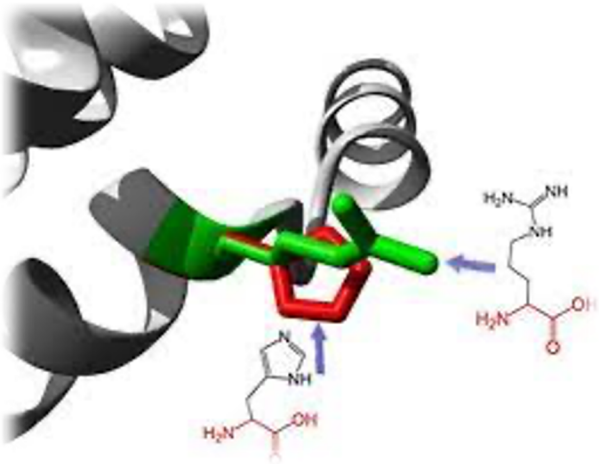
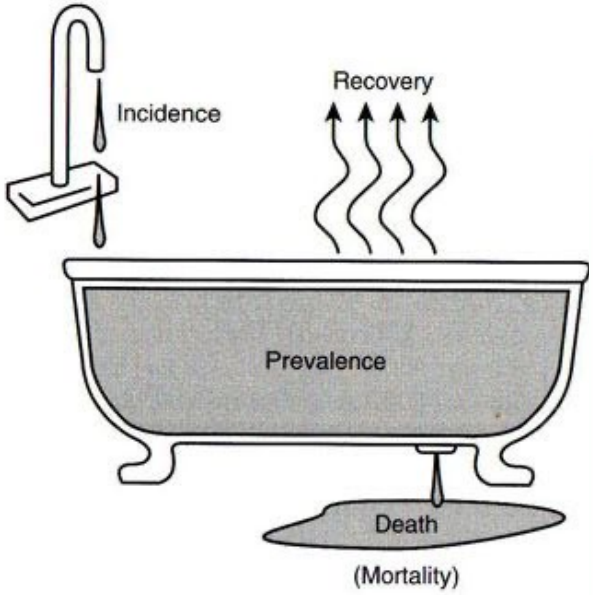
PREVENTION OF DEMENTIA
DEVELOPING COUNTRIES PERSPECTIVE

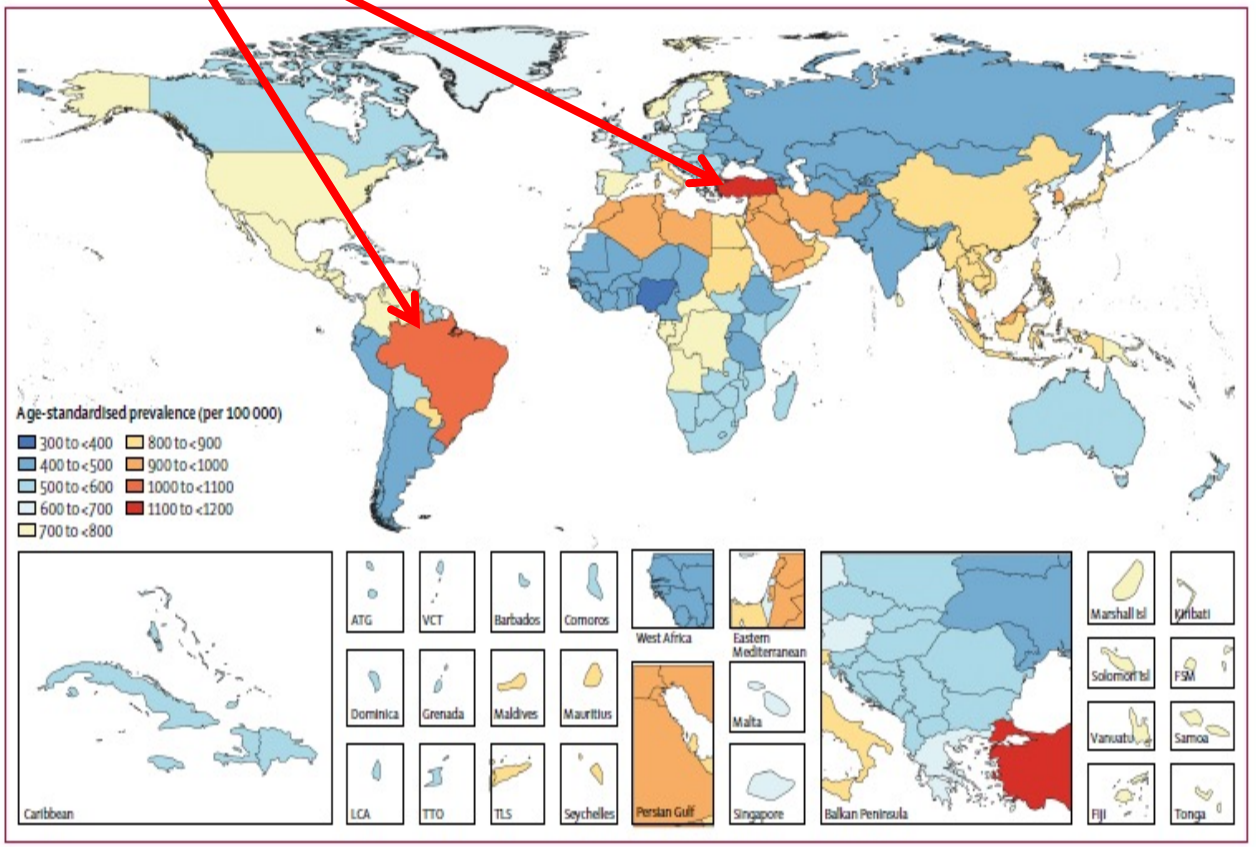
Dr Gautam Saha
President
SAARC

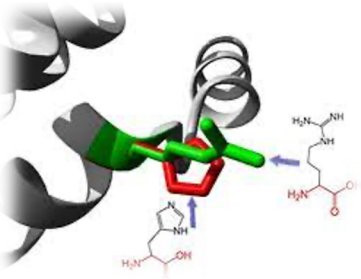


IS DEMENTIA INCREASING OR DECREASING?



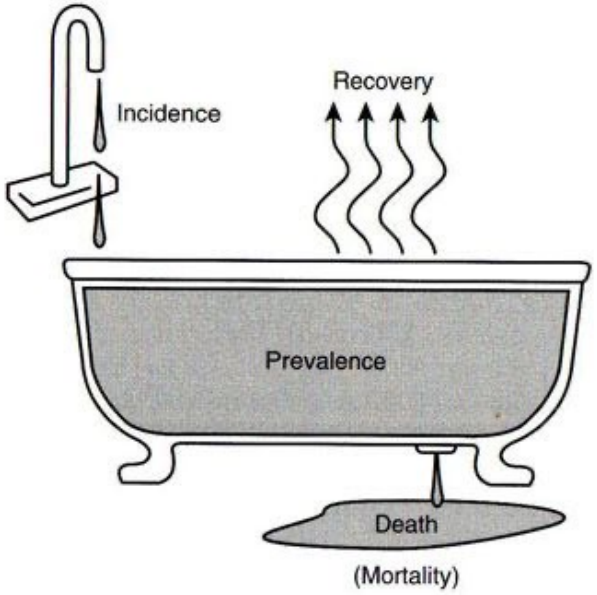
"Increases in overall prevalence related to an ageing population"





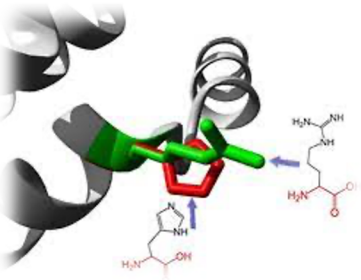
Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

