?	Table 3, 4,5, 6
	Are the numbers consistent in the text and the tables?	Page 11,12,13,
Discussion		
	Are the results succinctly summarized?	Page 14
	Are the implications of the results stated?	Page 15
	Are other interpretations considered and refuted?	Page 16
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	Are appropriate conclusions drawn?	Page 17

*PDF Proof "**Neuropsychological tests for the diagnosis of dementia: results of a survey in Italian memory clinics**", Alessandra Di Pucchio [1], Nicola Vanacore [1], Fabrizio Marzolini [1], Eleonora Lacorte[1], Teresa Di Fiandra [2], I-DemObs Group [3], Marina Gasparini [4]

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	X (pg.1,2)	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	X (pg 4,5)	Explain the scientific background and rationale for the investigation being reported
Objectives	X (pg 7,8)	State specific objectives, including any prespecified hypotheses
Methods		
Study design	X (pg 8)	Present key elements of study design early in the paper
Setting	X (pg 8)	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants		(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls X (pg 8) *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	X (pg9,10)	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	X (pg 9,10)	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	X (pg 17)	Describe any efforts to address potential sources of bias
Study size	n.a*	Explain how the study size was arrived at
Quantitative variables	X (pg9)	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	X (pg 10,11)	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

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(*e*) Describe any sensitivity analyses

Continued on next page

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Results		
Participants	**n.a***	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	**n.a***	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	**X (pg 11,12)**	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	**X (pg 13.,14)**	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	**n.a***	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	**X (pg 14.15)**	Summarise key results with reference to study objectives
Limitations	**X (pg 17)**	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	**X (pg 17)**	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	**n.a***	Discuss the generalisability (external validity) of the study results
Other information		
Funding	**X** (pg 18)	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

***n.a not applicable**

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Use of neuropsychological tests for the diagnosis of dementia: a survey of Italian memory clinics

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Use of neuropsychological tests for the diagnosis of dementia: a survey of Italian memory clinics

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ABSTRACT

Aim. Providing an overview of the neuropsychological tests used in Italian memory clinics (defined as Centers for Cognitive Disorders and Dementias – CCDD in Italy) for the diagnosis of cognitive disorders and dementias.

Methods. A total of 501 CCDDs, out of all 536 active CCDDs, were surveyed between February 2014 and August 2015 to verify the characteristics of the centers who performed a comprehensive neuropsychological assessment (NPA), defined as the administration of at least one test for verbal and visual episodic memory, attention, constructional praxis, verbal fluency, and executive functions (Minimum Core Tests - MCT), as part of the diagnostic process.

Results. A total of 45.7% of Italian CCDDs performed a comprehensive MCT as part of the diagnostic process. The logistic regression model showed that the probability of including at least one psychologist in the team was higher in the CCDDs that reported using a comprehensive NPA (OR=4.55; 95% CI: 2.92-7.1), that CCDDs in Southern Italy had a lower probability of using an MCT (OR = 0.56; 95% CI: 0.35-0.89), and that the use of an MCT was higher in University/ISRH CCDDs (OR = 10.97; 95% CI: 3.85-31.25).

Conclusion. Almost half of the CCDDs administered a set of MCTs; while the remaining centers only performed few tests or screening procedures. The neuropsychological tests used in Italian CCDDs were comparable to those used in other European countries. Performing a comprehensive NPA remains the best way to assess and monitor cognitive deficits over time, thus further debate on the current status of NPAs in clinical practice is needed.

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Article summary (strengths and limitations of this study)

- The study provides an overview of the frequency of use and the availability of neuropsychological assessment (NPA) in a large and representative number of Italian

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memory clinics (defined as Centers for Cognitive Disorders and Dementias – CCDD in Italy).

- a limitation of the study is its being based on data from self-reported questionnaires, administered to health professionals in charge of enrolled CCDDs which could potentially over-estimate the actual scenario.

Key words

Neuropsychological test; Memory clinic; Survey research; Dementia; Alzheimer disease, Diagnosis;

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organization that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. *Grant funding for research but no other competing interests.*

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INTRODUCTION

Cognitive testing is consistently considered as extremely relevant in the diagnosis and follow-up of patients with dementia. International guidelines [1-2] specifically address its use in addition to clinical investigation - the so-called incremental validity [3]. A neuropsychological assessment (NPA) is aimed at defining the severity of dementia, but also at confirming a diagnostic hypothesis. Once dementia is diagnosed, a simple "omnibus" test (e.g. Mini-Mental State Examination – MMSE; Milan Overall Dementia Assessment - MODA) can provide a deterioration score, which is useful for the clinical monitoring over time [4]. However, in case of patients with subtle cognitive complaints but maintaining normal daily life activities, possible preclinical impairments can only be detected through a comprehensive NPA. The specific tool to be chosen in each case can vary (for a review, see Ngo and Holroyd-Leduc [5]), but it should always be proven to have strong psychometric properties.

