10° CONVEGNO NAZIONALE SUI CENTRI DIURNI ALZHEIMER

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PROGRAMMA SCIENTIFICO

SIAMO PRONTI AD USARE I NUOVI FARMACI PER L'ALZHEIMER ?
(SE E QUANDO ARRIVERANNO)

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Alzheimer's & Dementia: Translational Research & Clinical Interventions 4 (2018) 195-214

Alzheimer & Dementia

Featured Article

Alzheimer's disease drug development pipeline: 2018

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Abstract

Introduction: Treatments for Alzheimer's disease (AD) are needed due to the growing number of individuals with preclinical, prodromal, and dementia forms of AD. Drug development for AD therapies can be examined by inspecting the drug development pipeline as represented on clinicaltrials.gov.

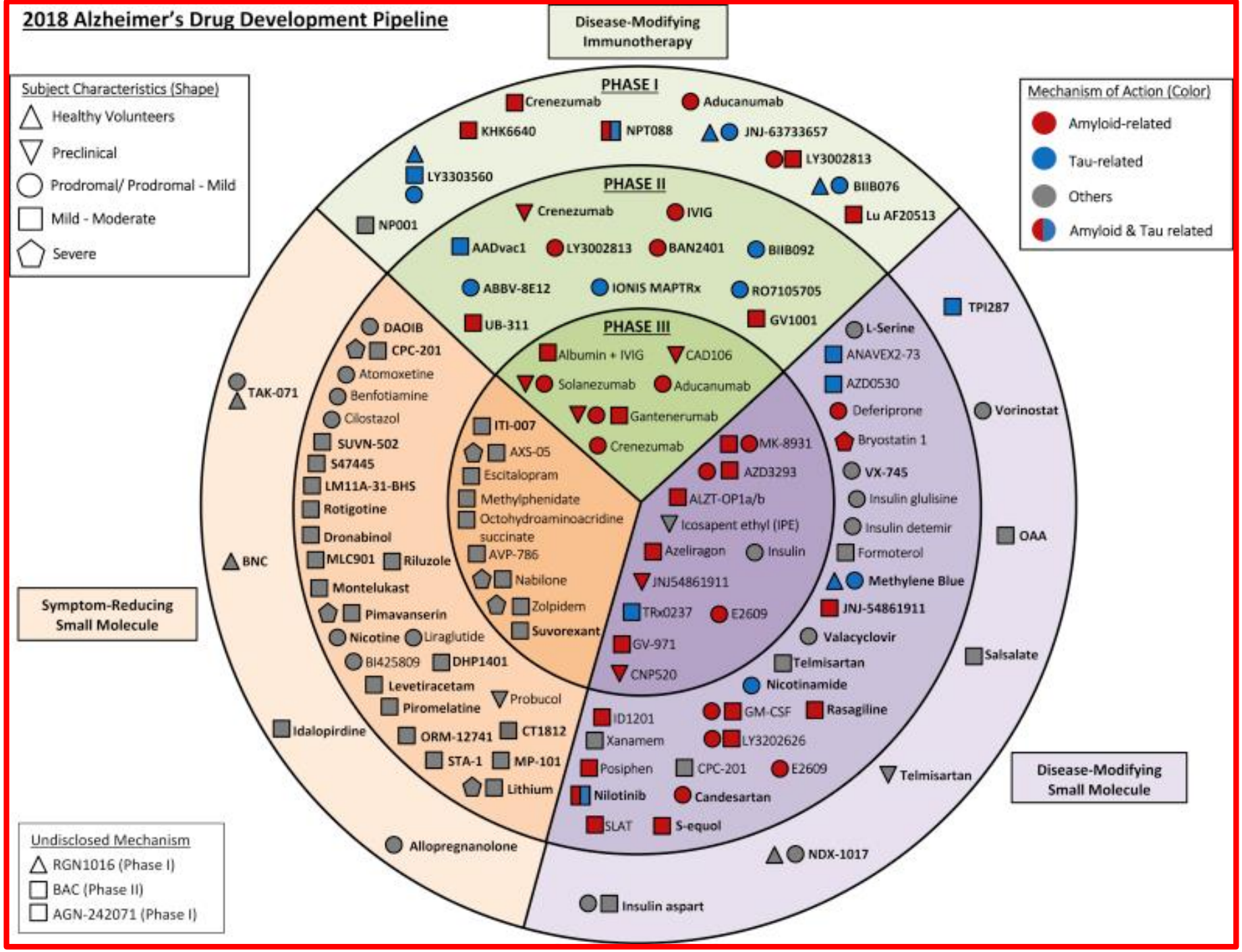
Methods: Clinicaltrials.gov was assessed as of January 30, 2018 to determine AD therapies represented in phase I, phase II, and phase III.

Results: There are 112 agents in the current AD treatment pipeline. There are 26 agents in 35 trials in phase III, 63 agents in 75 trials in phase II, and 23 agents in 25 trials in phase I. A review of the mechanisms of actions of the agents in the pipeline shows that 63% are disease-modifying therapies, 22% are symptomatic cognitive enhancers, and 12% are symptomatic agents addressing neuropsychiatric and behavioral changes. Trials in phase III are larger and longer than phase II or phase I trials, particularly those involving disease-modifying agents. Comparison with the 2017 pipeline shows that there are four new agents in phase III, 14 in phase II, and eight in phase I. Inspection of the use of biomarkers as revealed on clinicaltrials.gov shows that amyloid biomarkers are used as entry criterion in 14 phase III disease-modifying agent trials and 17 disease-modifying agent trials in phase II. Twenty-one trials of disease-modifying agents in phase II did not require biomarker confirmation for AD at trial entry.

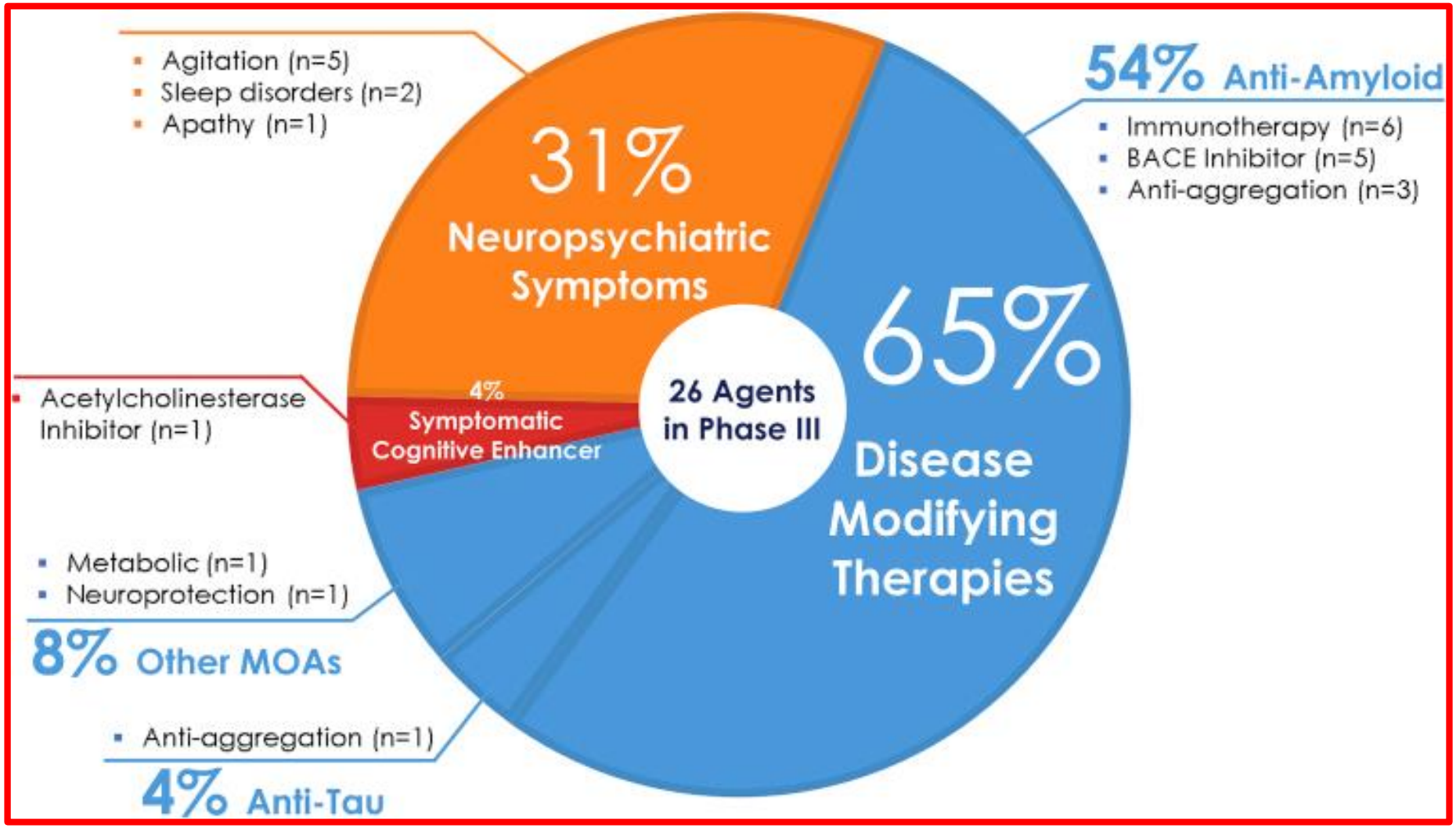
Discussion: The AD drug development pipeline is slightly larger in 2018 than in 2017. Trials increasingly include preclinical and prodromal populations. There is an increase in nonamyloid mechanisms of action for drugs in earlier phases of drug development. Biomarkers are increasingly used in AD drug development but are not used uniformly for AD diagnosis confirmation.

Table 1
Agents currently in phase III of Alzheimer's disease drug development (as of January 30, 2018)

Agent	Agent mechanism class	Mechanism of action	Therapeutic purpose	Clinicaltrials.gov ID	Status	Sponsor	Start date	Estimated end date
Aducanumab	Anti-amyloid	Monoclonal antibody	Remove amyloid (DMT)	NCT02484547	Recruiting	Biogen	September-15	April-22
				NCT02477800	Recruiting	Biogen	August-15	March-22
Albumin + immunoglobulin	Anti-amyloid	Polyclonal antibody	Remove amyloid (DMT)	NCT01561053*	Active, not recruiting	Grifols	March-12	December-17
ALZT-OP1a + ALZT-OP1b (cromolyn + ibuprofen)	Anti-amyloid, anti-inflammatory	Mast cell stabilizer (cromolyn), anti-inflammatory (ibuprofen)	Reduce neuronal damage; mast cells may also play a role in amyloid pathology (DMT)	NCT02547818	Recruiting	AZTherapies, Pharma Consulting Group, KCAS Bio, APCER Life Sciences	September-15	November-19
AVP-786	Neurotransmitter based	Sigma 1 receptor agonist; NMDA receptor antagonist	Improve neuropsychiatric symptoms (agitation)	NCT02442765	Recruiting	Avanir	September-15	July-18
				NCT02446132	Recruiting-EXT	Avanir	December-15	March-21
AZD3293 (LY3314814)	Anti-amyloid	BACE1 inhibitor	Reduce amyloid production (DMT)	NCT02245737*	Active, not recruiting	AstraZeneca, Eli Lilly	September-14	September-19
				NCT02783573	Recruiting	AstraZeneca, Eli Lilly	July-16	March-21
				NCT02972658	Recruiting-EXT	AstraZeneca, Eli Lilly	March-17	September-20


2018 Alzheimer's Drug Development Pipeline
Disease-Modifying Immunotherapy
Subject Characteristics (Shape)
Healthy Volunteers
Preclinical
Prodromal/ Prodromal - Mild
Mild - Moderate
Severe
Mechanism of Action (Color)
Amyloid-related
Tau-related
Others
Amyloid & Tau related
PHASE I
Crenezumab
Aducanumab
KHK6640
NPT088
JNJ-63733657
LY3002813
LY3303560
BIIB076
NP001
Lu AF20513
PHASE II
Crenezumab
IVIG
AADvac1
LY3002813
BAN2401
BIIB092
ABBV-8E12
IONIS MAPTRx
RO7105705
UB-311
GV1001
PHASE III
Albumin + IVIG
CAD106
Solanezumab
Aducanumab
Gantenerumab
Crenezumab
TPI287
L-Serine
ANAVEX2-73
AZD0530
Deferiprone
Bryostatin 1
VX-745
Insulin glulisine
Insulin detemir
Formoterol
Methylene Blue
JNJ-54861911
Valacyclovir
Telmisartan
Nicotinamide
GM-CSF
Rasagiline
LY3202626
CPC-201
E2609
Telmisartan
Candesartan
S-equol
NDX-1017
Insulin aspart
Vorinostat
OAA
Salsalate
Disease-Modifying Small Molecule
DAOIB
CPC-201
Atomoxetine
Benfotiamine
Cilostazol
SUVN-502
S47445
LM11A-31-BHS
Rotigotine
Dronabinol
MLC901
Riluzole
Montelukast
Pimavanserin
Nicotine
Liraglutide
BI425809
DHP1401
Levetiracetam
Piromelatine
Probucol
ORM-12741
CT1812
STA-1
MP-101
Lithium
Idalopirdine
Allopregnanolone
TAK-071
BNC
ITI-007
AXS-05
Escitalopram
Methylphenidate
Octohydroaminoacridine succinate
AVP-786
Nabilone
Zolpidem
Suvorexant
MK-8931
AZD3293
ALZT-OP1a/b
Icosapent ethyl (IPE)
Azeliragon
Insulin
JNJ54861911
TRx0237
E2609
GV-971
CNP520
ID1201
Xanamem
Posiphen
Nilotinib
SLAT
Symptom-Reducing Small Molecule
Undisclosed Mechanism
RGN1016 (Phase I)
BAC (Phase II)
AGN-242071 (Phase I)

Mechanisms of action of agents in phase III.



