Pieter Jelle Visser - selected references

1 Vos, S. J., van Rossum, I. A., Verhey, F., Knol, D. L., Soininen, H., Wahlund, L. O. ... & Visser, P. J. (2013). Prediction of Alzheimer disease in subjects with amnestic and nonamnestic MCI. *Neurology, 80,* 1124-1132.
Notes: OBJECTIVE: To compare the predictive accuracy of beta-amyloid (Abeta)1-42 and total tau in CSF, hippocampal volume (HCV), and APOE genotype for Alzheimer disease (AD)-type dementia in subjects with amnestic mild cognitive impairment (aMCI) and nonamnestic mild cognitive impairment (naMCI). METHODS: We selected 399 subjects with aMCI and 226 subjects with naMCI from a multicenter memory clinic-based cohort. We measured CSF Abeta1-42 and tau by ELISA (n = 231), HCV on MRI (n = 388), and APOE epsilon4 (n = 523). Follow-up was performed annually up to 5 years. Outcome measures were progression to AD-type dementia and cognitive decline. RESULTS: At least 1 follow-up was available for 538 subjects (86%). One hundred thirty-two subjects with aMCI (38%) and 39 subjects with naMCI (20%) progressed to AD-type dementia after an average follow-up of 2.5 years. CSF Abeta1-42, tau, Abeta1-42/tau ratio, HCV, and APOE epsilon4 predicted AD-type dementia in each MCI subgroup with the same overall diagnostic accuracy. However, CSF Abeta1-42 concentration was higher and hippocampal atrophy less severe in subjects with naMCI compared with aMCI. This reduced the sensitivity but increased the specificity of these markers for AD-type dementia in subjects with naMCI. CONCLUSIONS: AD biomarkers are useful to predict AD-type dementia in subjects with aMCI and naMCI. However, biomarkers might not be as sensitive for early diagnosis of AD in naMCI compared with aMCI. This may have implications for clinical implementation of the National Institute on Aging and Alzheimer's Association criteria

2 Visser, P. J., Vos, S., van, R., I, & Scheltens, P. (2012). Comparison of International Working Group criteria and National Institute on Aging-Alzheimer's Association criteria for Alzheimer's disease. *Alzheimers and Dementia, 8,* 560-563.
Notes: Two sets of research criteria for Alzheimer's disease are now available: those published by an International Working Group in 2007, and the recommendations published by the National Institute on Aging and the Alzheimer's Association (NIA-AA) in 2011. They both provide guidelines for the diagnosis of asymptomatic and symptomatic Alzheimer's disease. The coexistence of two sets of criteria for the same disorder raises the question of which set of criteria should be preferred. A comparison of the criteria revealed differences in approach, terminology, and use of cognitive markers and biomarkers. Most persons who meet the International Working Group criteria will also meet the NIA-AA criteria and vice versa. However, the NIA-AA criteria allow for a subclassification of persons based on biomarker results within each diagnostic category. Further research is needed to validate the criteria. Modifications are likely to be made before the criteria can be used in daily practice

3 Visser, P. J., Verhey, F., Knol, D. L., Scheltens, P., Wahlund, L. O., Freund-Levi, Y. et al. (2009). Prevalence and prognostic value of CSF markers of Alzheimer's disease pathology in patients with subjective cognitive impairment or mild cognitive impairment in the DESCRIPA study: a prospective cohort study. *Lancet Neurol., 8,* 619-627.
Notes: BACKGROUND: Alzheimer's disease (AD) pathology is common in patients with amnestic mild cognitive impairment (aMCI) without dementia, but the prevalence of AD pathology in patients with subjective cognitive impairment (SCI) and non-amnestic mild cognitive impairment (naMCI) is unknown. AD is characterised by decreased CSF concentrations of Abeta(42) and increased concentrations of tau. We investigated the prevalence of a CSF AD profile in patients with SCI, naMCI, or aMCI and the association of this profile with cognitive outcome in each group. METHODS: Patients with SCI, naMCI, aMCI, and neurologically healthy controls were recruited from 20 memory clinics across Europe, between January, 2003, and June, 2005, into this prospective cohort study. A CSF AD profile was defined as an abnormal ratio of Abeta(42):tau. Patients were assessed annually up to 3 years. Outcome measures were changes in memory, overall cognition, mini-mental state examination (MMSE) score, daily function, and progression to AD-type

dementia. FINDINGS: The CSF AD profile was more common in patients with SCI (31 of 60 [52%]), naMCI (25 of 37 [68%]), and aMCI (56 of 71 [79%]) than in healthy controls (28 of 89 [31%]). The profile was associated with cognitive decline in patients with naMCI (memory, MMSE, and daily function) and in patients with aMCI (MMSE and daily function). In patients with aMCI, a CSF AD profile was predictive of AD-type dementia (OR 26.8, 95% CI 1.6-456.4). INTERPRETATION: AD is a common cause of SCI, naMCI, and aMCI and is associated with cognitive decline in patients with naMCI or aMCI. Patients with SCI might be in the early stages of AD, and cognitive decline might become apparent only after longer follow-up. FUNDING: European Commission; Ana Aslan International Foundation
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4 Visser, P. J. & Knopman, D. S. (2009). Amyloid imaging in the prediction of Alzheimer-type dementia in subjects with amnestic MCI. *Neurology, 73,* 744-745.