Several attempts were made, over the years, to harmonize and uniform cognitive assessment in dementia. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD) was created in 1986 by the National Institute of Aging (NIA) to standardize the procedures for the evaluation and diagnosis of patients with Alzheimer's disease (AD). The neuropsychological battery proposed by CERAD includes tests for verbal fluency and naming, the MMSE, word list recall and recognition, constructional praxis, and recall of constructional praxis. The Word list recall test, in particular, was found to be the best in distinguishing between patients with AD and healthy controls [6]. In 2009, the AD Center (ADC) program of the NIA carried out a survey to gather data on assessment practices, including tools for the evaluation of the cognitive domain. The study designed a brief cognitive battery, to be used in ADCs [7]. However, as the authors pointed out, the battery resulted as appropriate for a first evaluation, but it did not prove as an adequate substitute for a comprehensive NPA. Moreover, it did not result as an adequate tool to detect subtle impairments as compared with the CERAD battery [8].

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As for Europe, the EFNS (European Federation of Neurological Societies) task force performed a survey on the neuropsychological tests used to detect dementia in 25 countries, with the objective of harmonizing their use across these countries [9]. The survey identified 213 different tools, pointing out that not all of them were validated in each country. Specifically, 18-21 countries reported using verbal memory tests, but only the tests used in 11-14 of these countries were validated. These findings highlighted the critical issue of the psychometric solidity of the tools used in clinical practice, and their reliability. It also underlined a difficulty in selecting which tests are to be used for the assessment and diagnosis of dementia, due to differences in the cultural context, in clinical and research practice, and in health care policies.

Further recommendations were recently proposed for a comprehensive NPA [10-11], as it may work as a good predictor of progression from subtle impairments to AD.,–These recommendations pointed out the need of exploring the major cognitive domains – episodic memory, constructional praxis, attention, verbal fluency and executive functions (Table 1).

Table 1 - Recommendations for Neuropsychological assessment for dementia:

CERAD[6]	UDS[a][7]	CIMA-Q battery[10]	Finney *et al*[11]
Boston Naming Test Constructional praxis Mini-Mental State Exam Recall of constructional praxis Verbal Fluency Word list memory Word list recall Word list recognition	Animal list generation Boston naming test Digit symbol Digit span forward & backward Logical Memory, story A Mini Mental State Exam Trail Making Test (A - B) Vegetable list generation	Animal fluency Auditory Verbal Boston naming Digit Symbol Learning Test Line Object decision Orientation Rey Trail Making Test (A-B)	Assessment (MOCA) Boston naming test COWAT Hopkins / California verbal learning test Mattis Dementia Rating Scale Mini Mental State Exam Montreal Cognitive Rey-Osterrieth complex Figure Stroop test Trail Making Test (A- B) Wisconsin card sorting test
[a] low sensitivity (73.6%) and specificity (70.8%) for MCI			

The Italian scenario

Italy is structured in 18 regions and 2 self-administered provinces, and its NHS is organized at national, regional, and local level. At a national level, the Ministry of Health, supported by several

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specialized agencies, establishes the basic principles and objectives of the health system, defines the core health services to be guaranteed across the country, and distributes to each region its quote of national funds. Regions are substantial self-administered in defining of the structure of their local health systems, and are responsible for organizing and delivering health care. At a local level, public and community health services, and primary care is directly delivered by local health authorities (Aziende Sanitarie Locali), while secondary and specialized care is either directly delivered by ASLs or accessible through public hospitals or accredited private structures.

The diagnosis, treatment and support of people with dementia within the Italian NHS is currently managed by different health and social health services. Memory clinics are defined, within the Italian NHS, as Centers for Cognitive Disorders and Dementias (CCDD) and can be based in public, territorial, outpatient services, hospitals or University hospitals, or Institute for Scientific Research and Healthcare (ISRH). The team of healthcare professionals involved in these centers includes neurologists, geriatricians and psychiatrists, and financial support is provided by the NHS. CCDDs are specifically dedicated to the assessment, diagnosis and management of dementias, and are entitled to prescribe specific pharmacological treatments for Alzheimer Disease (i.e. donepezil, rivastigmine, galantamine, memantine) and/or behavioral and psychological symptoms of dementia (i.e. antipsychotic drugs) based on the diagnosis and the treatment plan. In 2000, a first survey of all Italian CCDDs was performed within the Cronos study, a project implemented by the Italian Ministry of Health and the Italian National Institute of Health, that identified about 500 memory clinics in Italy.[12]

Two more surveys, one performed in 2002 and the second in 2006, aimed at identifying and characterizing the activities carried out by memory clinics. Their objective was to acknowledge the importance of the role of memory clinics in the diagnosis and treatment of people with dementia, but also to assess the wide variability in their distribution and characteristics at a regional and local level [13-14].

