Subjective cognitive decline as the first symptom of Alzheimer's Disease

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Disclosure

Within the last five years:

Advisor fee: AC Immune, Via Med, Janssen Cilag,

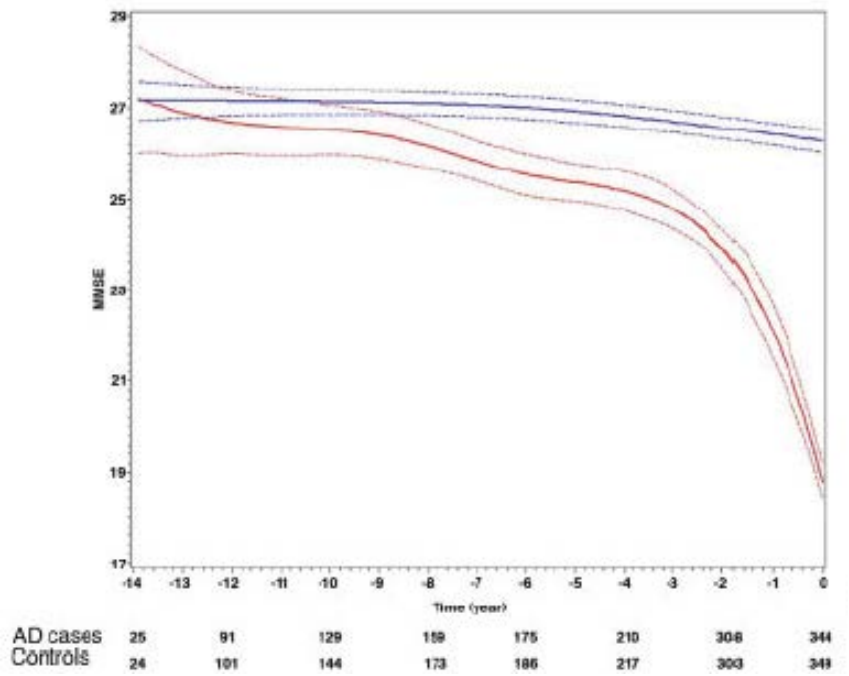
Novartis, GE Healthcare, Lilly, Piramal Imaging, Roche,

UCB, Astra Zeneca, Schwabe, Nutricia, Octapharma

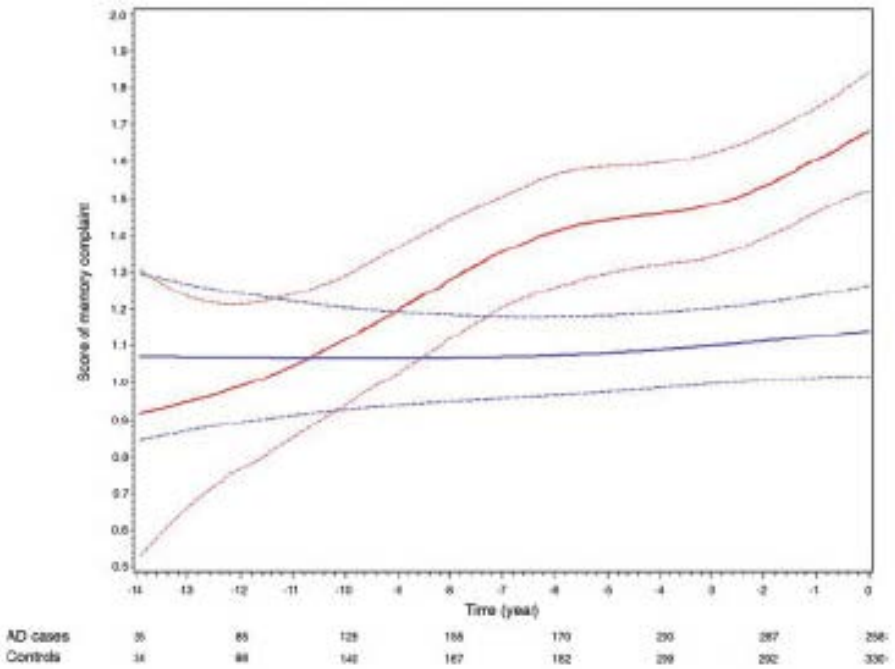
Speaker fee: Pfizer, Esai, Novartis, GE Healthcare