5 Visser, P. J. & Verhey, F. R. (2008). Mild cognitive impairment as predictor for Alzheimer's disease in clinical practice: effect of age and diagnostic criteria. *Psychological Medicine, 38,* 113-122.
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BACKGROUND: We investigated whether the predictive accuracy of mild cognitive impairment (MCI) for Alzheimer-type dementia (AD) in a clinical setting is dependent on age and the definition of MCI used. METHOD: Non-demented subjects older than 40 (n=320) who attended a memory clinic of a university hospital were reassessed 5 years later for the presence of AD. MCI was diagnosed according to the criteria of amnestic MCI, mild functional impairment (MFI), ageing-associated cognitive decline (AACD), and age-associated memory impairment (AAMI). The main outcome measure was the area under the curve (AUC) of a receiver operating characteristic (ROC) curve. Analyses were conducted on the entire sample and on subgroups of subjects aged 40-54, 55-69 and 70-85 years. RESULTS: A diagnosis of AD at follow-up was made in 58 subjects. Four of them were in the 40-54 age group, 29 in the 55-69 age group and 25 in the 70-85 age group. The diagnostic accuracy in the entire sample was low to moderately high with AUCs ranging from 0.56 (AACD) to 0.75 (amnestic MCI). A good predictive accuracy with an AUC >0.80 was only observed in subjects aged 70-85 using the criteria of amnestic MCI (AUC=0.84). CONCLUSIONS: The predictive accuracy of MCI for AD is dependent on age and the definition of MCI used. The predictive accuracy is good only for amnestic MCI in subjects 70-85 years. As subjects with prodromal AD are often younger than 70, the usefulness of MCI as predictor of AD in clinical practice is limited

6 Visser, P. J. & Brodaty, H. (2006). MCI is not a clinically useful concept. *International Psychogeriatrics, 18,* 402-409.
Notes: Department of Psychiatry and Neuropsychology, University of Maastricht, Maastricht, The Netherlands. pj.visser@np.unimaas.nl

7 Visser, P. J., Kester, A., Jolles, J., & Verhey, F. (2006). Ten-year risk of dementia in subjects with mild cognitive impairment. *Neurology, 67,* 1201-1207.
Notes: Department of Psychiatry and Neuropsychology, University of Maastricht, Maastricht, The Netherlands. pj.visser@np.unimaas.nl
OBJECTIVE: To investigate the 10-year risk of dementia in subjects with mild cognitive impairment (MCI) ages 40 to 85 years. METHODS: We selected subjects from a memory clinic if they met one of the following definitions of MCI: cognitive complaints (n = 181), aging-associated cognitive decline (AACD) (n = 163), mild functional impairment (n = 86), or amnestic MCI (n = 64). Subjects were reassessed after 2, 5, and 10 years. The risk of dementia was calculated with Kaplan-Meier statistics. Analyses were conducted in the entire sample and in subgroups of subjects aged 40 to 54 years, 55 to 69 years, and 70 to 85 years. RESULTS: The 10-year risk of dementia was 0.27 (95% CI 0.20 to 0.34) in subjects with

cognitive complaints, 0.28 (95% CI 0.21 to 0.35) in subjects with AACD, 0.44 (95% CI 0.32 to 0.56) in subjects with mild functional impairment, and 0.48 (95% CI 0.35 to 0.61) in subjects with amnestic MCI. Ninety-one percent of the demented subjects had probable AD. The risk of dementia increased with increasing age for all MCI definitions ($p < 0.001$). Depending on the MCI definition used, the risk for dementia ranged from 0 to 0.06 in subjects aged 40 to 54 years, from 0.37 to 0.52 in subjects aged 55 to 69 years, and from 0.77 to 1.0 in subjects aged 70 to 85 years. CONCLUSIONS: The majority of subjects with MCI do not progress to dementia at the long term. Age strongly influences the dementia risk. MCI often represents the predementia stage of a neurodegenerative disorder in elderly subjects but rarely in younger subjects