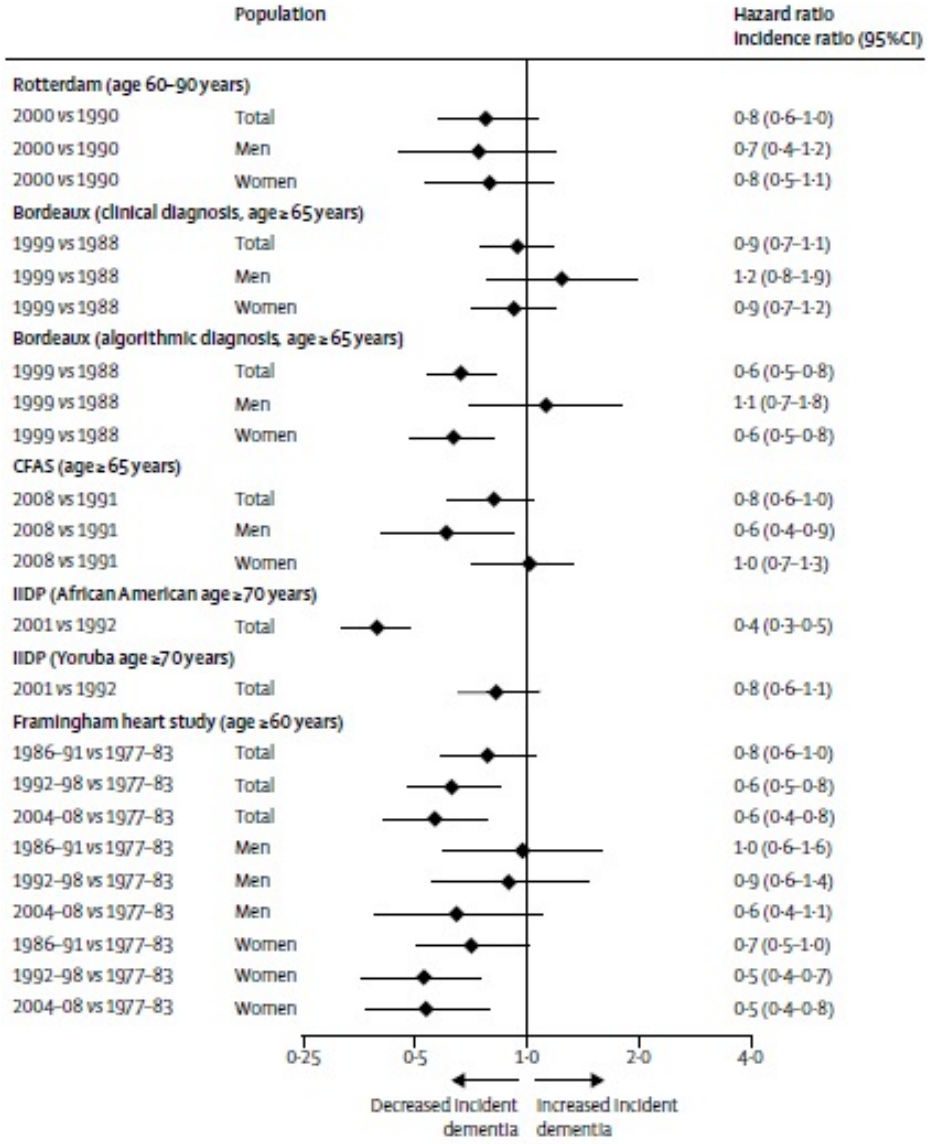
GBD 2016 Dementia Collaborators*



USA, the UK, France, Netherlands
age-specific incidence rates are lower

“BUT LMIC INCIDENCE IS INCREASING”





Extent of the problem …..

By 2030 will increase to 65.7 million

By 2050 ….. ……115.4 million

Unless effective means of reducing incidence are introduced

No curative treatment is available…
No PROVEN disease-modifying agent yet

The 21st Century is the **Century of neurodegenerative disease**

DISEASE PREVENTION

Primary prevention	Secondary prevention	Tertiary prevention
• **Reduce incidence** of disease • **By intervening before disease onset through** • Promoting initiation & maintenance of good health, or • Eliminating potential causes of disease.	• **Prevent a disease at very early or preclinical phases** from progressing to more overt, manifest disease	• **Managing manifest disease & its complications** • Aiming to maximize quality of life

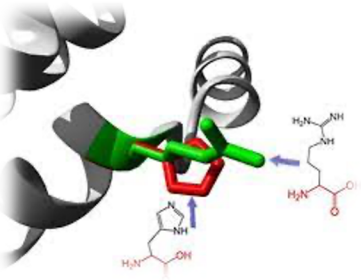
The prevalence of dementia would be reduced by 50% if risk reduction strategies were successful in delaying its onset by 5 years

RESERVE as a concept accounting for the "difference between an individual's clinical picture and their neuropathology"

Review Article

Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance

Yaakov Stern[a,*], Eider M. Arenaza-Urquijo[b], David Bartrés-Faz[c,d,e], Sylvie Belleville[f], Marc Cantilon[g], Gael Chetelat[h], Michael Ewers[i], Nicolai Franzmeier[i], Gerd Kempermann[j], William S. Kremen[k], Ozioma Okonkwo[l], Nikolaos Scarmeas[m,n], Anja Soldan[o], Chinedu Udeh-Momoh[p], Michael Valenzuela[q], Prashanthi Vemuri[r], Eero Vuoksimaa[s], and the Reserve, Resilience and Protective Factors PIA Empirical Definitions and Conceptual Frameworks Workgroup

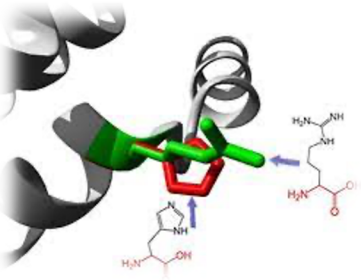


RESEREVE: BRAIN (BR)+COGNITIVE (CR)+MAINATINENECE (BM)

Review Article

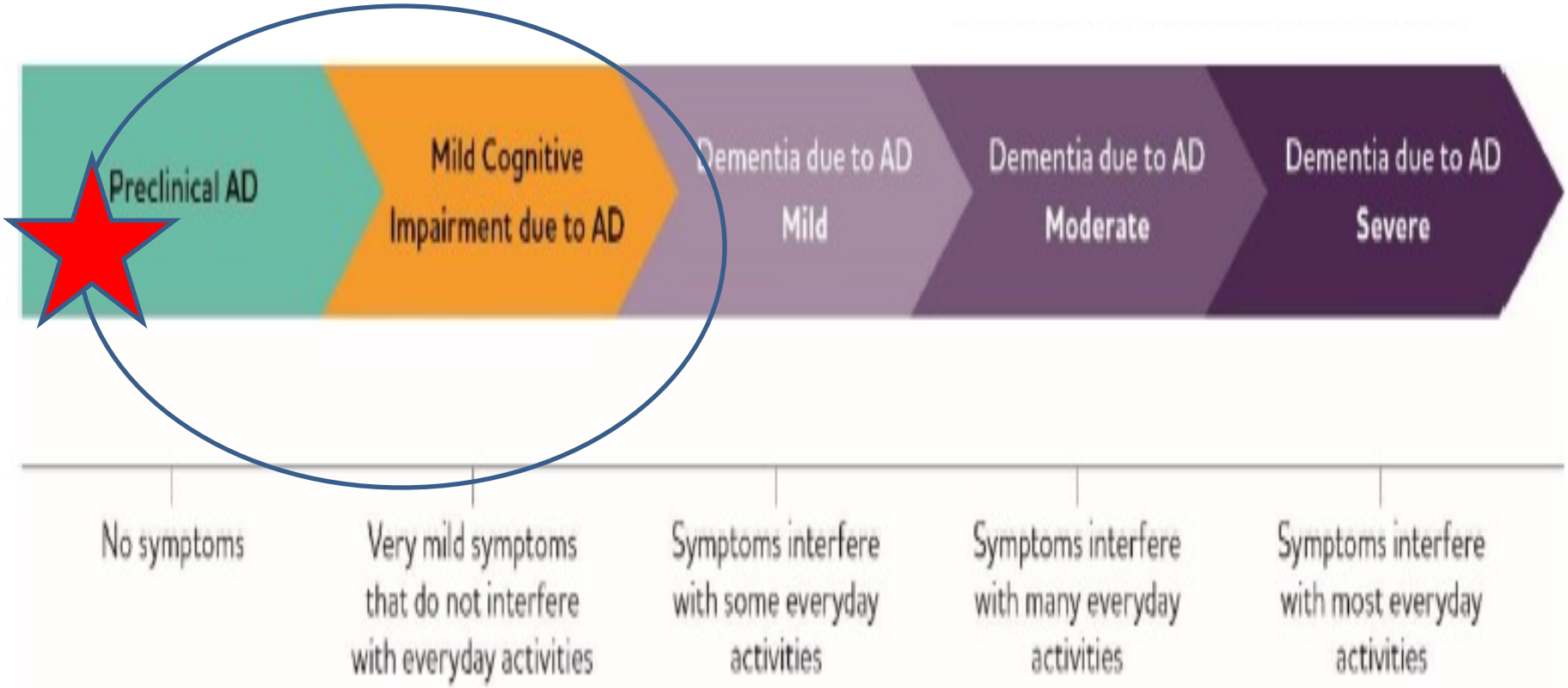
Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance

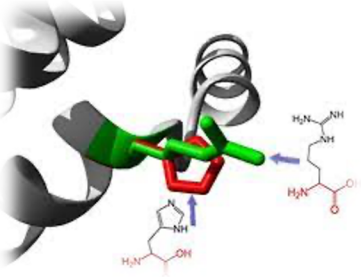
Yaakov Stern[a,*], Eider M. Arenaza-Urquijo[b], David Bartrés-Faz[c,d,e], Sylvie Belleville[f], Marc Cantilon[g], Gael Chetelat[h], Michael Ewers[i], Nicolai Franzmeier[i], Gerd Kempermann[j], William S. Kremen[k], Ozioma Okonkwo[l], Nikolaos Scarmeas[m,n], Anja Soldan[o], Chinedu Udeh-Momoh[p], Michael Valenzuela[q], Prashanthi Vemuri[r], Eero Vuoksimaa[s], and the Reserve, Resilience and Protective Factors PIA Empirical Definitions and Conceptual Frameworks Workgroup



BR is conceived as neurobiological capital
CR refers to the adaptability (i.e., efficiency, capacity, flexibility)
BM reduced development over time of age-related brain changes and pathology based on genetics or lifestyle

Subjective Cognitive Impairment





Risk factor

Is education level important in reducing dementia ?

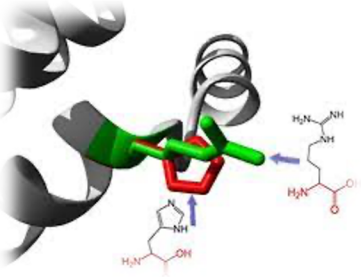
Higher childhood education levels and **lifelong** higher educational attainment reduce dementia risk

Influence of young adult cognitive ability and additional education on later-life cognition

William S. Kremen[a,b,c,1], Asad Beck[b,d], Jeremy A. Elman[a,b], Daniel E. Gustavson[a,b], Chandra A. Reynolds[e], Xin M. Tu[b,f], Mark E. Sanderson-Cimino[a,b,d], Matthew S. Panizzon[a,b], Eero Vuoksimaa[g], Rosemary Toomey[h], Christine Fennema-Notestine[a,b,i], Donald J. Hagler Jr.[a,b,i], Bin Fang[a,b], Anders M. Dale[a,b,i,j], Michael J. Lyons[h], and Carol E. Franz[a,b,1]

in cognitive-intellectual activities, are frequently considered indices of cognitive reserve, but whether their effects are truly causal remains unclear. In this study, after accounting for general cognitive ability (GCA) at an average age of 20 y, additional education, occupational complexity, or engagement in cognitive-intellectual activities accounted for little variance in late midlife cognitive functioning in men age 56–66 ($n = 1009$). Age 20 GCA accounted for 40% of variance in the same measure in late midlife and approximately 10% of variance in each of seven cognitive domains. The other factors each accounted for <1% of the variance in cognitive outcomes. The impact of these other factors likely reflects reverse causation—namely, downstream effects of early adult GCA. Supporting that idea, age 20 GCA, but not education, was associated with late midlife cortical surface area ($n = 367$). In our view, the most parsimonious expla-

Few further gains with education after age 20 years



Risk factor

Is education level important in reducing dementia?

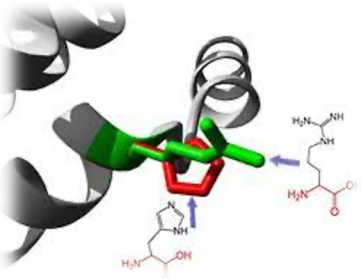
EDUCATION: 7 % PAF

GLOBAL LITERACY RATE IS 86.3 %

Table 1
Literacy Rate Trend in India 1951-2011

Census Year	Persons	Decadal Increase	Males	Females	Gender gap
1951	18.33		27.16	8.86	18.30
1961	28.3	9.97	40.40	15.35	25.05
1971	34.45	6.15	45.96	21.97	23.99
1981	43.57	9.12	56.38	29.76	26.62
1991	52.21	8.64	64.13	39.29	24.84
2001	64.83	12.62	75.26	53.67	21.59
2011	74.04	9.21	82.14	65.46	16.68

Source: Census Of India



Does retirement affect cognitive decline ?

Higher Retirement age and more cognitively demanding jobs have less cognitive deterioration (memory/fluency) !

INDIA

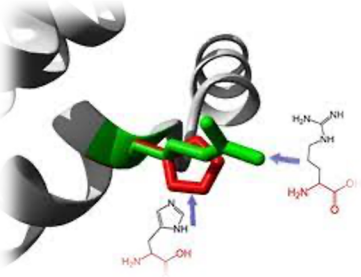
7th Pay commission

Retirement age: 62 yrs.

Worldwide

Denmark

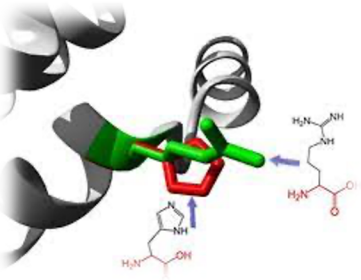
Retirement age: **67 yrs**.



Does cognitive intervention helps in General population/ MCI ?

GENERAL POPULATION
Three systematic reviews
No effect on general cognition

MCI
One RCT/2 metanalysis/1 Systematic review
Inconclusive: only improves QoI



Risk factor

Does HEARING LOSS affect cognitive decline ?

