

ALZHEIMERI TÕVE MARKERID: KLIINILISED KORRELATSIOONID

Juhan Reimand, MD, PhD
radioloog-vanemarst
Põhja-Eesti Regionaalhaigla



SISUKORD

01. PATOFÜSIOLOGIA
Amüloidkaskaad
Alzheimeri tõve diagnoos

02. AMÜLOID
CSF, PET ja plasma

03. TAU
CSF, PET ja plasma

04. NÜÜD JA TULEVIKUS
Mida kasutada?



01.

PATOFÜSIOLOGIA

DIAGNOOS AJALOOLISELT



PATOLOGIA

Kuldne standard



KLIINILINE DIAGNOOS

**SENSITIIVSUS
SPETSIIFILISUS**

71 – 87%

44 – 71%

Kliinilise diagnoosi täpsus USA ekspertkeskustes

Beach et al., J Neuropathol Exp Neurol. 2012

DIAGNOOS TÄNAPÄEVAL



PATOLOGIA

Kuldne standard



KLIINILINE DIAGNOOS



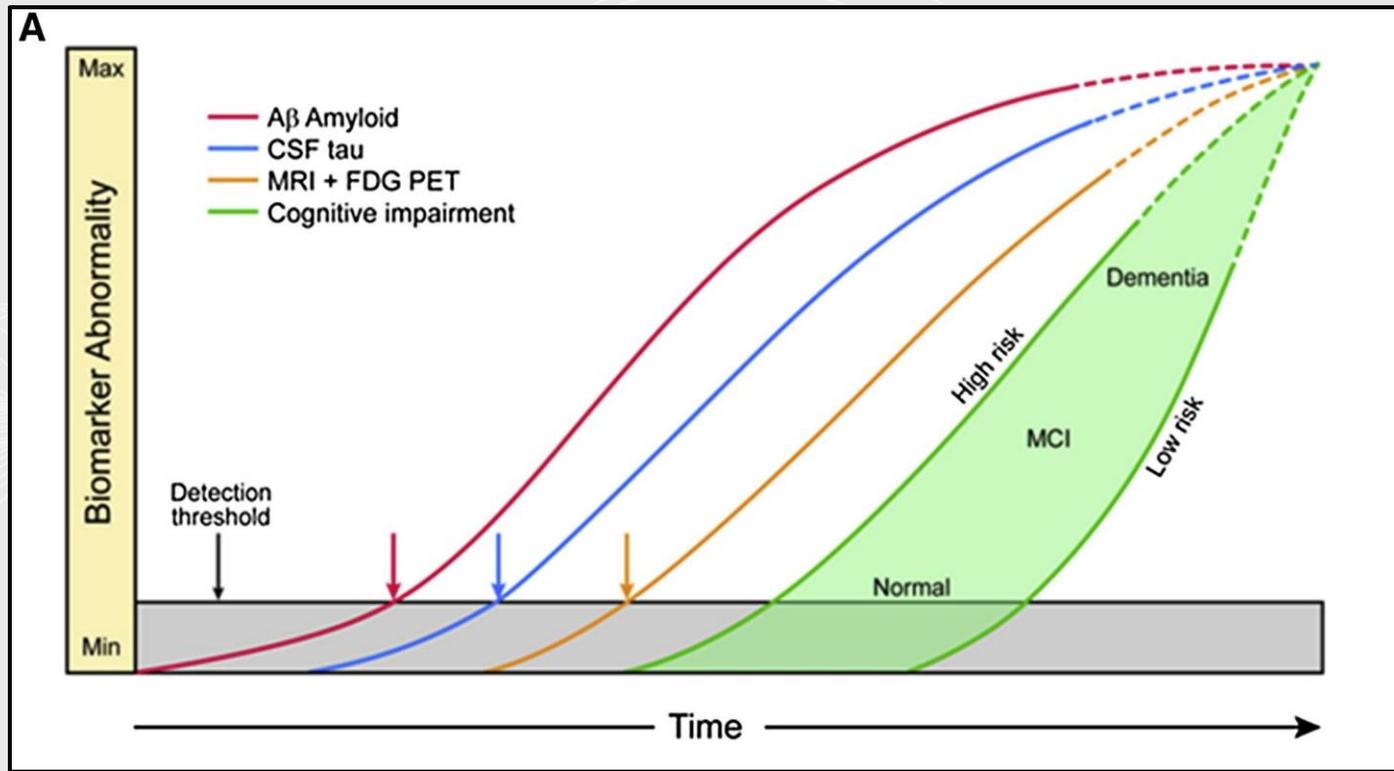
KUVAMINE

MRI, PET

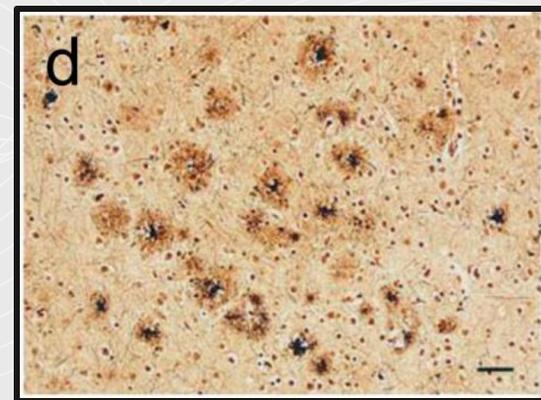
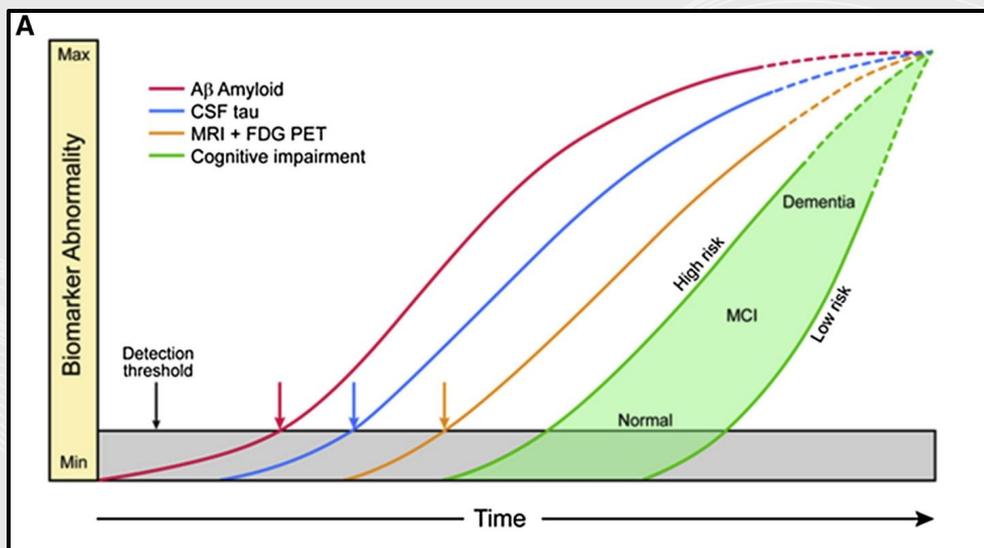


LABOR

Liikvor, veri



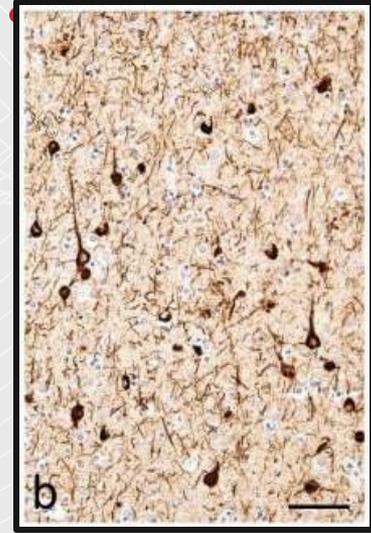
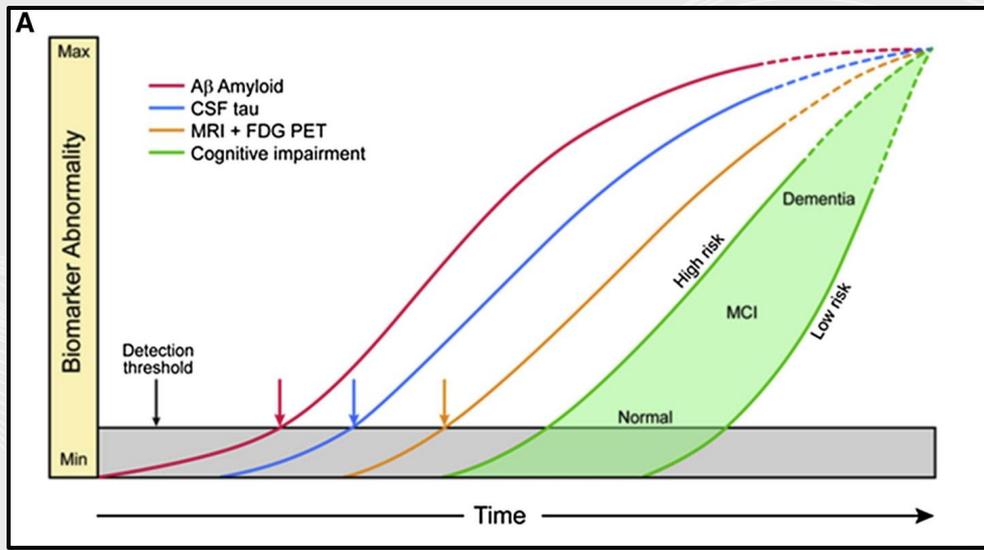
ALZHEIMERITÕVE PATOLOOGILINE KASKAAD