The antibody aducanumab reduces Aβ plaques in Alzheimer's disease

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Alzheimer's disease (AD) is characterized by deposition of amyloid-β (Aβ) plaques and neurofibrillary tangles in the brain, accompanied by synaptic dysfunction and neurodegeneration. Antibody-based immunotherapy against Aβ to trigger its clearance or mitigate its neurotoxicity has so far been unsuccessful. Here we report the generation of aducanumab, a human monoclonal antibody that selectively targets aggregated Aβ. In a transgenic mouse model of AD, aducanumab is shown to enter the brain, bind parenchymal Aβ, and reduce soluble and insoluble Aβ in a dose-dependent manner. In patients with prodromal or mild AD, one year of monthly intravenous infusions of aducanumab reduces brain Aβ in a dose- and time-dependent manner. This is accompanied by a slowing of clinical decline measured by Clinical Dementia Rating—Sum of Boxes and Mini Mental State Examination scores. The main safety and tolerability findings are amyloid-related imaging abnormalities. These results justify further development of aducanumab for the treatment of AD. Should the slowing of clinical decline be confirmed in ongoing phase 3 clinical trials, it would provide compelling support for the amyloid hypothesis.

Table 1 | Baseline characteristics

Characteristic		Placebo ($n=40$)	Aducanumab 1 mg kg^{-1} ($n=31$)	Aducanumab 3 mg kg^{-1} ($n=32$)	Aducanumab 6 mg kg^{-1} ($n=30$)	Aducanumab 10 mg kg^{-1} ($n=32$)	Total ($n=165$)*
Years of age (mean ± s.d.)		72.8 ± 7.2	72.6 ± 7.8	70.5 ± 8.2	73.3 ± 9.3	73.7 ± 8.3	72.6 ± 8.1
Female sex (*n* (%))		23 (58)	13 (42)	17 (53)	15 (50)	15 (47)	83 (50)
ApoE ε4 (*n* (%))	Carriers	26 (65)	19 (61)	21 (66)	21 (70)	20 (63)	107 (65)
	Non-carriers	14 (35)	12 (39)	11 (34)	9 (30)	12 (38)	58 (35)
Clinical stage (*n* (%))	Prodromal	19 (48)	10 (32)	14 (44)	12 (40)	13 (41)	68 (41)
	Mild	21 (53)	21 (68)	18 (56)	18 (60)	19 (59)	97 (59)
MMSE (mean ± s.d.)		24.7 ± 3.6	23.6 ± 3.3	23.2 ± 4.2	24.4 ± 2.9	24.8 ± 3.1	24.2 ± 3.5
Global CDR (*n* (%))	0.5	34 (85)	22 (71)	22 (69)	25 (83)	24 (75)	127 (77)
	1	6 (15)	9 (29)	10 (31)	5 (17)	8 (25)	38 (23)
CDR-SB (mean ± s.d.)		2.66 ± 1.50	3.40 ± 1.76	3.50 ± 2.06	3.32 ± 1.54	3.14 ± 1.71	3.18 ± 1.72
FCSRT sum of free recall score (mean ± s.d.)		15.2 ± 8.5	13.2 ± 9.0	13.8 ± 8.0	14.4 ± 8.3	14.6 ± 8.3	14.3 ± 8.3
PET SUVR composite score (mean ± s.d.)		1.44 ± 0.17	1.44 ± 0.15	1.46 ± 0.15	1.43 ± 0.20	1.44 ± 0.19	1.44 ± 0.17
AD medications use† (*n* (%))		24 (60)	19 (61)	28 (88)	20 (67)	17 (53)	108 (65)

Percentages are rounded to the nearest integer. AD, Alzheimer's disease; ApoE ε4, apolipoprotein E ε4 allele; CDR, Clinical Dementia Rating; CDR-SB, Clinical Dementia Rating—Sum of Boxes; FCSRT, Free and Cued Selective Reminding Test; MMSE, Mini-Mental State Examination; PET, positron emission tomography; SD, standard deviation; SUVR, standard uptake value ratio.

*Number of patients dosed.

†Cholinesterase inhibitors and/or memantine.

Table 2 | Summary of adverse events and most common adverse events

		Aducanumab			
Adverse event (*n* (%))	Placebo ($n=40$)	1 mg kg^{-1} ($n=31$)	3 mg kg^{-1} ($n=32$)	6 mg kg^{-1} ($n=30$)	10 mg kg^{-1} ($n=32$)
Any adverse event	39 (98)	28 (90)	27 (84)	28 (93)	29 (91)
Serious event	15 (38)	3 (10)	4 (13)	4 (13)	12 (38)
Discontinuing treatment due to an adverse event	4 (10)	3 (10)	2 (6)	3 (10)	10 (31)
Common adverse events					
ARIA	2 (5)	2 (6)	4 (13)	11 (37)	15 (47)
Headache	2 (5)	5 (16)	4 (13)	8 (27)	8 (25)
Urinary tract infection	4 (10)	3 (10)	2 (6)	4 (13)	5 (16)
Upper respiratory tract infection	6 (15)	2 (6)	2 (6)	2 (7)	6 (19)
Diarrhoea	3 (8)	0	6 (19)	1 (3)	3 (9)
Arthralgia	2 (5)	0	6 (19)	2 (7)	1 (3)
Fall	8 (20)	3 (10)	2 (6)	2 (7)	2 (6)
Superficial siderosis of CNS	0	2 (6)	1 (3)	2 (7)	4 (13)
Constipation	0	3 (10)	1 (3)	1 (3)	3 (9)
Nausea	2 (5)	2 (6)	5 (16)	0	1 (3)
Anxiety	4 (10)	4 (13)	1 (3)	1 (3)	1 (3)
Nasopharyngitis	0	1 (3)	5 (16)	0	1 (3)
Cough	2 (5)	3 (10)	1 (3)	0	1 (3)
Alanine aminotransferase increased	0	3 (10)	0	1 (3)	0
Aspartate aminotransferase increased	0	3 (10)	0	0	1 (3)

Common adverse events are those with an incidence of $\geq 10\%$ in any aducanumab treatment group. Incidence of ARIA based on adverse event reporting. Adverse events of ARIA-E (oedema) and ARIA-H (micro-haemorrhage) are both coded to the MedDRA preferred term of amyloid-related imaging abnormalities, and ARIA-H (superficial siderosis) codes to the MedDRA preferred term of superficial siderosis of the CNS. ARIA, amyloid-related imaging abnormalities; CNS, central nervous system; MedDRA, Medical Dictionary for Regulatory Activities.

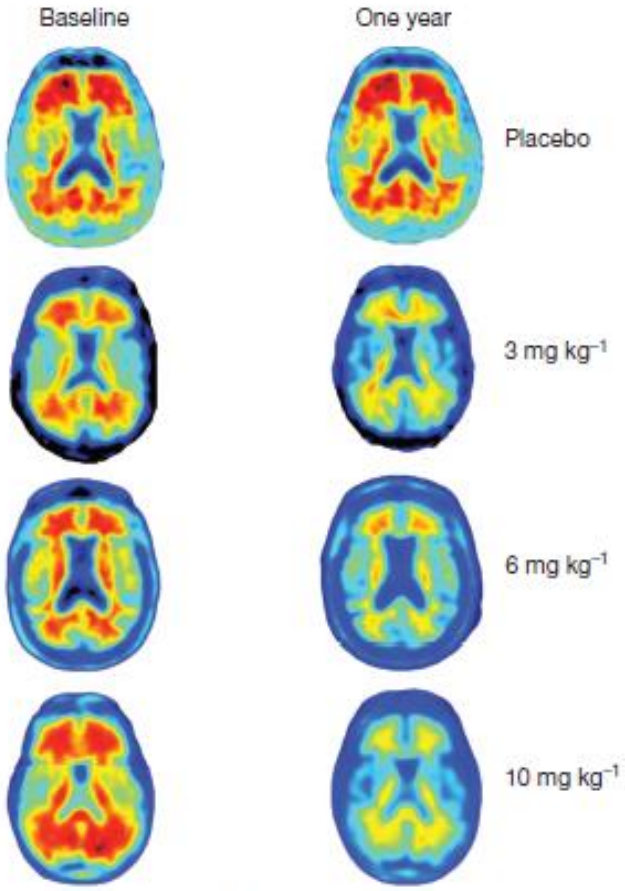

Figure 1 | Amyloid plaque reduction with aducanumab: example amyloid PET images at baseline and week 54. Individuals were chosen

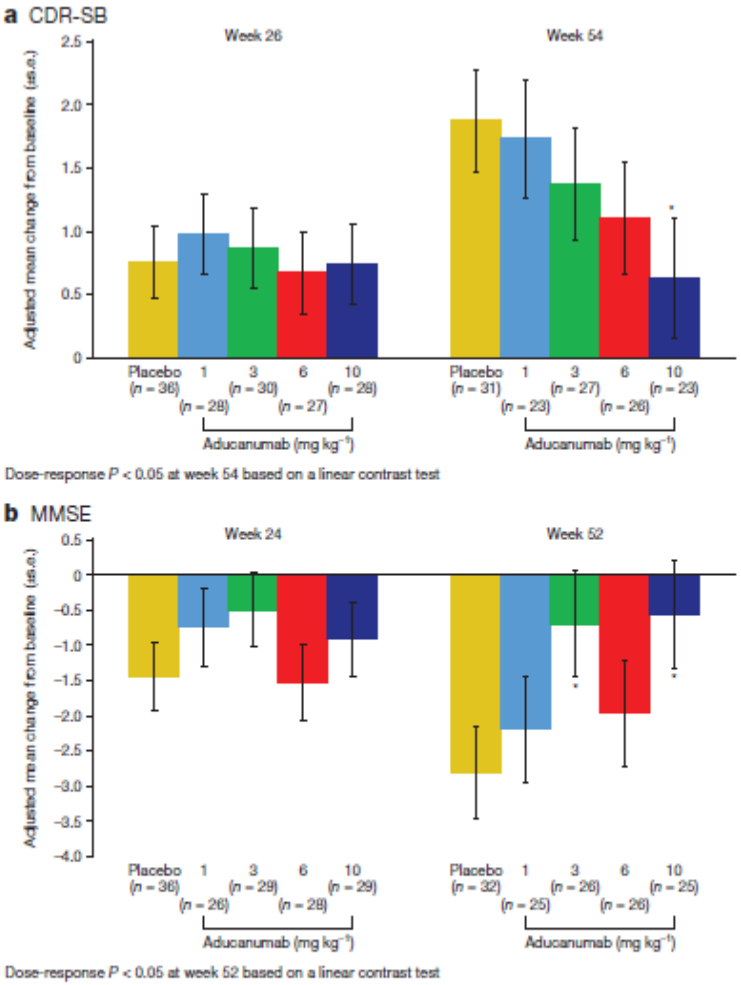

Figure 3 | Aducanumab effect (change from baseline) on CDR-SB and MMSE. a, b, Aducanumab effect on CDR-SB (**a**) and MMSE (**b**). *$P < 0.05$ versus placebo; two-sided tests with no adjustments for multiple comparisons. CDR-SB and MMSE were exploratory endpoints. Adjusted mean ± s.e. Analyses using ANCOVA. CDR-SB, Clinical Dementia Rating—Sum of Boxes; MMSE, Mini Mental State Examination.

Extended Data Table 1 | Change from baseline in amyloid PET SUVR values (a secondary endpoint at 6 months), and in exploratory clinical endpoints at the end of the placebo-controlled period (6-month data also shown for amyloid PET)

		Aducanumab				
Adjusted mean ± SE change from baseline for:	Placebo	1 mg kg^{-1}	3 mg kg^{-1}	6 mg kg^{-1}	10 mg kg^{-1}	p-value (dose-response)
Amyloid PET SUVR values						
At 6 months	(n=34)	(n=26)	(n=27)	(n=23)	(n=27)	
	−0.005 ± 0.018	−0.030 ± 0.020	−0.087 ± 0.020**	−0.143 ± 0.022***	−0.205 ± 0.020***	<0.0001
At 1 year†	(n=30)	(n=21)	(n=26)	(n=23)	(n=21)	
	0.003 ± 0.021	−0.055 ± 0.024	−0.135 ± 0.022***	−0.210 ± 0.024***	−0.268 ± 0.025***	<0.0001
CDR-SB‡	(n=31)	(n=23)	(n=27)	(n=26)	(n=23)	
	1.87 ± 0.41	1.72 ± 0.46	1.37 ± 0.43	1.11 ± 0.44	0.63 ± 0.47*	<0.05
MMSE‡	(n=32)	(n=25)	(n=26)	(n=26)	(n=25)	
	−2.81 ± 0.67	−2.18 ± 0.75	−0.70 ± 0.75*	−1.96 ± 0.75	−0.56 ± 0.76*	<0.05
NTB overall Z score†	(n=29)	(n=23)	(n=26)	(n=24)	(n=24)	
	−0.11 ± 0.08	−0.25 ± 0.09	−0.13 ± 0.08	−0.19 ± 0.09	−0.10 ± 0.09	NS
FCSRT: sum of free recall score†	(n=31)	(n=23)	(n=25)	(n=25)	(n=25)	
	−2.33 ± 1.07	−1.63 ± 1.24	−1.25 ± 1.20	−4.04 ± 1.21	−0.69 ± 1.20	NS

*P < 0.05; **P < 0.01; ***P < 0.001 versus placebo; two-sided tests with no adjustments for multiple comparisons.
†At week 54.
‡At week 52.
Analyses using ANCOVA. ApoE ε4, apolipoprotein E ε4 allele; CDR-SB, Clinical Dementia Rating—Sum of Boxes; FCSRT, Free and Cued Selective Reminding Test; MMSE, Mini-Mental State Examination; NS, not significant; NTB, neuropsychological test battery; SE, standard error; SUVR, standard uptake value ratio.