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The 2002 survey showed a wide variability between memory clinics, both in the type of cognitive tests adopted, and their use. About 50% of memory clinics declared to perform a NPA, but such a percentage was probably over-estimated due to an unclear definition of "*what*" a NPA should actually be. The ADAS-cog (Alzheimer's Disease Assessment Scale – cognitive subscale) resulted to be the most frequently used tool, despite it being proven as useful for the monitoring, but not for the diagnosis of dementia. On the other hand, only 5.6-18% of the structures reported using a test for episodic memory, attention and/or language. The study highlighted two main issues: i) a higher probability of misdiagnosis in the memory clinics that did not use a NPA, and ii) a need to improve the psychometric properties of some of the adopted tools. In 2008, Bianchi & Dai Prà [15] published a review of all Italian normative studies published from 1987 to 2007, and provided new standards to choose the best tools to be used in clinical practice. The results of the review support the use of short batteries to test patients with advanced dementia, and to administer a core assessment of episodic memory to subjects in the preclinical stages of the disease.

The Italian "National Dementia Plan" (NDP), in 2014, redefined the existing memory clinics renaming them as "Centers for Cognitive Disorders and Dementias" (CCDD), but maintaining their central role in the network of health care and social care services, and recognizing the need to reorganize services for dementia in integrated care pathways [16]. The INIH actively participated in the development of the NDP, and was also entrusted, within the 2013 program of research actions of the National Centre for Disease Prevention and Control (NCDPC), funded by the ~~il~~MoH, with the management of the national project: "Survey of the social and health services dedicated to dementias and creation of a specific website: Observatory for dementias".

A new survey was conducted in 2015[17], as part of this project. The methodology and methodological issues of the survey are reported in a dedicate publication [17]

This study had the objective of describing the use of neuropsychological tests for the diagnosis of cognitive disorders and dementia within the Italian CCDDs, and to investigate the possible

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relationship between the use of these tests and the presence or absence of a psychologist in the multidisciplinary teams working in CCDDs.

MATERIALS AND METHODS

Surveyed services

A total of 536 CCDDs were surveyed from February 2014 to August 2015 at a national level. The methodology used to carry out the survey of all health and social services currently available in Italy for people with dementia is reported in a dedicated paper [17]. A list of all CCDDs was obtained contacting designed representatives from each region, as these structures are heterogeneously distributed across the territory [17].

The survey was included in action 1.2 of the objective 1 of the Italian national plan of dementia [16]. No ethical approval or informed consent was used as all respondents were public institutions and all questions were about services' activities.

Survey questionnaire

A standardized form, designed to identify structure, process, and outcome indicators, was used to gather information on the type of NPA tools, and the clinical scales, tests and batteries used in CCDDs, for the diagnosis and assessment of dementias.

Information on the presence of a psychologist in the staff, on the type of service (e.g. part of a hospital, territorial, or university structure, or an ISRH), on the overall percentage of patients

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assisted per year, and on the proportion of patients who receive a comprehensive neuropsychological assessment was also included.

The questionnaire was administered to all health professionals in charge of enrolled CCDDs. The completed forms were collected through a specifically designed online platform, and data were exported for statistical analyses (see supplementary data).

Minimum core tests

Neuropsychological tests were classified according to the cognitive and functional domains they investigated. Based on compendia of cognitive testing[18-19] and the recommendations from the Italian Neuropsychological Society [20], the following categories were defined: i) screening test, ii) batteries for global assessment, iii) tests for memory, attention, executive functions, constructional abilities, iv) emotional status and behavior. Naming tests were categorized separately from semantic fluency tests, due to their validation studies being of low quality.

To verify the use of a comprehensive NPA in the diagnosis of cognitive disorders and dementia, we identified a Minimum Core Tests (MCT). We defined as MCT an essential set of tests for the evaluation of the main cognitive functions., including at least one test for each of the following cognitive domains: both verbal and visual episodic memory, attention, constructional praxis, verbal fluency, and executive functions. A set of test meeting these requirements, in fact, according to the compendia and the recommendations from the INS[18-19], would allow a CCDD to detect both the presence of subtle cognitive impairments and different patterns of dementia.