Amüloid- β

Jack et al., Neuron. 2013

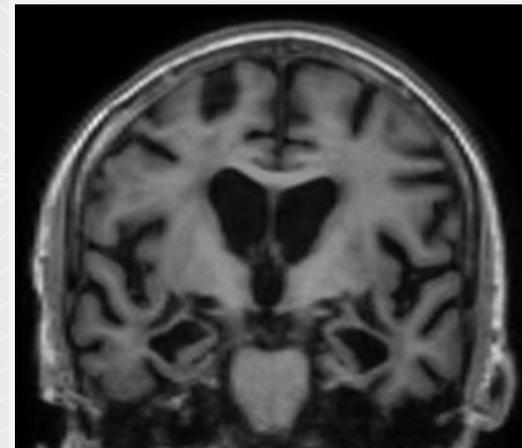
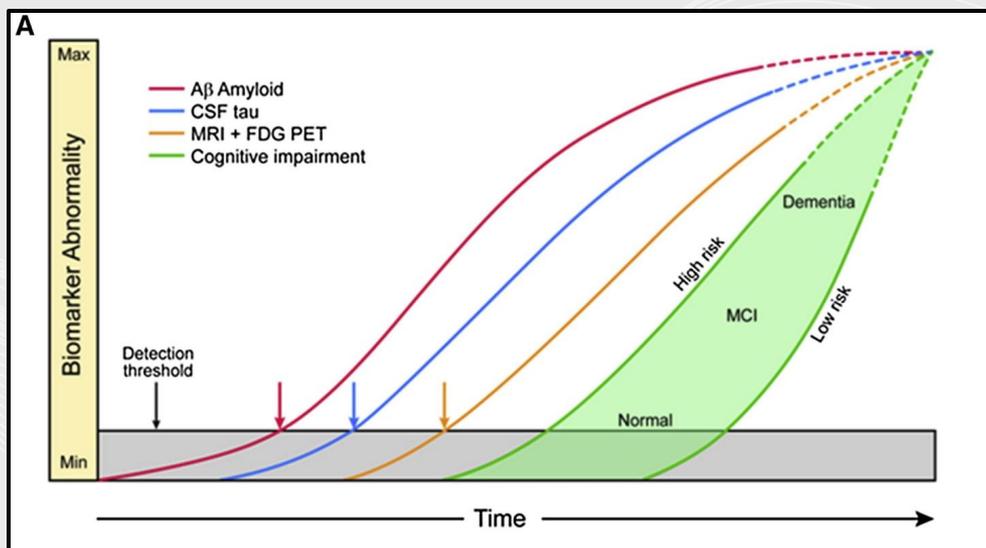
Montine et al., Acta Neuropathol. 2012



Amüloid- β



Tau



Amüloid- β

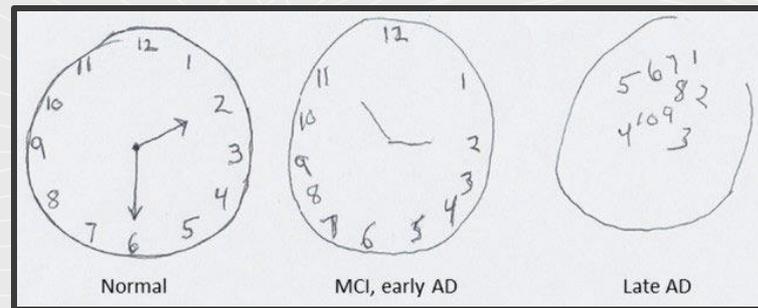
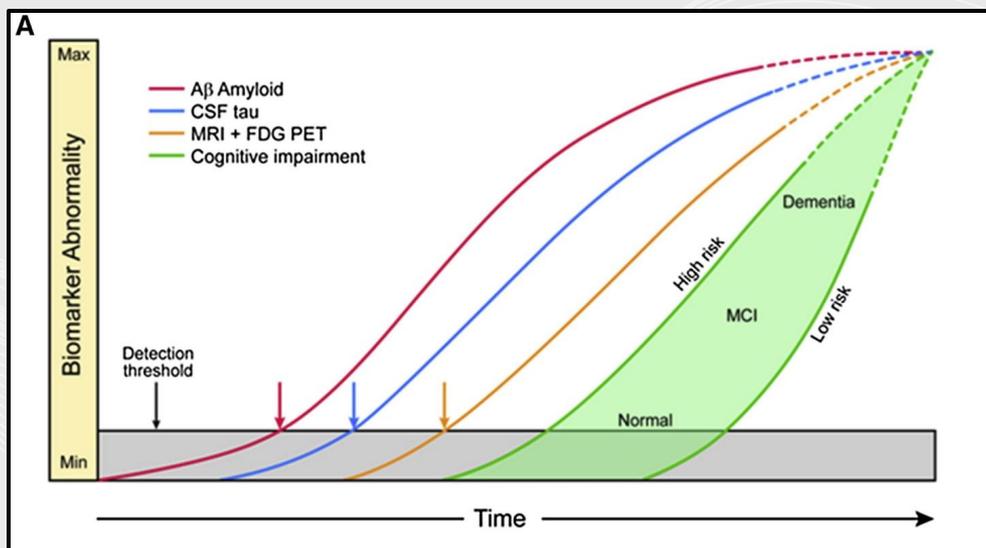