CLINICAL DEMENTIA RATING SCALE (CDR) ESTESA (*)

N. B.: assegnare punteggio solo se il deficit dipende da deterioramento cognitivo e non da altre cause

DEMENZA:	ASSENTE CDR 0	MOLTO LIEVE CDR 0.5	LIEVE CDR 1	MODERATA CDR 2	GRAVE CDR 3
Memoria	Nessuna perdita di memoria o smemoratezza occasionale ed irrilevante	Lieve smemoratezza permanente; parziale rievocazione di eventi	Perdita memoria moderata e più rilevante per eventi recenti con interferenza nelle attività quotidiane	Perdita memoria severa: materiale nuovo perso rapidamente	Perdita memoria grave; rimangono alcuni frammenti
Orientamento	Perfettamente orientato	Ben orientato eccetto lieve difficoltà nell'orientamento temporale	Moderato deficit nell'orientamento temporale; orientato nello spazio durante la visita ma altrove può essere disorientato	Severo disorientamento temporale, spesso spaziale	Orientamento solo personale
Giudizio e soluzione di problemi	Risolve bene i problemi quotidiani e gestisce bene sia gli affari che le finanze; giudizio adeguato rispetto al passato	Lieve compromissione nella soluzione di problemi, analogie e differenze (prove di ragionamento)	Difficoltà moderata di gestione dei problemi, analogie e differenze; giudizio sociale di solito conservato	Difficoltà severa di esecuzione di problemi, analogie e differenze; giudizio sociale compromesso	Incapace di dare giudizi o di risolvere problemi
Vita di comunità	Usuali livelli di autonomia funzionale nel lavoro, acquisti, attività di volontariato e relazioni sociali	Lieve compromissione nel lavoro, acquisti, attività di volontariato e relazioni sociali	Incapace di compiere indipendentemente queste attività anche se può ancora essere coinvolto in alcune; appare normale ad una esame casuale	Nessuna pretesa di fuori In grado di essere portato fuori casa	attività indipendente casa. Non in grado di uscire fuori casa
Casa e hobbies	Vita domestica, hobbies e interessi intellettuali ben conservati	Vita domestica, hobbies e interessi intellettuali lievemente compromessi	Lieve ma sensibile compromissione della vita domestica; abbandono dei lavori domestici più difficili e degli hobbies ed interessi più complicati	Conservati solo semplici lavori domestici, interessi ridotti, non sostenuti	Nessuna funzione domestica conservata
Cura personale	Interamente capace propria	di curarsi della persona	Richiede sollecitazione per la normale cura personale	Richiede assistenza per abbigliamento, igiene e cura personale	Richiede molta assistenza per cura personale; spesso incontinenza urinaria

CDR 4: DEMENZA MOLTO GRAVE Il paziente presenta severo deficit del linguaggio o della comprensione, problemi nel riconoscere i familiari, incapacità a deambulare in modo autonomo, problemi ad alimentarsi da solo, nel controllare la funzione intestinale o vescicale

CDR 5: DEMENZA TERMINALE Il paziente richiede assistenza totale perché completamente incapace di comunicare, in stato vegetativo, allettato, incontinente

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Staging Dementia Using Clinical Dementia Rating Scale Sum of Boxes Scores:

A Texas Alzheimer's Research Consortium Study

Sum of Boxes Staging Category

CDR Sum of Boxes Range	Staging Category
0	Normal
0.5–4.0	Questionable cognitive impairment
0.5–2.5	Questionable impairment
3.0–4.0	Very mild dementia
4.5–9.0	Mild dementia
9.5–15.5	Moderate dementia
16.0–18.0	Severe dementia

Abbreviation: See Table 1.

RAND CORPORATION

Research Report

JAKUB P. HLÁVKA, SOEREN MATTKE, JODI L. LIU

Assessing the Preparedness of the Health Care System Infrastructure in Six European Countries for an Alzheimer's Treatment

About This Report

This report shows the potential magnitude of health care infrastructure constraints in the evaluation and treatment of early-stage Alzheimer's disease with a future disease-modifying therapy in six European countries. This research was sponsored by Biogen and conducted within RAND Health, a division of the RAND Corporation. A profile of RAND Health, abstracts of its publications, and ordering information can be found at www.rand.org/health. The authors thank the following subject-matter experts for sharing their insights into clinical practices and patient needs in the six countries: Antonio del Olmo, Lutz Frölich, Michael Karran, Pierre Krolak-Salmon, José Luis Molinuevo, Matthew Norton, Patrizia Spadin, Anders Wimo, and Bengt Winblad. The authors also thank Jon Sussex and Peter Hudomiet for their valuable feedback on this report.

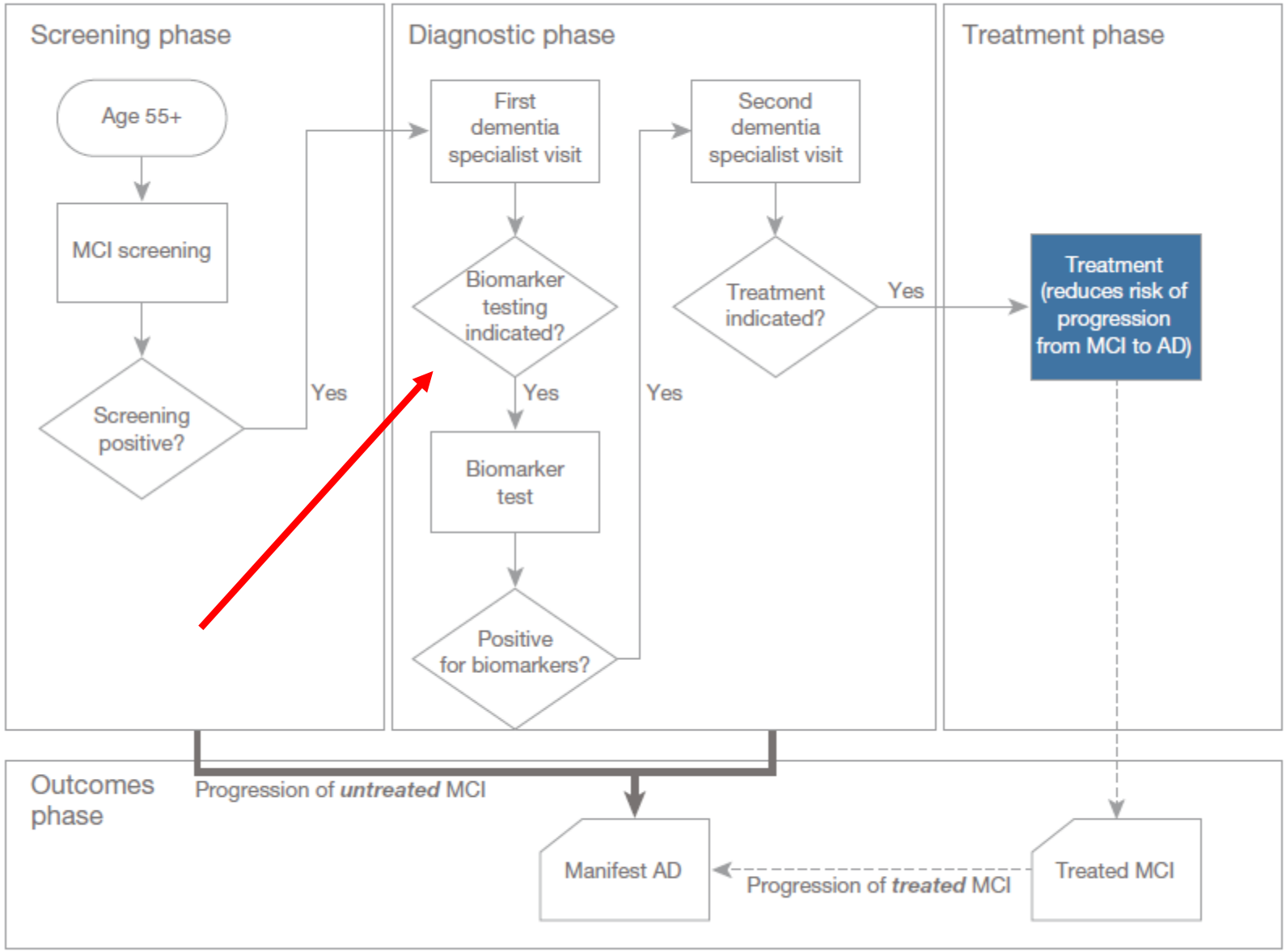
TABLE 1

Alzheimer's Disease-Modifying Therapy Candidates in Phase 2 and Phase 3 Clinical Trials, as of September 2018

Candidate	Sponsor	Clinical Trial Phase	Expected Primary Completion Date	National Clinical Trial Identifier
Anti–beta-amyloid antibodies				
Aducanumab (BIIB037)	Biogen[a]	Phase 3	January 2020	NCT02477800
Crenezumab	Hoffman-La Roche	Phase 3	August 2020	NCT02670083
Gantenerumab	Hoffman-La Roche	Phase 3	May 2022	NCT03443973, NCT03444870
BAN2401	Eisai/Biogen	Phase 2	July 2018	NCT01767311
LY3002813[b]	Eli Lilly	Phase 2	October 2020	NCT03367403
Anti-tau antibodies				
ABBV-8E12	AbbVie	Phase 2	December 2020	NCT02880956
RO7105705	Genentech	Phase 2	September 2020	NCT03289143
BACE inhibitors				
Elenbecestat (E2609)	Eisai/Biogen	Phase 3	March 2021	NCT03036280
CNP520	Novartis/Amgen/Banner Alzheimer's Institute	Phase 2/3	July 2024	NCT03131453
Vaccines				
CAD106 (anti–beta amyloid)	Novartis	Phase 2/3	August 2024	NCT02565511
AADvac1 (anti-tau)	Axon Neuroscience	Phase 2	June 2019	NCT02579252

FIGURE 1

Conceptual Framework for the Patient Journey



SOURCE: Liu et al., 2017.

NOTE: AD = Alzheimer's dementia.

TABLE 2

Estimated Workforce to Supply Dementia Specialist Visits

	Neurologists	Geriatricians	Geriatric or Old-Age Psychiatrists	Specialists per 100,000 People
France	2,571	1,756	—	6.7
Germany	6,607	2,149	10,943	24.0
Italy	6,508	1,415	1,578	16.0
Spain	2,719	970	735	9.5
Sweden	—	450	1,349	18.2
United Kingdom	1,755	1,332	1,761	7.3

SOURCES: Eurostat, 2017; European Geriatric Medicine Society, 2018.

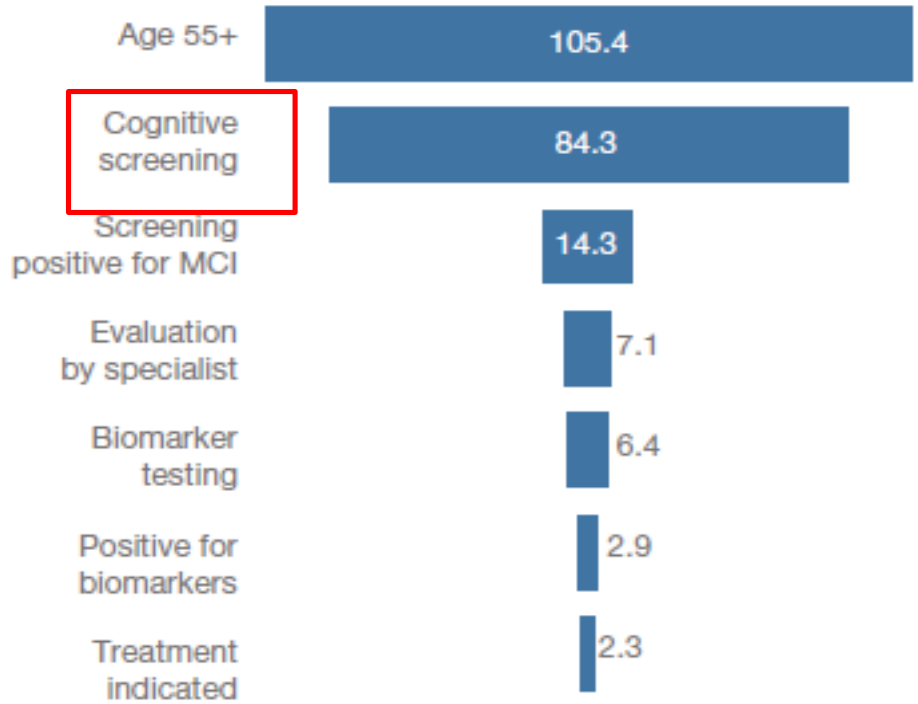
NOTES: The numbers of neurologists and psychiatrists are based on 2014–2016 data from Eurostat (most recent for each country). The number of geriatricians is based on 2012–2017 data from European Geriatric Medicine Society (most recent for each country). Based on expert input about the specialists involved in diagnosis of MCI due to Alzheimer's disease, we do not include geriatric psychiatrists in France and neurologists in Sweden.