All tests, batteries, and clinical scales that are currently validated in the Italian population were listed and included in the survey questionnaire with the objective of collecting data on the neuropsychological tests routinely used in Italian CCDDs for the diagnosis of dementias **(Table 2).**

Table 2 - Most frequently used neuropsychological tests, batteries and clinical scales in Italy

	Italian normative studies

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Test or battery	
Digit-span	Orsini et al, 1987[21]
Corsi spatial span	Orsini et al, 1987[21]
Babcock' short-tale	Carlesimo et al, 2002[22]
Rey 15-word	Carlesimo et al, 1996[23]
Rey Complex Figure (RCF)	Carlesimo et al, 2002[22]
Attentional Matrices	Spinnler & Tognoni, 1987[24]
Stroop test	Caffarra et al, 2002[25]
Trail Making Test (TMT)	Giovagnoli et al, 1996[26]
Frontal Assessment Battery (FAB)	Appollonio et al, 2005[27]
Modified Wisconsin Card Sorting Test (MCST)	Caffarra et al, 2004[28]
Phonemic word fluency test (FAS)	Carlesimo et al, 1996[23]
Semantic word fluency test	Novelli et al, 1986[29]
Visual naming	Sartori et al, 1988[30]
Aachener Aphasia naming test (AAT)	Luzzatti et al, 1996[31]
Clock' drawing	Mondini et al, 2003[32]
Drawings copy	Carlesimo et al, 2002[22]
Oral-facial apraxia	Spinnler & Tognoni, 1987[24]
Ideomotor apraxia	Spinnler & Tognoni, 1987[24]
Coloured Progressive Matrices (CPM)	Carlesimo et al, 1996[23]
Standard Progressive Matrices (SPM)	Caffarra et al, 2003[33]
Mini-Mental State Examination	Measso et al, 1993[34]
Milan Overall Dementia Assessment (MODA)	Brazzelli et al, 1994[35]
Mental Deterioration Battery (MDB)	Carlesimo et al, 1996[23]
Alzheimer's Disease Assessment Scale (ADAS)	Fioravanti et al, 1994[36]
Clinical and Behavioral Scales	
Activities of Daily Living (ADL)	Katz ,1963[37]
Instrumental Activities of Daily Living (IADL)	Lawton & Brody, 1969[38]
Geriatric Depression Scale (GDS)	Yesavage et al, 1983[39]
Frontal Behavioral Inventory (FBI)	Alberici et al, 2007[40]
Insight Scale	Ott et al, 1996[41]
Neuropsychiatric Inventory (NPI)	Cummings et al, 1994[42]

Statistical analysis

The frequency of the use of neuropsychological tests for the diagnosis of dementia was calculated and reported as percentages. A chi square test was used to compare the number of services reporting the use of MCT.

A regression logistic model was also designed to assess the association between the use of a minimum core of neuropsychological tests, the geographical distribution and type of CCDDs, and

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the presence of at least one psychologist in the staff. ORs and their 95% Confidence Intervals (CIs) were calculated within the model. P-values lower than 0.05 (5%) were considered as statistically significant. All statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS- Version 23.0).

RESULTS

A total of 501 (93.5%) centers returned the completed forms: 219 (43.7%) from Northern Italy, 87 (17.4%) from Central Italy, and 195 (38.9%) from Southern Italy and the islands. The response rate resulted similar across the different areas. The geographical distribution and type of CCDDs are reported in table 3.

Table 3 – Distribution of the Centers for Cognitive Disorders and Dementias included in the survey according to type and geographical distribution

Type of CCDD	Geographical distribution			
	Northern Italy N (%)	Central Italy N (%)	Southern Italy N (%)	Total N (%)
Hospital	148 (67.6)	43 (49.4)	75 (38.5)	266 (53.1)
Territorial Services	53 (24.2)	31 (35.6)	112 (57.4)	196 (39.1)
University/ISRH	18 (8.2)	13 (14.9)	8 (4.1)	39 (7.8)
Total	219 (43.7)	87 (17.4)	195 (38.9)	501 (100)

CCDD – Center for Cognitive Disorders and Dementias

Table 4 reports data on the use of NP tools in Italian CCDDs. The results from the present survey (2015) were also compared with the results from the 2002 survey.

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Table 4 - Comparison between the Neuropsychological tests used in Italian CCDDs based on the results from two different surveys

	Tests in use during the 2002 survey[13-14]	Tests in use during the current survey
Domains-Functions /Test	%	%
Memory		
Rey 15-words	11	65
Babcock' short-tale	11.2	69.6
RCF recall	-	52.2
Corsi spatial span	12	46.4
Digit-span	4.8	52.8
Visual memory	1.3	-
Language		
AAT	1.5	17.8
Visual naming	-	17
Semantic word fluency test	15.3	61.2
Token test	13.3	-
Constructional abilities		
Drawings copy	-	52.4
RCF – copy	5.6	55.4
Clock' drawing	9.7	83.6
Attention		
Stroop test	2.3	33.2
TMT-A	1.3	51.6
Attentional Matrices	18.4	54.4
Executive functions		
SPM	6.1	41.4
CPM	1.3	33.2
MCST	0.3	24.2
TMT-B	1.3	51.6
FAS	17.1	61.8
Clinical and Behavioral Scales		
ADAS-cog	24	2.4
MDB	-	22.6
MODA	23.5	29.8
WAIS-R	3.1	-
MoCA	-	6.6