τ

Tau



Neuro-
degeneratsioon



Amüloid-β



τ

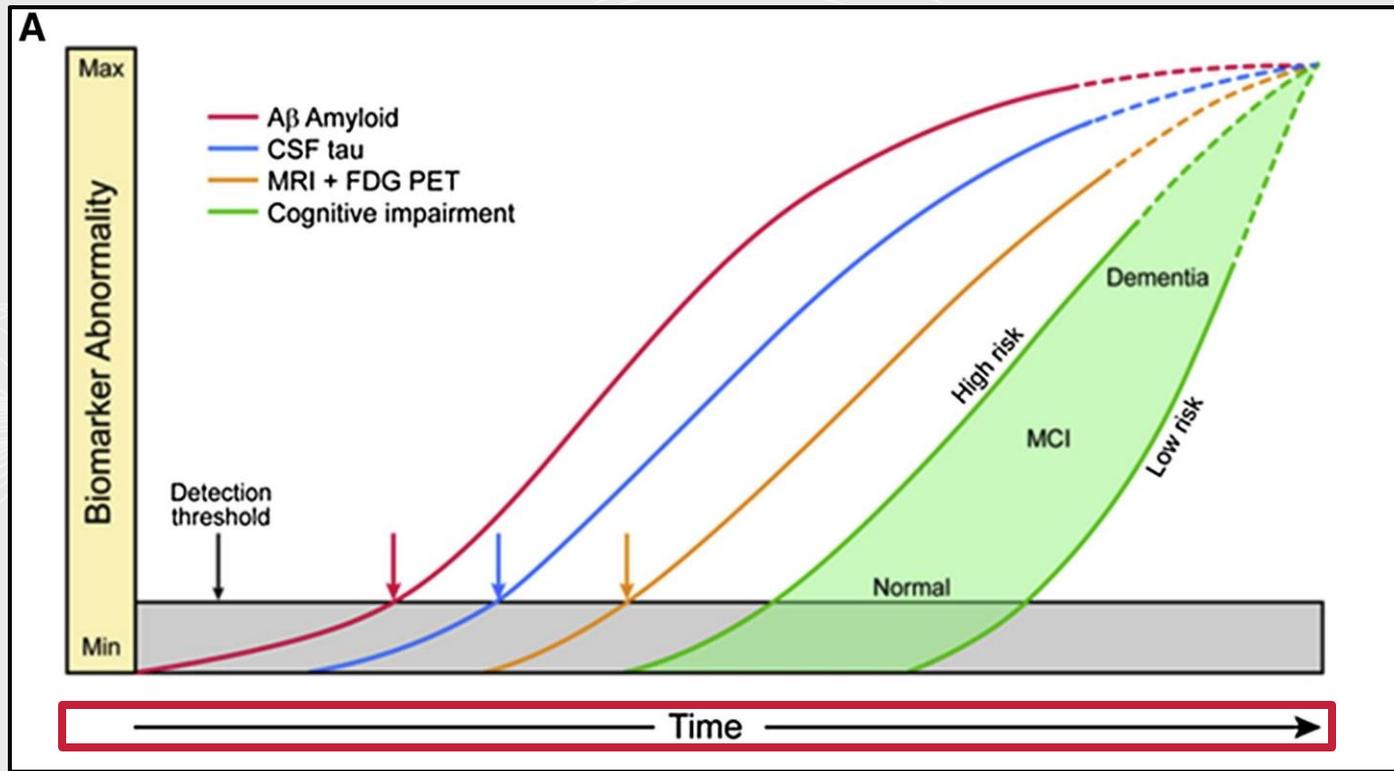
Tau



Neuro-
degeneratsioon



Kliinilised
sümptomid



AMÜLOID 20 AASTAT ENNE SÜMPTOMEID

ALZHEIMER = AMÜLOID

AT(N) profiles	Biomarker category	
A-T-(N)-	Normal AD biomarkers	
A+T-(N)-	Alzheimer's pathologic change	Alzheimer's continuum
A+T+(N)-	Alzheimer's disease	
A+T+(N)+	Alzheimer's disease	
A+T-(N)+	Alzheimer's and concomitant suspected non Alzheimer's pathologic change	
A-T+(N)-	Non-AD pathologic change	
A-T-(N)+	Non-AD pathologic change	
A-T+(N)+	Non-AD pathologic change	

A - Amüloid

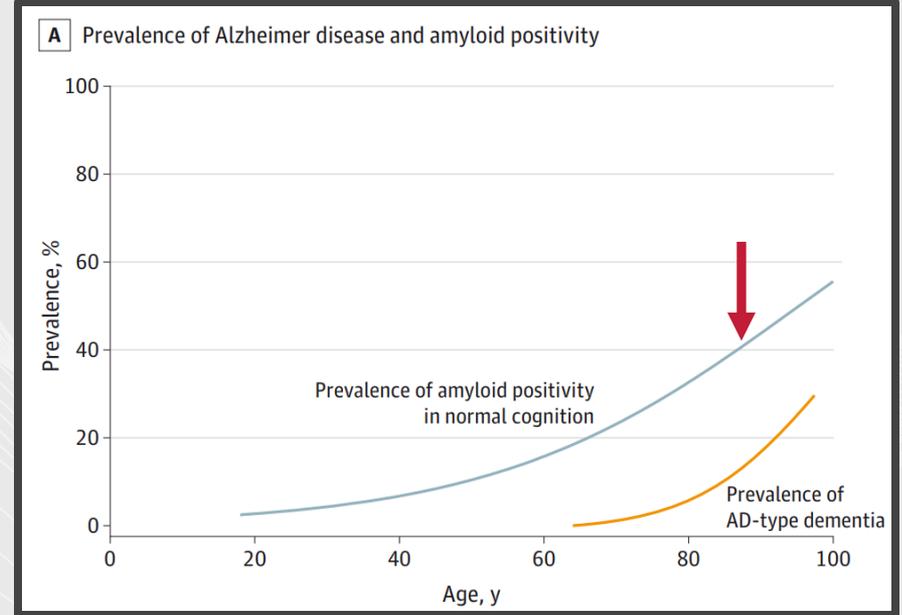
T - Tau

N - Neurodegeneratsioon

ALZHEIMER = AMÜLOID?

AT(N) profiles	Biomarker category	
A-T-(N)-	Normal AD biomarkers	
A+T-(N)-	Alzheimer's pathologic change	Alzheimer's continuum
A+T+(N)-	Alzheimer's disease	
A+T+(N)+	Alzheimer's disease	
A+T-(N)+	Alzheimer's and concomitant suspected non Alzheimer's pathologic change	
A-T+(N)-	Non-AD pathologic change	
A-T-(N)+	Non-AD pathologic change	
A-T+(N)+	Non-AD pathologic change	

Jack et al., *Alzheimers Dement.* 2018



Jansen et al., *JAMA.* 2015

ALZHEIMER = AMÜLOID?

