Preventie van Dementie: levensstijl of wonderpil

Prof Dr PP De Deyn

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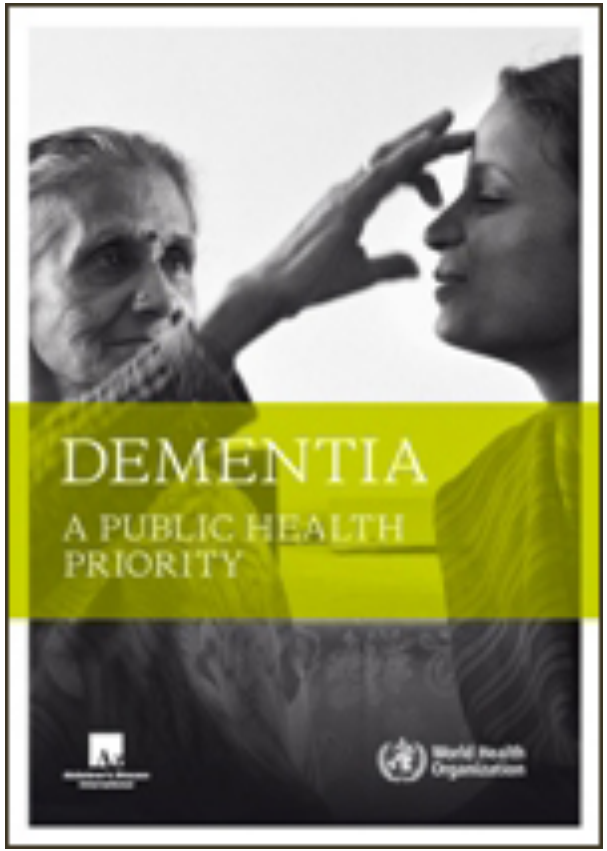
Dementie: a public health priority!

- Prevalentie stijgt
  - 270.000 → 670.000 (2050) in Nederland
  - 200.000 → 480.000 (2050) in België
  - 45 miljoen → 135 miljoen (2050) wereldwijd

- Voorlopig geen genezing mogelijk
- Dementie is één van de duurste ziekten
- Belasting mantelzorgers is hoog
  - grijze druk ↑

Preventie van dementie = belangrijk!

Global action against dementia
G8 Dementia Summit
11/12/13
#G8dementia



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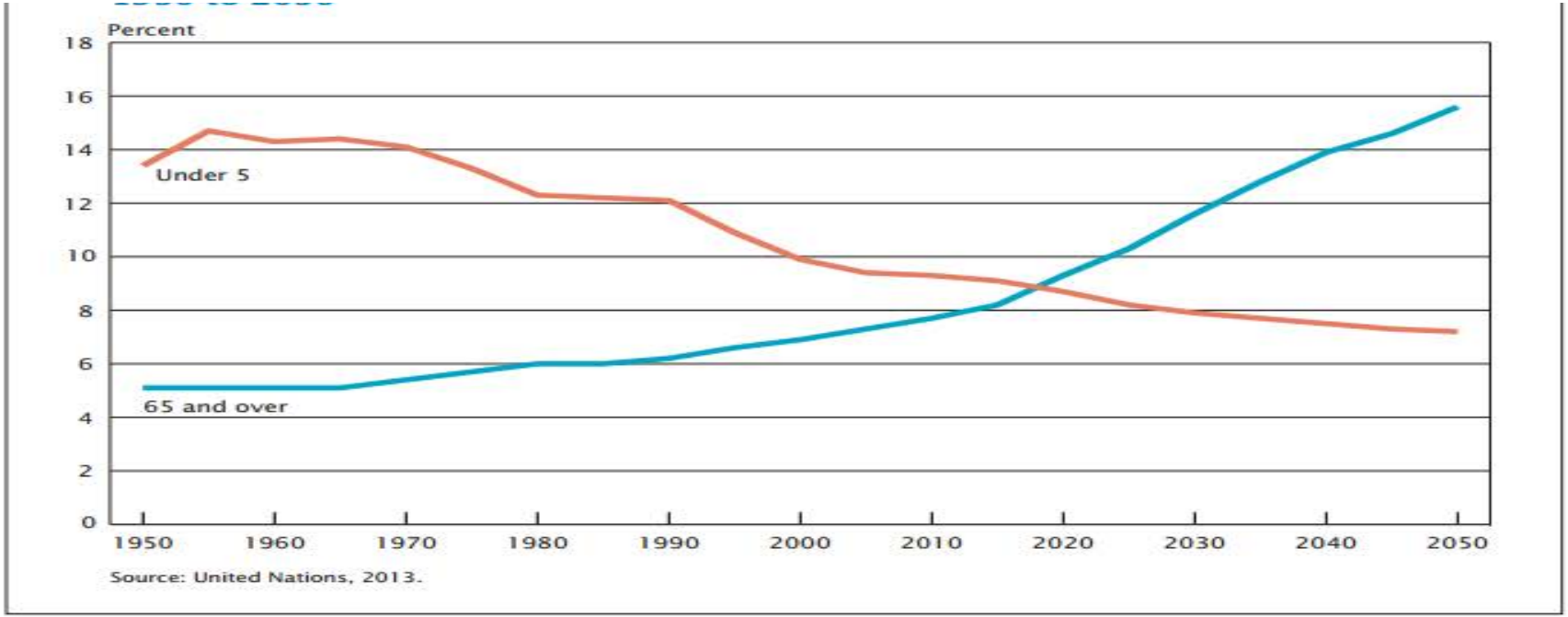
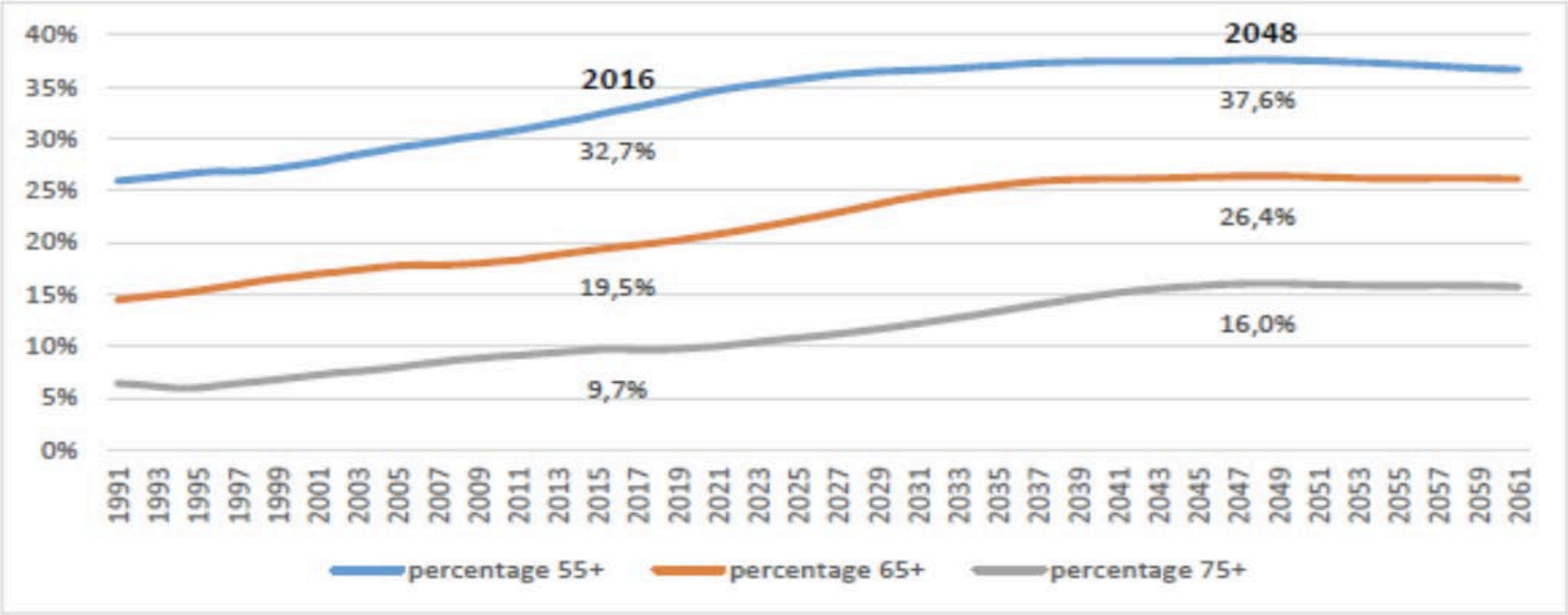
Oudere Bevolking Groeiend Wereldwijd



He et al. U.S. Census Bureau, International Population Reports, P95/16-1, *An Aging World: 2015*

Oudere Bevolking Groeiend in België



Bron: 1991-2016: waarnemingen FOD Economie – Algemene Directie Statistiek (ADS); 2017-2061: vooruitzichten, Federaal Planbureau …

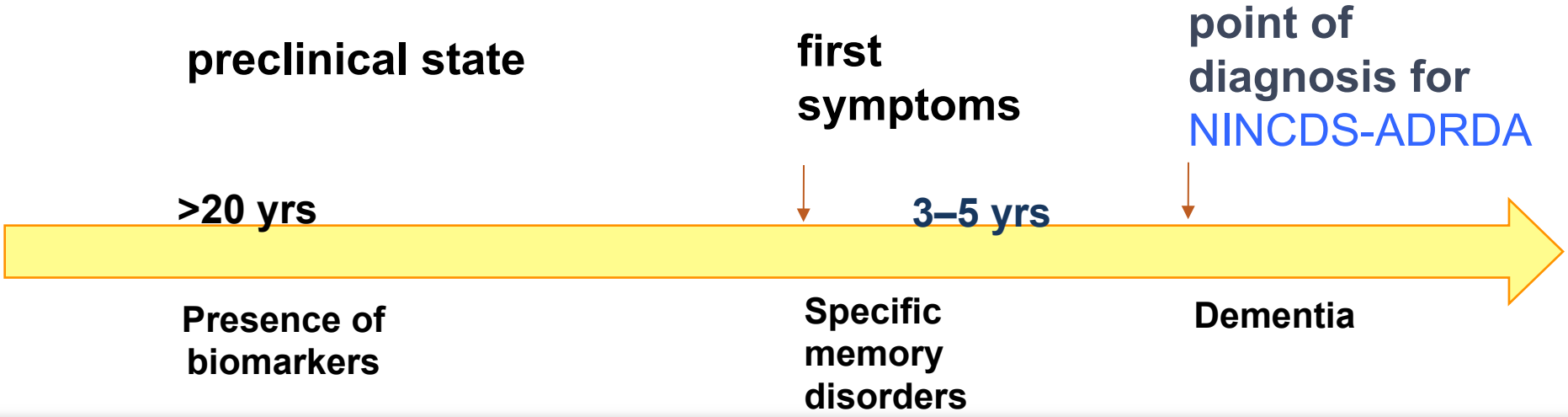
Vroegdetectie van Dementie: kan het ?