RCF: Rey Complex Figure; AAT: Aachener Aphasia naming test; TMT: Trail Making Test; SPM: Standard Progressive Matrices; CPM: Coloured Progressive Matrices; MCST: Modified Wisconsin Card Sorting Test; FAS: Phonemic word fluency test; ADAS-cog: Alzheimer's Disease Assessment Scale- cognitive subscale; MDB: Mental Deterioration Battery; MODA: Milan Overall Dementia Assessment; WAIS-R: Wechsler Adult Intelligence Scale-Revised; MoCA: Montreal Cognitive Assessment

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A total of 229 (45.7%) of the included CCDDs reported using a comprehensive NPA for the diagnosis of dementia, meeting the criteria for the MCT (table 5).

Of the 229 CCDDs that reported using an MCT, 81.7% included a psychologist in the team (table 5). The majority of services that used an MCT were based in Northern Italy (55.5%) and were hospital services (60.3%), while the lower frequency of services using an MCT was reported in Southern Italy and the Islands (25.3%) (table 5).

Table 5 - Geographical distribution, type of structure, and presence of at least a psychologist in the CCDDs that used and did not use a Minimum core set of neuropsychological tests.

	Use of a Minimum core set of neuropsychological tests		
	Yes (n= 229) (%)	**No (n=272) (%)**	**p value**
Geographical distribution of CCDDs			
Northern Italy	127 (55.5%)	92 (33.8%)	
Central Italy	44 (19.2%)	43 (15.8%)	0.001
Southern Italy and Islands	58 (25.3%)	137 (50.4%)	
Type of CCDD			
Territorial Services	57 (24.9%)	139 (51.1%)	
Hospital	138 (60.3%)	128 (47.1%)	0.001
University/ISRH	34 (14.8%)	5 (1.8%)	
Psychologist (at least one)	187 (81.7%)	119 (43.8%)	0.001

CCDD: Center for Cognitive Disorders and Dementias

ISRH: Institute for Scientific Research and Healthcare

The logistic regression model showed that the probability of including at least one psychologist in the team was higher in the CCDDs that reported using a comprehensive NPA (OR=4.55; 95% CI: 2.92-7.1). The model also showed that CCDDs in Southern Italy had a lower probability of using an MCT (OR = 0.56; 95% CI: 0.35-0.89), and that the probability of using an MCT was higher in University/ISRH CCDDs (OR = 10.97; 95% CI: 3.85-31.25) (Table 6).

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Table 6 - Logistic regression model showing the association between the use of a minimum core of neuropsychological tests in CCDDs and their geographical distribution and type, and the presence of at least one psychologist in the staff.

	OR	95% CI		p value
		Lower	Upper	
Psychologist (at least one)				
Not	1.00			
Yes	4.55	2.91	7.10	0.001
Geographical distribution of CCDDs				
Northern Italy	1.00			
Central Italy	1.13	0.63	2.02	0.685
Southern Italy - Islands	0.56	0.35	0.89	0.014
Type of CCDD				
Territorial Services	1.00			
Hospital	1.96	1.28	3.02	0.002
University/IRCSS	10.97	3.85	31.25	0.001

CCDD: Center for Cognitive Disorders and Dementias

DISCUSSION AND CONCLUSION

The present survey provides an overview of the use and the availability of NPA in Italian CCDDs. Some previous studies gathered information on the tools used to assess and diagnose dementia, but they either included a limited number of centers [43], or involved only representatives of national neurological associations [9]. Our study specifically focused on healthcare centers that directly manage people with dementia with the objective of describing the approach to cognitive testing in patients with dementia within the public national health system.

The first, relevant finding was a considerable difference between the 2002 survey and this survey in both in the type of tools adopted and their use. Some of the tools were used much more sporadically due to either their low sensitivity (e.g. Visual Memory), or their inadequacy in identifying dementia (WAIS-r). Some other tools, instead, are now considerably less widespread (e.g. ADAS-cog) as they were introduced in clinical practice due to their diffusion as an outcome measure in clinical trials on cholinesterase inhibitors. On the other hand, a considerable increase was observed in the

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use of some key tools for the early diagnosis of dementia, such as tests for episodic memory, phonemic and semantic fluency, executive functions, and constructional abilities.