AT(N) profiles	Biomarker category	
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A+T+(N)+	Alzheimer's disease	
A+T-(N)+	Alzheimer's and concomitant suspected non Alzheimer's pathologic change	
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A-T-(N)+	Non-AD pathologic change	
A-T+(N)+	Non-AD pathologic change	

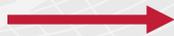
KLIINILINE DIAGNOOS:

- 1) Kliinilised sümptomid
- 2) Amüloid + tau

DIAGNOSTILISED VÕIMALUSED



Amüloid- β



τ

Tau



Neuro-
degeneratsioon



Kliinilised
sümptomid

1. Amüloid PET
2. CSF $A\beta_{42}$
3. (Plasma $A\beta_{42/40}$)

1. CSF p-tau
2. Tau PET
3. (Plasma p-tau)

1. MRT
2. FDG PET
3. CSF t-tau



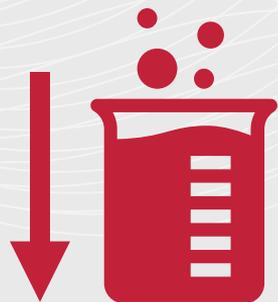
02.

AMÜLOID



LIIKVOR (CSF)

Alzheimeri tõbi



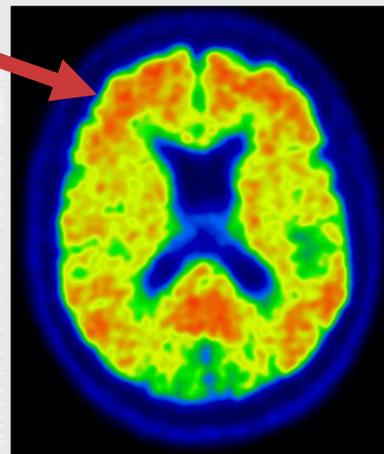
$A\beta_{42}$

Norm

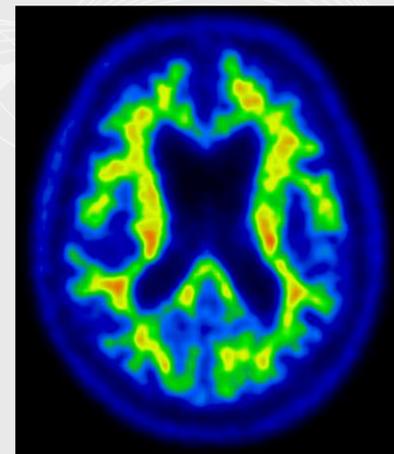


POSITRONEMISSION- TOMOGRAAFIA (PET)

Alzheimeri tõbi



Norm





LIIKVOR (CSF)

Veeslahustuva $A\beta_{42}$ tuvastamine

Kaasnev p-tau and t-tau analüüs
Odavam

Interventsionaalne protseduur
Metoodiline variatsioon
Teatud kliinilised situatsioonid



POSITRONEMISSION- TOMOGRAAFIA (PET)