JAMA Otolaryngol

Associatic

Function,

A System

David G. Loughrey, BA(

Brian A. Lawlor, MD, FR

Outcome	No. of Participants/Events	r Value (95% CI)
Attention	5159/11	−0.16 (−0.24 to −0.07)
Delayed recall	3808/7	−0.10 (−0.16 to −0.04)
Fluency	4629/9	−0.08 (−0.12 to −0.04)
Global cognition	7702/15	−0.15 (−0.18 to −0.11)
Immediate recall	6747/15	−0.14 (−0.20 to −0.09)
Processing speed	10660/20	−0.13 (−0.18 to −0.08)
Reasoning	3128/12	−0.17 (−0.25 to −0.10)
Semantic memory	2906/10	−0.14 (−0.20 to −0.08)
Visuospatial ability	669/5	−0.11 (−0.19 to −0.03)
Working memory	4855/9	−0.10 (−0.15 to −0.05)
Summary	15620/113	−0.12 (−0.14 to −0.10)

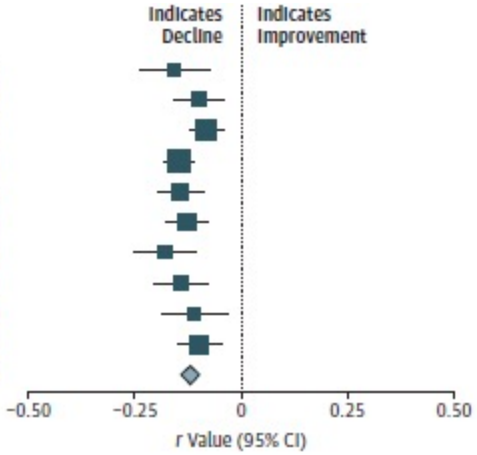
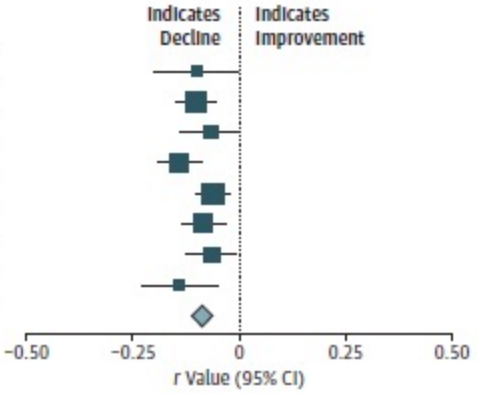
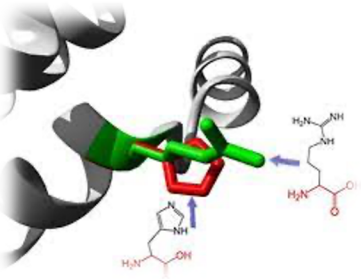


Figure 3. Forest Plot of Correlations for Cognition Cohort Outcomes

Outcome	No. of Participants/ Events	r Value (95% CI)
Attention	5159/11	−0.10 (−0.20 to 0.00)
Delayed recall	3808/7	−0.10 (−0.15 to −0.05)
Fluency	4629/9	−0.07 (−0.14 to 0.01)
Global cognition	7702/15	−0.14 (−0.19 to −0.09)
Immediate recall	6747/15	−0.06 (−0.10 to −0.02)
Processing speed	10660/20	−0.08 (−0.14 to −0.03)
Reasoning	3128/12	−0.06 (−0.12 to 0.00)
Semantic memory	2906/10	−0.14 (−0.23 to −0.05)
Summary	15620/113	−0.09 (−0.11 to −0.07)

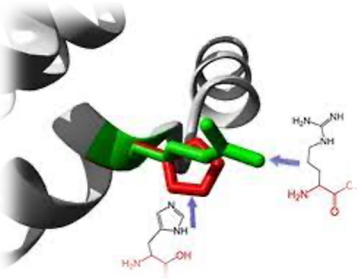


Increased
risk of dementia
(OR 1.3 per 10 Db)



Would Hearing aids help ?

Hearing aid use was the largest factor protecting from decline (regression coefficient β for higher episodic memory 1.53; p<0.001) adjusting for protective and harmful factors



CLINICAL INVESTIGATION

Longitudinal Relationship Between Hearing Aid Use and Cognitive Function in Older Americans

Asri Maharani, PhD, Piers Dawes, PhD,† James Nazroo, PhD,‡ Gindo Tampubolon, PhD,‡ Neil Pendleton, PhD,* and on behalf of the SENSE-Cog WP1 group*

JAGS 2018

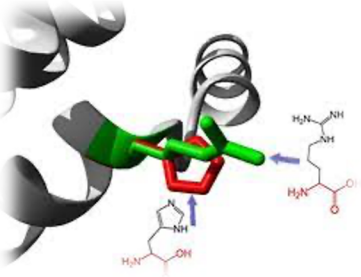
Risk factor

Does HEARING LOSS affect cognitive decline ?

INDIA
63 MILLION PEOPLE HAVE HEARING LOSS
(NHM, 2022)

WORLWIDE
430 MILLION PEOPLE HAVE HEARING LOSS
(WHO, 2021)

PAF: 8 %

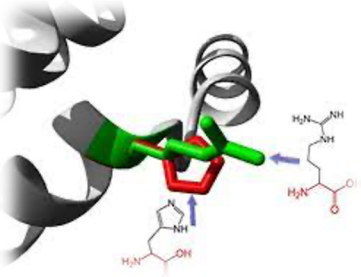


https://nhm.gov.in/index1.php?lang=1&level=2&sublinkid=1051&lid=606#:~:text=Hearing%20loss%20is%20the%20most,at%206.3%25%20in%20Indian%20population.

Is TBI a risk for Dementia ?

Studies: Maximum risk within 6 m of
single TBI (OR: 1.6)/Severe TBI (OR: 2.1)/Multiple TBI (OR: 2.8)

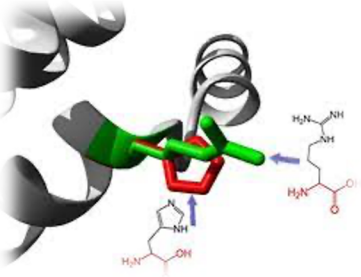
Cohort study of 28 815 older adults with concussion
Those taking statins had a 13% reduced risk of dementia



Is TBI a risk for Dementia ?

Single, severe TBI is associated in humans, and mouse models, with widespread hyperphosphorylated tau pathology

India has the rather unenviable distinction of having the highest rate of head injury in the world



https://indianheadinjuryfoundation.org/traumatic-brain-injury/

Is Hypertension a risk for dementia ?

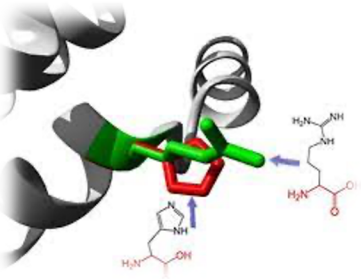
Yes

Persistent **midlife** (after 40) hypertension is associated with increased risk of a late life dementia

Framingham data (McGrath et al., 2017)
> 130 mm Hg associated with increased risk

Reduced brain volumes and increased white matter hyperintensity volume

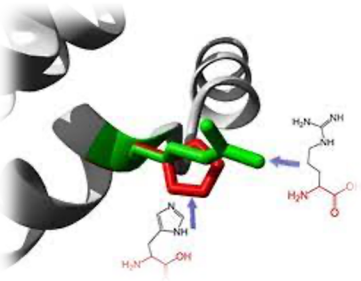
BP declines in later life and this decline is associated with dementia development



Does ANTIHYPERTENSIVES help?