Cognitive performance and cognitive complaints before AD onset

PAQUID study, n=3.477, age >65 J., 14 years follow-up



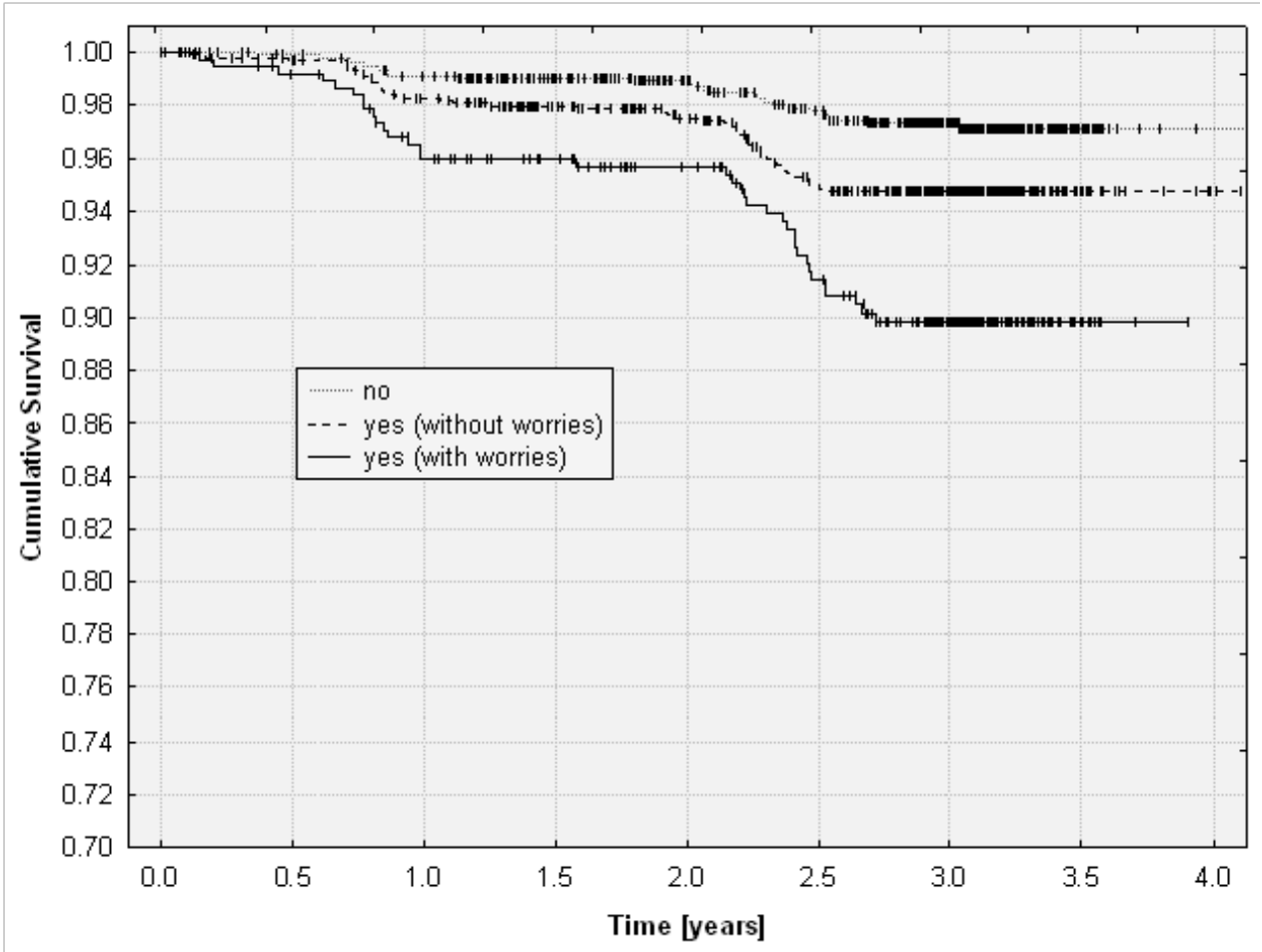
MMSE



Cognitive complaints

Amieva et al., Ann Neurol., 2008