Box 2. Interceptor Project, Italy

In December 2017, Italy launched the Interceptor Project to help identify people at higher risk of developing Alzheimer's disease, with the goal of improving their quality of care (Alzheimer Europe, 2017). The initiative aims to enroll 400 patients ages 50 to 85 with mild cognitive impairment and develop strategies to identify patients with the highest risk of developing Alzheimer's dementia and thus the greatest likelihood of benefiting if a new treatment becomes available ("Italy Launches Pioneering Project to Identify Alzheimer's Risk," 2017). The Italian Ministry of Health expects to collect comprehensive data based on neuropsychological assessments, CSF tests, and PET and MRI scans over a period of three years, which is expected to help inform the selection of the most appropriate biomarkers for nationwide screening for patients with a higher risk of progressing toward Alzheimer's dementia. One of the stated goals, moreover, is to better understand which patients are most likely to benefit from a novel therapy, thus increasing the system's sustainability (Ministero della Salute, 2017).

FIGURE 2

Expected Patient Demand at Each Stage of the Patient Journey in the Six European Countries in 2019 (millions)



NOTE: The number of expected patients is from France, Germany, Italy, Spain, Sweden, and the United Kingdom.

- A disease-modifying therapy for patients with MCI due to Alzheimer's disease becomes available in 2020. We assume the therapy would be an anti–beta-amyloid monoclonal antibody, as candidates that target beta-amyloid are the furthest along in clinical trials, that would be delivered by intravenous administration.

- We assume the following treatment characteristics: Treatment would be delivered by intravenous infusion every four weeks over one year, following protocols for a typical immunotherapy; and treatment would reduce the relative risk of progression from MCI to Alzheimer's dementia by 50 percent.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 February 2018
CPMP/EWP/553/95 Rev.2
Committee for Medicinal Products for Human Use (CHMP)

Guideline on the clinical investigation of medicines for the treatment of Alzheimer's disease

Draft agreed by CNSWP	December 2015
Adopted by CHMP for release for consultation	28 January 2016
Start of public consultation	01 February 2016
End of consultation (deadline for comments)	31 July 2016
Agreed by CNSWP	December 2017
Adopted by CHMP	22 February 2018
Date of coming into effect	1 September 2018

This guideline replaces 'Guideline on medicinal products for the treatment of Alzheimer's disease and other dementias' (CPMP/EWP/553/95 Rev. 1).

Efficacy endpoints in AD Dementia

For patients with **established** AD dementia, efficacy should be assessed in the following domains:

1) cognition, as measured by objective tests (cognitive endpoint);
2) (instrumental) activities of daily living (functional endpoint);
3) overall clinical response, as reflected by global assessment (global endpoint)

Efficacy endpoints in Prodromal AD/MCI due to AD

The use of a composite scale with a combined assessment of cognition and its impact on daily functioning as a single primary endpoint is also considered appropriate in this population.

Efficacy endpoints in Preclinical AD

For the time being there is no "gold standard" for assessment of treatment effect in patients with preclinical AD

Until a biomarker will be qualified as a reliable surrogate measure of treatment effect in absence of a clinically observable change, patients should be followed up for a sufficient time to capture relevant cognitive changes.

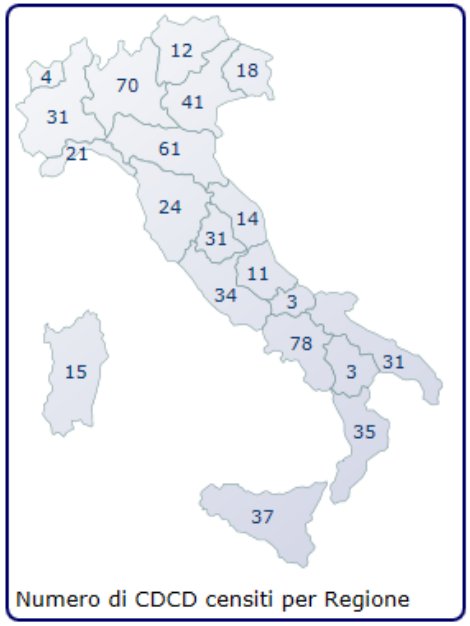
IL CONTESTO DEI SERVIZI IN ITALIA

Nuovo sito dell'Osservatorio Demenze

https://demenze.iss.it

La mappa *on line* dei Servizi per Demenze in Italia

593 CDCD*



Numero di CDCD censiti per Regione

553 Centri diurni **

Numero di Centri Diurni censiti per Regione

1304 Strutture residenziali***

Numero di Strutture Residenziali censite per Regione

Ann Ist Super Sanità 2017 | Vol. 53, No. 3: 246-252
DOI: 10.4415/ANN_17_03_11

Survey of health and social-health services for people with dementia: methodology of the Italian national project

Alessandra Di Pucchio[1], Teresa Di Fiandra[2], Fabrizio Marzolini[1], Eleonora Lacorte[1], SQoDS Group* and Nicola Vanacore[1]

[1]*Centro Nazionale Prevenzione delle Malattie e Promozione della Salute, Istituto Superiore di Sanità, Rome, Italy*
[2]*Direzione della Prevenzione, Ministero della Salute, Rome, Italy*
**the members of the SQoDS Group are listed before the References*

Abstract
People with dementia have special assistance needs. Worldwide problem is to ensure access to quality health services. Our study supported by the Italian Ministry of Health reports methodology features of a large survey project conducted to identify and to collect information on health and social health services for people with dementia in Italy. Among all Italian regions, about two thousand services available to individuals with dementia disease and their caregivers were identified. These services included memory clinics, daycare centers and residential care facilities, totally or partially covered by the public healthcare service. A survey questionnaire was designed to collect information and a web-platform system was developed to manage data from all services. Of great importance, the web-platform is capable to display surveyed services as an on-line map regularly updated and easily accessible from the Dementia Observatory website (www.iss.it/demenza).

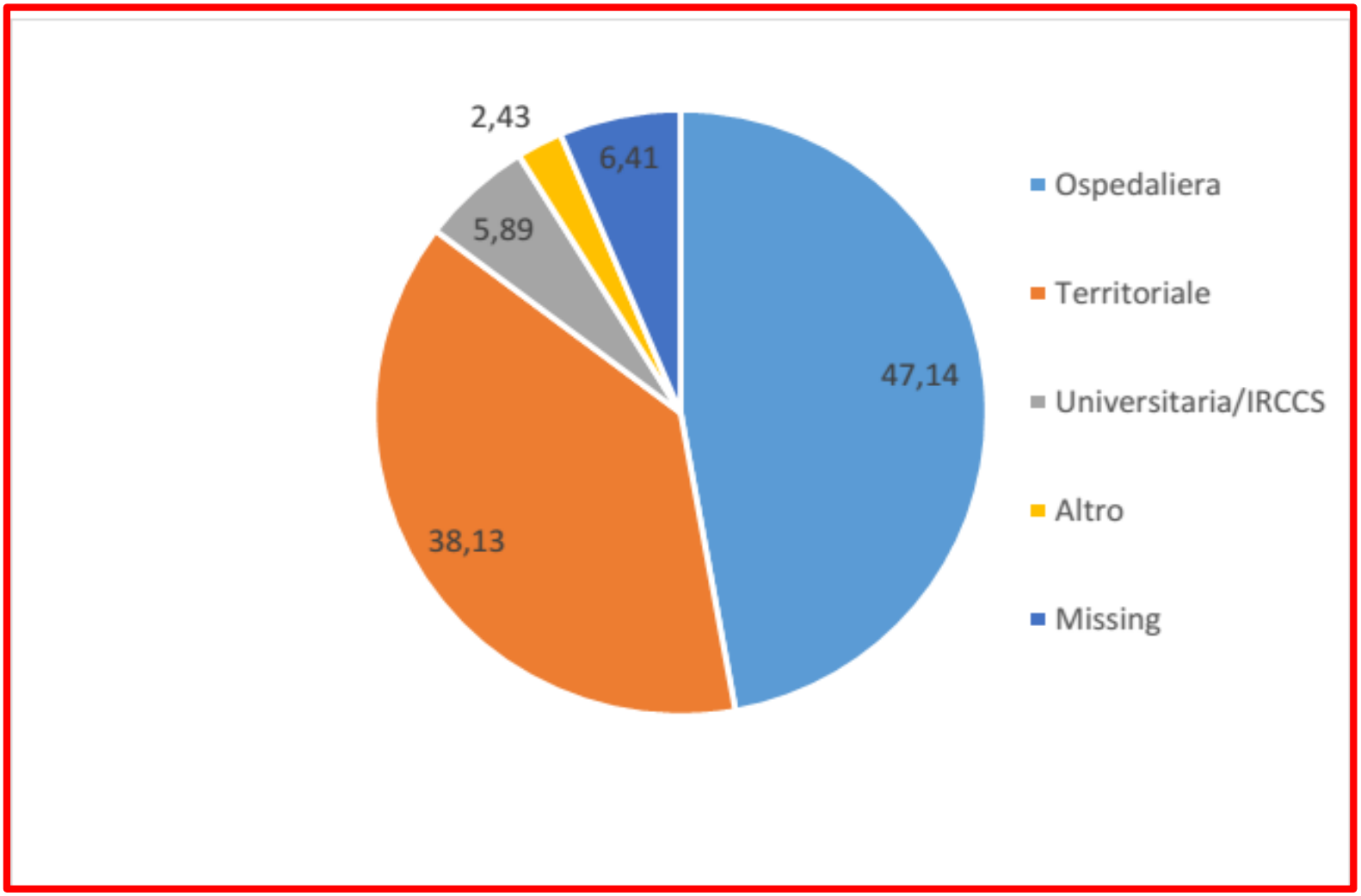
Key words
- dementia
- survey research
- memory clinic
- day care and residential care service
- web-platform system

CDCD

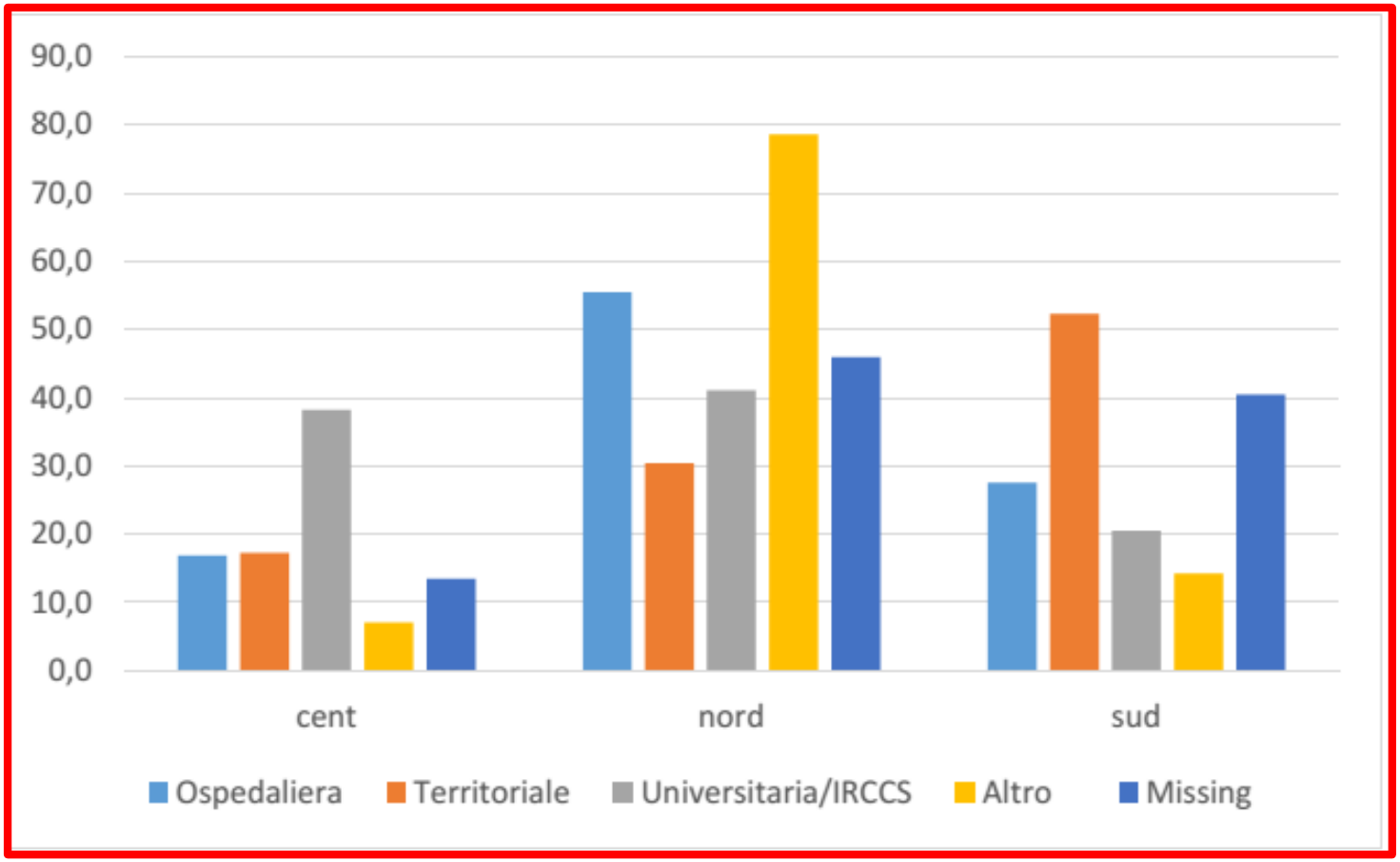
Tab.1 Distribuzione di frequenza dei 577 CDCD per Region