Mogelijke biomerkers voor vroegdiagnostiek van dementie

- **Beeldvorming :**
  - MRI: brain, ventricles, hippocampal volumes
  - fMRI: brain activation
  - MRS: NAA
  - PET: FDG, beta-amyloid deposition (C11-PIB), receptor studies
  - SPECT: rCBF, receptor studies
- **Hersenvocht merkers**
  - Beta-amyloid, tau, phoshpo-tau
  - Novel protein markers for neurodegeneration/AD

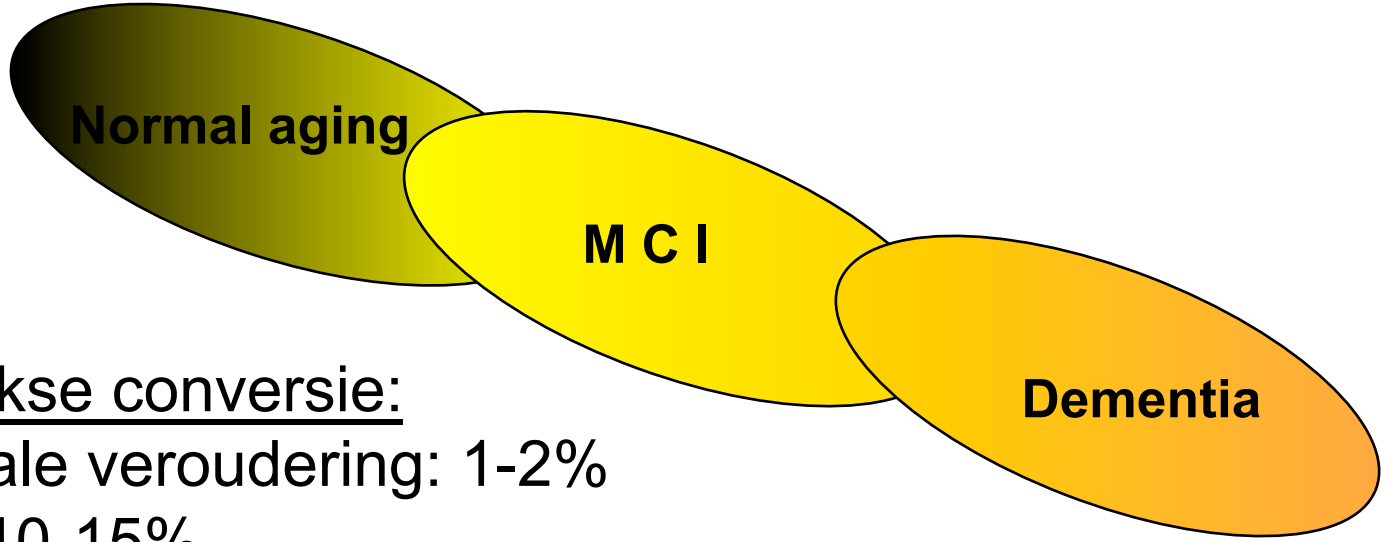
Genomics - proteomics – metabolomics etc ...

Is het mogelijk de ziekte van Alzheimer vroegtijdig te detecteren ?



AD

MCI Concept
Milde Cognitieve Stoornis



<u>Jaarlijkse conversie:</u>
Normale veroudering: 1-2%
MCI: 10-15%

Diagnostische prestatie van hersenvocht biomarkers?

ELSEVIER

Neurobiology of Aging 29 (2008) 1143–1159

NEUROBIOLOGY OF AGING

www.elsevier.com/locate/neuaging

Diagnostic performance of a CSF-biomarker panel in autopsy-confirmed dementia

Sebastiaan Engelborghs [a,b], Karen De Vreese [e], Tom Van de Casteele [e], Hugo Vanderstichele [e], Bart Van Everbroeck [c], Patrick Cras [c,d], Jean-Jacques Martin [c], Eugeen Vanmechelen [e], Peter Paul De Deyn [a,b,c,*]

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Available online 10 April 2007

CSF biomarkers for early dementia diagnosis bij mensen met klachten over geheugen

Association between CSF biomarkers and incipient Alzheimer's disease in patients with mild cognitive impairment: a follow-up study

Oskar Hansson, Henrik Zetterberg, Peder Buchhave, Elisabet Londos, Kaj Blennow, Lennart Minthon

Lancet Neurol 2006; 5: 228–34
Published Online February 6, 2006
DOI:10.1016/S1474-4422(06)70355-6
See Reflection and Reaction page 198

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Correspondence to: Prof Kaj Blennow, Institute of Clinical Neuroscience, Department of Experimental Neuroscience, Sahlgrenska University Hospital, Mölndal S-431 80 Göteborg, Sweden kaj.blennow@neuro.gu.se

Summary

Background Disease-modifying treatment strategies for Alzheimer's disease have led to an urgent need for biomarkers to identify the disease at a very early stage. Here, we assess the association between CSF biomarkers and incipient Alzheimer's in patients with mild cognitive impairment (MCI).

Methods From a series of 180 consecutive patients with MCI, we assessed 137 who underwent successful lumbar puncture at baseline. Patients at risk of developing dementia were followed clinically for 4–6 years. Additionally, 39 healthy individuals, cognitively stable over 3 years, served as controls. We analysed CSF concentrations of β amyloid$_{1-42}$ (Aβ42), total tau (T-tau), and phosphorylated tau (P-tau$_{181}$) using Luminex xMAP technology.

Findings During follow-up, 57 (42%) patients with MCI developed Alzheimer's disease, 21 (15%) developed other forms of dementia, and 56 (41%) remained cognitively stable for 5·2 years (range 4·0–6·8). A combination of CSF T-tau and Aβ42 at baseline yielded a sensitivity of 95% and a specificity of 83% for detection of incipient AD in patients with MCI. The relative risk of progression to Alzheimer's disease was substantially increased in patients with MCI who had pathological concentrations of T-tau and Aβ42 at baseline (hazard ratio 17·7, p<0·0001). The association between pathological CSF and progression to Alzheimer's disease was much stronger than, and independent of, established risk factors including age, sex, education, *APOE* genotype, and plasma homocysteine. The combination of T-tau and Aβ42/P-tau$_{181}$ ratio yielded closely similar results (sensitivity 95%, specificity 87%, hazard ratio 19·8).

Interpretation Concentrations of T-tau, P-tau$_{181}$, and Aβ42 in CSF are strongly associated with future development of Alzheimer's disease in patients with MCI.

Introduction

The prevalence of dementia doubles every 5 years from the age of 65 so that around 40% in the age-group 90–95 years are affected. With increasing life expectancy across the world, dementia is a rapidly growing socioeconomic and medical problem.[1] Alzheimer's disease is the most common cause of dementia. The pathogenic process of Alzheimer's disease probably starts decades before the clinical onset of the disease.[2] During this preclinical period there is a gradual loss of axons and neurons, and at a certain threshold the first symptoms, most often impaired episodic memory, appear. At this stage patients do not fulfil the criteria for dementia and may be diagnosed with mild cognitive impairment (MCI). However, MCI is a very common syndrome in elderly people and has a multitude of causes. Even though around 40–60% of patients with the syndrome develop Alzheimer's disease during the first 5 years, many have a stable form of memory impairment.[3,4] Moreover, early stages of vascular dementia or dementia with Lewy bodies, for example, can be preceded by MCI.[4] Depression can also mimic the syndrome.

So far, there is no established method to predict progression to Alzheimer's disease in individuals with MCI. New tools to aid in the diagnostic work-up of individuals with MCI would be of fundamental public-health importance. Such methods would be of even greater significance if new drug candidates, such as β-sheet breakers, β-secretase inhibitors, and amyloid β$_{1-42}$ (Aβ42) immunotherapy, prove to have disease-arresting effects. These types of drugs are likely to have the best efficacy in the early or even preclinical phase of the disease when the synaptic and neuronal loss has not become too widespread.[5,6] In fact, lack of tools to detect preclinical Alzheimer's disease has been suggested to be one of the main obstacles for the development of new treatments.[7]

Early studies indicated that CSF biomarkers could be useful for defining a subgroup of patients with MCI at especially high risk of developing Alzheimer's disease.[5,8,9] However, the clinical follow-up in these studies has been short, generally only about 1–2 years.[5,8,9] In view of the fact that each year MCI progresses to Alzheimer's disease in 8–15% of patients, a very extensive follow-up period (>4–5 years) would be needed to ascertain whether a patient with stable MCI really does not have incipient Alzheimer's disease.[5] Moreover, when assessing the accuracy of a diagnostic test, the study should preferably include a consecutive series of patients from a relevant clinical population.[10–12] However, the participants with MCI included in CSF studies have generally been highly

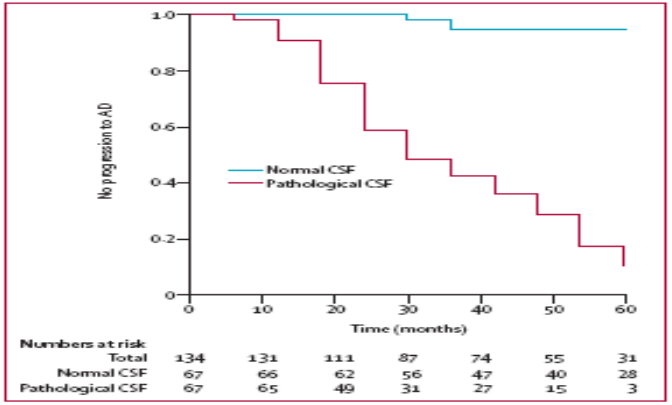

Figure 2: Kaplan–Meier estimates of the rate of progression to Alzheimer's disease in patients with MCI who have either normal CSF or pathological CSF at baseline

Numbers at risk are the number of patients with MCI at each time point who had not developed any type of dementia and for whom clinical follow-up was still ongoing. Cut-off values for pathological CSF were >350 ng/L for T-tau and <530 ng/L for Aβ42. The incidence of Alzheimer's disease in patients with MCI who had pathological CSF (n=67) was 27% per year compared with 1% per year in patients with normal CSF (n=67).

A combination of CSF T-tau and Aβ$_{1-42}$ at baseline yielded a sensitivity of 95% and a specificity of 83% for detection of incipient AD in patients with MCI.

The relative risk of progression to Alzheimer's disease was substantially increased in patients with MCI who had pathological concentrations of T-tau and Aβ$_{1-42}$ at baseline

CSF biomarkers for early dementia diagnosis

ORIGINAL CONTRIBUTION

Diagnosis-Independent Alzheimer Disease Biomarker Signature in Cognitively Normal Elderly People

Geert De Meyer, PhD; Fred Shapiro, MLS; Hugo Vanderstichele, PhD; Eugeen Vanmechelen, PhD; Sebastiaan Engelborghs, MD, PhD; Peter Paul De Deyn, MD, PhD; Els Coart, PhD; Oskar Hansson, MD; Lennart Minthon, MD; Henrik Zetterberg, MD, PhD; Kaj Blennow, MD, PhD; Leslie Shaw, PhD; John Q. Trojanowski, MD, PhD; for the Alzheimer's Disease Neuroimaging Initiative

Objective: To identify biomarker patterns typical for Alzheimer disease (AD) in an independent, unsupervised way, without using information on the clinical diagnosis.

Design: Mixture modeling approach.

Setting: Alzheimer's Disease Neuroimaging Initiative database.

Patients or Other Participants: Cognitively normal persons, patients with AD, and individuals with mild cognitive impairment.

Main Outcome Measures: Cerebrospinal fluid–derived β-amyloid protein 1-42, total tau protein, and phosphorylated tau_{181P} protein concentrations were used as biomarkers on a clinically well-characterized data set. The outcome of the qualification analysis was validated on 2 additional data sets, 1 of which was autopsy confirmed.

