



36th Global Conference of
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European Brain Council's Rethinking Alzheimer's Disease: Scaling up health systems' readiness

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RETHINKING ALZHEIMER'S DISEASE

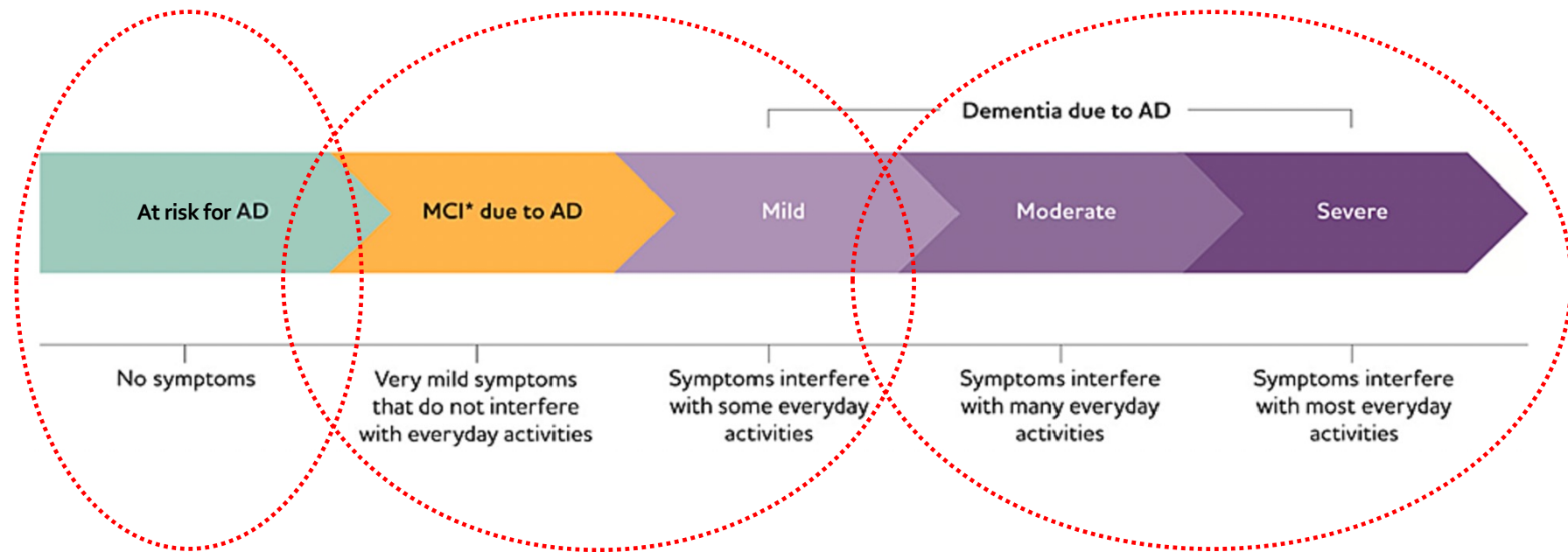
DETECTION AND DIAGNOSIS

□ LIST OF ENDORSERS

To help improve the quality of life and care for people living with AD in Europe, the following organisations endorse the RETHINKING Alzheimer's disease White Paper, including the call to action and policy recommendations.

- | | | |
|---|-------|--|
|  | | Ace Alzheimer Center Barcelona*,
<i>Spain</i> |
|  | | Dementia Research Network,
<i>Ireland</i> |
|  | | European Academy of Neurology,
<i>Austria</i> |
|  | | European Institute of Women's Health,
<i>Ireland</i> |
|  | | Masaryk University, Faculty of Medicine,
<i>Czech Republic</i> |
|  | | Memory Center of the University Hospitals of Geneva,
<i>Switzerland</i> |
|  | | Réseau Mémoire Alois,
<i>France</i> |
|  | | St. Anne's University Hospital Brno,
<i>Czech Republic</i> |
|  | | Tallaght University Hospital
<i>Ireland</i> |
|  | | University of Geneva,
<i>Switzerland</i> |
|  | | Women's Brain Project,
<i>Switzerland</i> |