Regione	N CDCD	% CDCD
Lombardia	72	12.48
Emilia Romagna	61	10.57
Piemonte	31	5.37
Veneto	41	7.11
Liguria	21	3.64
Trentino Alto Adige	12	2.08
Friuli Venezia Giulia	18	3.12
Valle d'Aosta	4	0.69
Totale Nord	**260**	**45.06**
Lazio	34	5.89
Marche	14	2.43
Toscana	24	4.16
Umbria	31	5.37
Totale centro	**103**	**17.85**
Abruzzo	11	1.91
Basilicata	3	0.52
Calabria	36	6.24
Campania	78	13.52
Molise	3	0.52
Puglia	31	5.37
Sardegna	15	2.60
Sicilia	37	6.41
Totale Sud e Isole	**214**	**37.09**
Totale Italia	**577**	**100**

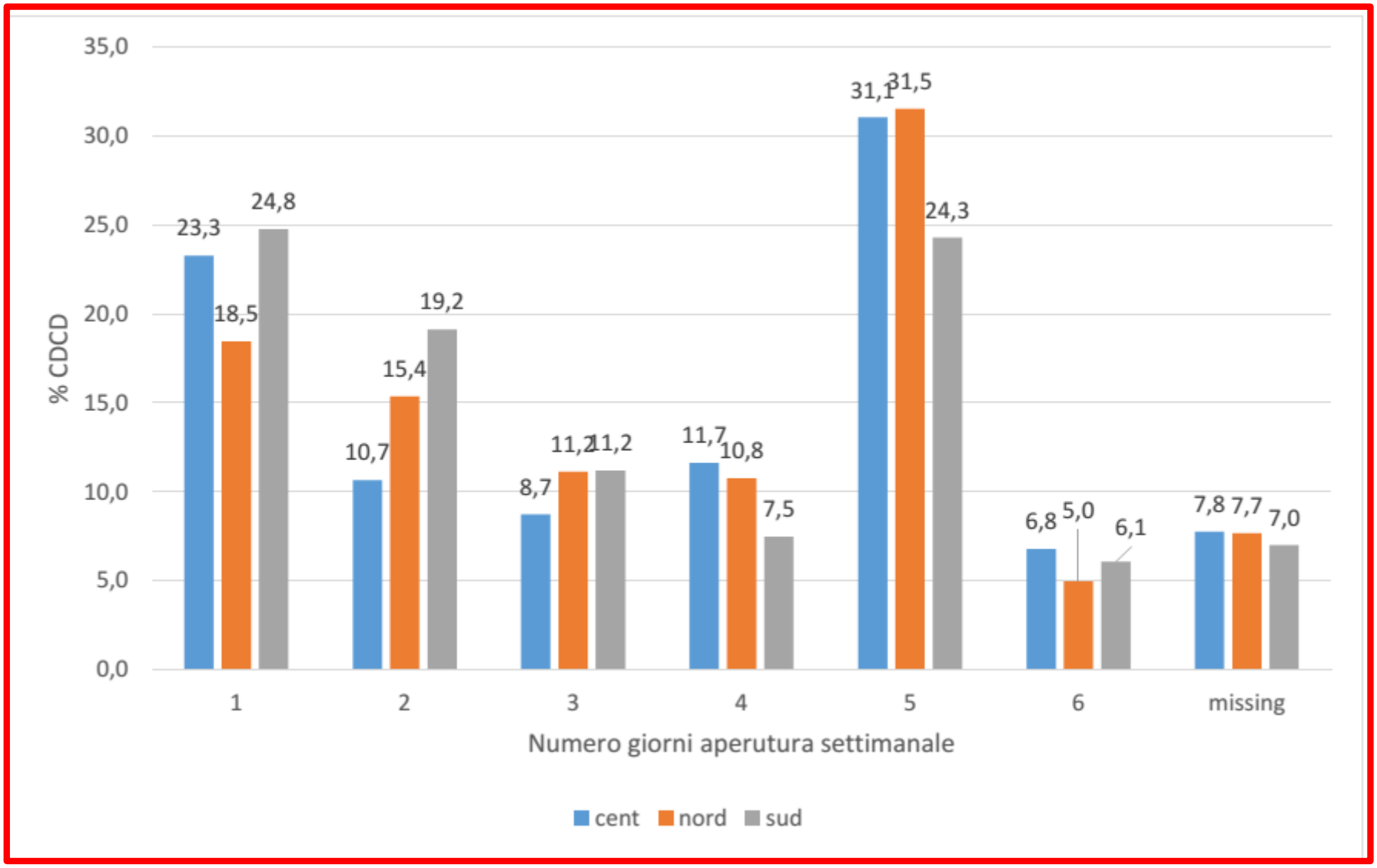
DISTRIBUZIONE PER TIPOLOGIA DI CDCD



DISTRIBUZIONE PER TIPOLOGIA ED AREA GEOGRAFICA DI CDCD



GIORNI DI APERTURA SETTIMANALE DEI CDCD



PERSONALE CHE LAVORA NEI CDCD

Staff members	Permanent		Non-permanent		Missing		N
Geriatrician	234	81.82	25	8.74	27	9.44	286
Neurologist	256	80.76	41	12.93	20	6.31	317
Psychiatrist	72	75.79	6	6.32	17	17.89	95
Psychologist	174	52.73	144	43.64	12	3.64	330
Social worker	78	77.23	7	6.93	16	15.84	101
Nurse	256	83.66	4	1.31	46	15.03	306
Speech ther.	32	74.42	2	4.65	9	20.93	43
Physiotherapist	39	68.42	8	14.04	10	17.54	57
Occupational ther.	14	60.87	7	30.43	2	8.70	23

Activity/service	Northern regions		Central regions		Southern regions	
	N	%	N	%	N	%
Clinical assessment	236	90,8	96	93,2	194	90,7
Neuropsychology	231	88,8	95	92,2	184	86,0
Routine blood tests	193	74,2	69	67,0	148	69,2
Brain MRI	178	68,5	67	65,0	133	62,1
Brain CT-scan	190	73,1	68	66,0	141	65,9
EEG	129	49,6	40	38,8	81	37,9
SPECT/ 18FDG PET	152	58,5	44	42,7	94	43,9
Genetic testing	86	33,1	26	25,2	43	20,1
Brain fMRI	61	23,5	25	24,3	45	21,0
Volumetric MRI	43	16,5	22	21,4	32	15,0
CSF AD biomarkers	110	42,3	28	27,2	36	16,8
Total CCDDs	260		103		214	

Open Access Research

BMJ Open

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

Alessandra Di Pucchio,[1] Nicola Vanacore,[1] Fabrizio Marzolini,[1] Eleonora Lacorte,[1] Teresa Di Fiandra,[2] I-DemObs Group, Marina Gasparini[3]

Nello studio condotto in Italia intervistando 501 referenti di CDCD è stato possibile calcolare che nell'Italia del Sud e Isole viene effettuata una valutazione neurolopsicologica completa con una frequenza inferiore al 44% rispetto alle strutture del Nord Italia

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

A	B	C	D	E
		95% CI		
	OR	Lower	Upper	P value
Psychologist (at least one)				
Not	1.00			
Yes	4.55	2.91	7.10	0.001
Geographical distribution of CCDD				
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, Centre for Cognitive Disorders and Dementias; IRCSS, Institute for Scientific Research and Healthcare.

IL CONTESTO

REGISTER OF COMMISSION EXPERT GROUPS and Other Similar Entities

Home
How is the register organised
Expert groups explained
Quick search
Advanced search
News
Meetings
Calls for applications
Contact the register
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Print as PDF

Group Details - Commission Expert Group

Details | Additional Information | Meetings | Subgroups | Statistics | Members

Name: Group of Governmental experts on Dementias (E02984) — **Closed**

Policy Area: Public Health

Lead DG: SANTE - DG Health and Food Safety

Type: Informal, Permanent

Scope: Limited

Mission: Coordination and exchange of views with Member States on dementia policies

Task: Assist the Commission in the preparation of legislative proposals and policy initiatives

Contact: SANTE-CONSULT-C1@ec.europa.eu

Publication in RegExp: 05 Dec 2013

Link to Website: http://ec.europa.eu/health/major_chronic_diseases/diseases/alzheimer/index_en.htm

Last updated: 05 Jun 2018

I PIANI NAZIONALI DEMENZA

PRESIDENZA
DEL CONSIGLIO DEI MINISTRI
CONFERENZA UNIFICATA

PROVVEDIMENTO 30 ottobre 2014.

Accordo, ai sensi dell'articolo 9, comma 2, lett. *c)* del decreto legislativo 28 agosto 1997, n. 281, tra il Governo, le regioni e le province autonome di Trento e di Bolzano, le province, i comuni e le comunità montane sul documento recante: «Piano nazionale demenze - Strategie per la promozione ed il miglioramento della qualità e dell'appropriatezza degli interventi assistenziali nel settore delle demenze». (Rep. atti n. 135/CU).

LA CONFERENZA UNIFICATA

Nell'odierna seduta del 30 ottobre 2014:

Monitoraggio dello stato di recepimento del PND a livello regionale *(aggiornamento Novembre 2017)*

Regione	Documento di riferimento per il recepimento del PND	Principali indicazioni nei documenti di recepimento		
		Ri-denominazione CDCD	Segnalati nodi assistenza e rete Servizi	Progettualità riprogrammazione Servizi
Lazio	DCA n. 448 del 22/12/2014	si	si	Si
Marche	DGR n. 107 del 23/2/2015	si	si	Si
Toscana	DGR 147 del 23/02/2015	si	si	si
Liguria	DGR n.267 del 13/3/2015; DGR n.55 del 26/01/2017	si	si	si
Veneto	Delibera 653/2015 del 15/05/2015	si	si	si
P.A. Trento	Delibera n.719 del 6/05/2015	si	si	Si
Campania	Decreto commissariale n.52 del 29/05/2015	si	si	Si
Emilia Romagna	DGR n.990 del 27/06/2016	si	si	Si
Puglia	DGR n.1034 del 14/07/2016 (BUR Puglia n.88 del 29/7/16)	no	no	no
Umbria	DGR n.1019 del 12/09/2016	no	no	no
Piemonte	DGR n. 37-4207 del 14/11/2016	si	si	si

Note: tutta la documentazione è stata inserita formalmente sul sito dell'Osservatorio Demenze (www.iss.it/demenze) in una sezione dedicata alla normativa regionale

* Solo la P.A. Trento

è consultabile sul sito dell'Osservatorio salute (www.salute.gov)

Alcol e giovanissimi: negli ospedali un caso su 5 di intossicazione acuta da ...

Metformina, nessun rischio se usata per diabete gestazionale nei ...

Tac spirale per i forti fumatori: ecco i centri per lo screening dettagliato ...

Celiachia e colon irritabile: non basta togliere il glutine, occorrono ...

Come fare a dormire meglio? Un pigiama di lana può darvi una mano,ma ...

Appello al ministero dalla Federazione Alzheimer Italia: si finanzi il piano nazionale demenze

Al 14 novembre hanno firmato 116.000 persone

Presidenza del Consiglio dei Ministri

CONFERENZA UNIFICATA

Accordo, ai sensi dell'articolo 9, comma 2, lettera c), del decreto legislativo 28 agosto 1997, n. 281, tra il Governo, le Regioni e le Province Autonome di Trento e Bolzano e gli Enti locali sui documenti "Linee di indirizzo nazionali sui Percorsi Diagnostico Terapeutici Assistenziali (PDTA) per le demenze" e "Linee di indirizzo nazionali sull'uso dei Sistemi informativi per caratterizzare il fenomeno delle demenze".

Repertorio atti n. 130/CU del 26 ottobre 2017

LA CONFERENZA UNIFICATA

Linee di indirizzo Nazionali sui Percorsi Diagnostico Terapeutici Assistenziali per le demenze

Tavolo per il monitoraggio del recepimento ed implementazione del Piano Nazionale Demenze

5/07/2017

Linee di indirizzo Nazionali sull'uso dei Sistemi Informativi per caratterizzare il fenomeno delle demenze

Tavolo per il monitoraggio del recepimento e implementazione del Piano Nazionale Demenze

5/07/2017

QUALI SONO I PDTA PER LE DEMENZE

Regione Lombardia

ASL Brescia

PERCORSO
DIAGNOSTICO-TERAPEUTICO-ASSISTENZIALE
DECADIMENTO COGNITIVO/DEMENZA

Settembre 2011

Regione Lombardia

ASL Milano

e le Aziende Ospedaliere, IRCCS, ASP(Aziende di Servizi alla Persona), Università sotto elencate

Percorso Preventivo-Diagnostico-Terapeutico-Assistenziale Riabilitativo (PDTAR)
per la popolazione e i pazienti con demenza

011 - da aggiornare entro dicembre 2013 o prima
SL di componenti del Gruppo di lavoro - se emergeranno
novità clinicamente rilevanti

REGIONE PIEMONTE

ReSS

REGIONE PIEMONTE

PERCORSO
DIAGNOSTICO
TERAPEUTICO sulla
DIAGNOSI PRECOCE
DELLE DEMENZE

ULSS21 LEGNAGO

Azienda USL Roma D

REGIONE LAZIO

IL SISTEMA ASSISTENZIALE INTEGRATO DI PRESA IN CARICO
DEL PAZIENTE CON MALATTIA DI ALZHEIMER O ALTRA
FORMA DI DEMENZA NELLA ASL ROMA D