This might be explained by a progressive increase in the number of available cognitive tests between the year 1987, when the Study of Standardization by Spinnler & Tognoni [24] was published, and the year 2000, when the AEUs were created. About 49 studies were carried out during these 13 years, and 64 in the following 10 years. This caused a progressive shifting from "historical" tests (e.g. the WAIS scales) to new tests specifically designed to target the demographical changes of the population, and the trend is still ongoing (see Barletta-Rodolfi et al [20]).

When comparing results from this survey with data from other European countries [9], no substantial differences were observed in the type of tests used. All cognitive domains resulted to be assessed in a quite homogeneous way, despite a degree of variability in some tools (e.g. in language and verbal memory). However, two specificities emerged. First, the tests aimed at assessing abstract thinking (e.g. Raven's Progressive Matrices) resulted as widely used in Italy, while their use seemed to be much less frequent in other European countries. Second, all tests used in Italian structures were validated on the Italian population, and thus resulted as having good psychometric properties.

Results from the survey showed also that the majority of CCDDs administering an MCT included at least a psychologist in the team. About 46% of the centers offered an MCT, with significant differences between the centers in Northern Italy and the centers in Central and Southern Italy. The CCDDs in Northern Italy seemed to have a better profile, while the CCDDs in Central and Southern Italy seemed to have similar organizational characteristics. The importance of including an operator specifically trained to administer NPA tools was first highlighted in 1985, when the American Psychological Association (APA) defined and detailed the required standards for neuropsychological examiners [44]. Italy included these requirements within the expertise of

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professional psychologists (l. 56/89; D.M. 24/7/2006). However, uncertainties still exist on *who can do what*. Moreover, any health professional who administer NP tests should be specifically trained, and a constant interaction between neuroanatomical specialties and cognitive and clinical psychology should be maintained when interpreting the results from any type of NP test.

Results from the present survey also showed that more than half of the included CCDDs based their screening procedures mainly on the administration of rough cognitive (e.g. MMSE) and functional (e.g. ADL, IADL) scales, or a small set tests. This lack of expertise raises the issue of *what is an NPA and what is it thought to be*.

The knowledge on the clinical manifestations of AD considerably increased starting from 1984, when the NINCDS-ADRDA criteria for the diagnosis of probable AD were established [45].

The NINCDS-ADRDA criteria were then revised by the NIA [46], due to the need to clearly discriminate AD from either other conditions leading to dementia (e.g. Frontotemporal Dementia, Primary Progressive Aphasia), or non-amnestic forms of AD. The core clinical criteria for a diagnosis of all-cause dementia require the presence of cognitive or behavioral symptoms involving at least two cognitive domains among memory, judgment, visuospatial abilities, language and behavior. The new criteria to define a diagnosis of probable AD, also require an either amnestic or non-amnestic significant initial cognitive deficit, and, in case of a non-amnestic AD, concomitant linguistic, visuospatial and executive dysfunctions.

Therefore, the NPA needs to quantify the deficit, but also to define a pattern of scores that can provide a diagnostic clue on the possible etiology, considering that cognitive functions depend on neural network involving different brain areas [47].

A recent review highlighted that mild cognitive impairments may be undetected by simple mental status examination and brief screening tests[48, 49]. Short cognitive tests, however, are still widespread in clinical practice, in particular in countries where healthcare policies are defined based

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on their cost-effectiveness, and specifically, on the costs of tools and instruments, the time needed to administer them, and the costs related to misdiagnoses (false positives and/or false negatives).

This kind of tests are currently being promoted by some international programs to optimize the cognitive screening in primary care [50-51], where the prevalence of undiagnosed cases is high [4]. However, CCDDs, that are designed as second-/third-level referral units, should use this type of tests as part of the clinical examination and in the monitoring over time of already diagnosed patients, rather than adopt them as diagnostic tools, considering their intrinsic limitations (for a review, see Brown, 2016 [52]). A comprehensive NPA thus, is currently the best way to assess and quantify cognitive deficits [47], and should be the minimum requirement for the diagnosis of dementia.

The main strength of this survey is the inclusion of structures based on the whole national territory. This study can be of support in understanding the functioning of Italian CCDDs and the type of NP tools used in clinical practice to assess people with cognitive complaints.

This is an extremely relevant issue, considering also that potentially disease-modifying treatments are currently under development, that will require more sensitive neuropsychological measures for the early identification of cognitive disorders and dementia.

The main limitation of this survey is its being based on self-administered questionnaires, thus potentially over-estimating the scenario. The misuse of NP tests could prevent an homogeneity in the evaluation criteria, and the comparability of data from different CCDDs.

The number and type of tests used in the diagnostic process of dementia should follow recommendations from the Italian Neuropsychological Society included in the National Guidelines, thus closing the gap between cognitive neurosciences and public health.

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The external validity of our results refers to all Italian CCDDs (501 out of all the 536 active CCDDs were surveyed). This information can also be useful to compare the use of Neuropsychological tests between memory clinics from different countries.