The spectrum of Alzheimer's disease



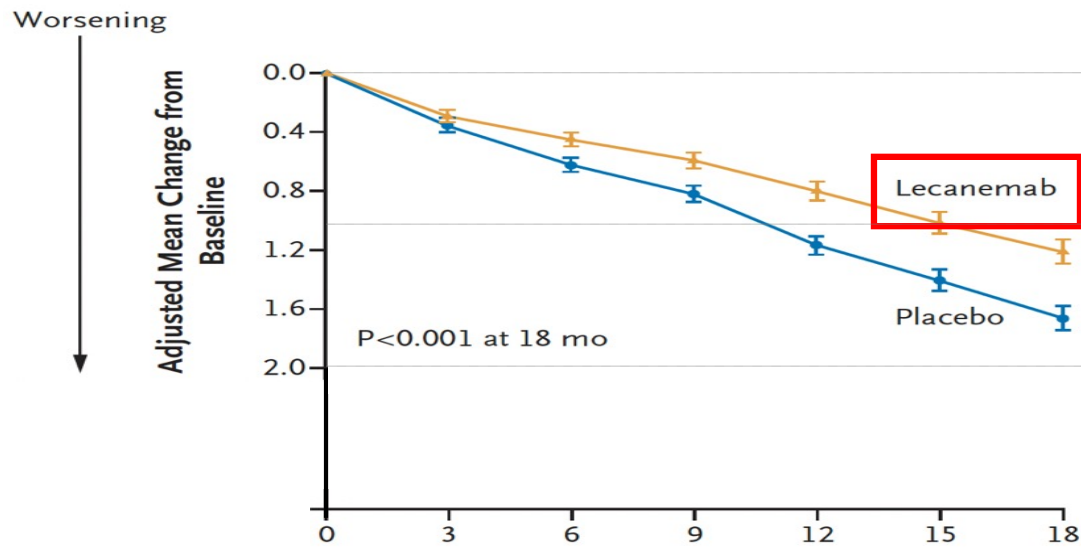
The at risk state is the next frontier

Attention will need to be increasingly given to the MCI and mild dementia stage

Most patients are still diagnosed in the moderate to severe stages

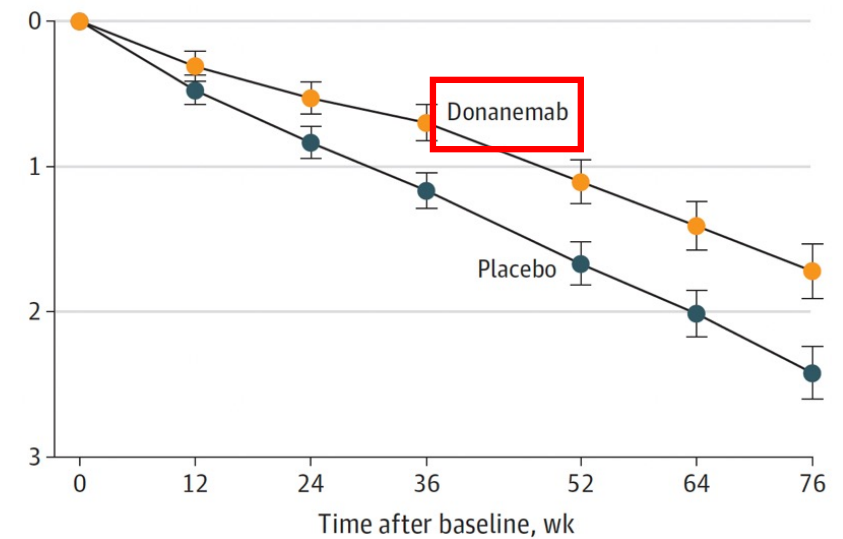
Anti-amyloid monoclonal antibodies are going to change the way we treat and regard AD

0.45 points (27%)