AUTORI: DR. VITTORIO CHINNI – DIRETTORE F.F. DISTRETTO SANITARIO XIII° MUNICIPIO
DR. GIOVANNI MANCINI – DIRETTORE F.F. UOC NEUROLOGIA – ASL RM D
DR.SSA DANIELA SGROI – DIRETTORE AREA DIP. CURE PRIMARIE – ASL RM D
DR.SSA CATERINA IVARDO – DIRIGENTE MEDICO AREA DIP. CURE PRIMARIE
DR.SSA MARIA LAURA MAZZARA – RESPONSABILE UOS INTEGRAZIONE SOCIO-SANITARIA DISTRETTO XIII° MUNICIPIO

ELENCO DELLE UNITÀ OPERATIVE COINVOLTE:

UOC Neurologia Ospedale G.B. Grassi
Poliambulatori Distrettuali Specialistici di Neurologia e Geriatria della ASL RM D
Area Dipartimentale Cure Primarie ASL RM D
UOC Direzione Sanitaria dei Distretti Fiumicino e Municipi XIII, XV, XVI
Centri Assistenza domiciliare e residenziale dei Distretti Fiumicino e Municipi XIII, XV, XVI
UOS Integrazione Socio-sanitaria dei Distretti Fiumicino e Municipi XIII, XV, XVI
Servizi Sociali del Comune di Fiumicino e dei Municipi XIII, XV e XVI del Comune di Roma

Rete provinciale per la diagnosi, cura ed assistenza delle demenze con il mod
organizzativo dei Centri per i Disturbi Cognitivi (CDC) : Tab.1 e Tab.2

Tab.1 *La rete per le demenze della Provincia di Modena*

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

La rete provinciale per le Demenze

- 7 Centri Distrettuali per i Disturbi Cognitivi
- 3 CDC Ospedalieri (Neurologia e Geriatria del NOCSAE di Baggiovara, Neurologia Osp. di Carpi)
- 1 Nucleo Ospedaliero Demenze c/o Villa Igea Modena (20 p.l. cod. 56)
- 3 Nuclei Alzheimer per Assistenza Residenziale Temporanea
(Mirandola: 15 p.l.,Modena: 20 p.l., Pavullo: 7 p.l.; nuova attivazione Formigine 1.09.2013: 10 posti)
- 3 CD Alzheimer (Carpi: 23 posti, Modena «9 Gennaio: 20 posti, Modena «Mingucci»; 20 posti)
- 5 Associazioni di Volontariato che garantiscono una serie di interventi in sinergia con AUSL ed Enti locali
- Accordo aziendale con i MMG per la presa in carico del pz con demenza e della sua famiglia

Nel 2013 seguite 15.000 persone con demenza, 2778 nuove diagnosi di cui 1300 AD , 5195 progetti attivi dei MMG

Monitoraggio del Piano Nazionale Demenze (PND)

Tavolo di confronto con le Regioni e gli altri portatori di interesse

Nel corso del 2018 ha lavorato essenzialmente per:

- supportare tutte le attività che garantiscono la gestione e il continuo aggiornamento dell' **«Osservatorio demenze»** (esame normative regionali, analisi dati survey, manutenzione mappa ecc.)
- **completare la stesura dei due documenti di approfondimento previsti dal PND: Etica e comunità amiche della demenza**

Special Article

THE EFFECT OF DIFFERENT DIAGNOSTIC CRITERIA ON THE PREVALENCE OF DEMENTIA

TIMO ERKINJUNTTI, M.D., PH.D., TRULS ØSTBYE, M.D., M.P.H., RUNA STEENHUIS, PH.D., C.PSYCH., AND VLADIMIR HACHINSKI, M.D., D.SC.(MED.)

TABLE 3. PREVALENCE OF DEMENTIA IN THE CSHA COHORT AS DIAGNOSED BY VARIOUS CLASSIFICATION SYSTEMS, ACCORDING TO AGE GROUP.*

AGE GROUP	NO.	DSM-III	DSM-III-R	DSM-IV	ICD-9	ICD-10	CAMDEX	CLINICAL CONSENSUS
yr		number of subjects (percent)						
65–74	391	85 (21.7)	41 (10.5)	43 (11.0)	17 (4.3)	8 (2.0)	7 (1.8)	57 (14.6)
75–84	931	245 (26.3)	149 (16.0)	114 (12.2)	41 (4.4)	28 (3.0)	49 (5.3)	184 (19.8)
≥85	557	216 (38.8)	136 (24.4)	100 (18.0)	36 (6.5)	22 (3.9)	36 (6.5)	152 (27.3)
Total	1879	546 (29.1)	326 (17.3)	257 (13.7)	94 (5.0)	58 (3.1)	92 (4.9)	393 (20.9)

*CSHA denotes the Canadian Study of Health and Aging.

I CRITERI NIA (NATIONAL INSTITUTE ON AGING)

ELSEVIER

Alzheimer's & Dementia

Alzheimer's & Dementia ■ (2011)

FASE PRECLINICA

Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup

Reisa A. Sperling[a,*], Paul S. Aisen[b], Laurel A. Beckett[c], David A. Bennett[d], Suzanne Craft[e],

The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease

Marilyn S. Albert[a,*], Steven T. DeKosky[b,c], Dennis Dickson[d], Bruno Dubois[e],

MCI due to AD

DEMENTIA due to AD

The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging and the Alzheimer's Association workgroup

Guy M. McKhann[a,b,*], David S. Knopman[c], Howard Chertkow[d,e], Bradley T. Hyman[f],

I CRITERI IWG
(INTERNATIONAL WORKING GROUP)

2007

Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS–ADRDA criteria

Bruno Dubois*, Howard H Feldman*, Claudia Jacova, Steven T DeKosky, Pascale Barberger-Gateau, Jeffrey Cummings, André Delacourte, Douglas Galasko, Serge Gauthier, Gregory Jicha, Kenichi Meguro, John O'Brien, Florence Pasquier, Philippe Robert, Martin Rossor, Steven Salloway, Yaakov Stern, Pieter J Visser, Philip Scheltens

2010

Revising the definition of Alzheimer's disease: a new lexicon

Bruno Dubois, Howard H Feldman, Claudia Jacova, Jeffrey L Cummings, Steven T DeKosky, Pascale Barberger-Gateau, André Delacourte, Giovanni Frisoni, Nick C Fox, Douglas Galasko, Serge Gauthier, Harald Hampel, Gregory A Jicha, Kenichi Meguro, John O'Brien, Florence Pasquier, Philippe Robert, Martin Rossor, Steven Salloway, Marie Sarazin, Leonardo C de Souza, Yaakov Stern, Pieter J Visser, Philip Scheltens

2014

Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria

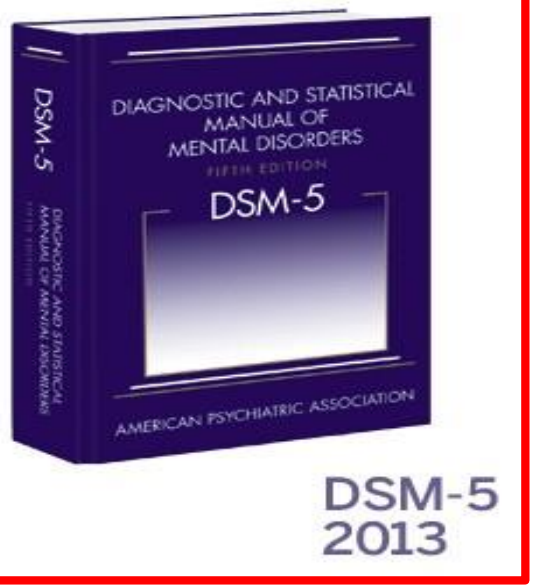
Bruno Dubois, Howard H Feldman, Claudia Jacova, Harald Hampel, José Luis Molinuevo, Kaj Blennow, Steven T DeKosky, Serge Gauthier, Dennis Selkoe, Randall Bateman, Stefano Cappa, Sebastian Crutch, Sebastiaan Engelborghs, Giovanni B Frisoni, Nick C Fox, Douglas Galasko, Marie-Odile Habert, Gregory A Jicha, Agneta Nordberg, Florence Pasquier, Gil Rabinovici, Philippe Robert, Christopher Rowe, Stephen Salloway, Marie Sarazin, Stéphane Epelbaum, Leonardo C de Souza, Bruno Vellas, Pieter J Visser, Lon Schneider, Yaakov Stern, Philip Scheltens, Jeffrey L Cummings

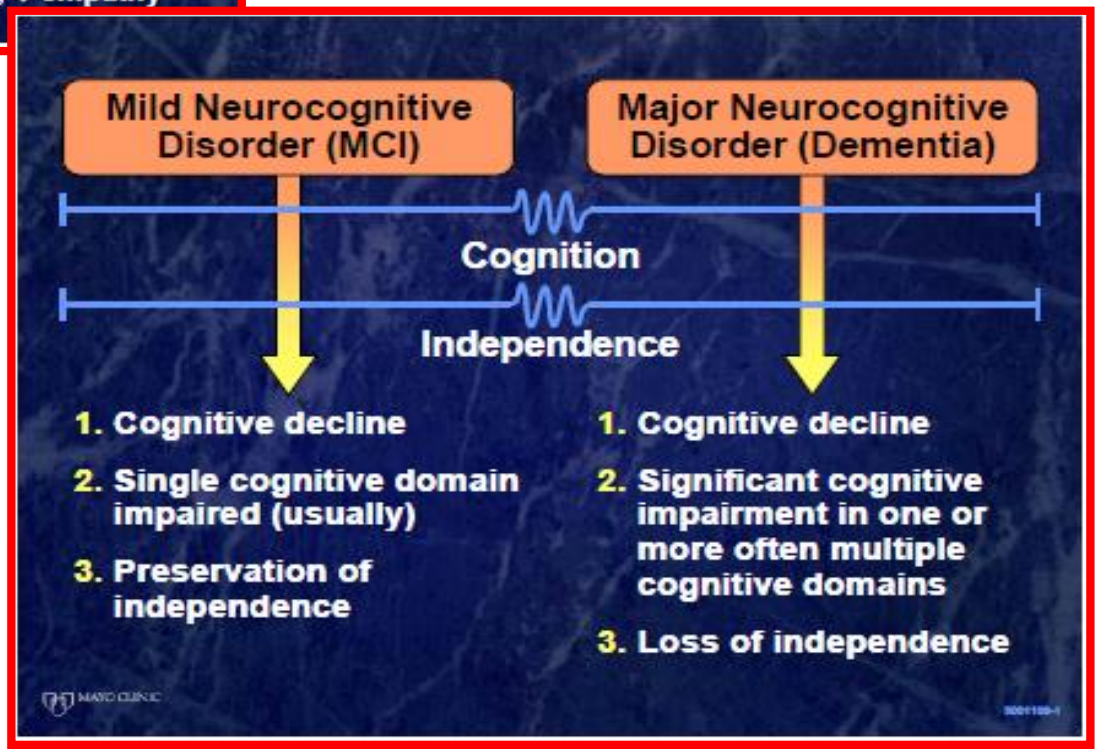
Neurocognitive Disorders

Domains

Domain	Tasks
Complex attention	Major: diminished, multiple stimuli Mild: takes longer
Executive abilities	Major: abandon complex activities Mild: ↑ effort, multi-tasking
Learning/memory	Major: repeat self in conversation Mild: recent events, occas repeat
Language	Major: anomia, paraphasias Mild: ↓ naming, word finding
Visuoconstruction Visuoperception	Major: not driving, ↓ navigation Mild: maps, effort
Social cognition	Major: insensitivity social contexts Mild: subtle personality, ↓ empathy

MAYO CLINIC





Published in final edited form as:

Harv Rev Psychiatry. 2015 ; 23(5): 320–328. doi:10.1097/HRP.0000000000000090.

DSM-5 and mental disorders in older individuals: an overview

Perminder S. Sachdev, MD, PhD, FRANZCP[1,2,*], **Adith Mohan, MBBS, MRCPsych, FRANZCP**[1,2], **Lauren Taylor, MBBS**[2], and **Dilip V. Jeste, MD**[3]