Results: Using the US Alzheimer's Disease Neuroimaging Initiative data set, a cerebrospinal fluid β-amyloid protein 1-42/phosphorylated tau_{181P} biomarker mixture model identified 1 feature linked to AD, while the other matched the "healthy" status. The AD signature was found in 90%, 72%, and 36% of patients in the AD, mild cognitive impairment, and cognitively normal groups, respectively. The cognitively normal group with the AD signature was enriched in apolipoprotein E ε4 allele carriers. Results were validated on 2 other data sets. In 1 study consisting of 68 autopsy-confirmed AD cases, 64 of 68 patients (94% sensitivity) were correctly classified with the AD feature. In another data set with patients (n=57) with mild cognitive impairment followed up for 5 years, the model showed a sensitivity of 100% in patients progressing to AD.

Conclusions: The mixture modeling approach, totally independent of clinical AD diagnosis, correctly classified patients with AD. The unexpected presence of the AD signature in more than one-third of cognitively normal subjects suggests that AD pathology is active and detectable earlier than has heretofore been envisioned.

Arch Neurol. 2010;67(8):949-956

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CSV biomerkers voor vroegdiagnose ?

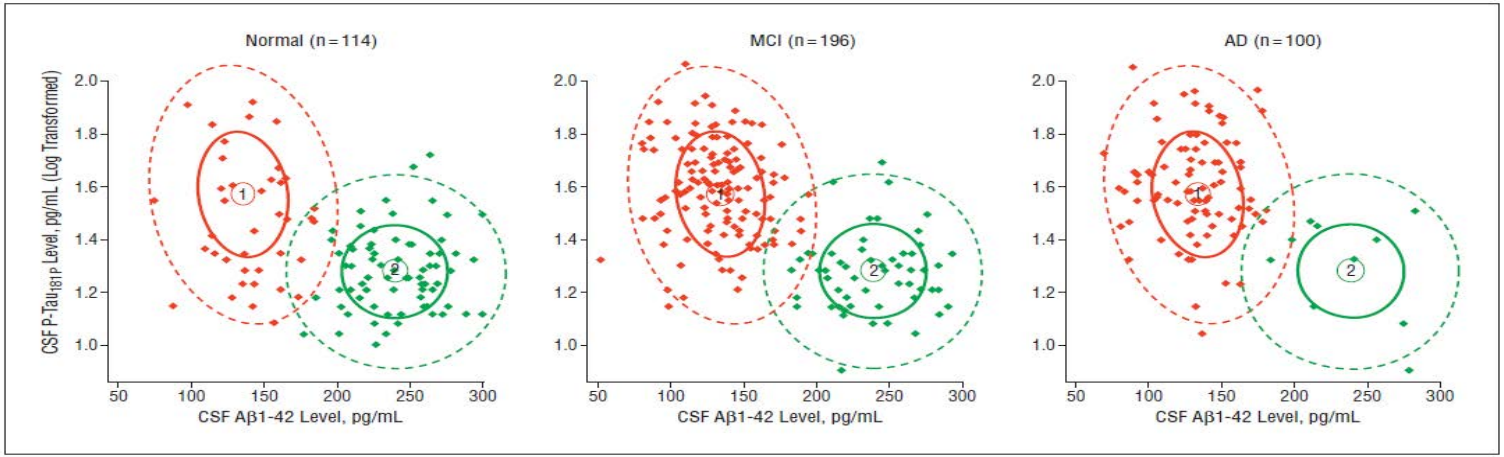

Figure 4. A combined cerebrospinal fluid–derived β-amyloid protein 1-42 (CSF Aβ1-42)/CSF phosphorylated tau_{181P} (CSF P-Tau_{181P}) mixture model applied to the subject groups. Densities of each signature are represented with confidence ellipses, and signature membership of the subject based on the mixture is indicated with the corresponding color (signature 1 is the Alzheimer disease [AD] signature [red]; signature 2 is the healthy signature [green]). MCI indicates mild cognitive impairment.

Pathological biomarker profile ($A\beta_{1\text{-}42}$ & P-tau_{181P}):

- AD: 90%
- MCI: 72%
- **Controls: 36%**

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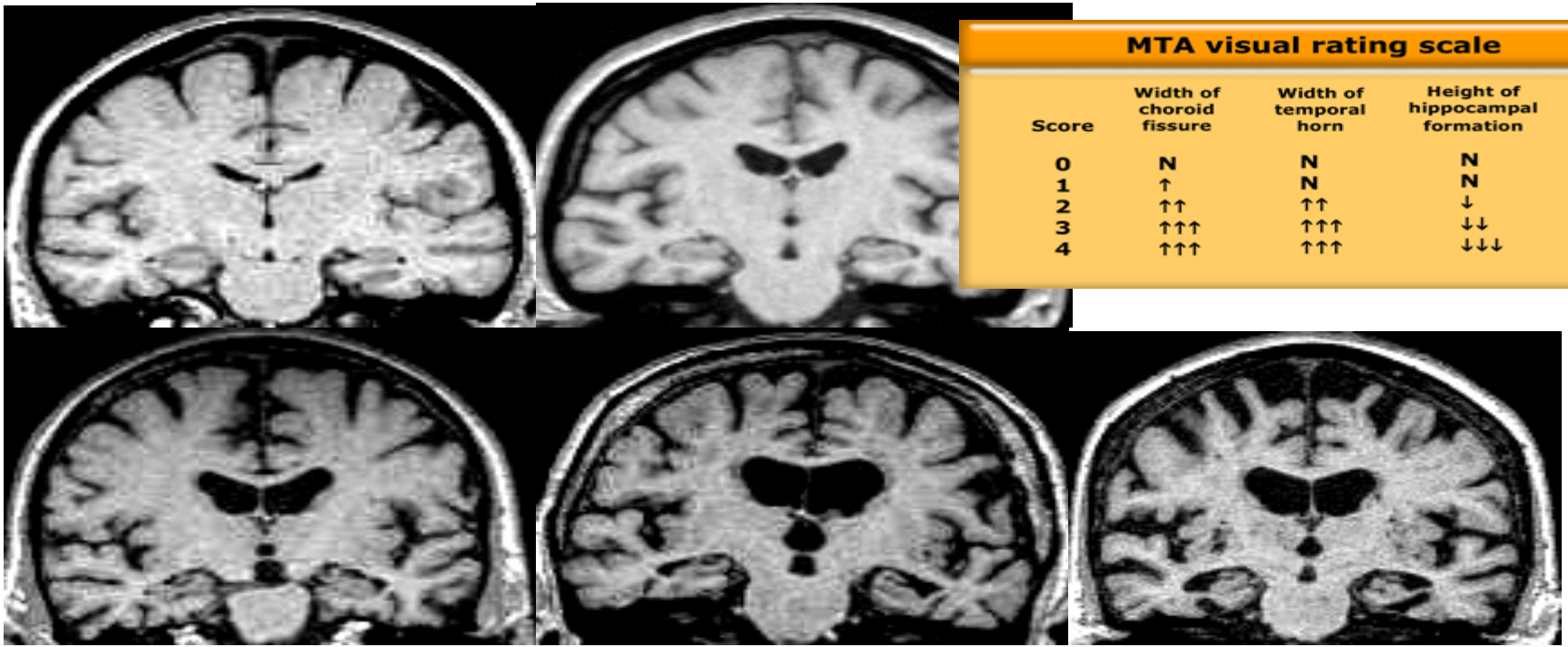
Slaapkwabatrofie



MTA visual rating scale

Score	Width of choroid fissure	Width of temporal horn	Height of hippocampal formation
0	N	N	N
1	↑	N	N
2	↑↑	↑↑	↓
3	↑↑↑	↑↑↑	↓↓
4	↑↑↑	↑↑↑	↓↓↓

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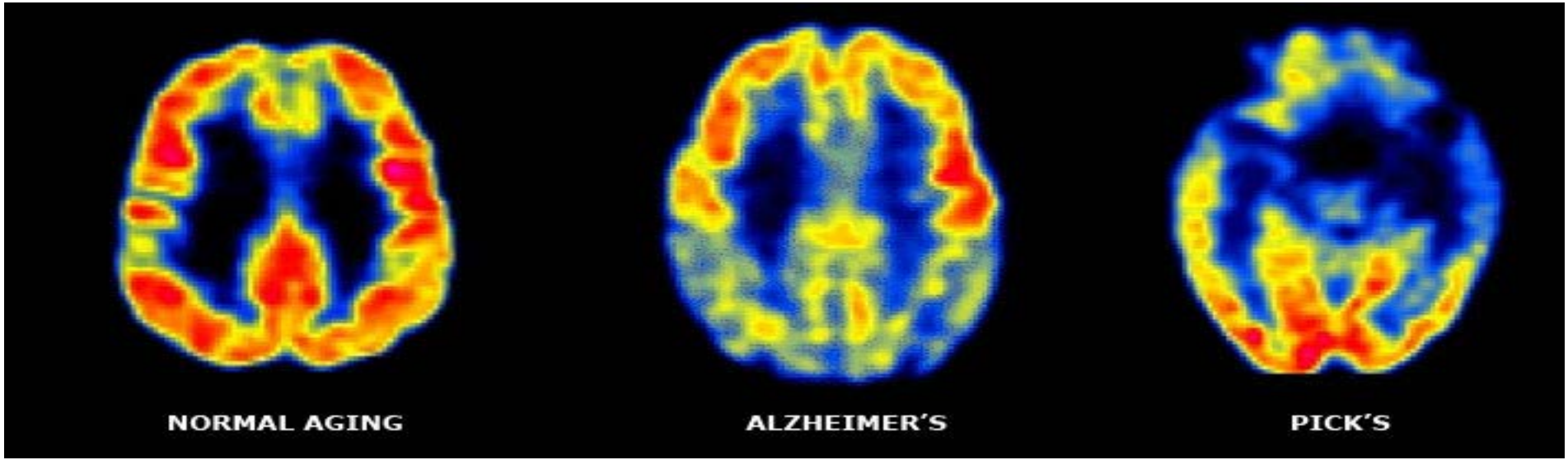
FDG-Glucose metabolism