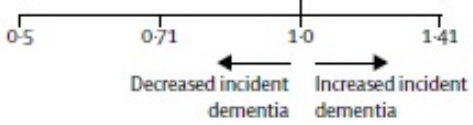
SPRINT in 9361 hypertensive adults
2 arms: **Intensive vs Standard**
14.6 vs 18.3 cases/1000 person-years of MCI

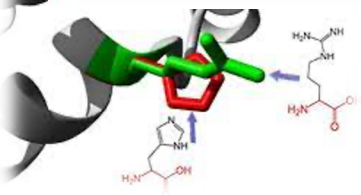
4 Meta-analysis using Anti-hypertensives have suggested decline in Dementia rates



	Studies (individuals, n)	Dementia cases, n	Hazard ratio (95% CI)	p value for heterogeneity
Angiotensin-converting enzyme inhibitors				
Alone or in combination (vs no drug users)	6 (12 521)	1100	0·97 (0·82–1·15)	0·32
Alone (vs no drug users)	6 (11 112)	895	1·03 (0·83–1·27)	0·72
Alone or in combination (vs other drug users)	6 (7794)	1080	1·11 (0·96–1·29)	0·43
Alone (vs other drug users)	6 (6385)	875	1·16 (0·93–1·46)	0·48
Angiotensin II receptor blockers				
Alone or in combination (vs no drug users)	3 (5737)	595	0·84 (0·58–1·21)	0·09
Alone (vs no drug users)	3 (5073)	476	0·78 (0·5–1·22)	0·24
Alone or in combination (vs other drug users)	3 (4559)	720	0·88 (0·71–1·09)	0·62
Alone (vs other drug users)	3 (4039)	629	0·76 (0·53–1·09)	0·62
β blockers				
Alone or in combination (vs no drug users)	6 (12 668)	1258	0·86 (0·75–0·98)	0·58
Alone (vs no drug users)	5 (9826)	888	0·96 (0·77–1·20)	0·27
Alone or in combination (vs other drug users)	6 (7794)	1080	0·95 (0·83–1·10)	0·41
Alone (vs other drug users)	5 (5544)	752	1·07 (0·89–1·30)	0·39
Calcium channel blockers				
Alone or in combination (vs no drug users)	6 (12 469)	1098	0·87 (0·75–1·01)	0·97
Alone (vs no drug users)	6 (11 174)	900	0·92 (0·75–1·14)	0·97
Alone or in combination (vs other drug users)	6 (7794)	1080	1·04 (0·86–1·24)	0·26
Alone (vs other drug users)	6 (6639)	908	1·09 (0·89–1·35)	0·5
Diuretics				
Alone or in combination (vs no drug users)	6 (12 588)	1257	0·87 (0·76–0·99)	0·52
Alone (vs no drug users)	6 (10 623)	934	0·97 (0·76–1·24)	0·16
Alone or in combination (vs other drug users)	6 (7794)	1080	0·95 (0·83–1·09)	0·91
Alone (vs other drug users)	6 (5961)	782	1·05 (0·83–1·33)	0·26
Any antihypertensive drugs				
Alone or in combination (vs no drug users)	6 (14 520)	1865	0·88 (0·79–0·98)	0·65

χ^2=3·35, df=5; p=0·65, I^2=0·0%





Does STATINS help in preventing Dementia
In cohort with vascular risk ?

Cochrane Library

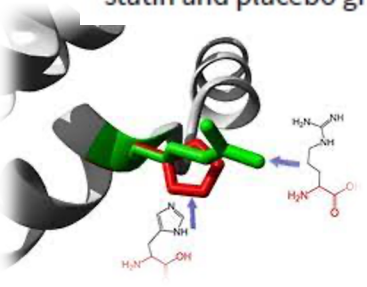
Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

[Intervention Review]

Statins for the prevention of dementia

We included two trials with 26,340 participants aged 40 to 82 years of whom 11,610 were aged 70 or older. All participants had a history of, or risk factors for, vascular disease. The studies used different statins (simvastatin and pravastatin). Mean follow-up was 3.2 years in one study and five years in one study. The risk of bias was low. Only one study reported on the incidence of dementia (20,536 participants, 31 cases in each group; odds ratio (OR) 1.00, 95% confidence interval (CI) 0.61 to 1.65, moderate quality evidence, downgraded due to imprecision). Both studies assessed cognitive function, but at different times using different scales, so we judged the results unsuitable for a meta-analysis. There were no differences between statin and placebo groups on five different cognitive tests (high quality evidence). Rates of treatment discontinuation due to non-fatal adverse events were less than 5% in both studies and there was no difference between statin and placebo groups in the risk of withdrawal due to adverse events (26,340 participants, 2 studies, OR 0.94, 95% CI 0.83 to 1.05).

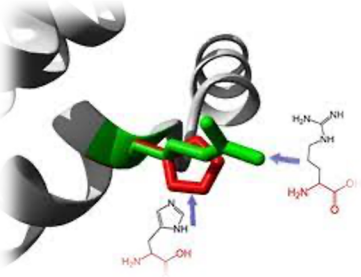


Does DM enhance risks in dementia ?

Meta-analyses of 2.3 million
DM is risk for all cause dementia (RR: 1.6)
(Chatterjee et al., 2016)

Increase risk with duration/severity of DM

? Metformin protecting against dementia
(Conflicting data)

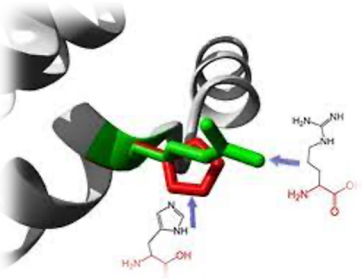


Intensive diabetic control individuals does not decrease the risk of Dementia

Does Physical inactivity enhance risks in dementia ?

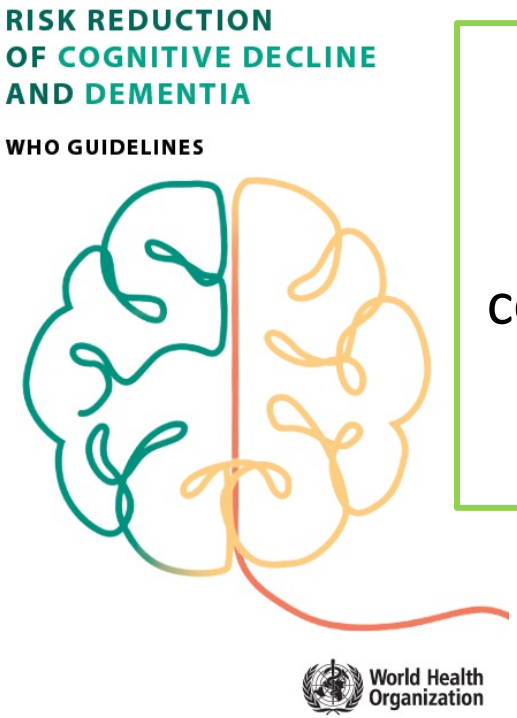
Meta-analyses of longitudinal observational studies of 1–21 years duration showed exercise to be associated with reduced risk of dementia

HUNT study: At least weekly midlife moderate-to-vigorous physical activity (breaking into a sweat) 25-year period of follow-up (Zotcheva et al., 2018)

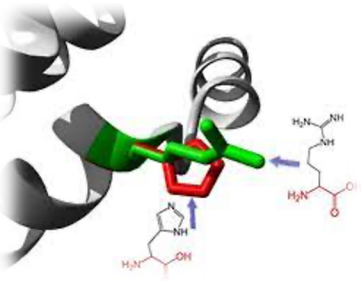


Does exercise helps?

3 Meta-analysis



"the evidence points towards physical activity having a small, beneficial effect on normal cognition, with a possible effect in MCI, mostly due to aerobic exercise"

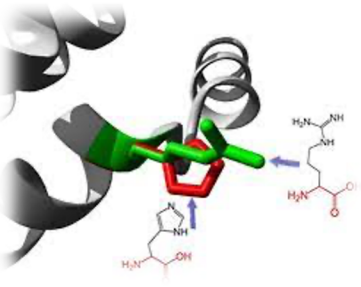


Risk factor

Does obesity enhance risks in dementia ?

19 longitudinal studies including 589 649 people aged 35 to 65 years, followed up for up to 42 years

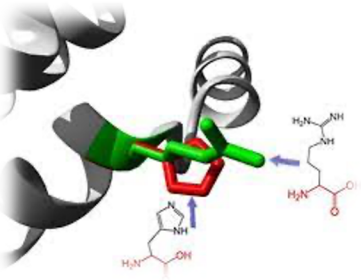
obesity (BMI ≥ 30; RR 1.3) but not being overweight (BMI 25–30; RR 1.1) was associated with late-life dementia



Does reducing weight helps?