Subjective decline in memory as a risk indicator of AD



AgeCoDe
n=2.423,
cognitively normal
36 months follow-up

SCD without worries

HR: 3.04

CI: 1.36-6.81

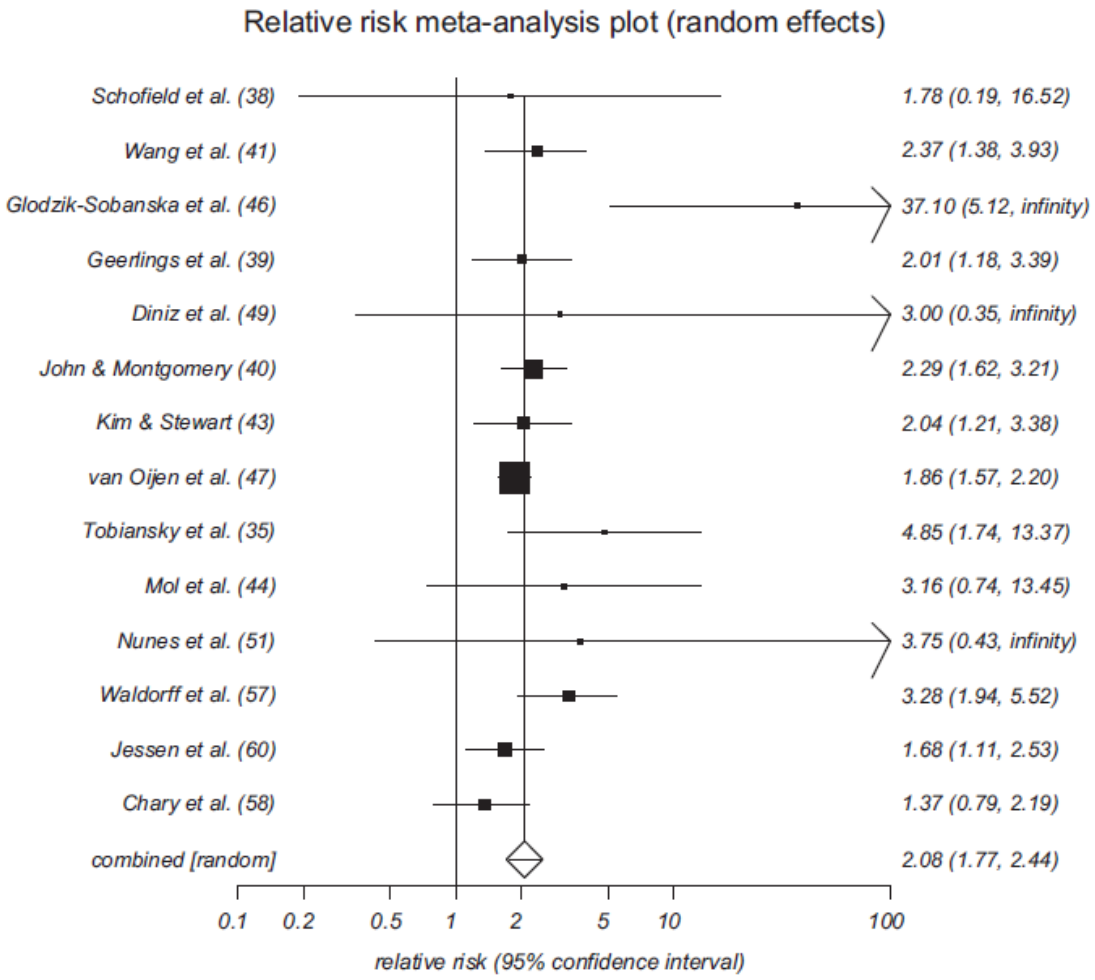