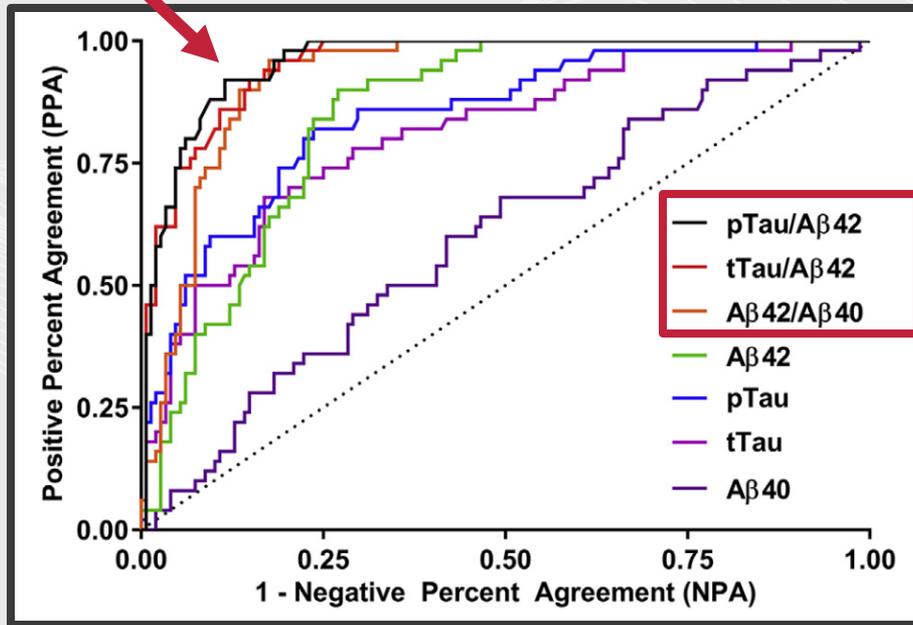
Amüloid- β ladustuste tuvastamine

Topograafiline informatsioon
Tulemuste visuaalne kontroll

Madalam kättesaadavus
Kiirguskoormus



KAS VAJA KASUTADA CSF $A\beta_{40}$



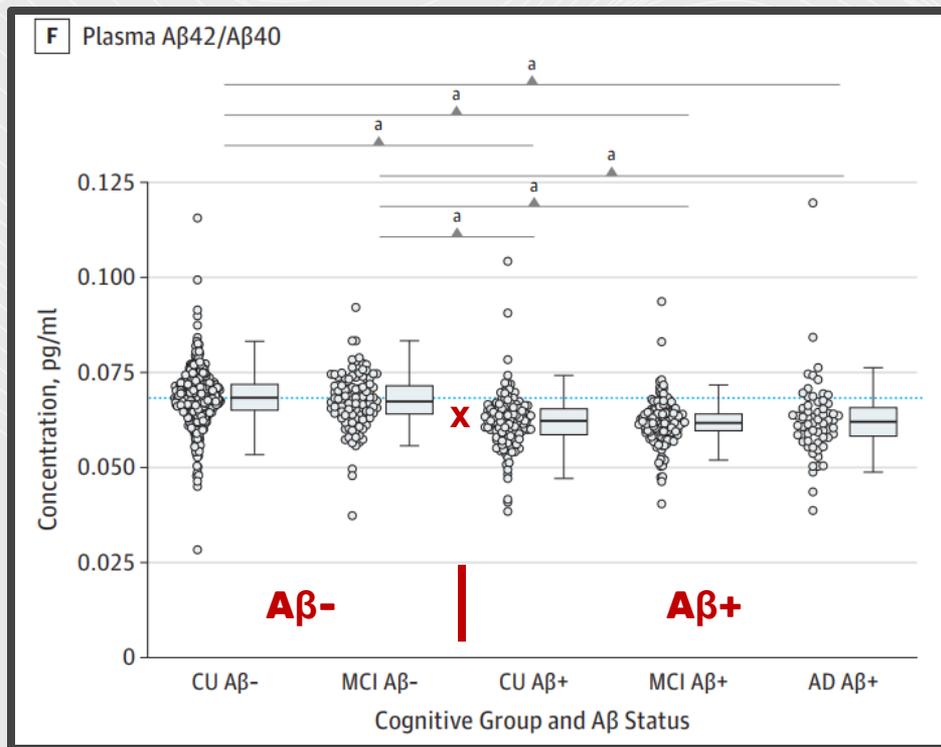
AMÜLOID?

$$A\beta_{40/42} > A\beta_{42}$$

ALZHEIMERI TÕBI?

$$A\beta_{40/42} \text{ VÕI } p\text{-tau}/A\beta_{42}$$

PLASMA AMÜLOID?





03.

TAU

CSF TAU



P-TAU181

Näitab Alzheimeri tõve
patoloogiat

AIN

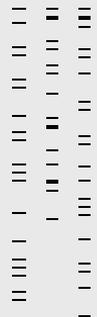


(T-)TAU

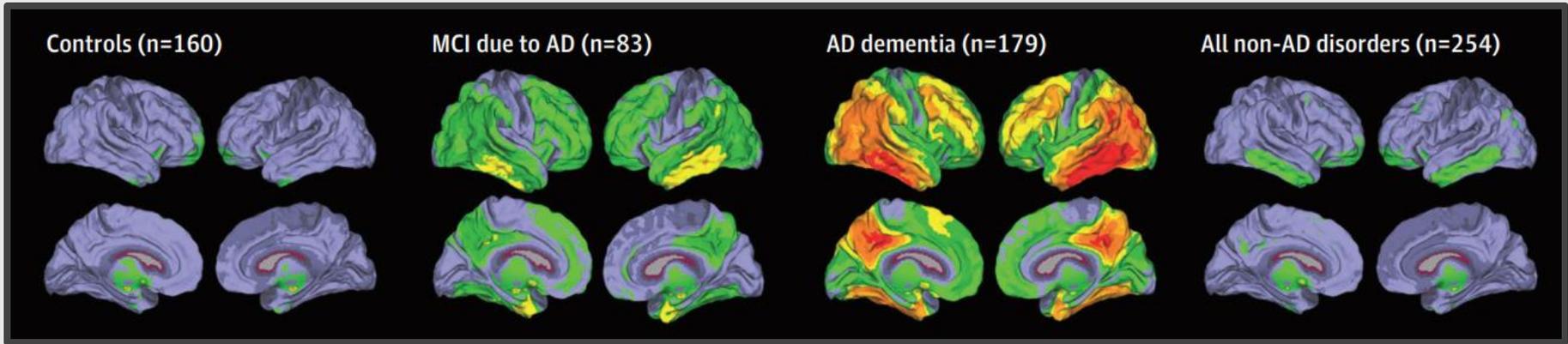
Mittespetsiifilistem
rakukahjustuse marker