Meta-analysis: Weight loss of 2 kg or more in people with BMI greater than 25 was associated with a significant improvement in attention and memory (over 8–48 weeks) (Veronese et al., 2017)

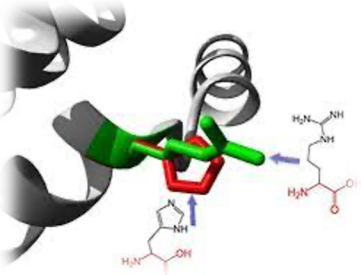
No long term data/for prevention of dementia



Does alcohol consumption enhance risks in dementia ?

Heavy drinking is associated with brain changes, cognitive impairment, and dementia, a risk known for centuries

Risk associated with EOD
Drinking in moderation (less than 21 units per week) was protective (17 % lesser risk)



Right sided hippocampal atrophy on MRI

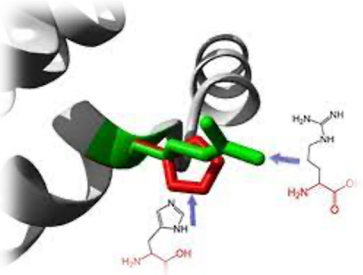
Does smoking/air pollutants enhance risks in dementia ?

Smokers are at higher risk of dementia than nonsmokers

Higher risk of premature death before the age at which they might have developed dementia

Stopping smoking, even when older, reduces this risk

Passive smoking and cognition loss: data is scarce



Exposure to PM 2.5, NO2, and carbon monoxide were all associated with increased dementia risk

Risk factor

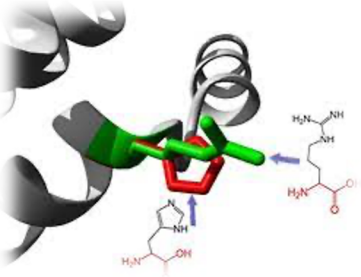
Does depression/reduced social contact increase dementia ?

Late life depression (not early) is associated with increase incident dementia (within 5 yrs)
?epiphenomenon

JOINT FAMILY SYSTEM ?

Animal models: SSRI beneficiary in amyloid plaques generation

SOCIAL CONTACT: is protective for dementia
Being single and widowed (late life) have increased risk



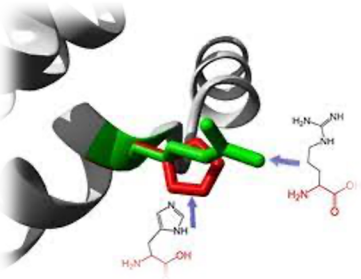
Is DIET protective in dementia ?

Observational studies have focused on individual components ranging from folate and B vitamins, Vitamin C, D, E, and selenium as
potential protective factors

Whole diet: Mediterranean diet/nordic diet

960 + COHORT: Green leafy vegetables, equivalent to 1.3 servings PER DAY: Significantly less cognitive decline over 5 years (Morris et al., 2018)

Akbaraly et al (2019): Assessed three midlife dietary in 8255 people, followed up for a mean of nearly 25 years, found neither pattern protected from dementia, except in those with cardiovascular disease

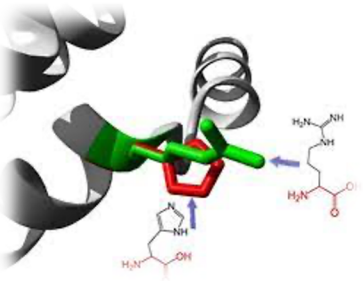


Role of Dietary interventions ?

Cochrane review: No role of RCTs of supplements (A, B, C, D, and E; calcium, zinc, copper, and multivitamins trials, n-3 fatty acids, antioxidant vitamins, and herbs) in preventing dementia in mid-late life; No role of Vit B/E in MCI; No role of multi-nutrient drinks

INDIGENOUS DIET ?

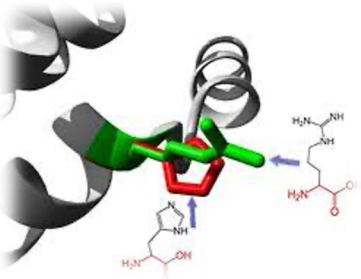
2 Meta-analysis (desired effect on global cognition) and WHO guidelines recommend Mediterranean diet

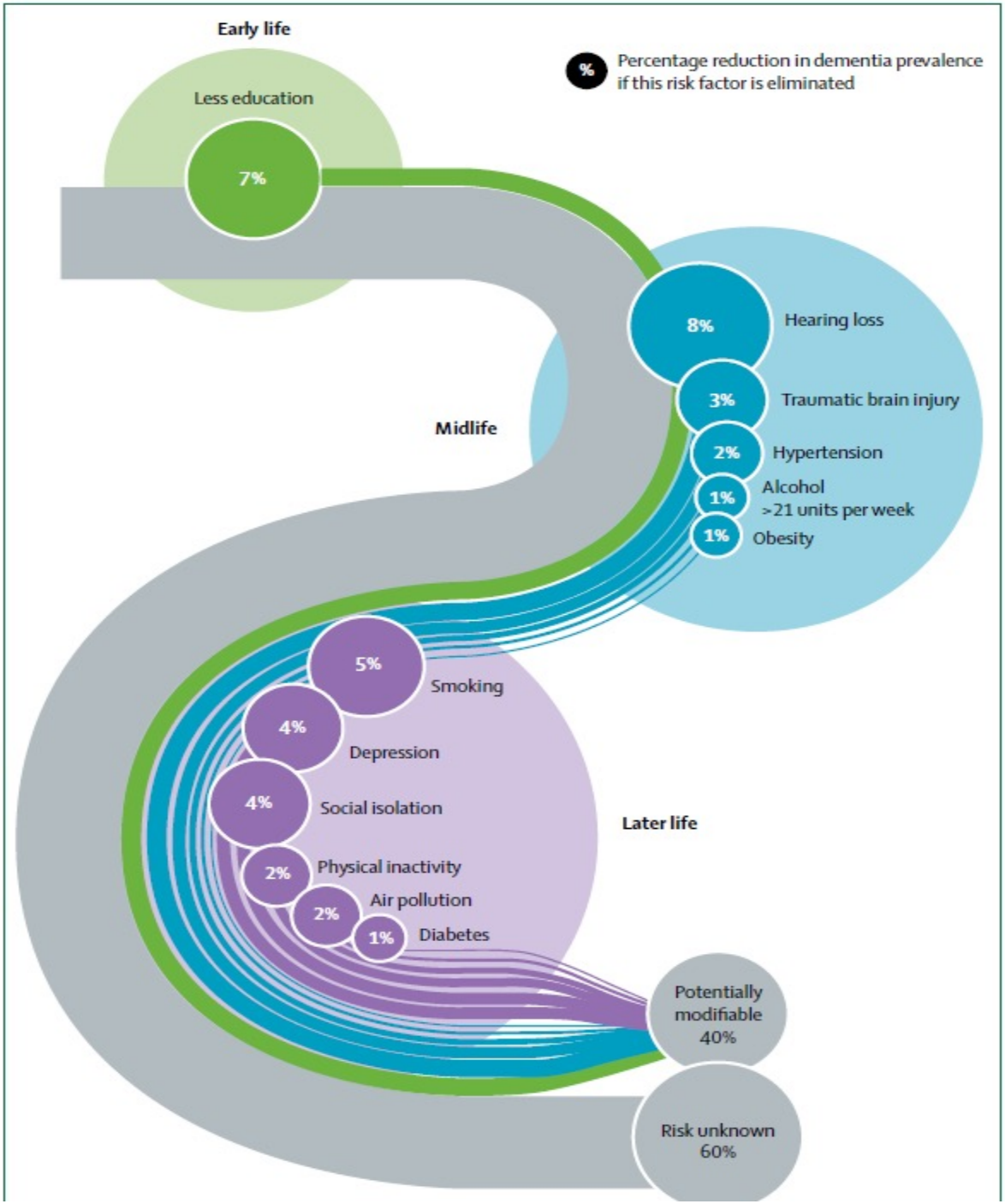


Risk factor

INDIA: 41 % PAF

Overall the evidence for treating hypertension is strongest and high blood pressure throughout midlife increases the risk of dementia even without stroke