SCD with worries

HR: 6.54

CI: 2.82-15.20

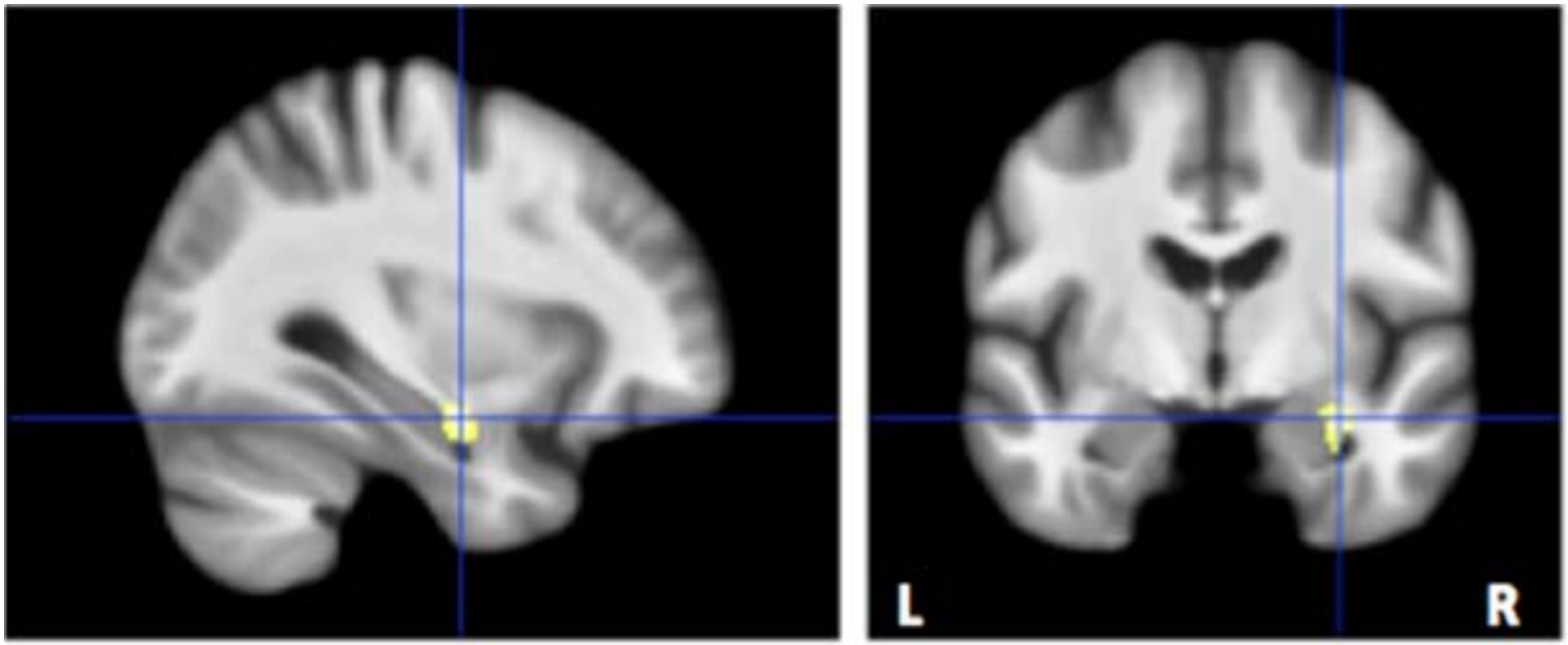
Jessen, Arch. Gen. Psychiatry, 2010

Meta-analysis of risk of dementia in subjective cognitive decline (SCD) in epidemiological studies