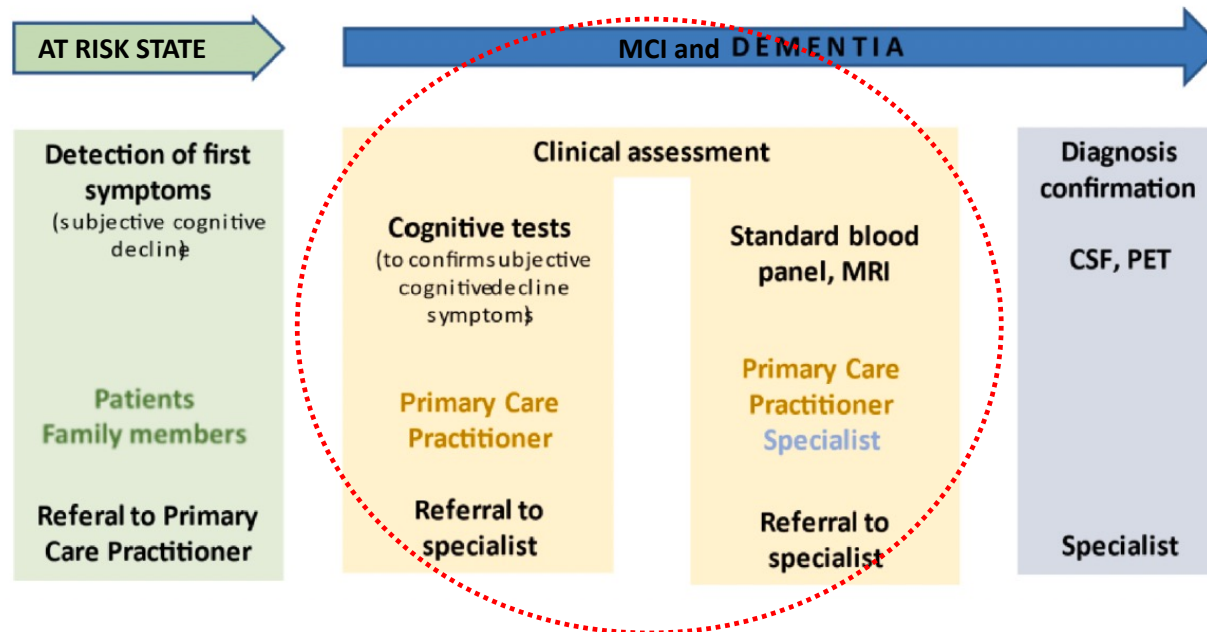
van Dyck et al., *N Engl J Med* 2023; 388:9-21

0.70 points (29%)



Sims et al., *JAMA* doi:10.1001/jama.2023.13239

Current detection and diagnosis pathway



Still today, >90% of patients are diagnosed with just cognitive tests and CT/MRI

PROJECT EXECUTIVE BOARD							RESEARCH ASSISTENTS		
	G Frisoni	F Nobili	C Festari	F Massa	M Cotta Ramusino	S Orini		F Gandolfo	Nicolosi

EXTERNAL REVIEW		SCIENTIFIC ADVISORY BOARD					
	W Van der Flier		B Dubois	M Boada Rovira	C Ritchie	O Hansson	P Scheltens

THE PANEL								

WORKFLOW

		Cognitive complaints																
ASSESSMENT		CLINICAL ASSESSMENT ¹ SCREENING OF BPSD COGNITIVE SCREENING TESTS																
W0 SYNDROMIC HYPOTHESIS		Suspected MCI or mild dementia																
ASSESSMENT		BLOOD (INCL. TSH, B12, FOLATES)			DETAILED NPSY BATTERY			MRI (OR CT) ²		EEG IN SPECIFIC CASES								
W1 SYNDROMIC PROFILE BASED ON W0-W1 ASSESSMENT		Amnesic cognitive impairment and disproportionate medial temporal lobe atrophy	Predominant visuo-spatial impairment and parieto-occipital atrophy	Predominant language impairment (i.e., logopenic, agrammatic/non-fluent or semantic) and consistent focal atrophy in the dominant hemisphere.	Frontal behavioural and/or dysexecutive syndrome with cortical atrophy	Dysexecutive and/or visuospatial deficits, and at least one among alertness fluctuations, visual hallucinations, REM behavioural disorders, parkinsonism	Non-amnesic, mainly dysexecutive deficit, ocular motor dysfunction and parkinsonism	Non-amnesic, mainly dysexecutive deficits and symptoms of neocortical dysfunction (in particular, apraxia), along with asymmetric parkinsonism and asymmetric brain atrophy	Cognitive impairment, and MRI with negative or inconsistent result.	No cognitive impairment	Non-amnesic cognitive deficit along with pseudo-bulbar signs and/or parkinsonism and with extensive relevant vascular damage on MRI	Atypical course (e.g., rapid onset and progression) associated with unusual symptoms or biological, neurophysiological or neuroimaging findings						
W2 CLINICAL DIAGNOSIS		Typical AD syndrome	Atypical AD syndrome PCA Logopenic PPA		Agrammatic or semantic PPA	bvFTD or vAD	LB spectrum DLB PD-MCI	PSP spectrum	CBS	No clear hypothesis		Psychiatric conditions, worried well, SCD	Vascular cognitive impairment	Other neurological disorders (e.g., LOE, CJD, AE)				
		Suspected AD			Suspected FTL		Suspected LBD		Suspected motor tauopathy									
ASSESSMENT		CSF biomarkers				FDG-PET		DAT-SPECT		FDG-PET			CSF biomarkers					
W2		A-	A+T	A borderline	A+T	Normal	Abnormal but not typical of FTL	Abnormal and typical of FTL	Positive	Negative	Normal	Abnormal and typical of CBS	Abnormal and typical of PSP	Abnormal but not typical of CBS	Abnormal but not typical of PSP	A+T	A+T	A- or borderline
W3 BIOMARKER BASED DIAGNOSIS		⊕	⊕	⊕	⊕	⊕	⊕	FTLD	LBD DLB	DLB still possible PD-MCI excluded	⊕	CBS	PSP					
ASSESSMENT		FDG-PET		amyloid PET		CSF biomarkers		MIBIG scintigraphy		CSF biomarkers		CSF biomarkers		FDG-PET				
W3		Abnormal and typical of AD	Normal or abnormal but not typical of AD	Neg	Pos	A+T	A-	A+T	Pos	Neg	A+T	A-	A borderline or A+T	A-	A+T	Biomarker choice according to FDG-PET pattern	More biomarkers needed*	According to FDG-PET pattern
W3 ETIOLOGICAL DIAGNOSIS		AD	⊕	AD	AD	AD	fvAD excluded Review all the collected information	⊕	⊕	⊕	AD	CBS not due to AD	Review all the collected information	AD excluded	AD	AD		