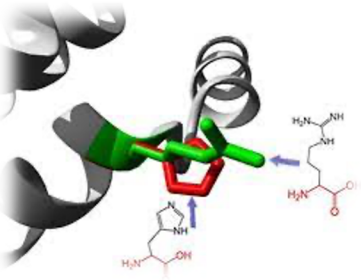


Targeted on individuals

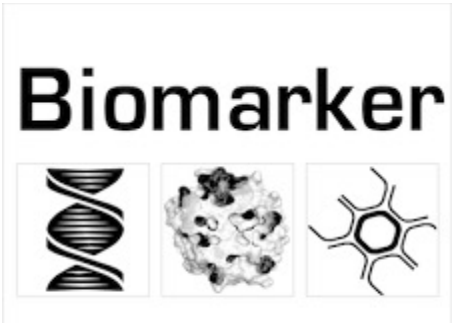
- Treat hypertension and aim for SBP <130 mm Hg in midlife
- Use hearing aids for hearing loss; we need to help people wear hearing aids as many find them unacceptable, too difficult to use, or ineffective
- Avoid or discourage drinking 21 or more units of alcohol per week
- Prevent head trauma where an individual is at high risk
- Stopping smoking is beneficial regardless of age
- Reduce obesity and the linked condition of diabetes by healthy food availability and an environment to increase movement
- Sustain midlife, and possibly late-life physical activity

The Lancet Commissions

Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission



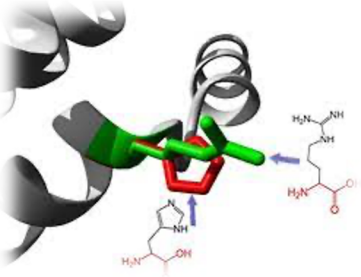
Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, Amit Dias, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Adesola Ogunniyi, Vasiliki Orgeta, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

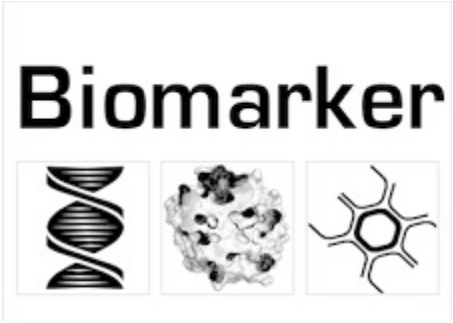


Detection of Alzheimer's disease

NEURODEGENERATION

Hippocampal volume loss and entorhinal cortex and medial temporal cortical thinning



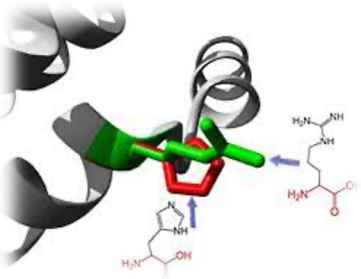


Detection of Alzheimer's disease

Amyloid imaging | Is not diagnostic test

PET positivity: was associated with a higher probability of developing Alzheimer's disease compared with amyloid negative (10 yr follow up)

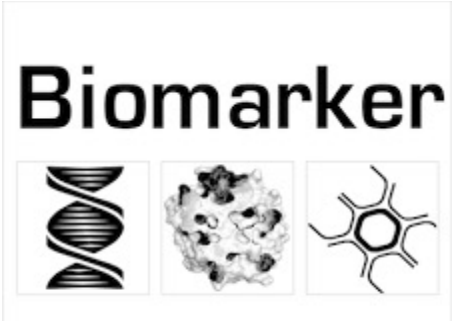
PET AMYLOID Plaques in the in normal population from less than
3% at age 50–59 years to around 40% at age 80–89 years



JAMA Neurology | Original Investigation

Prevalence and Outcomes of Amyloid Positivity Among Persons Without Dementia in a Longitudinal, Population-Based Setting

Rosebud O. Roberts, MB, ChB, MS; Jeremiah A. Aakre, MPH; Walter K. Kremers, PhD; Maria Vassilaki, MD, PhD; David S. Knopman, MD; Michelle M. Mielke, PhD; Rabe Alhurani, MBBS, MS; Yonas E. Geda, MD, MSc; Mary M. Machulda, PhD; Preciosa Coloma, MD, PhD; Barbara Schauble, MD, PhD; Val J. Lowe, MD; Clifford R. Jack Jr, MD; Ronald C. Petersen, MD, PhD



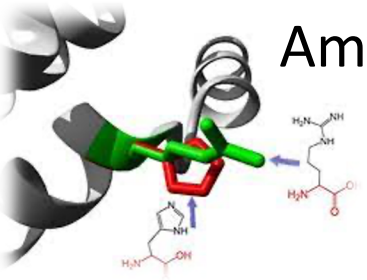
Detection of Alzheimer's disease

Amyloid imaging

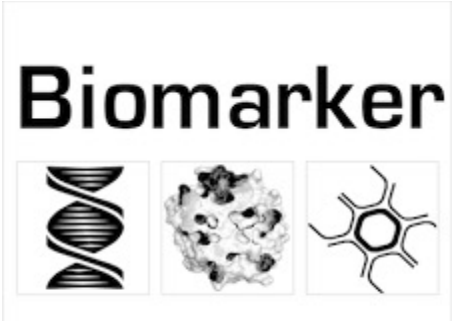
	Normal state 1	Amyloidosis state 2	Neurodegeneration state 3	Amyloidosis and neurodegeneration state 4	Mild cognitive impairment and amyloidosis and neurodegeneration state 5	Mild cognitive impairment and neurodegeneration state 6
60 years	0·2 (0·06–0·8)	1·3 (0·6–2·5)	3·6 (1·1–14·2)	7·1 (4·5–10·9)	93·5 (91·1–95·0)	57·2 (48·2–67·9)
65 years	0·5 (0·14–1·8)	2·5 (1·2–4·9)	4·3 (1·4–15·0)	10·7 (6·8–16·2)	91·7 (89·2–93·5)	55·4 (46·6–65·8)
70 years	1·1 (0·34–3·5)	4·7 (2·4–8·7)	5·5 (2·0–16·6)	15·5 (10·0–22·8)	88·6 (85·8–90·6)	52·2 (43·8–62·4)
75 years	2·2 (0·74–6·5)	7·8 (4·1–14·0)	7·3 (2·9–19·0)	20·8 (13·7–29·7)	83·8 (80·7–86·2)	47·4 (39·6–57·0)
80 years	3·7 (1·3–9·8)	11·1 (6·0–18·7)	9·3 (3·9–20·9)	24·4 (16·4–33·8)	75·8 (72·2–78·7)	40·0 (33·1–48·6)
85 years	4·7 (1·8–11·0)	11·5 (6·5–18·5)	9·7 (4·3–19·3)	23·1 (15·8–31·2)	63·7 (59·6–67·2)	30·0 (24·5–37·2)
90 years	3·8 (1·5–8·2)	8·2 (4·7–12·9)	7·1 (3·3–13·3)	16·8 (11·5–22·6)	46·7 (42·7–50·2)	19·1 (15·3–24·3)

Data are relative risk (95% CI) or %. Reproduced from Brookmeyer and Abdalla[185] by permission of Elsevier.