[1]Centre for Healthy Brain Ageing (CHeBA), School of Psychiatry, UNSW Australia

[2]Neuropsychiatric Institute, Prince of Wales Hospital, Sydney, Australia

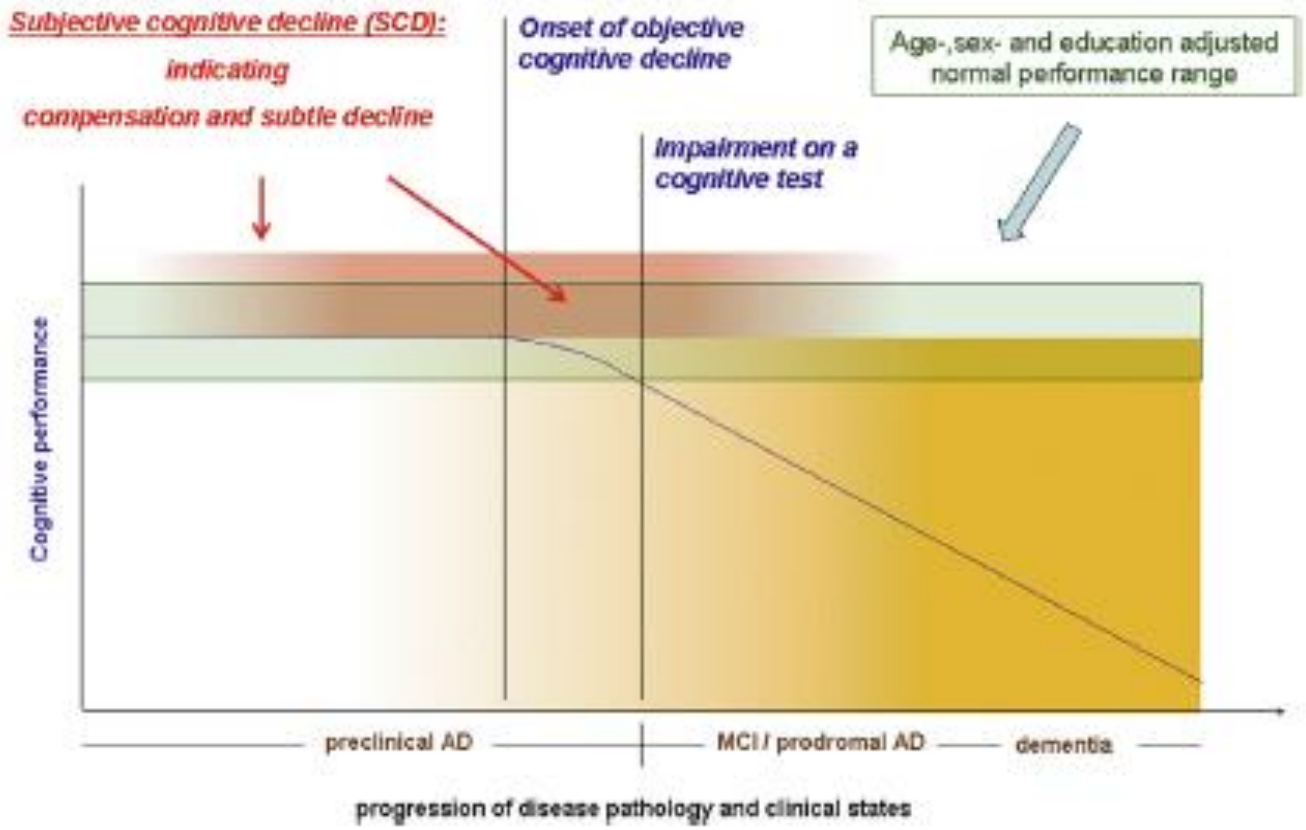
[3]Department of Psychiatry and Neurosciences, University of California, San Diego, California, USA

The criteria for Major NCD do have some differences from DSM-IV dementia: i) Major NCD requires significant decline in only one cognitive domain; ii) unlike DSM-IV dementia, impairment in memory is not essential for Major NCD; and iii) the functional threshold for diagnosing Major NCD is that cognitive deficits 'interfere with independence in everyday activities', in contrast with the DSM-IV requirement of 'significantly interferes with work or social activities or relationships with others'. The determination of 'significant' cognitive decline is based both on subjective concern of an individual or a knowledgeable informant or a clinician, as well as the objective demonstration of substantial impairment in cognitive performance on an objective measure. The latter is ideally a formal neuropsychological assessment, but a brief "bedside" assessment by the clinician would suffice for this criterion. If a formal assessment is available, the performance typically falls 2 or more standard deviations (SD) below the normative mean (or below the 3rd percentile) on the test administered. It is expected that these changes will lead to a more rational and operational approach to the diagnosis of Major NCD or dementia.

The DSM-5 criteria for Mild NCD differ from those for Major NCD by *severity* of the cognitive deficits and the consequent *functional impairment*. The cognitive decline in this case is stated to be 'modest', with the guideline that neuropsychological test performance in Mild NCD is in the range 1 to 2 SD below the normative mean, or between the 3rd and 16th percentiles. Formal neuropsychological testing is not mandated, and clinicians may rely on 'bedside' assessments and apply their 'clinical judgment'. There is an acknowledgement however, that formal assessment by a clinical neuropsychologist is the standard to aspire to given that cognitive deficits in Mild NCD are subtler than in Major NCD and may be more difficult to establish with 'bedside' testing. If serial assessments are available for any individual, they may more objectively document decline, but cautious interpretation is recommended owing to practice effects, variable test-retest reliability, and the dearth of normative data on cognitive decline.[51]

F. Jessen et al. / Alzheimer's & Dementia ■ (2014) 1–9

Course of cognitive symtomes in AD



JAMDA

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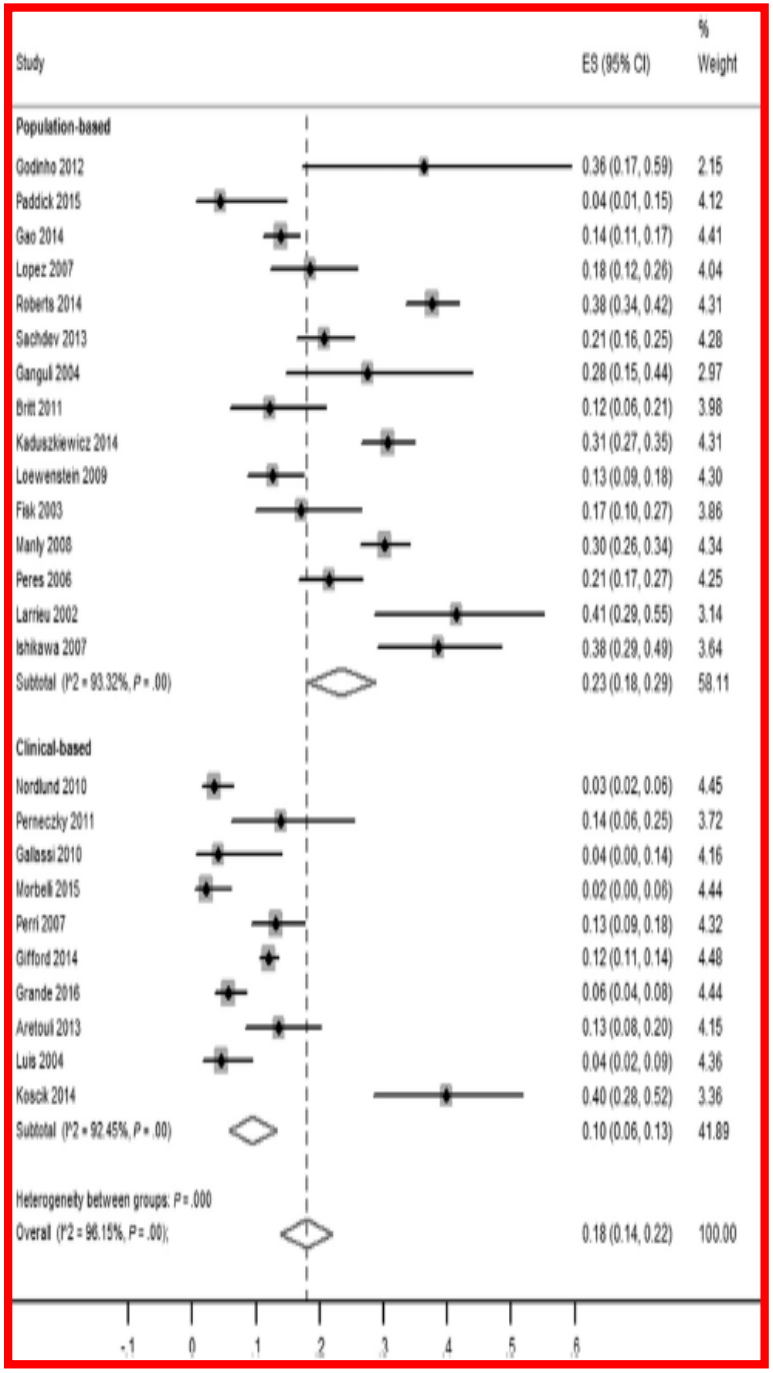
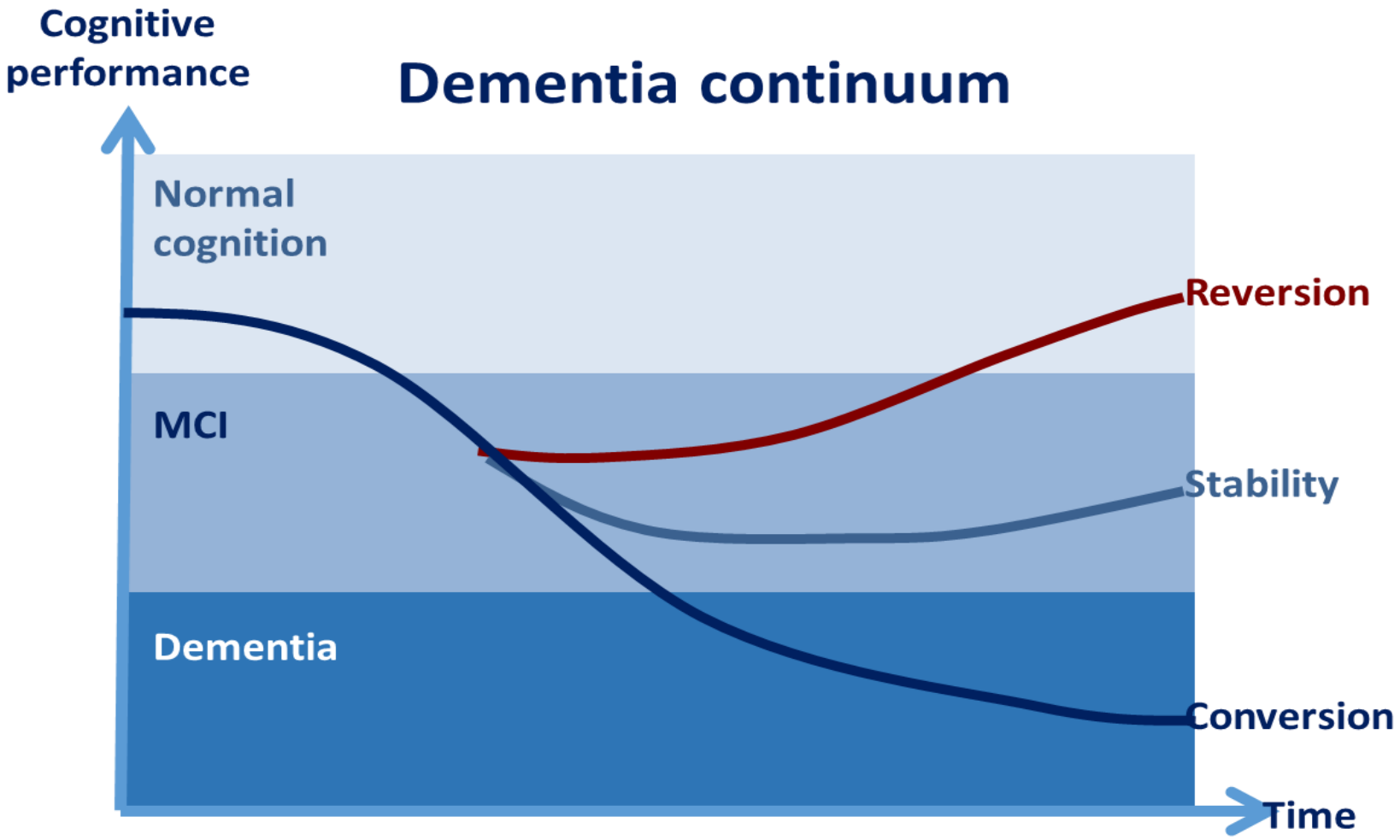
Original Study

Spontaneous Reversion of Mild Cognitive Impairment to Normal Cognition: A Systematic Review of Literature and Meta-Analysis

Marco Canevelli MD[a,*], Giulia Grande MD[b], Eleonora Lacorte MSci[c], Elisa Quarchioni MStat[c], Matteo Cesari PhD[d,e], Claudio Mariani MD[b], Giuseppe Bruno PhD[a], Nicola Vanacore PhD[c]



Reversione alla normalità del MCI



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DOI 10.3233/JAD-180416
IOS Press

A Systematic Review and Meta-Analysis on the Prevalence of Dementia in Europe: Estimates from the Highest-Quality Studies Adopting the DSM IV Diagnostic Criteria

Ilaria Bacigalupo[a,*], Flavia Mayer[a], Eleonora Lacorte[a], Alessandra Di Pucchio[a], Fabrizio Marzolini[a], Marco Canevelli[b], Teresa Di Fiandra[c] and Nicola Vanacore[a]
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[c]*General Directorate for Health Prevention, Ministry of Health, Rome, Italy*

PREVALENZA PER DEMENZA IN EUROPA (Lobo et al. 2000)

6.4%

Age – group	Prevalenza X 100 ab maschi	Prevalenza X 100 ab femmine
65-69	1.6	1
70-74	2.9	3.1
75-79	5.6	6
80-84	11	12.6
85-89	12.8	20.2
90 +	22.1	30.8

Analisi pooled dei dati
11 studi pubblicati dal 1991-1997
Criteri clinici DSM III-R; CAMDEX, AGECAT
Nessuna valutazione di qualità

PREVALENZA PER DEMENZA IN EUROPA (Bacigalupo et al. 2018)

7.1%

Age – group	Prevalenza X 100 ab maschi	Prevalenza X 100 ab femmine
65-69	0.9	1.1
70-74	2.1	2.2
75-79	4.6	5.6
80-84	9.0	13.3
85-89	13.9	26.4
90 +	31.2	38.9

Meta-analisi
9 studi pubblicati dal 2002-2015
Criteri clinici DSM IV
Valutazione di qualità con checklist ADI
Due studi includono anche pazienti istituzionalizzati.