ATN

CJD, insult, infektsioon, FTD, tuumor



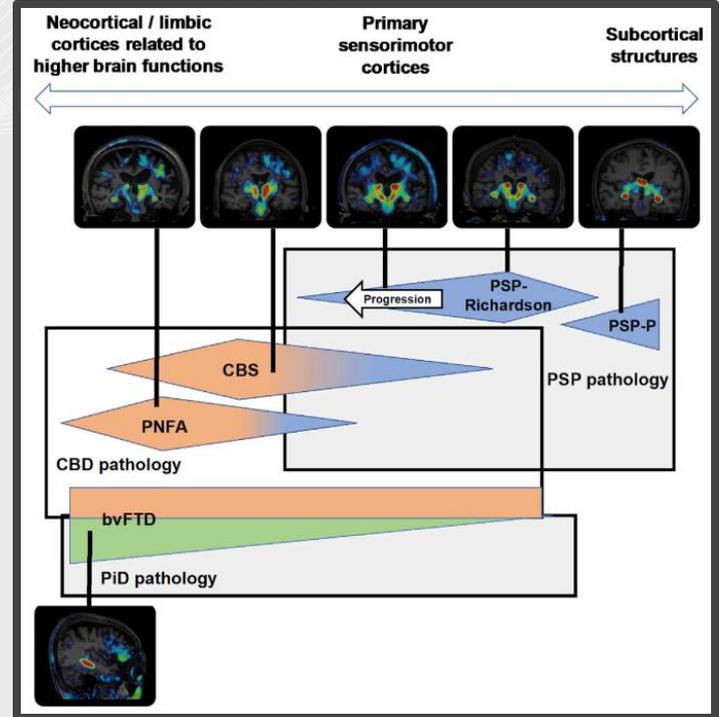
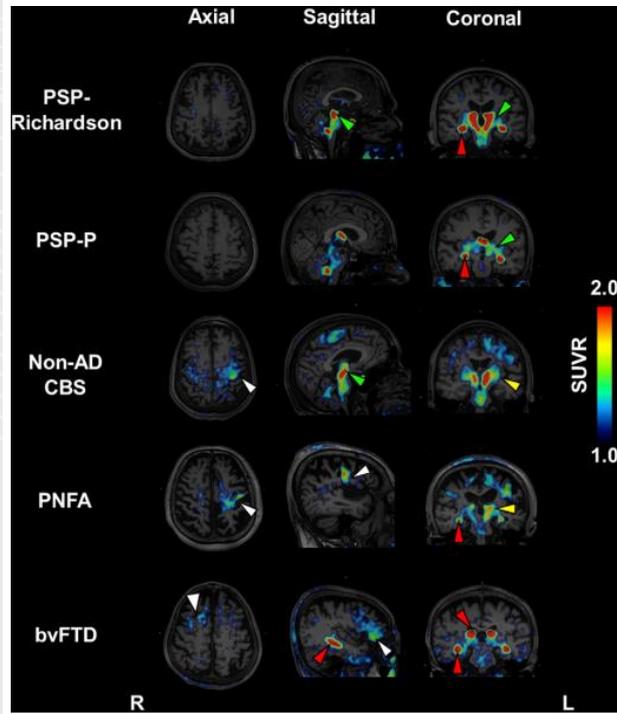
FLORTAUCIPIR PET



- Näitab Alzheimeri tõvele iseloomulikku 3R/4R taud
- FDA kasutusluba



UUED TAU PET MÄRKAINED

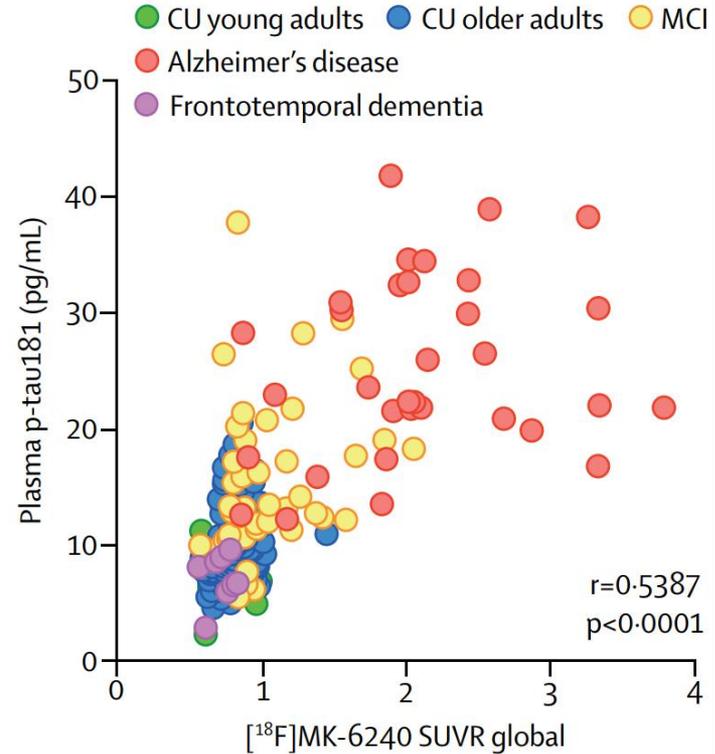
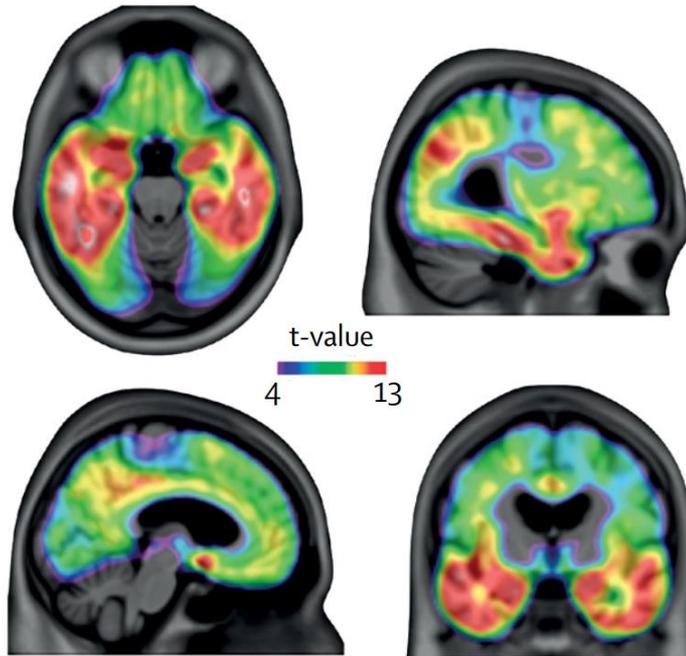