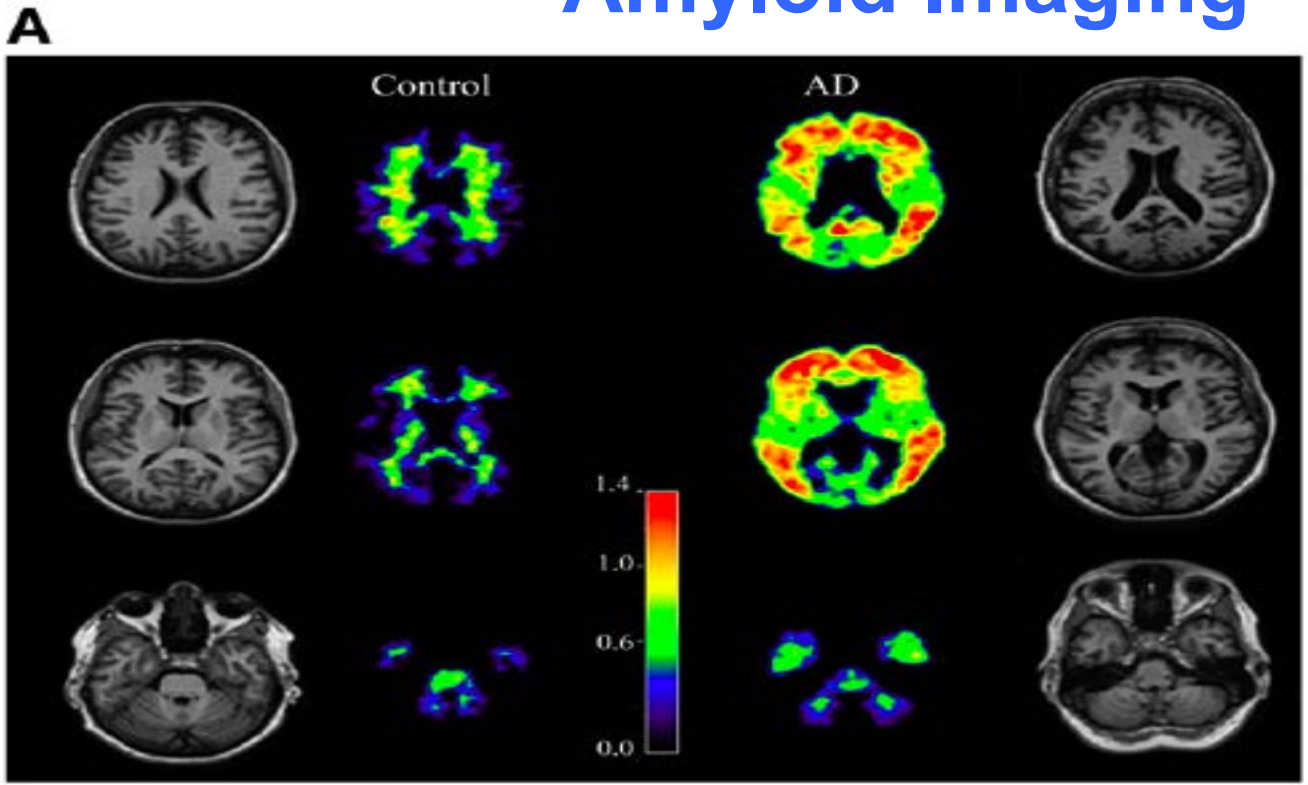
Journal of Nuclear Medicine, published on January 21, 2009 as doi:10.2967/jnumed.108.056499

Detection of Alzheimer Pathology In Vivo Using Both ^{11}C-PIB and ^{18}F-FDDNP PET

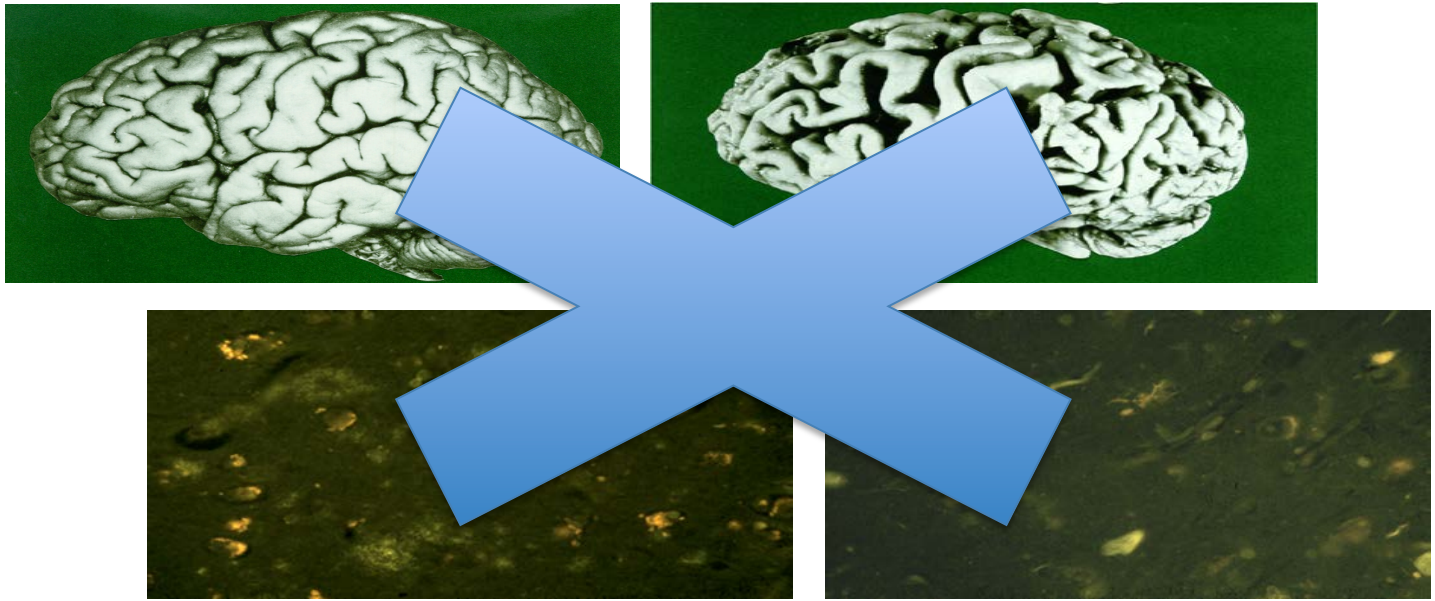
Nelleke Tolboom[1,2], Maqsood Yaqub[1], Wiesje M. van der Flier[2], Ronald Boellaard[1], Gert Luurtsema[1], Albert D. Windhorst[1], Frederik Barkhof[3], Philip Scheltens[2], Adriaan A. Lammertsma[1], and Bart N.M. van Berckel[1]

[1]Department of Nuclear Medicine and PET Research, VU Un
Neurology and Alzheimer Centre, VU University Medical Ce
University Medical Centre, Amsterdam, The Netherlands

In-vivo PET Amyloid Imaging



Gouden Standaard ??



Preventie
van
Dementie
?

Leefstijl en preventie ?

Risicofactoren voor dementie

- ApoE ε4 allele (7%)

- Educatie/opleiding (8%)
- Hoorverlies (9%)
- Hoge bloeddruk (2%)
- Obesitas (1%)
- Roken (5%)
- Depressie (4%)
- Eenzaamheid (2%)
- Diabetes (1%)
- Fysieke inactiviteit (3%)

Potentieel modificeerbare risicofactoren (PAR 35%)

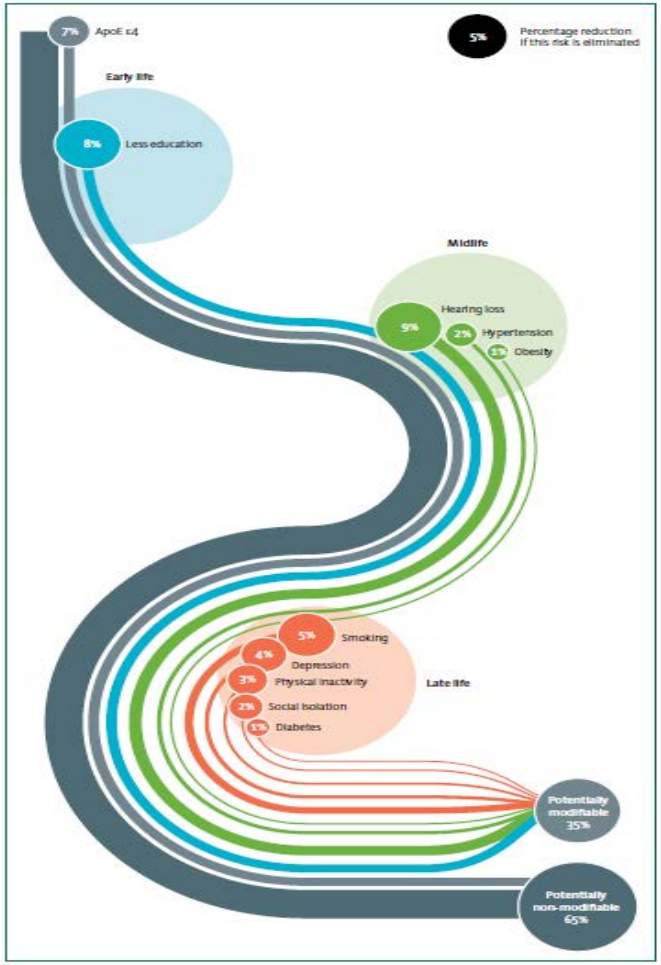


Figure 4: Life-course model of contribution of modifiable risk factors to dementia
Numbers are rounded to nearest integer. Figure shows potentially modifiable or non-modifiable risk factors.

PAR = Populatie Attributieve Risico's

Livingston G et al Lancet 2017

Strategieën

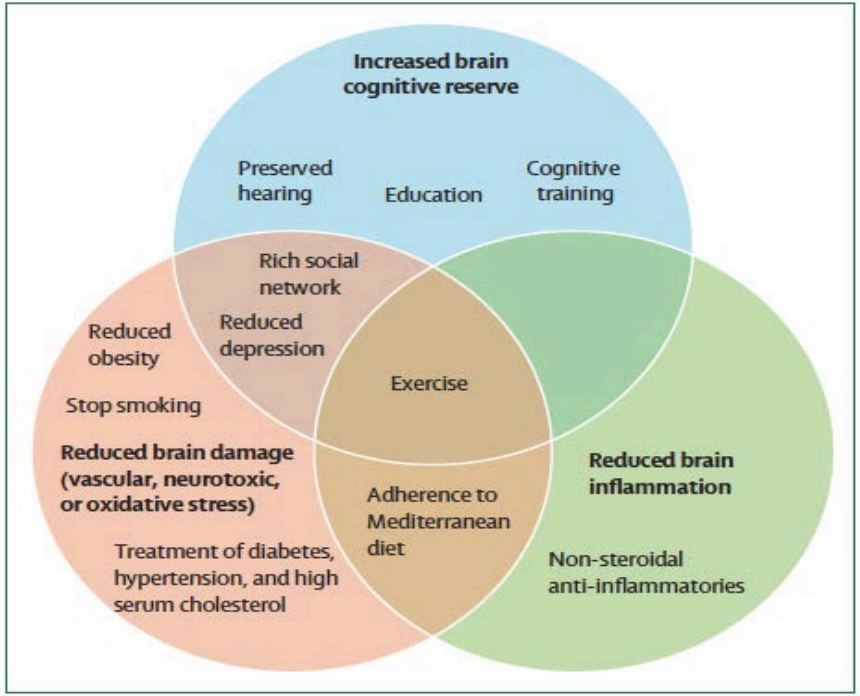


Figure 5: Potential brain mechanisms for preventive strategies in dementia

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Vrijsen *et al. BMC Public Health* (2021) 21:1344
https://doi.org/10.1186/s12889-021-11415-2

BMC Public Health

RESEARCH ARTICLE Open Access

Knowledge, health beliefs and attitudes towards dementia and dementia risk reduction among descendants of people with dementia: a qualitative study using focus group discussions

J. Vrijsen[1*], E. L. M. Maeckelberghe[2], R. Broekstra[1,3], J. J. de Vries[4], A. Abu-Hanna[5], P. P. De Deyn[4], R. C. Oude Voshaar[6], F. E. Reesink[4], E. Buskens[1], S. E. de Rooij[7] and N. Smidt[1]

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Ze wisten het !!

Table 2 Identified risk factors for dementia by the focus group participants

Non-modifiable risk factors	Modifiable risk factors	Modifiable risk factors (suspicions)
Age	Poor diet (e.g., salt)	Sleeping behaviour
Genetics	Physical inactivity	Stress
Family history	Smoking	Traumatic experiences
	Alcohol use	Mental wellbeing
	Cognitive activities	
	High cholesterol	
	Hypertension	
	Diabetes	
	Cardiovascular diseases	

The risk factors loneliness, obesity and renal dysfunction were not mentioned by the group.