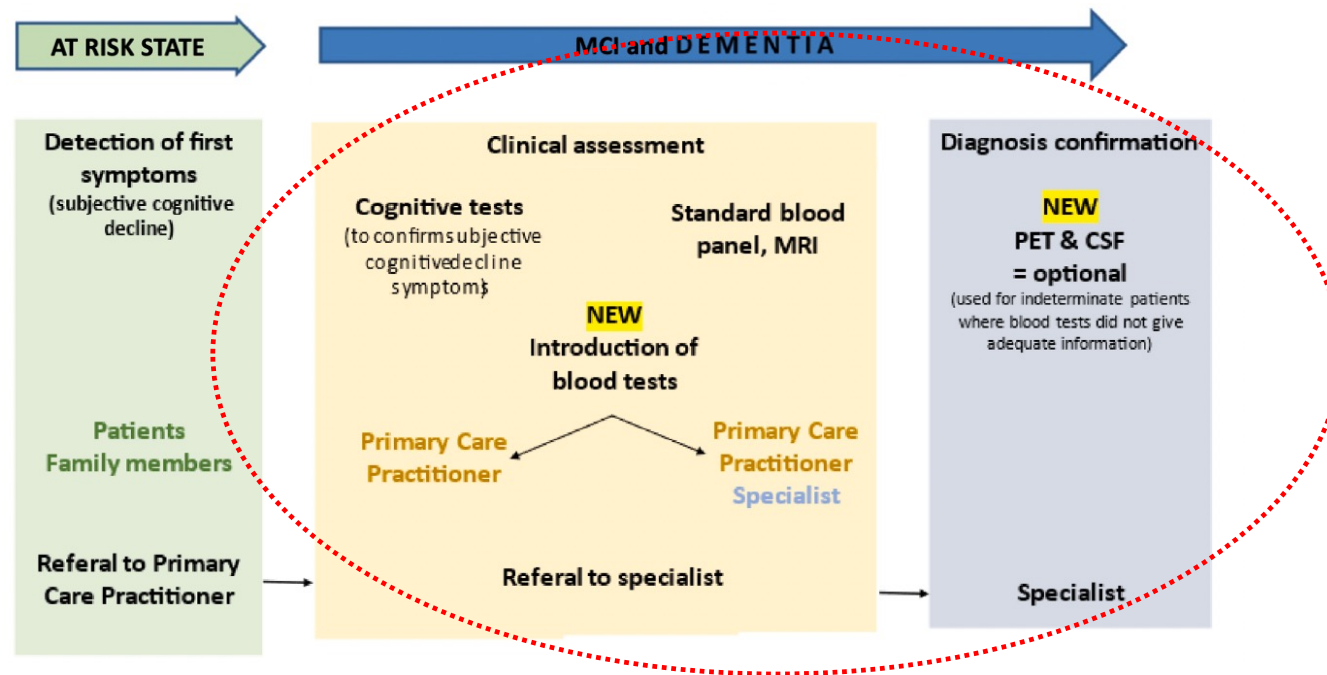
AD: Alzheimer's disease
 AE: autoimmune encephalitis
 BPSD: behavioural and psychological symptoms of dementia
 bvFTD: behavioural variant frontotemporal dementia
 CBS: corticobasal syndrome
 CJD: Creutzfeldt-Jacob disease
 CSF: cerebrospinal fluid
 CT: computed tomography
 DAT: dopamine transporter
 DLB: dementia with Lewy body
 EEG: electroencephalography
 FDG: 18F-fluorodeoxyglucose
 FTL: frontotemporal lobar degeneration
 fvAD: frontal variant of AD
 LBD: Lewy body disease
 LOE: late-onset epilepsy
 MCI: mild cognitive impairment
 MIBIG: metaiodobenzylguanidine
 MRI: magnetic resonance imaging
 NPSY: neuropsychology
 PCA: posterior cortical atrophy
 PD: Parkinson's disease
 PET: positron emission tomography
 PPA: primary progressive aphasia
 PSP: progressive supranuclear palsy
 SCD: subjective cognitive decline
 SPECT: single-photon emission computed tomography