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Author Guarantee Statement: No ethical approval or informed consent was used such respondents were all public institutions and questions were about services activity.

Contributorship statement. All authors contributed extensively to the work presented in this paper. A.DP. contributed to the conception and design of the work, to the acquisition and interpretation of data for the work and drafting the work; F.M. and E.L. contributed to the acquisition of data for the work and revising it critically; T.DF. contributed to the conception of the work and revising it critically; M.G. contributed to the design of the work, interpretation of data for the work and in writing the work; I.B., M.B., M.C., P.C., A.C., A.Cr. (Alessio Crestini), F.Ma. (Flavia Mayer), L.P., P.P. (in the IDemObsGroup) contributed to the acquisition of data for the work, in giving technical support and with conceptual advice; N.V. is the principal investigator of the project that provided financial support for the paper, and contributed to the conception and design of the work, the analysis and interpretation of data for the work, and in critically revising the work. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Data sharing statement: not applicable

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This supplementary data include a translation of some items related to the investigation on neuropsychological tools used in clinical practice for the diagnosis of dementia. Information on these tools are included in the survey questionnaire that was designed to collect data, in a standardized form, on Italian memory clinics. The full survey questionnaire is available in Italian upon request. Moreover, an overall description of the methodology used in this survey is available in a dedicated paper (Di Pucchio a et al, 2017).

The survey questionnaires included five sections, and all questions were specifically formulated to collect information on:
1. Location and registry service;
2. Access to the service;
3. Organizational aspects of the services;
4. Treatments and services provision;
5. Data on activities and patient numbers.

A group of researchers, including specialists in dementia, epidemiologists, and members of target services, participated in the development of the survey questionnaires and ensured the validity of included questions (content validity).

Table 1 shows a description of the topics included in the survey questionnaire for Italian memory clinics.

Table 1 – Section/Domain and topics included in the survey questionnaire for memory clinics

Section/Domain and Topics
Location and registry service
Detailed information on service's location, name, phone number and address; type of services provided; type of funding and methods of reimbursement
Access to service
Operating days and hours per week
Ways to access the service (e.g. phone reservation; wording for medical prescription*)
Organizational aspects of the services
Staff profile and composition
Waiting time to access the service
Procedures and service documentation *(Availability of structured procedures for data collection on the activity; Availability of documentation on integrated care pathways)*
Treatments and services
Provided services *(i.e. Pharmacological and non-pharmacological interventions; Non-pharmacological interventions provided to caregivers)*
Referral to other health professionals and access to care coordination
Neuropsychological tools used in the assessment and diagnosis of dementia
Data on activities and number of patients
Number of patients with and without a diagnosis of dementia during the last year
Patients assessed per month
Patients referred for a first assessment per month
Number of patients in charge visited per year (at least one time per year)

Note: The full survey questionnaire is available in Italian upon request

In the "Treatments and services" section of the survey questionnaire, we included a question on the neuropsychological tools used in the assessment and diagnosis of dementia. We asked referents of the memory clinics to select from a predefined list (table 2) all neuropsychological tests, batteries and clinical

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scales routinely used within their memory clinic for the assessment and diagnosis of dementias. Further test could also be added if not included in the list.

Table 2 – List of Neuropsychological tests, batteries and clinical scales included in the survey questionnaire for memory clinics.

Aachener Aphasie Test (AAT)
Activities of Daily Living (ADL)
Alzheimer's Disease Assessment Scale (ADAS)
Attention Matrices
Babcock' short tale
Clock drawing
Coloured Progressive Matrices (CPM)
Corsi spatial span
Digit Span
Drawings copy
Frontal Assessment Battery (FAB)
Frontal Behavioral Inventory (FBI)
Geriatric Depression Scale (GDS)
Ideomotor Apraxia
Insight Scale
Instrumental Activities of Daily Living (IADL)
Mental Deterioration Battery (MDB)
Milan Overall Dementia Assessment (MODA)
Mini-Mental State Examination (MMSE)
Modified Wisconsin Card Sorting Test (MCST)
Neuropsychiatric Inventory (NPI)
Oral-facial apraxia
Phonemic word fluency test (FAS)
Rey 15 words
Rey- Complex Figure (RCF)
Semantic word fluency test
Standard Progressive Matrices (SPM)
Stroop Trail Making Test (TMT)
Visual naming

A web-platform system, the "Dementia Observatory web-platform system", was developed to manage the large amount of data from a very high number of services. This system allowed to create and manage a database with data storage and retrieval functions.
The survey questionnaire was self-administered, completed in an electronic form by the clinical representative of each service. The questionnaire included both closed questions with pre-coded options, and open questions. For the majority of questions answers were required.