Oproep van 67 zorgprofessionals

- investeer in preventie van dementie -

Aanbevelingen:

- Informeren van het grote publiek, risicogroepen en medische professionals van het potentieel van dementie preventie (d.m.v. publiekscampagnes)
- Ondersteuning bij aanpassen van leefstijl d.m.v. e-health en gecombineerde leefstijl interventies voor mensen *at risk*
- Samenleving inrichten zodat voor iedereen een gezonde keuze gemakkelijker wordt (bijv suikertaks)

≡ Menu nrc.nl› abonneer

O opinie

Martijn van Winkelhof, Gerjoke Wilmink, Philip Scheltens, Marcel Olde Rikkert, Erik Scherder, Karine van 't Land, Edo Richard, Bertine Lahuis, Geert Jan Biessels & Ruben Wenselaar

21 oktober 2019

Leestijd 5 minuten

Opslaan in leeslijst

Laten we de duurste ziekte aanpakken - dementie

Dementie is niet alleen een nare aandoening, maar ook een dure. Genoeg redenen om te investeren in preventie, schrijven *67 zorgprofessionals*. 'Minister, maak er werk van.'

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Maar, is er iets wat we kunnen doen..???

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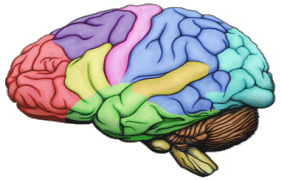
Yes…The ‘Big Five’ for Optimal Brain Function



1. **Physical activity**
2. **Nutrition**
3. **Mental stimulation**
4. **Socialization**
5. **Creativity and attitude – stress reduction**

Maar is dat allemaal zo evidence based ?

Body & Mind…

For starters….*'What is good for your heart is ALSO good for your brain'* – the Heart – Brain axis

Share common risk factors...cholesterol, high blood pressure, obesity, arterial damage, plaque build up…SO…
…..when you watch your cholesterol, maintain a healthy weight, and exercise for your heart, your brain benefits too.

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Here's why we need to move:

- The brain has over one billion neurons
- Heart beats roughly 120, 000 times
- 25% of the blood flow goes to the brain
- What is good for our hearts is also good for our brains

- Hersendood !! Denk even na !!

…stay healthy…

1: Physical Activity:

Daily, at least two and a half hours per week:

- ***Daily tasks*** (use the stairs, gardening, vigorous cleaning)
- ***Swimming*** (works joints/muscles without drag of gravity)
- ***Dancing or aerobics*** (exercises brain as well, fun)
- ***Biking/stationary bike*** (but protect your brain with a helmet!!)
- ***Tai-chi, yoga, Qui gon*** (strength, balance, concentration, de-stress)
- ***Walking, walking, walking***……..

2:Nutrition:

Basics: your brain needs good fuel!
***Avoid*:** saturated fats, processed meats, simple carbohydrates, salt;
Pile on: fruits, veggies, complex carbohydrates, grains & nuts, Oily fish & Omega-3 fatty acids

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Physical Activity

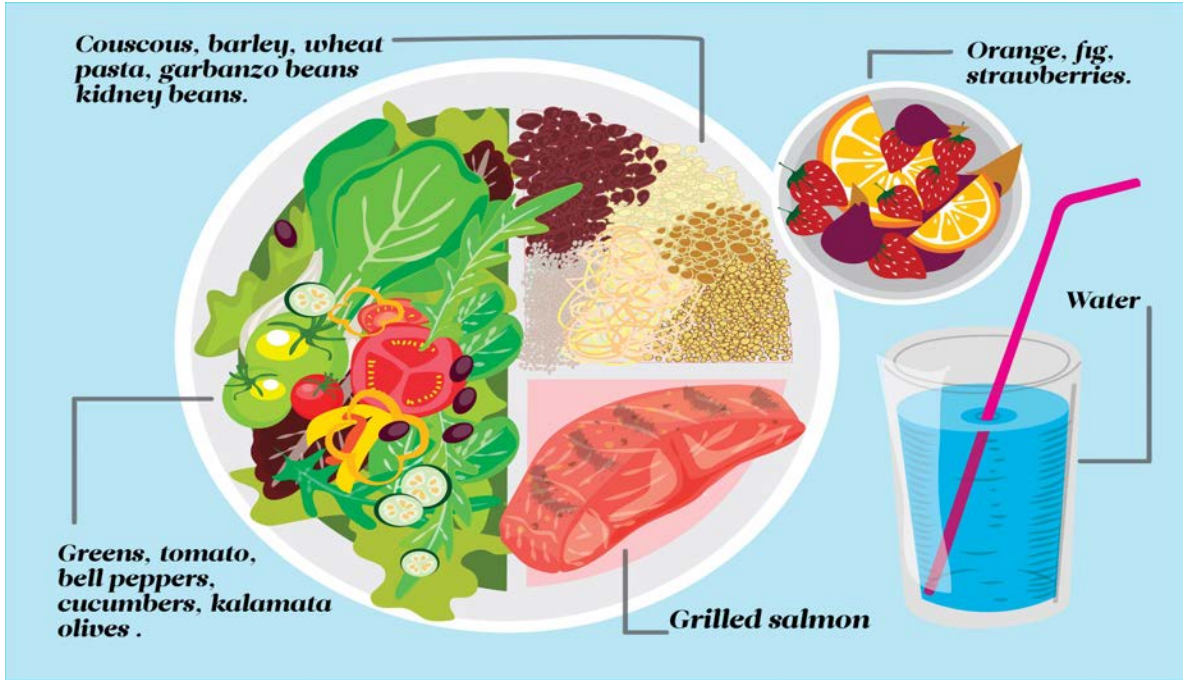
How can we increase our heart rate?

- Walking
- Running
- Dancing
- Gardening
- Yoga
- Biking
- Housework
- Lifting weights
- Swimming

Mowing the lawn
Walking the dog
Zumba
Kayaking
Hiking
Rock Climbing
Elliptical
Marching in Place
Playing with your kids

Diet and Nutrition

Mediterranean Diet



Dash Diet

DASH diet (Dietary Approaches to Stop Hypertension)
is rijk aan fruit, groenten, volle granen en magere zuivelproducten

What to eat

- Nuts, seeds, legumes, beans, whole grains
- Lean meats and fish
- Fruits
- Vegetables
- Olive oil

What to avoid

- Saturated and trans fats
- Processed foods
- Foods that are high in sodium and sugar
- Deep fried foods
- Unhealthy fast foods

ONTBIJT

Volkorenbrood

Havermout

Vezelrijke ontbijtgranen

Muesli

Fruit

Thee of koffie

Melk – sojaproduct

Zachte margarine

LUNCH

Fruit

Groenten

Notenpasta

Eieren

Cottage cheese

Mozzarella

Vis, kip of kalkoenfilet

Verse soep

WARME MAALTIJD

Helft groenten, liefst seizoensgebonden

Kwart aardappelen of volkoren granen (pasta, couscous)

Kwart vlees, vis, ei, peulvruchten of vervangproducten

Water

Soep

TUSSENDOORTJE

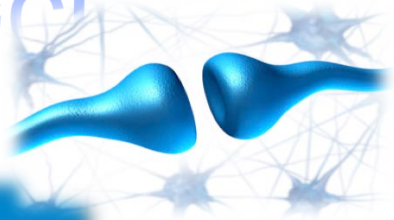
Groentjes

Handvol ongezouten noten

Fruit

Natuur yoghurt
- Zaden
- Agavesiroop
- Vers fruit
- Honing
- Noten
- …

..use your mind & connect..



3: Mental stimulation

'Exercise' your brain….

- Education is neuroprotective.
- Brain trainers.
- Puzzles, games, sensory stimulation, crosswords, reading, CST etc.
- **BUT** - ***Appropriate level -*** adapt to changing abilities!

`Use it or lose it!'

4: Socialisation

..remain socially connected.

- Humans are social creatures
- **Appropriate** socialization
- Work with known difficulties not against
- Trust in and inform others to help.

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Cognitive Stimulation

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Ways to stimulate your brain

- Learn a new language
- Read
- Learn a new skill
- Learn a new game
- Do word puzzles
- Drive a new way home (no GPS)
- Use your other hand to brush teeth/hair
- Embrace new and novel experiences

Social Engagement

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How to remain socially engaged

- Visit friends
- Visit family
- Join a book club
- Volunteer
- Start a game night
- Meet your neighbors
- Say Hi at the grocery store
- Try online dating
- Go to social meet ups

How to remain socially engaged
Ook ruimte voor persoonlijke invulling

How to remain socially engaged
Ook ruimte voor persoonlijke invulling

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…and manage stress and spirit..

5: Creativity, attitude & spirit:

Just as your brain dictates your feelings, your feelings affect your brain > stress hormones!!.

Manage and be aware of stress:

- Antidepressants (depression as risk factor)
- Aromatherapy,
- diet and exercise (e.g. tai chi, yoga etc.)
- Meditation (mindfulness – the here and now)

Be creative – be human!

- Music (singing for the brain)
- Art (art therapy)
- Dancing

Music can: Reduce anxiety, aid sleep, lower blood pressure, reduce stress hormones.

The creative brain: memory for music and emotion are in a different part of the brain from memory about 'things' and is often intact much longer in even sever dementia

This means these intact abilities can be tapped into in dementia

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Single Domain Lifestyle interventies toonden geen significante effecten – noch preventief noch symptomatisch

The Finger Study N= 1260

A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

Tiia Ngandu, Jenni Lehtisalo, Alina Solomon, Esko Levälahti, Satu Ahtiluoto, Riitta Antikainen, Lars Bäckman, Tuomo Hänninen, Antti Jula, Tiina Laatikainen, Jaana Lindström, Francesca Mangialasche, Teemu Paajanen, Satu Pajala, Markku Peltonen, Rainer Rauramaa, Anna Stigsdotter-Neely, Timo Strandberg, Jaakko Tuomilehto, Hilkka Soininen, Miia Kivipelto

Interpretation Findings from this large, long-term, randomised controlled trial suggest that a multidomain intervention could improve or maintain cognitive functioning in at-risk elderly people from the general population.