Mitchell et al., Acta Psychiatr Scand, 2014

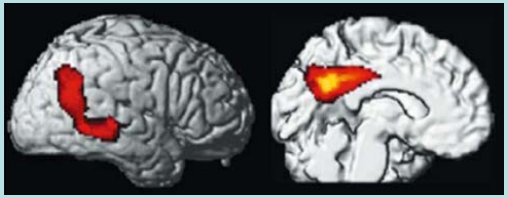
Voxel-based morphometry (VBM) in SMI



CO > SMI: p<0.001, whole brain, uncorrected; p<0.05, FWE – SVC (MTL)

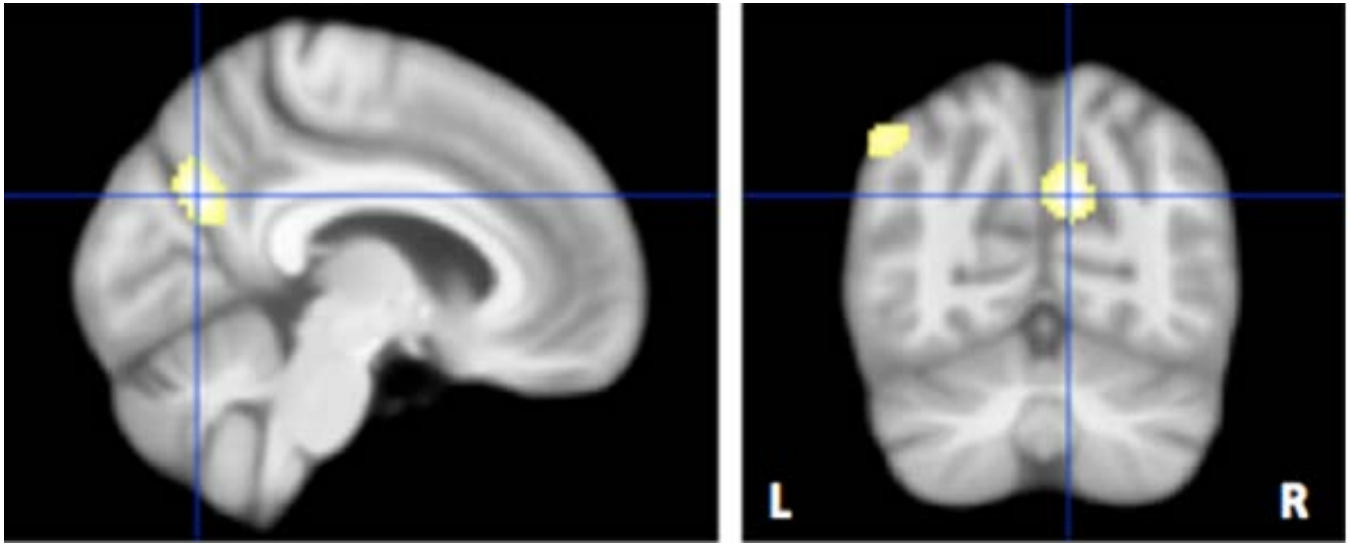
Scheef et al., Neurology, 2012

Glucose metabolism in SMI (FDG-PET)



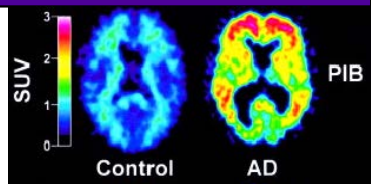
Hypometabolism in AD
Mosconi et al., 2005

CO > SMI:
p<0.001, whole brain, uncorrected
p<0.05, FWE - SVC (precuneus)