Some questions were also included to automatically check for already entered data, to avoid inconsistent answers.

All participants were invited to participate to the survey via email. An introductory cover letter was also sent to explain the objectives of the survey, specifying that the survey was carried out by the Italian NIH and that

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responding was required by the Ministry of Health. The cover letter included a link to access the online questionnaire. The contact name and address of the principal investigator, along with details on how and why the respondent was selected, and any potential benefits or harm resulting from the study were also provided.

To increase the number and accuracy of the responses to the survey different strategies were used, such as:
• keeping in contact with participants through follow-up emails after the initial message, and through telephone support;
• checking and correcting incorrect telephone and/or e-mail contacts;
• directly supporting respondents in completing the survey, when requested;
• contacting respondents who were initially unable to participate, but did not refuse to participate.

Data collected through the web-platform system were then exported in different formats for statistical analysis (SPSS ver. 20, IBM, USA). Null responses generated by typing errors or "impossible" responses to survey questions (i.e. to the question "how many days is the unit open?": outliers were considered numbers equal and/or lower than zero or higher than 7) were removed from calculations if not corrected within a given reference time.

The response rate of contacted services was used to describe the success of the survey, and considered as a primary measure of the quality of the survey.

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Questions to consider when preparing a report of findings from postal surveys (Table 4). *IN Burns KE, Duffett M, Kho ME, Meade MO, Adhikari NK, Sinuff T, Cook DJ; ACCADEMY Group. A guide for the design and conduct of self-administered surveys of clinicians. CMAJ. 2008 Jul 29;179(3):245-52.*

Section	Question	
Abstract		Page*
	Is the objective clearly stated?	Page 2
	Is the design of the study stated?	Page 2
	Is the study setting well described?	Page 2
	Is the survey population described?	Page 2
	Is the response rate reported?	Page 2
	Are the outcome measures identified?	Page 2
	Are the main results clearly reported?	Page 2
	Are the conclusions appropriate?	Page 2
Introduction		
	Is the problem clearly stated?	Page 4, 5
	Is the pertinent literature cited and critically appraised?	Page 5, 6
	Is the relevance of the research question explained?	Page 6, 7
	Is the objective clearly stated?	Page 7,8
Methods		
	Is the study design appropriate to the objective?	Page 8
	Is the setting clearly described?	Page 8
	Are the methods described clearly enough to permit other researchers to duplicate the study?	Page 8, 9,10, 11
	Is the survey sample likely to be representative of the population?	Page 8
	Is the questionnaire described adequately?	Page 8
	Have the validity and reliability of the questionnaire been established?	Page 8
	Was the questionnaire administered in a satisfactory way?	Page 8
	Are the statistical methods used appropriately?	Page 11
Results		
	Do the results address the objective?	Page 11,12, 13,
	Are all respondents accounted for?	Page 11
	Are the results clearly and logically presented?	Page 11,12, 13,
	Are the tables and figures appropriate?	Table 3, 4,5, 6
	Are the numbers consistent in the text and the tables?	Page 11,12,13,
Discussion		
	Are the results succinctly summarized?	Page 14
	Are the implications of the results stated?	Page 15
	Are other interpretations considered and refuted?	Page 16
	Are the limitations of the study and its results explained?	Page 17
	Are appropriate conclusions drawn?	Page 17

*PDF Proof "**Neuropsychological tests for the diagnosis of dementia: results of a survey in Italian memory clinics**", Alessandra Di Pucchio [1], Nicola Vanacore [1], Fabrizio Marzolini [1], Eleonora Lacorte[1], Teresa Di Fiandra [2], I-DemObs Group [3], Marina Gasparini [4]

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	X (pg.1,2)	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	X (pg 4,5)	Explain the scientific background and rationale for the investigation being reported
Objectives	X (pg 7,8)	State specific objectives, including any prespecified hypotheses
Methods		
Study design	X (pg 8)	Present key elements of study design early in the paper
Setting	X (pg 8)	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants		(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls X (pg 8) *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	X (pg9,10)	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	X (pg 9,10)	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	X (pg 17)	Describe any efforts to address potential sources of bias
Study size	n.a*	Explain how the study size was arrived at
Quantitative variables	X (pg9)	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	X (pg 10,11)	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

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(*e*) Describe any sensitivity analyses

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Results		
Participants	**n.a***	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	**n.a***	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	**X (pg 11,12)**	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	**X (pg 13.,14)**	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	**n.a***	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	**X (pg 14.15)**	Summarise key results with reference to study objectives
Limitations	**X (pg 17)**	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	**X (pg 17)**	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	**n.a***	Discuss the generalisability (external validity) of the study results
Other information		
Funding	**X** (pg 18)	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

***n.a not applicable**

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