Geen significant effect op geheugen

Lancet 2015; 385: 2255–63

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PreDIVA study

Effectiveness of a 6-year multidomain vascular care intervention to prevent dementia (preDIVA): a cluster-randomised controlled trial

Eric P Moll van Charante, Edo Richard*, Lisa S Eurelings, Jan-Willem van Dalen, Suzanne A Ligthart, Emma F van Bussel, Marieke P Hoevenaar-Blom, Marinus Vermeulen, Willem A van Gool*

Summary

Background Cardiovascular risk factors are associated with an increased risk of dementia. We assessed whether a

Lancet 2016; 388: 797–805

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PreDIVA study N= 3526, 70–78 jr

Procedures

Interventiegroep:

- ✓ 18 visites, om de vier maanden – 6 jaar
- ✓ per visite: nagaan van cardiovasculair relevante papameters :
  - ✓ rookgewoonten, fysische activiteit, gewicht, bloeddruk
  - ✓ Bloedonderzoek: glucose en lipidenprofiel
- ✓ Op basis van de resultaten:
  - ✓ Individuele levensstijladviezen en zo nodig interventies gebaseerd op vigerende richtlijnen
  - ✓ Wanneer aangewezen: medicatie voor hoge bloeddruk; lipidenstoornissen en type 2 diabetes en antithrombotica.
  - ✓ Medicatie gebruik werd verbeterd zo nodig/

Controle groep:

- ✓ Gewone zorg en klassiek cardiovasculair risicomanagenment

PreDIVA study Resultaten

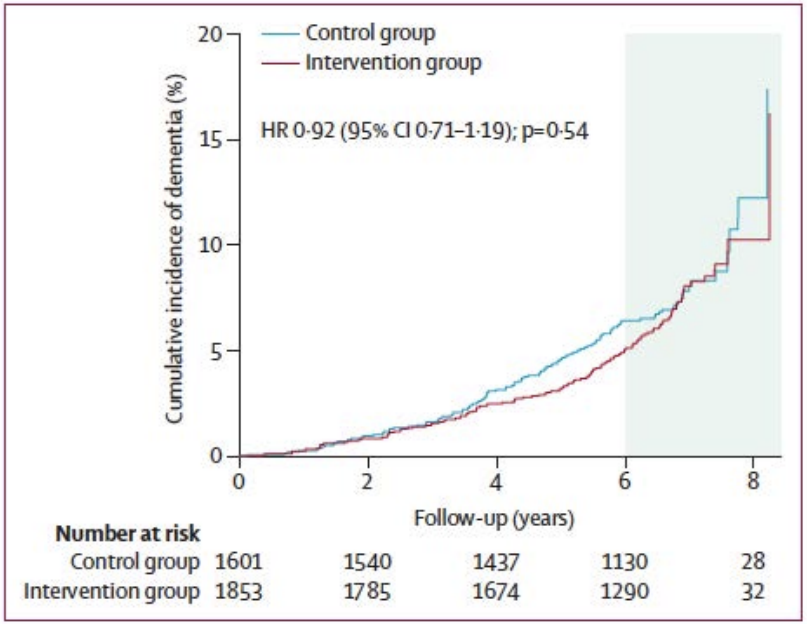

Figure 2: Kaplan-Meier plot of cumulative incidence of dementia

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MAPT study N= 1,680, ≥70 jr

MAPT STUDY: A MULTIDOMAIN APPROACH FOR PREVENTING ALZHEIMER'S DISEASE: DESIGN AND BASELINE DATA

B. Vellas[1,2,3], I. Carrie[1], S. Gillette-Guyonnet[1,2,3], J. Touchon[4], T. Dantoine[5], J.F.

a multidomain lifestyle intervention (cognitive training and advice on nutrition and physical activity), administered alone or in combination with n-3 polyunsaturated fatty acid supplementation

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MAPT study Resultaten

Interpretation

The multidomain intervention and polyunsaturated fatty acids, either alone or in combination, had no significant effects on cognitive decline over 3 years in elderly people with memory complaints. An effective multidomain intervention strategy to prevent or delay cognitive impairment and the target population remain to be determined, particularly in real-world settings.

Onze Nederlandse Vrienden

Project

Leefstijlonderzoek naar behoud van optimale cognitieve functie bij veroudering (MOCIA)

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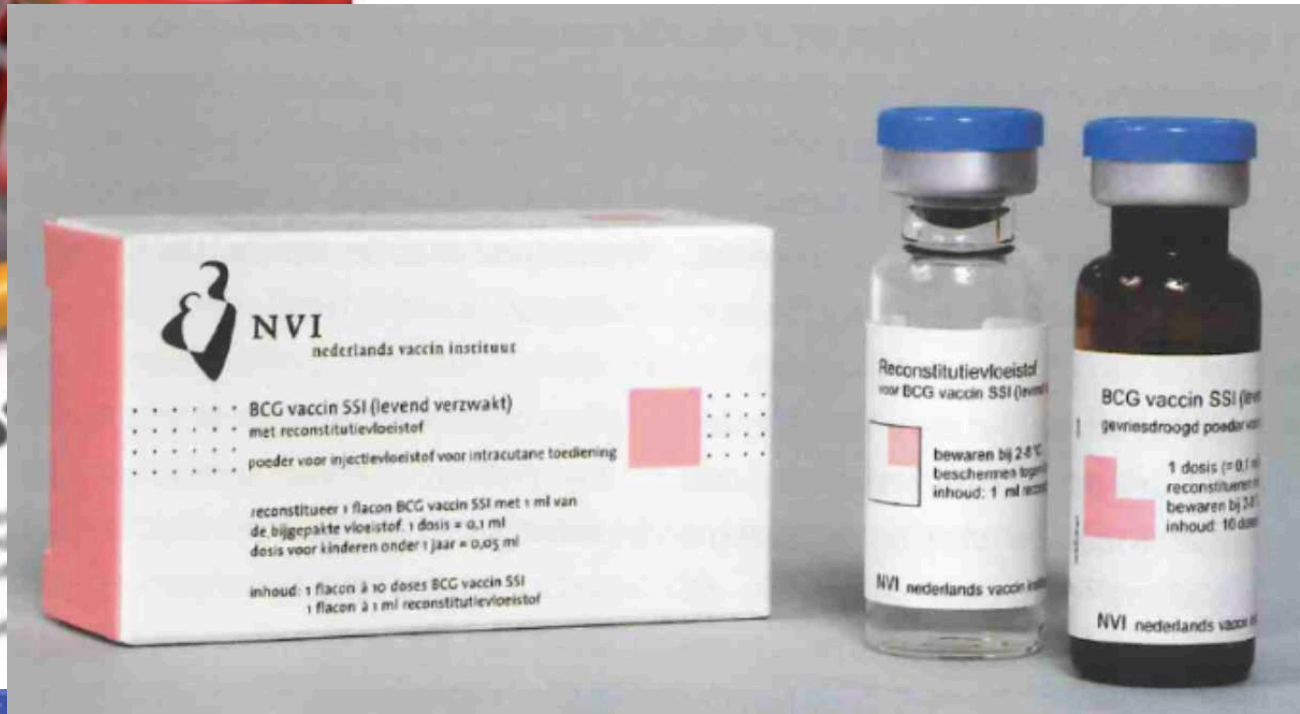
De TBC story : 1930

9 Openlucht-kuur in een lighal van het TBC-sanatorium Berg en Bosch te Bilthoven (R.K. Bouwblad, *1935*).

De TBC story : BCG Vaccin en tuberculostatica

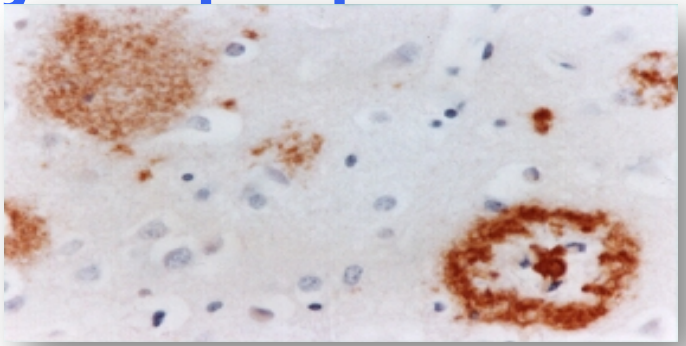


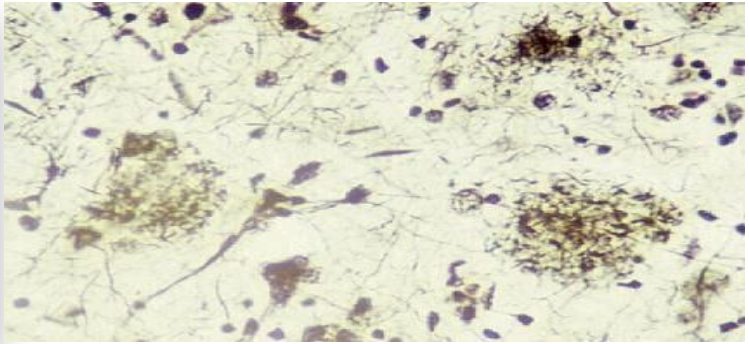
Naar een ziekteproces modificiërende aanpak

Wanneer een vaccin tegen Alzheimer ?

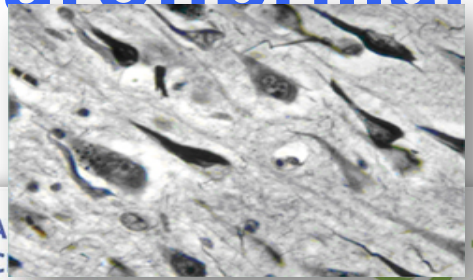
Neuropathologie dementie

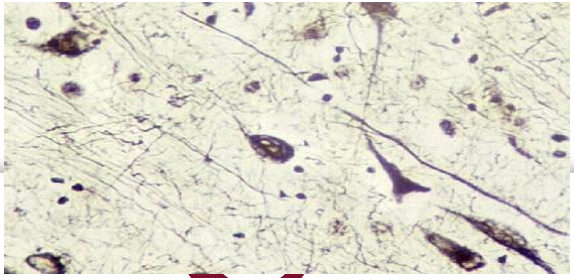
Amyloid plaques



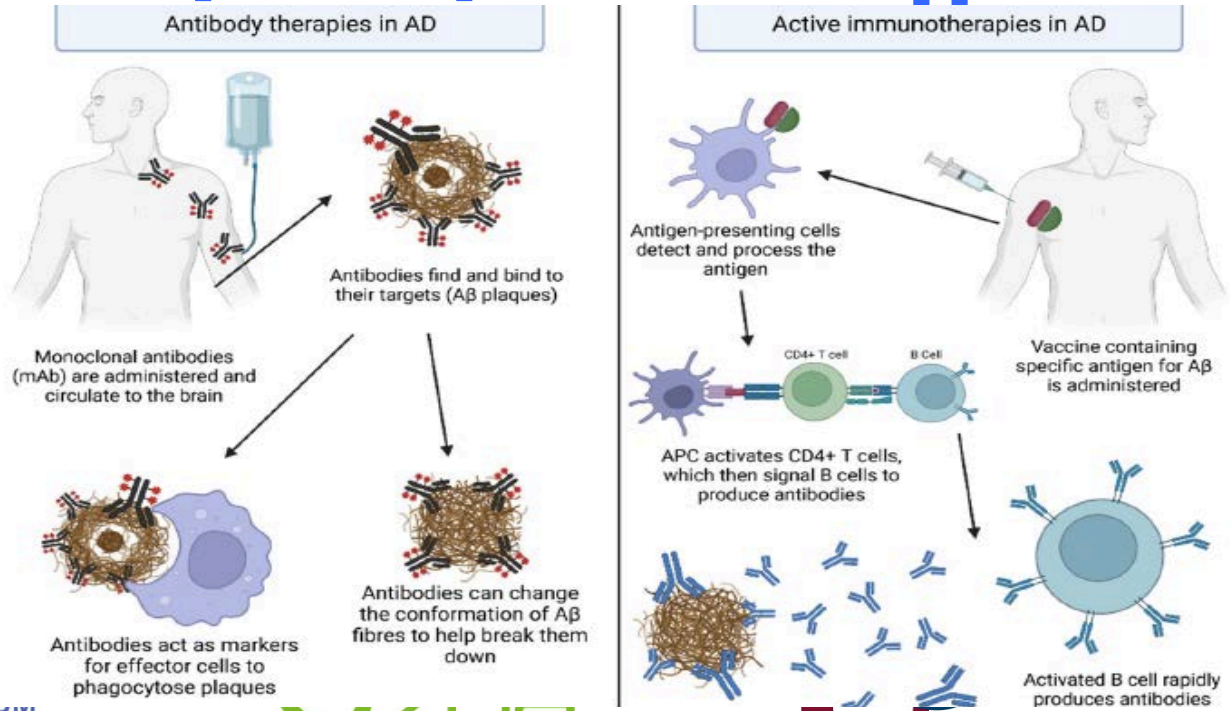


Neurofibrillaire kluwens





Vaccinatie versus



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Vaccination with AN-1792:
First demonstration of reversal of AD neuropathology ?