Table 2: **Ten-year risks by age of developing Alzheimer's disease for women based on amyloidosis alone and in the presence of neurodegeneration and mild cognitive impairment**



Amyloid PET positive scan: Helps in defining AD in uncertain etiology



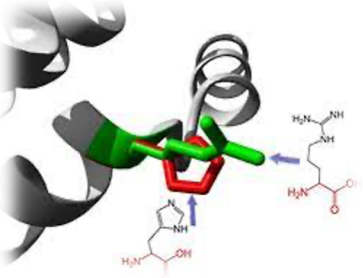
Detection of Alzheimer's disease

Fluid Markers (blood and CSF)

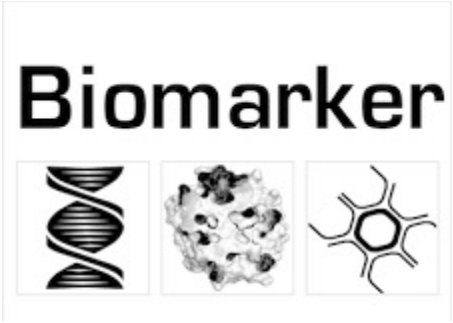
Aβ42: Most toxic form of Aβ peptide
and most widely accepted biomarker of AD

Aβ42/Aβ 40: Ratio in CSF is more accurate

CSF Aβ42/40 ratio and amyloid PET are
now considered interchangeable



Cheaper Blood Aβ42/40 amyloid biomarkers: correlate well with amyloid PET measurement and CSF concentrations of Aβ 42



Detection of Alzheimer's disease

Fluid Markers (blood and CSF)

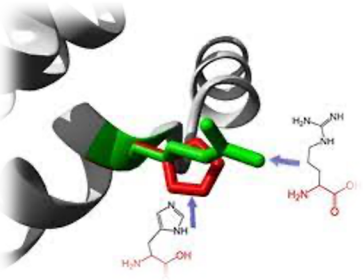
Neurofilament light protein in CSF is a marker for neurodegeneration

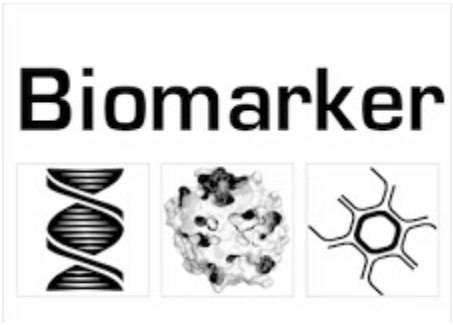
MARKS THE INTENSITY OF DISEASE PROCESS

CSF pTAU is considered a biomarker for AD (> T-Tau)

CSF P-tau 181: classical AD biomarker
CSF P-tau 217: d/f AD from FTD

Recently plasma P-tau 181/ P-tau 217 available



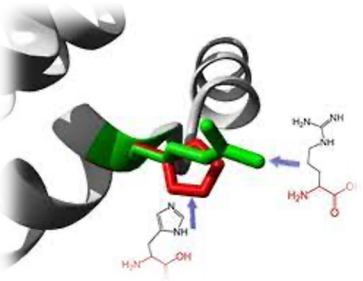


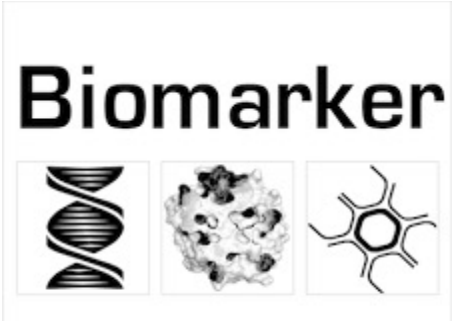
Detection of Alzheimer's disease

Amyloid/tua PET/fluid +
Has risk of developing Dementia
Individual level Prognostication not possible

Negative amyloid results can be useful for ruling out current Alzheimer's pathology

Blood biomarkers could be of value
in **LMIC**





When to use these Biomarker's any consensus ?

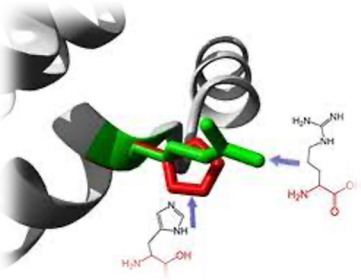
Five appropriate situations

1. SCI plus
2. MCI that is persistent, progressing, and unexplained
3. Patients with symptoms that suggest possible AD
4. MCI or dementia with an onset at an early age (<65)
5. Patients whose dominant symptom is a change in behavior

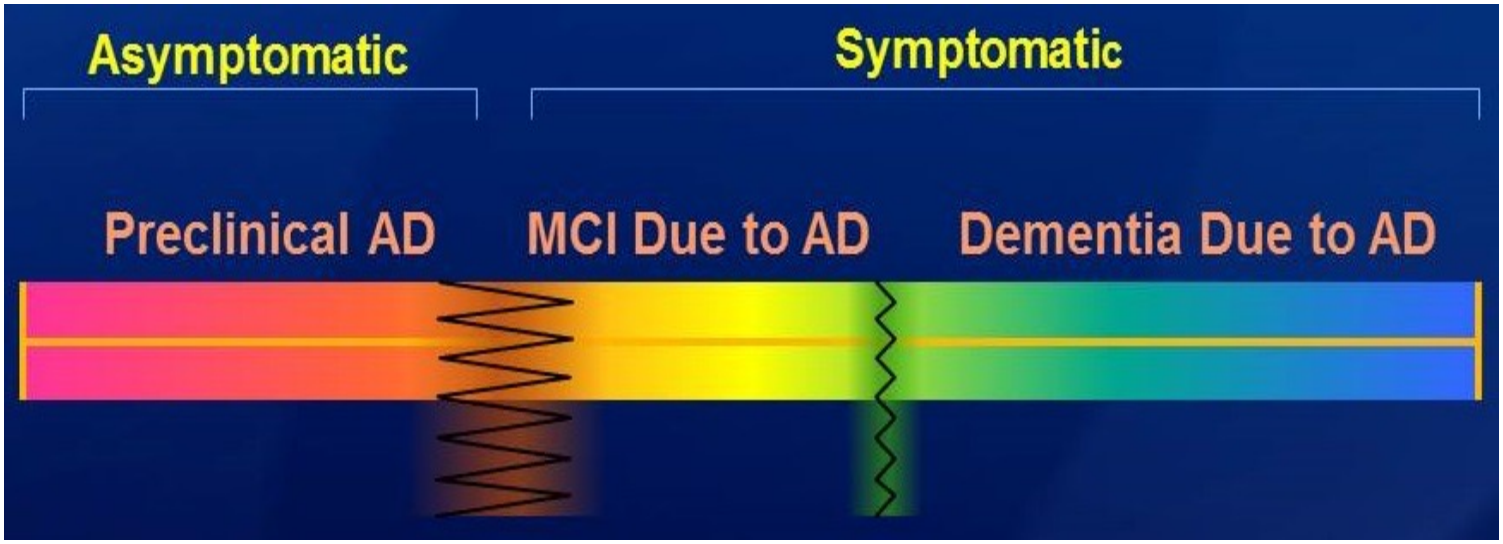
Review Article

Appropriate use criteria for lumbar puncture and cerebrospinal fluid testing in the diagnosis of Alzheimer's disease

Leslie M. Shaw[a], Jalayne Arias[b], Kaj Blennow[c], Douglas Galasko[d], Jose Luis Molinuevo[e], Stephen Salloway[f], Suzanne Schindler[g], Maria C. Carrillo[h], James A. Hendrix[h,*], April Ross[h], Judit Illes[i], Courtney Ramus[i], Sheila Fifer[j]



Subjective Cognitive Impairment



SCD *Plus*

- Subjective decline in memory rather than in other domains of cognition
- Onset of SCD within the last 5 years
- Age at onset of SCD ≥ 60 years
- Concerns (worries) associated with SCD
- Feeling of performing worse than others of the same age group
- Confirmation of cognitive decline by an informant
- Presence of the *APOEε4 genotype*
- Biomarker evidence for AD (defines preclinical AD)

Thanks