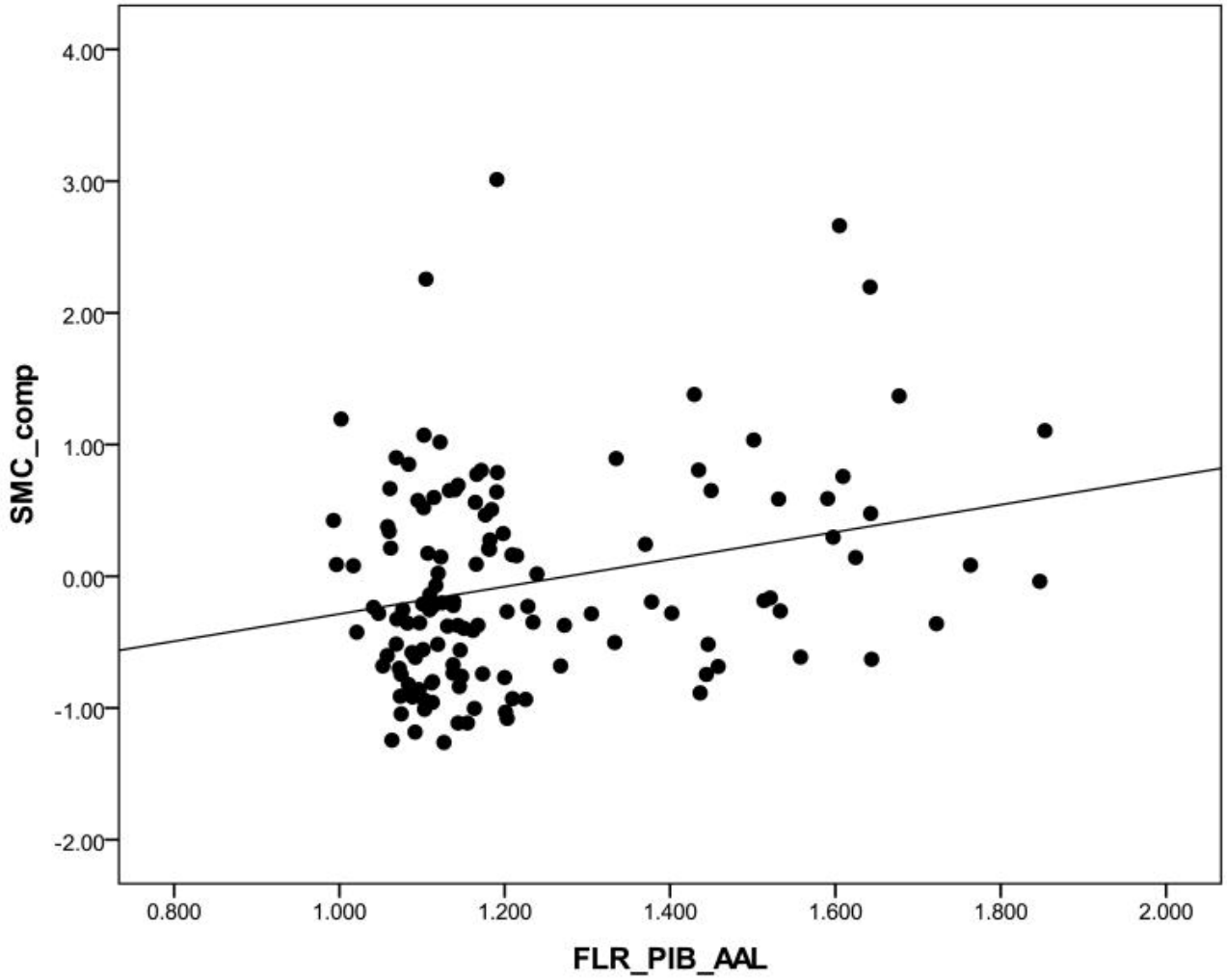


Scheef et al. Neurology, 2012

Amyloid deposition and SCD



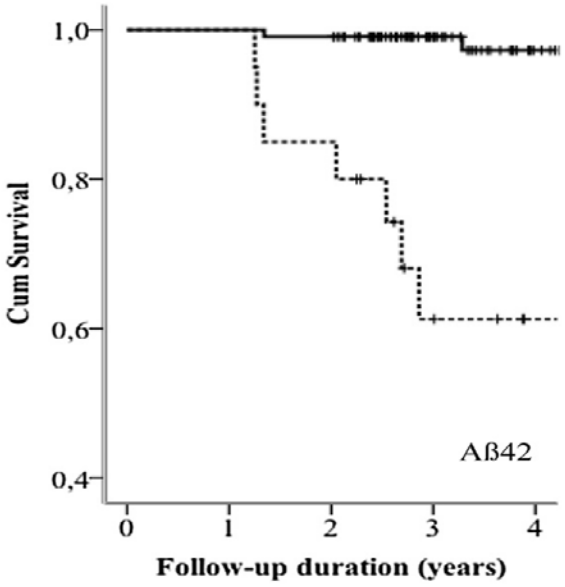
Klung et al., Ann Neurol., 2004



Amariglio et al., Neuropsychologia, 2012

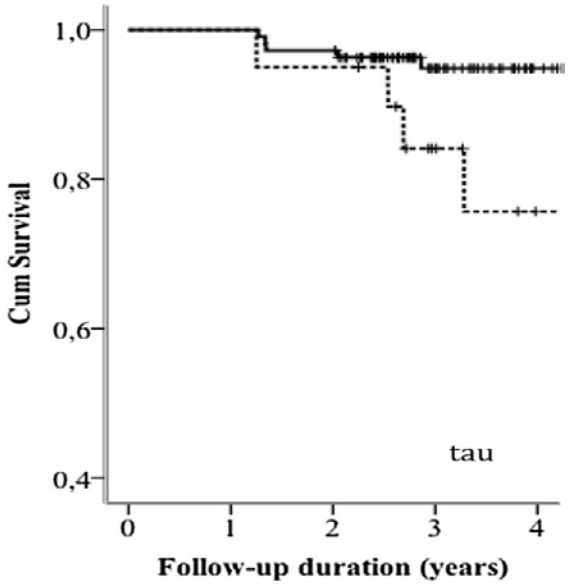
Prediction of MCI and dementia by CSF markers of AD in SCD