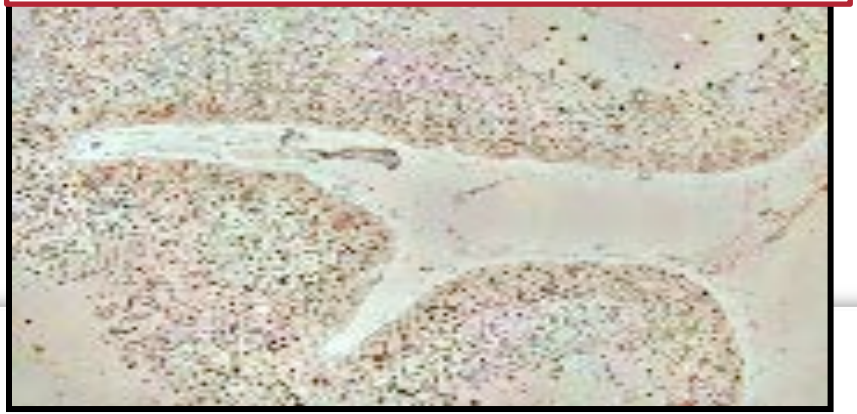
ARTICLES

Neuropathology of human Alzheimer disease after immunization with amyloid-β peptide: a case report

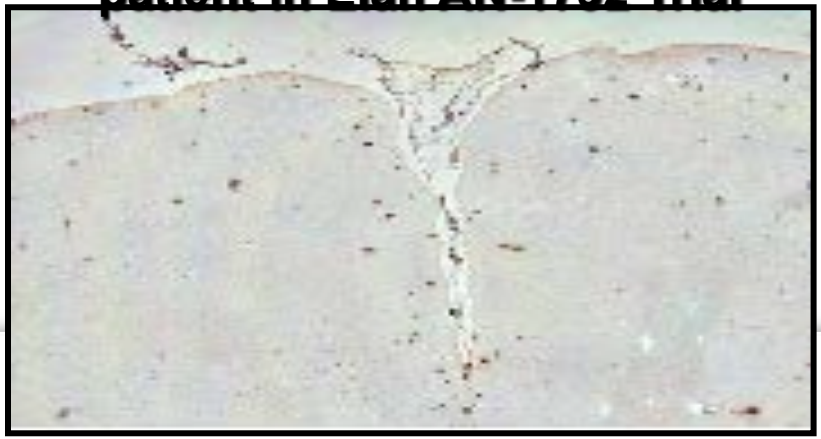
James A.R. Nicoll[1,2], David Wilkinson[1,3], Clive Holmes[1,3], Phil Steart[2], Hannah Markham[1,2] & Roy O. Weller[1,2]

NATURE MEDICINE • VOLUME 9 • NUMBER 4 • APRIL 2003

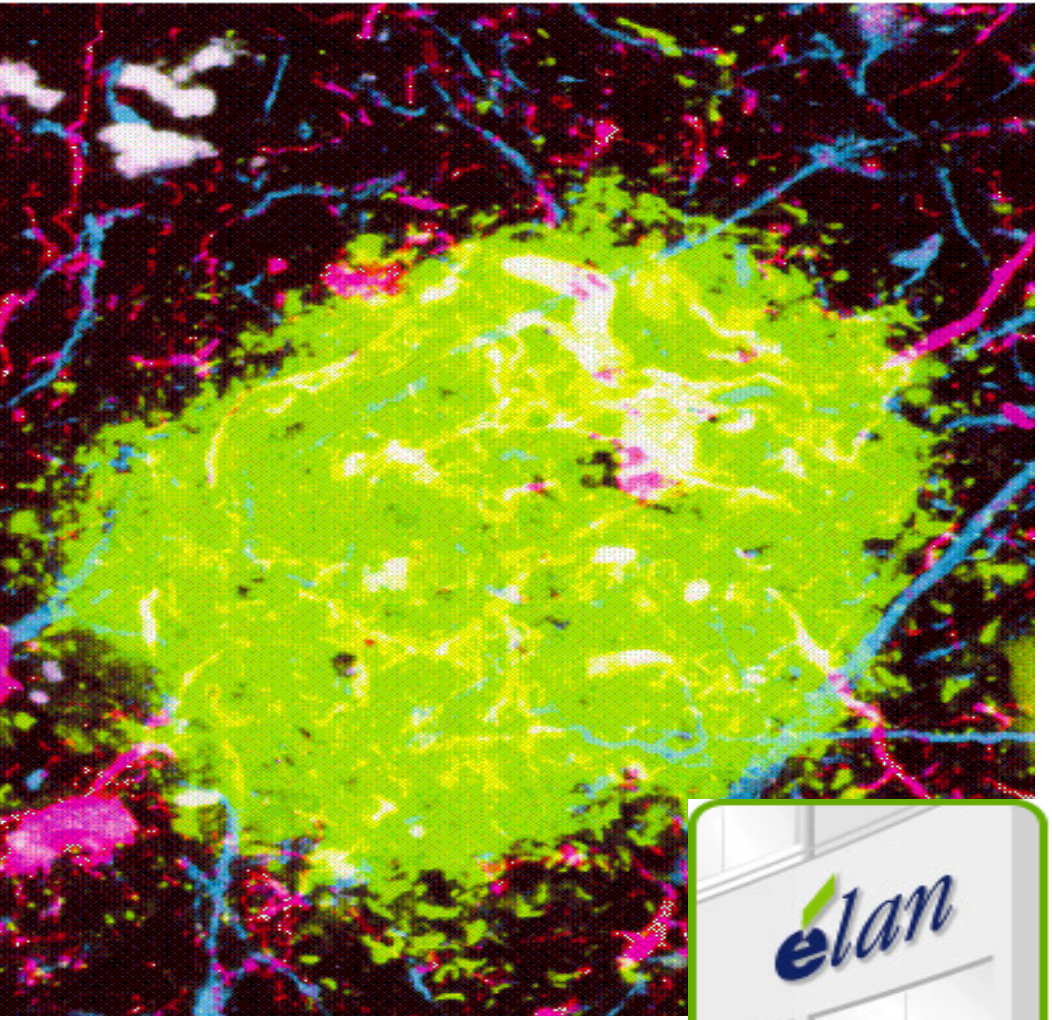
Parietal neocortex, non-immunized patient at comparable stage of AD



Parietal neocortex, immunized AD patient in Elan AN-1792 Trial



Nicoll et al. *Nat Med*. 2003;9:448-452.



Vaccination against Alzheimer's

Injecting people with small amounts of β-amyloid protein to raise an immunity to it.

But 6% of test patients got seriously ill.

tinued)

Drug	Mechanism	Sponsor	Study population	Admin	Phase	Results	Clinical Trial Identifier	Start date	Estin
Aducanumab (BIIB037)	Monoclonal anti-body	Biogen	Early AD	IV	III	Terminated	NCT02484547	2015 Sept	2019
			Early AD		III	Terminated	NCT02477800	2015 Aug	2019
			Early AD		III	Active, not recruit-ing	NCT04241068	2020 Mar	2023
Crenezumab (RG7412)	Monoclonal anti-body	Roche/AC Immune SA	Prodromal to mild AD	IV	III	Terminated	NCT02670083	2016 Mar	2019
			Prodromal to mild AD		III	Terminated	NCT03114657	2017 Mar	2019
			Prodromal to mild AD		III	Terminated	NCT03491150	2018 Apr	2019
Lecanemab (BAN2401)	Monoclonal anti-body	Biogen /Eisai	Early AD	IV	III	Recruiting	NCT03887455	2019 Mar	2024
			Preclinical AD		III	Recruiting	NCT04468659	2020 Jul	2027
Donanemab (LY3002813)	Monoclonal anti-body	Eli Lilly	Early symptomatic AD	IV	III	Recruiting	NCT04437511	2020 Jun	2023
			Preclinical AD		III	Recruiting	NCT05026866	2021 Aug	2027

isease; Admin, Route of administration; SC, subcutaneous; IM, intramuscular; IV, intravenous

The antibody aducanumab reduces Aβ plaques in Alzheimer's disease

Jeff Sevigny[1*], Ping Chiao[1*], Thierry Bussière[1*], Paul H. Weinreb[1*], Leslie Williams[1], Marcel Maier[2], Robert Dunstan[1], Stephen Salloway[3], Tianle Chen[1], Yan Ling[1], John O'Gorman[1], Fang Qian[1], Mahin Arastu[1], Mingwei Li[1], Sowmya Chollate[1], Melanie S. Brennan[1], Omar Quintero-Monzon[1], Robert H. Scannevin[1], H. Moore Arnold[1], Thomas Engber[1], Kenneth Rhodes[1], James Ferrero[1], Yaming Hang[1], Alvydas Mikulskis[1], Jan Grimm[2], Christoph Hock[2,4], Roger M. Nitsch[2,4]§ & Alfred Sandrock[1]§

50 | NATURE | VOL 537 | 1 SEPTEMBER 2016

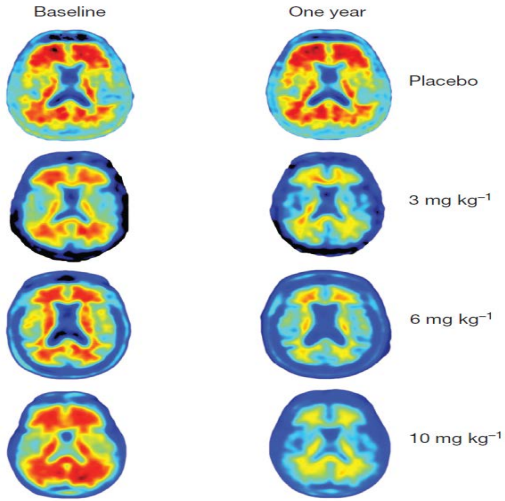


Figure 1 | Amyloid plaque reduction with aducanumab

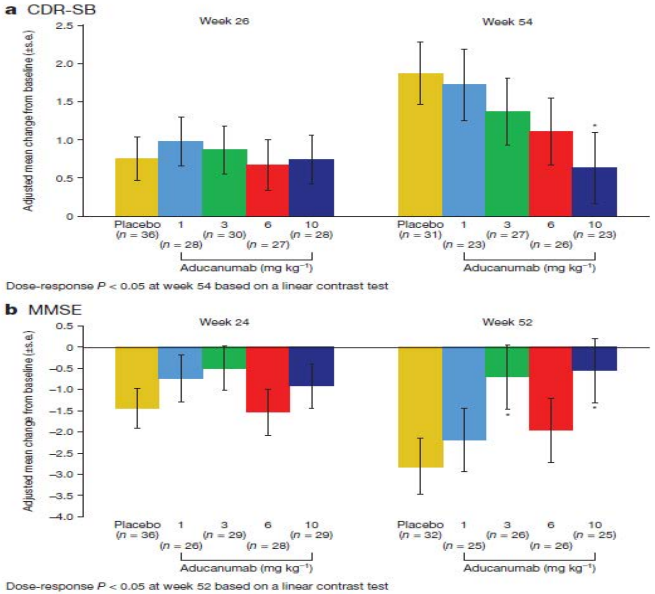


Table 2 | Summary of adverse events and most common adverse events

Adverse event (n (%))	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)
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)