W0, baseline general assessment
 W1, baseline detailed assessment
 W2, biomarker assessment
 W3, disambiguation of undefined diagnoses

¹ Neurological exam, physical exam, family, medical and social history
² CT should be performed only if MRI is unavailable or contraindicated.
³ Biomarker use: strongly recommended if age <70; recommended depending on individual patient feature if age 70-85. Not recommended if age >85. Bold font: strong agreement (>70%); regular font: moderate agreement (50%-69%).
⁴ Clinician will select the second-line biomarker according to the clinical-neuropsychological and MRI peculiarities of that specific case.

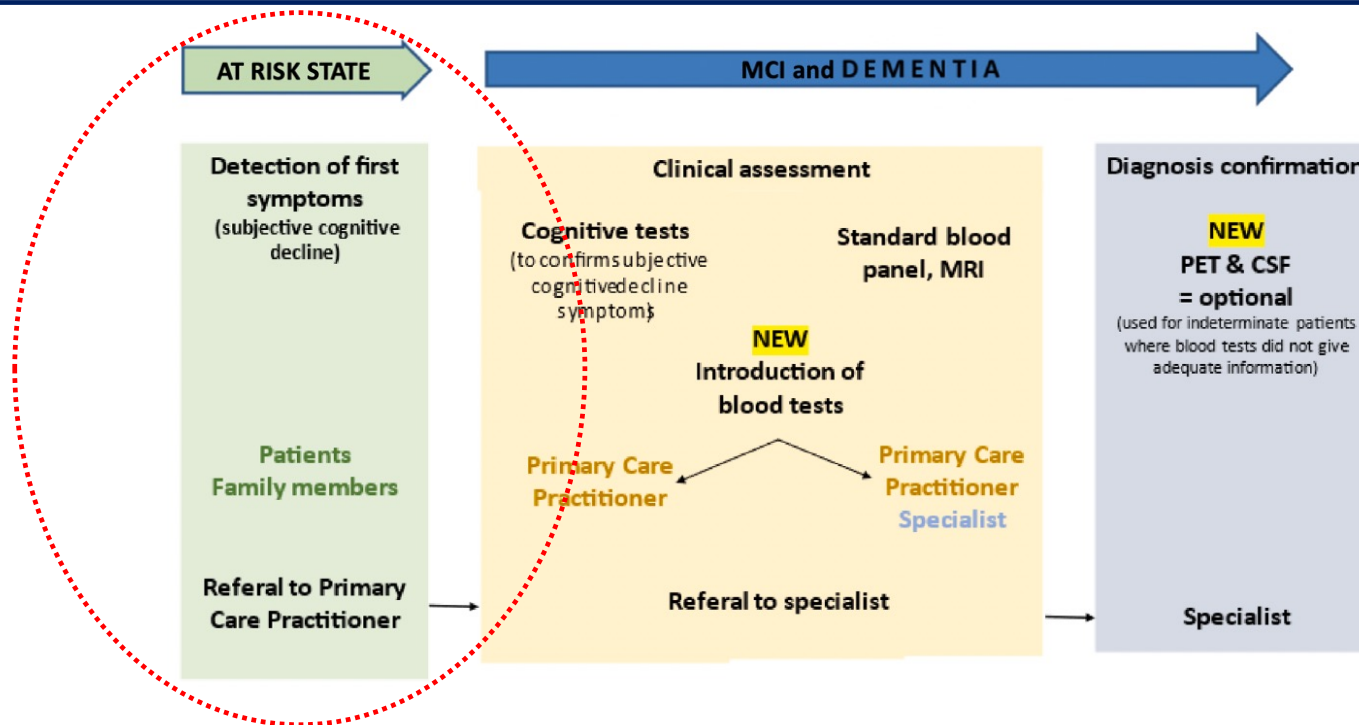
⊕ Assessment not further discussed in this initiative.
 ⊕ Reconsider diagnosis.