18F-PM-PBB3 PET

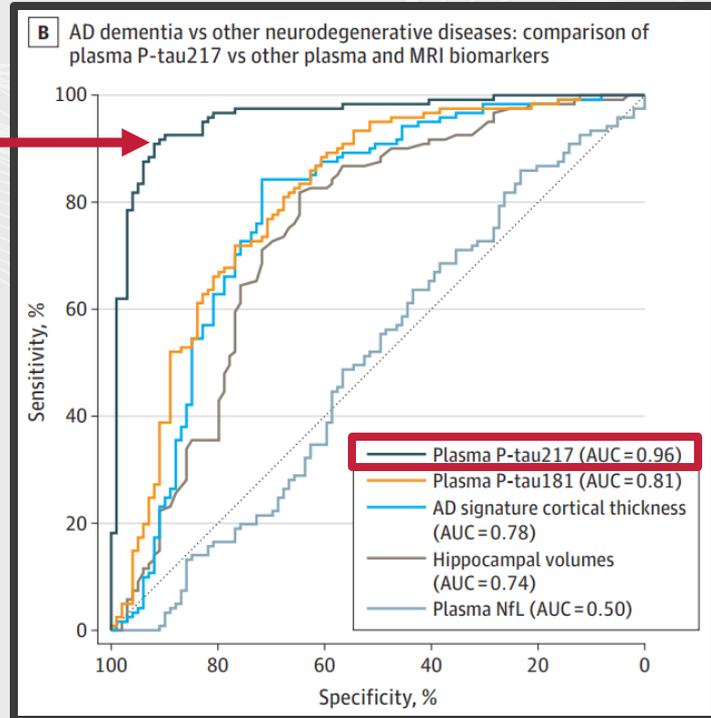
Teiste
tauopaatiate
tuvastamine

PLASMA P-TAU181

A Plasma p-tau181 vs tau [¹⁸F]MK-6240

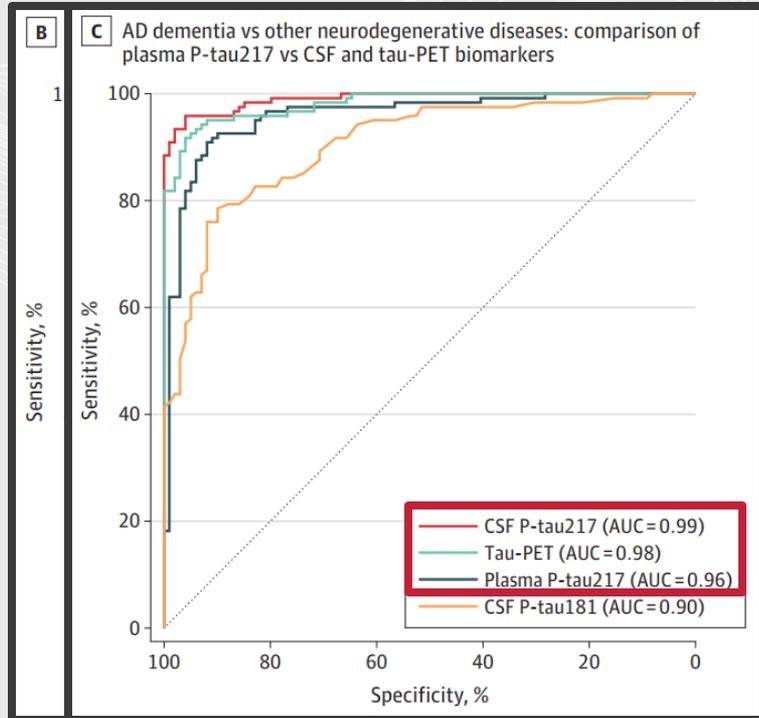


PLASMA P-TAU₂₁₇!



AD vs mitte AD:
P-tau₂₁₇ > p-tau₁₈₁, MRI, NfL

PLASMA P-TAU₂₁₇!



AD vs mitte AD:

P-tau₂₁₇ > p-tau₁₈₁, MRI, NFL

tau PET \approx CSF / plasma p-tau₂₁₇



04.

PRAEGU JA TULEVIKUS

BIOMARKERI VALIK

PRAEGU

AMÜLOID

- Valik CSF ja PETi vahel
- Plasmal kindlat rolli veel ei ole

TAU

- CSF p-tau181
- Flortaucipir tau PET sai FDA loa

NEURODEGENRATSIOON

- Strukturaalne MRT
- Vajadusel FDG PET



BIOMARKERI VALIK

PRAEGU

AMÜLOID

- Valik CSF ja PETi vahel
- Plasmal kindlat rolli veel ei ole

TAU

- CSF p-tau181
- Flortaucipir tau PET sai FDA loa

NEURODEGENRATSIOON

- Strukturaalne MRT
- Vajadusel FDG PET

TULEVIKUS

SKRIINING

- Plasma p-tau217 (ja $A\beta_{42/40}$)

TÄPSUSTAV

- Tau PET (uue põlvkond)
- Amüloid PET vajadusel

NEURODEGENRATSIOON

- Strukturaalne MRT



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US approves first new Alzheimer's drug in 20 years

🕒 7 June

The New York Times

How an Unproven Alzheimer's Drug Got Approved

Though some of its own senior officials said there was little evidence of benefit for patients, the F.D.A. nonetheless greenlighted Biogen's Aduhelm, or aducanumab.