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Lecanemab

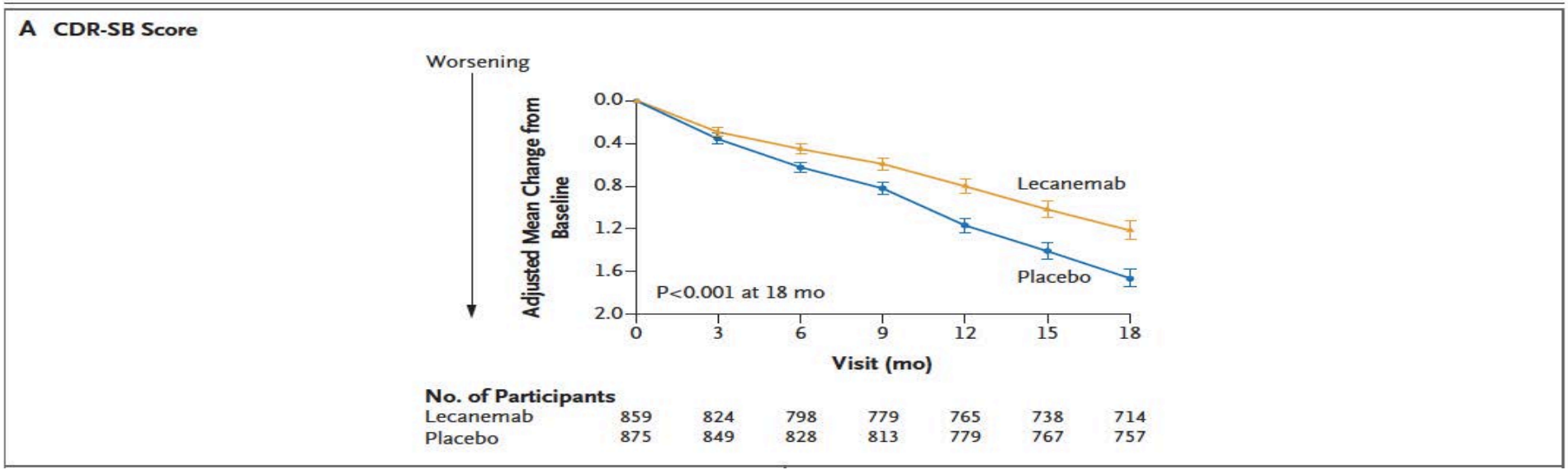
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Lecanemab in Early Alzheimer's Disease

C.H. van Dyck, C.J. Swanson, P. Aisen, R.J. Bateman, C. Chen, M. Gee, M. Kanekiyo, D. Li, L. Reyderman, S. Cohen, L. Froelich, S. Katayama, M. Sabbagh, B. Vellas, D. Watson, S. Dhadda, M. Irizarry, L.D. Kramer, and T. Iwatsubo

Ziekteproces beïnvloedend effect



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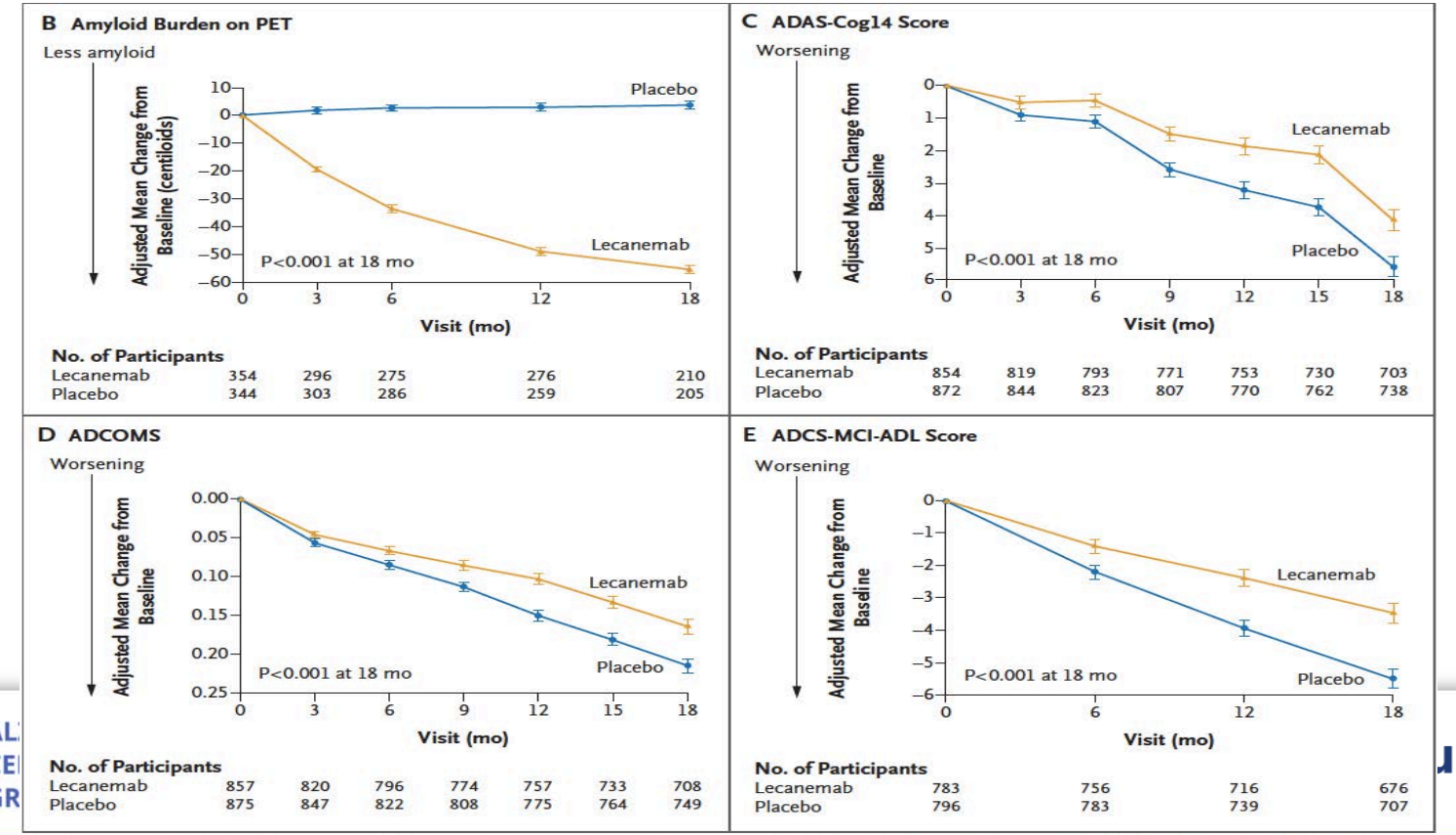
Ziekteproces beïnvloedend effect



Gecombineerd anti amyloid/tau

Incremental Innovation in Alzheimer's Disease Therapeutics
From Treatment to Disease Prevention

CURRENT THERAPIES — 2022 — *FUTURE OPPORTUNITIES IN DEVELOPMENT*

SYMPTOMATIC
- Cholinesterase inhibitors (e.g., donepezil)
- NMDA-receptor antagonists (e.g., memantine, amantadine)

1ST GENERATION DISEASE MODIFYING
- **Anti-Aβ mAbs** (e.g., aducanumab, lecanemab, donanemab)

NEXT GENERATION DISEASE MODIFYING
- **High-potency anti-Aβ mAbs** - improved patient access, safety, & efficacy
- **Anti tau-MTBR mAbs** – incremental efficacy
- **Others** (synuclein, vascular and glial biology)

PRIMARY & SECONDARY PREVENTION; TREATMENT
- **Aβ + Tau active vaccines**

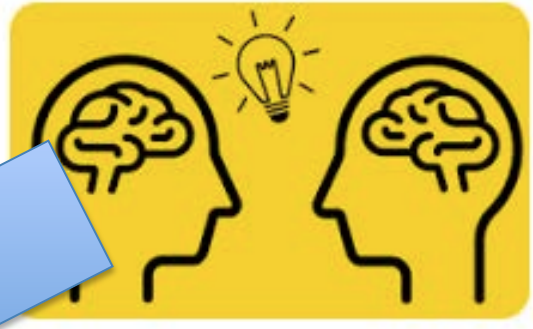
Aβ, amyloid beta; mAb, monoclonal antibody

Concluderend

30% van het aantal gevallen met dementie kan voorkomen worden door een gezonde leefstijl. [illegible] ond eten, voldoende bewegen [illegible] met roken helpen bij de preve[illegible]

https://www.alzheimer-ne[illegible]

Oorzaken en voorkome[illegible] heimer Nederla[illegible]



Een gezonde leefstijl dient uiteraard nagestreefd

EN

Er is hoop op een daadwerkelijke doorbraak met ziekteproces beïnvloedende medicinale interventies

Dank U

Vragen ?

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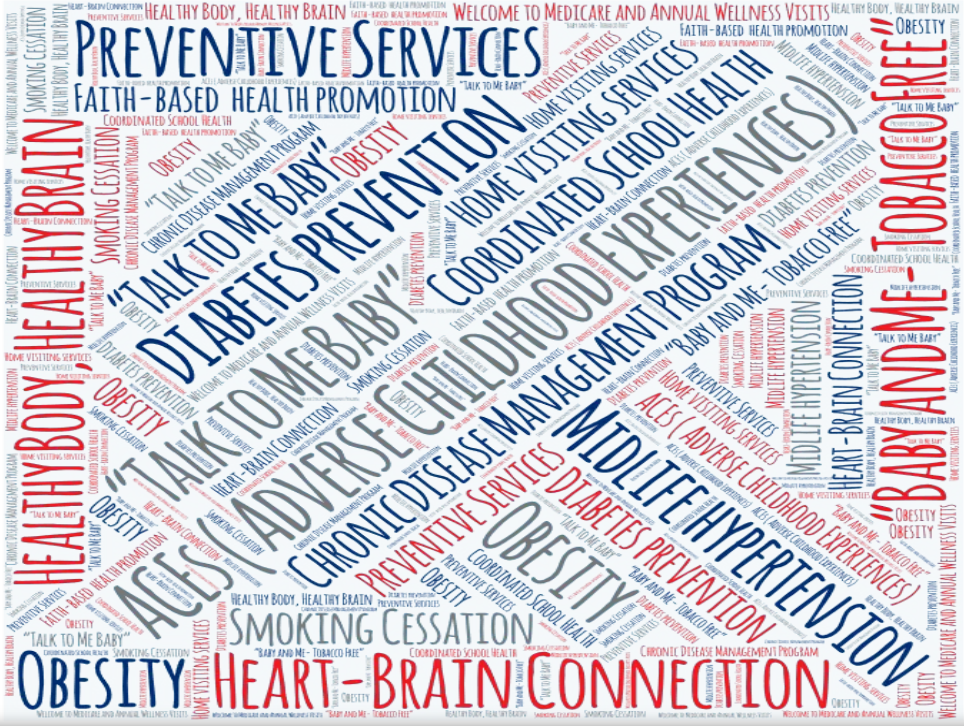
Optimale Cognitieve Gezondheid : Volksgezondheid Benadering



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