New detection and diagnosis pathway



Blood biomarkers of Alzheimer's pathology will radically change the future patient journey

New detection and diagnosis pathway



Blood biomarkers of Alzheimer's pathology will open the new patient journey for secondary prevention

Prevention

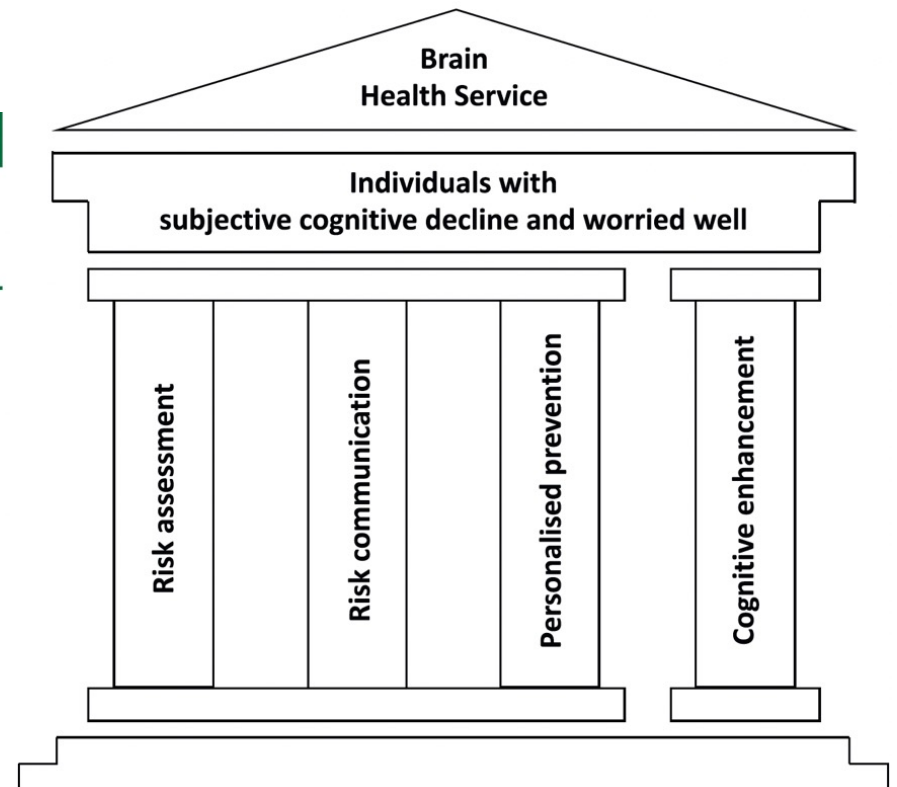
Health Policy

Dementia prevention in memory clinics: recommendations from the European task force for brain health services

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The Lancet Regional Health - Europe 2023;■: 100576 <https://doi.org/10.1016/j.lanepe.2022.100576>



The vision of secondary prevention of dementia and Alzheimer's disease

In 1945 hypertension was considered an untreatable natural consequence of ageing

- F.D. Roosevelt in Yalta, 1945
- His blood pressure was 260/150.
- Eight weeks later he had a bout up to 300/190 and died of intracranial hemorrhage at 3.35 pm on April 12, 1945, at the age of 65.

Bruenn HG. *Ann Int Med* 1970;72:579–91



Conclusions

- Diagnosis and care of dementia and AD are going to change dramatically in the coming years
- The biomarker-based diagnosis will need to be largely implemented in the clinic in patients with MCI and mild dementia
- Persons in the state at risk will be managed in novel memory clinics where risk assessment, risk communication, and risk reduction interventions will be delivered