RESEARCH ARTICLE

The Prevalence of Mild Cognitive Impairment in Diverse Geographical and Ethnocultural Regions: The COSMIC Collaboration

Perminder S. Sachdev[1,2]*, Darren M. Lipnicki[1], Nicole A. Kochan[1], John D. Crawford[1], Anbupalam Thalamuthu[1], Gavin Andrews[1], Carol Brayne[3], Fiona E. Matthews[4,5], Blossom C. M. Stephan[5], Richard B. Lipton[6,7], Mindy J. Katz[6], Karen Ritchie[8,9,10], Isabelle Carrière[8,9], Marie-Laure Ancelin[8,9], Linda C. W. Lam[11], Candy H. Y. Wong[12], Ada W. T. Fung[11], Antonio Guaita[13], Roberta Vaccaro[13], Annalisa Davin[13], Mary Ganguli[14,15,16], Hiroko Dodge[17,18], Tiffany Hughes[14], Kaarin J. Anstey[19], Nicolas Cherbuin[19], Peter Butterworth[19], Tze Pin Ng[20], Qi Gao[20], Simone Reppermund[1], Henry Brodaty[1,2], Nicole Schupf[21,22,23], Jennifer Manly[21,22,24], Yaakov Stern[21,22,24], Antonio Lobo[25,26], Raúl Lopez-Anton[25,27], Javier Santabárbara[25,28], Cohort Studies of Memory in an International Consortium (COSMIC)[¶]

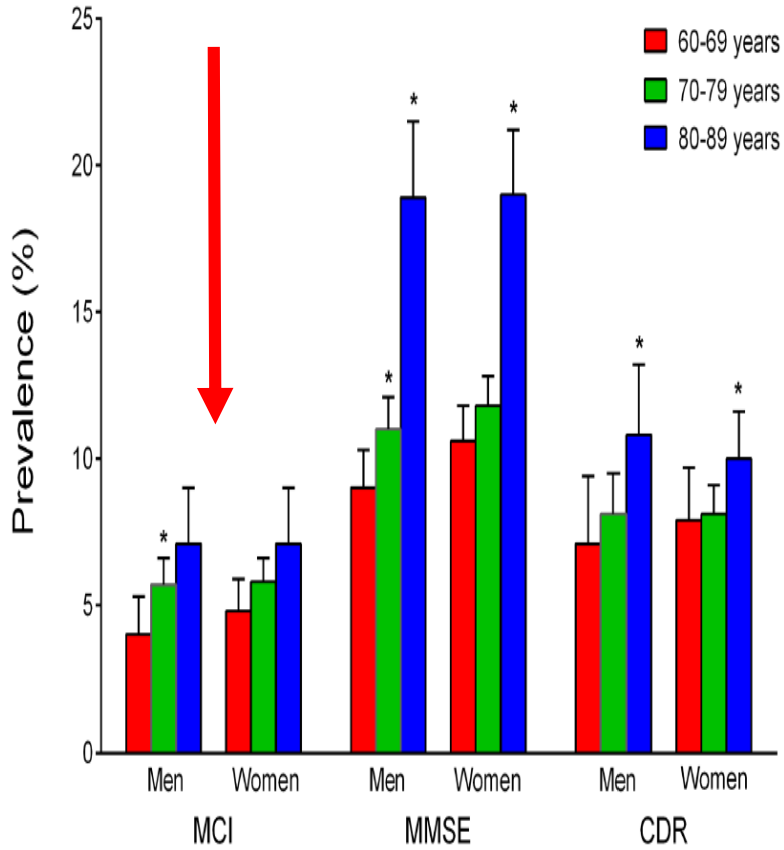

Fig 2. Crude prevalence estimates of mild cognitive impairment (MCI) among men and women of different age groups. Error bars indicate upper limits of 95% confidence intervals. Asterisks indicate a significant difference from: * 60–69 years; ** 70–79 years. There were no significant differences between men and women of the same age group for any classification approach. The objective cognitive impairment criteria for the classifications was performance in the bottom 6.681% of the relevant study for at least one harmonized cognitive domain (mild cognitive impairment), a Clinical Dementia Rating (CDR) of 0.5, or a Mini-Mental State Examination (MMSE) score 24–27.

STIMA DEI CASI CON MCI NELLA POPOLAZIONE ITALIANA (ISTAT 2016; Sachdev et al 2015)

classe-d'età	popolazione	tassi per 100 ab	casi attesi
60-69	7331158	4.5	329902
70-79	5635779	5.8	326875
80-89	3359904	7.1	238553
totale			895330

In Italia circa 1.000.000 di persone sono affette da demenza (5-7% pop. > 65 anni) e circa 900.000 con MCI (5.9 pop. > 60 anni)

QUALE IMPATTO SULLA PREVENZIONE E SUI SERVIZI ?

Strategic project promoted

by the Italian Medicines Agency (AIFA)

INTERCEPTOR PROJECT

ON EARLY DIAGNOSIS OF THE PRODROMAL STAGE OF ALZHEIMER DISEASE. THE PROGRESSION FROM MILD COGNITIVE IMPAIRMENT (MCI) TO DEMENTIA: THE ROLE OF BIOMARKERS IN EARLY INTERCEPTION OF PATIENTS CANDIDATE FOR PRESCRIPTION OF FUTURE DISEASE-MODIFYING DRUGS

Sponsor: AIFA (Agenzia Italiana del Farmaco) and Ministry of Health

Principal Investigator: Paolo Maria Rossini

Coordinating Committee: Institute of Neurology, Catholic University of The Sacred Heart, Rome, (Responsible: Paolo Maria Rossini); IRCCS Centro San Giovanni di Dio Fatebenefratelli, Brescia (Responsible: Stefano Cappa); IRCCS Foundation "Carlo Besta" Neurological Institute, Milan (Responsible: Fabrizio Tagliavini); National Institute of Health (Responsible: Nicola Vanacore); Associazione Italiana Malattia Alzheimer - AIMA (Responsible: Patrizia Spadin); Istituto Nazionale Ricovero e Cura Anziani – IRCCS-INRCA (Responsible: Fabrizia Lattanzio).

Study classification: This is a multicenter, interventional non therapeutic cohort study. It is a study aiming at finding new ways for early detection and diagnosis of medical conditions.

Biomarkers included in the study: MMSE; FCSRT; CSFp-tau and CSF p-tau/ABeta; (^{18}F)FDG-PET SCAN; Volumetric MRI; ApoE4; EEG.

Design: multicenter, interventional, non therapeutic, cohort study.

Number of patients in the study: 500.

3.7 Endpoints

Primary Endpoint

It shall be considered the conversion to Alzheimer's disease within 3.0 years after diagnosis of MCI, together with the assessment of the subjects remaining in a stable condition and of those showing a reversion to the normal cognitive profile. People with MCI who convert to other forms of dementia will be considered separately. The biomarker or a set of biomarkers will be evaluated which can predict the conversion to Alzheimer's disease with higher accuracy.

Secondary Endpoints

Evaluation of cost/benefit ratio of individual biomarker or combination of biomarkers compared to their accuracy to predict progression from MCI to AD and their financial sustainability, availability in the country and non-invasiveness for patients.

CONCLUSIONI

LA NEUROPATOLOGIA DELLE PERSONE ANZIANE SENZA DEMENZA

ANN NEUROL 2013;74:478–489

Much of Late Life Cognitive Decline Is Not due to Common Neurodegenerative Pathologies

Patricia A. Boyle, PhD,[1,2] Robert S. Wilson, PhD,[1,2,3] Lei Yu, PhD,[1,3]
Alasdair M. Barr, PhD,[4] William G. Honer, MD,[5]
Julie A. Schneider, MD,[1,3,6] and David A. Bennett, MD[1,3]

Results: Cognition declined a mean of about 0.11U per year (estimate = −0.109, standard error [SE] = 0.004, $p < 0.001$), with significant individual differences in rates of decline; the variance estimate for the individual slopes was 0.013 (SE = 0.112, $p < 0.001$). In separate analyses, global Alzheimer pathology, amyloid, tangles, macroscopic infarcts, and neocortical Lewy bodies were associated with faster rates of decline and explained 22%, 6%, 34%, 2%, and 8% of the variation in decline, respectively. When analyzed simultaneously, the pathologic indices accounted for a total of 41% of the variation in decline, and the majority remained unexplained. Furthermore, in random change

Participants

Participants came from two clinical-pathologic cohort studies of aging and dementia: the Religious Orders Study and the Memory and Aging Project[14,15]. The Religious Orders Study began in 1994 and involves older Catholic nuns, priests, and monks recruited from more than 40 groups across the United States. The Rush Memory and Aging Project began in 1997 and involves older lay persons recruited from retirement communities, subsidized housing facilities, and social service agencies in the Chicago metropolitan area. Persons in both studies agreed to annual clinical evaluations and brain autopsy at death. Written informed consent was obtained in each study after procedures were fully explained, and both studies were approved by the Institutional Review Board of Rush University Medical Center. The follow up participation rates for both studies exceed 95% of survivors and autopsy rates exceed 80%. At the time of these analyses, data were available from 856 deceased persons with at least 2 cognitive evaluations (mean number of annual evaluations=7.5, SD=3.8, range: 2-18 years); notably, more than 80% of the persons included in these analyses had 4 or more cognitive assessments, about 60% had 5 or more, and about 25% had more than 9 assessments.

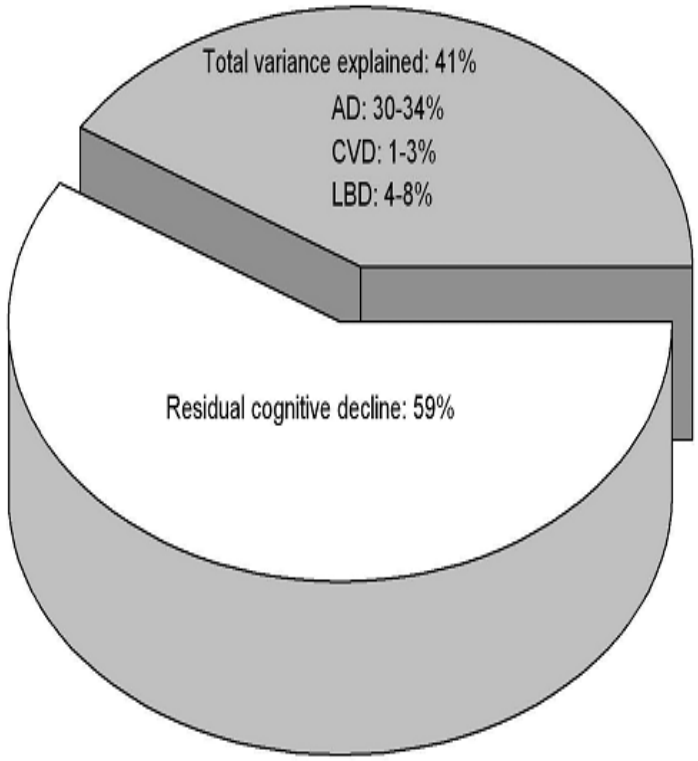

Figure 3.
Variation in cognitive decline explained by the pathologic indices (grey) and the residual, unexplained variation in cognitive decline (white) derived from fully adjusted models.

Published in final edited form as:
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Person-specific contribution of neuropathologies to cognitive loss in old age

Patricia A. Boyle[1,2], **Lei Yu**[1,3], **Robert S. Wilson**[1,2,3], **Sue E. Leurgans**[1,3], **Julie A. Schneider**[1,3,4], and **David A. Bennett**[1,3]

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Abstract

Objective—Mixed neuropathologies are the most common cause of dementia at the population level, but how different neuropathologies contribute to cognitive decline at the individual level remains unknown. We quantified the contribution of nine neuropathologies to cognitive loss at an individual level.

Methods—Participants (n=1,079) came from 2 longitudinal clinical-pathologic studies of aging. All completed 2+ cognitive evaluations (maximum = 22), died and underwent neuropathologic examinations to identify Alzheimer's disease (AD), other neurodegenerative diseases, and vascular pathologies. Linear mixed models examined associations of neuropathologies with cognitive decline and estimated the proportion of cognitive loss accounted for by each neuropathology at a person-specific level.

Results—Neuropathology was ubiquitous, with 94% of participants having 1+, 78% having 2+, 58% having 3+, and 35% having 4+. AD was most frequent (65%) but rarely occurred in isolation (9%). Remarkably, more than 230 different neuropathologic combinations were observed, each of which occurred in <6% of the cohort. The relative contributions of specific neuropathologies to cognitive loss varied widely across individuals. Although AD accounted for an average of about 50% of the observed cognitive loss, the proportion accounted for at the individual level ranged widely from 22% to 100%. Lewy bodies and hippocampal sclerosis also had potent effects, but again their impacts varied at the person-specific level.

Interpretation—There is much greater heterogeneity in the comorbidity and cognitive impact of age-related neuropathologies than currently appreciated, suggesting an urgent need for novel

evidence
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Best Practice OPEN ACCESS

Linee guida per la diagnosi, il trattamento e il supporto dei pazienti affetti da demenza

Antonino Cartabellotta[1*], Roberto Eleopra[2], Simone Quintana[3], Luca Pingani[4], Carlo Ferrarese[5], Fabrizio Starace[6], Marco Masina[7], Gianluigi Mancardi[8]

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- **QUALE EFFICACIA CLINICA PER I NUOVI FARMACI**

- **MALATTIA BIOLOGICA E MALATTIA CLINICA**
- **(RIFLESSIONE CRITICA SULL'USO DEI BIOMARCATORI)**

- **LE NUOVE CONOSCENZA ANATOMOPATOLOGICHE DELLA NEURODEGENERAZIONE**

- **FORMAZIONE DEGLI OPERATORI (DALLA DIAGNOSI ALLA TERAPIA)**

- **REDAZIONE DI PDTA**

- **APPLICAZIONE DEL PIANO NAZIONALE DELLE DEMENZE**

- **GOVERNO CLINICO DELLA DEMENZA DALLE ISTITUZIONI CENTRALI A QUELLE LOCALI**

Il tutto in un contesto di maggiore complessità … dal MCI alla demenza