HR: 16



Aß42	Numbers entering interval:		
>550 ng/l	108	107	35
<550 ng/l	20	17	5

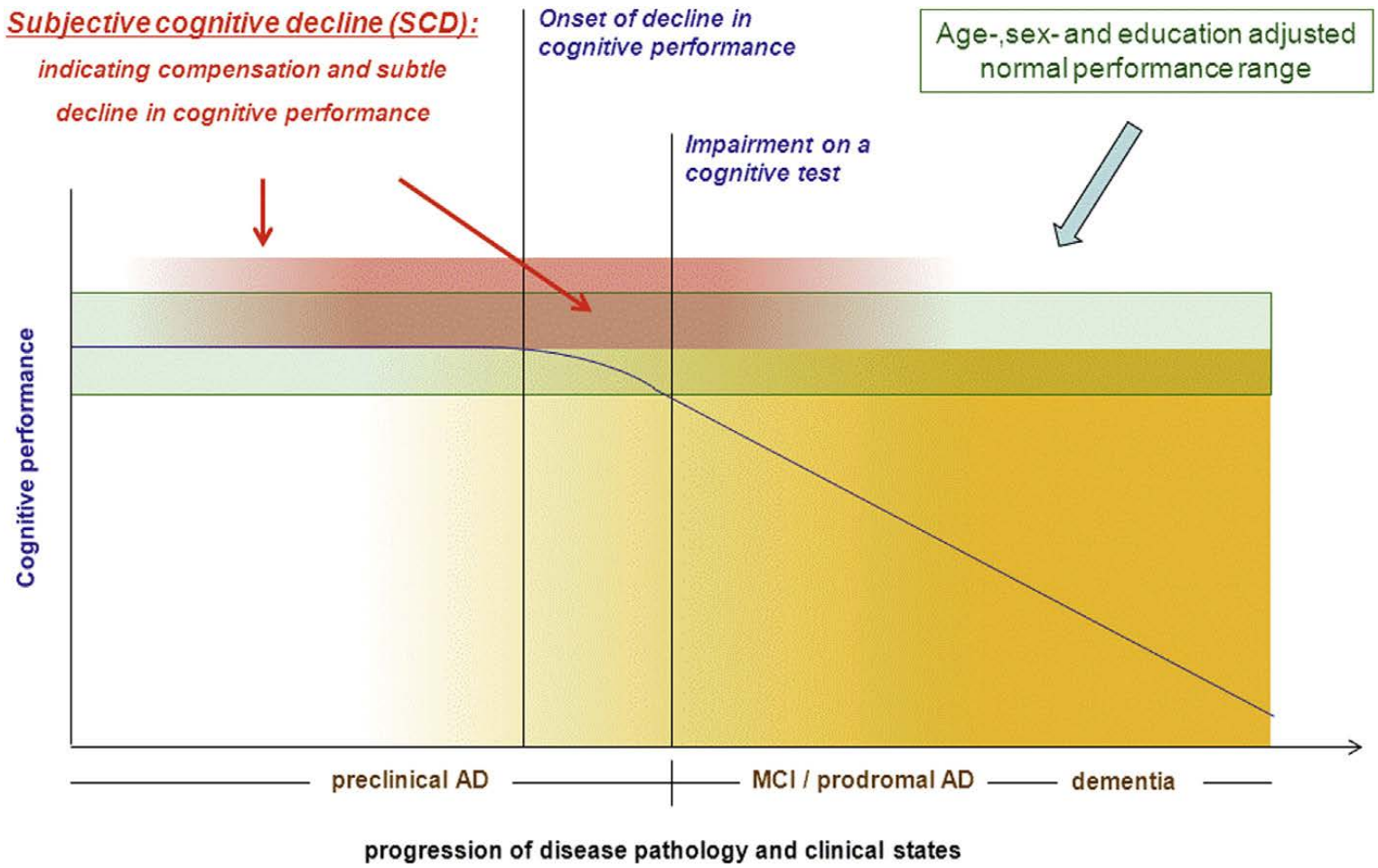
HR: 2.8



tau	Numbers entering interval:		
<375 ng/l	108	105	33
>375 ng/l	20	19	7

Van Harten et al. Alz & Dem, 2013

Conceptual framework for research on SCD in preclinical AD



Jessen et al., Subjective Cognitive Decline Initiative, Alz & Dem, 2014

Research criteria for subjective cognitive decline (SCD) in preclinical AD

- Self-experienced persistent decline in cognitive capacity in comparison with a previously normal status, and not related to an acute event
- Normal age-, gender- and education-adjusted performance on standardized cognitive tests, which are used to classify mild cognitive impairment (MCI) or prodromal AD
- 1 and 2 must be present

Exclusion criteria

- Mild cognitive impairment, prodromal AD, dementia
- Can be explained by a psychiatric* or neurological disease (apart form Alzheimer's disease) or by a medical disorder or by medication or by substance use

  **individual symptoms of depression or anxiety, which do reach the threshold of a disorder, are not considered exclusion criteria*

Jessen et al., Subjective Cognitive Decline Initiative, Alz & Dem, 2014

Features that increase the likelihood of preclinical AD in SCD : **SCD *plus***

- Subjective decline in memory, rather than in other domains of cognition
- Onset of SCD within the last five years
- Age at onset of SCD > 60 years
- Concerns (worries) associated with SCD
- Feeling of worse performance than other of the same age group

If available:

- Confirmation of cognitive decline by an informant
- Presence of the *APOE ε4* genotype
- Biomarker evidence for AD (defines preclinical AD)

Jessen et al., Subjective Cognitive Decline Initiative, Alz & Dem, 2014

Summary

- SCD may occur at the pre-MCI stage of AD (not in everybody)
- The presence of SCD in a subject increases the risk of future AD dementia
- SCD is not specific for AD
- The combination of SCD with AD biomakers is a promising approach for very early identification of subjects with AD
- SCD may represents the future condition for biomarker-based AD detection and early intervention