8 Visser, P. J., Scheltens, P., & Verhey, F. R. (2005). Do MCI criteria in drug trials accurately identify subjects with predementia Alzheimer's disease? *Journal of Neurology, Neurosurgery and Psychiatry, 76,* 1348-1354.
Notes: Department of Psychiatry, University Hospital Maastricht and Alzheimer Centre Limburg, Maastricht, Netherlands. pj.visser@np.unimaas.nl
BACKGROUND: Drugs effective in Alzheimer-type dementia have been tested in subjects with mild cognitive impairment (MCI) because these are supposed to have Alzheimer's disease in the predementia stage. OBJECTIVES: To investigate whether MCI criteria used in these drug trials can accurately diagnose subjects with predementia Alzheimer's disease. METHODS: MCI criteria of the Gal-Int 11 study, InDDEx study, ADCS memory impairment study, ampakine CX 516 study, piracetam study, and Merck rofecoxib study were applied retrospectively in a cohort of 150 non-demented subjects from a memory clinic. Forty two had progressed to Alzheimer type dementia during a five year follow up period and were considered to have predementia Alzheimer's disease at baseline. Outcome measures were the odds ratio, sensitivity, specificity, and positive and negative predictive value. RESULTS: The odds ratio of the MCI criteria for predementia Alzheimer's disease varied between 0.84 and 11. Sensitivity varied between 0.46 and 0.83 and positive predictive value between 0.43 and 0.76. None of the criteria combined a high sensitivity with a high positive predictive value. Exclusion criteria for depression led to an increase in positive predictive value and specificity at the cost of sensitivity. In subjects older than 65 years the positive predictive value was higher than in younger subjects. CONCLUSIONS: The diagnostic accuracy of MCI criteria used in trials for predementia Alzheimer's disease is low to moderate. Their use may lead to inclusion of many patients who do not have predementia Alzheimer's disease or to exclusion of many who do. Subjects with moderately severe depression should not be excluded from trials in order not to reduce the sensitivity

9 Visser, P. J., Verhey, F. R., Ponds, R. W., & Jolles, J. (2001). Diagnosis of preclinical Alzheimer's disease in a clinical setting. *International Psychogeriatrics, 13,* 411-423.
Notes: Department of Psychiatry and Neuropsychology, University of Maastricht, The Netherlands. pj.visser@np.unimaas.nl
INTRODUCTION: The aim of the study was to investigate whether the preclinical stage of Alzheimer's disease (AD) can be diagnosed in a clinical setting. To this end we investigated whether subjects with preclinical AD could be differentiated from subjects with nonprogressive mild cognitive impairment and from subjects with very mild AD-type dementia. METHODS: Twenty-three subjects with preclinical AD, 44 subjects with nonprogressive mild cognitive impairment, and 25 subjects with very mild AD-type dementia were selected from a memory clinic population. Variables that were used to differentiate the groups were demographic variables, the Mini-Mental State Examination score, performance on cognitive tests, measures of functional impairment, and measures of noncognitive symptomatology. RESULTS: Age and the scores for the delayed recall task could best discriminate between subjects with preclinical AD and subjects with nonprogressive mild cognitive impairment. The overall accuracy was 87%. The score on the Global Deterioration Scale and a measure of intelligence could best discriminate between subjects with preclinical AD and subjects with very mild AD-type dementia. The overall accuracy was 85%. CONCLUSIONS: Subjects with preclinical AD can be distinguished from subjects with

nonprogressive mild cognitive impairment and from subjects with very mild AD-type dementia. This means that preclinical AD is a diagnostic entity for which clinical criteria should be developed

10 Visser, P. J., Verhey, F. R., Ponds, R. W., Kester, A., & Jolles, J. (2000). Distinction between preclinical Alzheimer's disease and depression [see comments]. *Journal of the American Geriatrics Society, 48,* 479-484.
Notes: Department of Psychiatry and Neuropsychology, Institute of Brain and Behavior, University of Maastricht, The Netherlands ; ABSTRACT: OBJECTIVE: To assess the prevalence of depression in subjects with preclinical Alzheimer's disease (AD) and to investigate the possibility of differentiating subjects with preclinical AD and depression from subjects with depression- related cognitive impairment. DESIGN: A prospective, observational cohort study. SETTING: An outpatient memory clinic of a university-affiliated hospital. PARTICIPANTS: Nondemented subjects with cognitive impairment older than 55 years (n = 111) without neurological or somatic causes for the cognitive impairment. MEASUREMENTS: At baseline, data were collected on patient characteristics, the severity of depression, and cognitive functioning. The course of the cognitive impairment and the presence of dementia were assessed after 2 and 5 years. RESULTS: Twenty-five subjects had preclinical dementia with Alzheimer's type dementia at follow-up. Sixty percent of these subjects (n = 15) were depressed at baseline. Subjects with depression and preclinical AD had at baseline a poorer performance on the cognitive tasks and were older than the subjects with depression-related cognitive impairment. Logistic regression with backward step selection selected age and memory performance as the best predictors for Alzheimer's type dementia in the depressed subjects. The specificity of these predictors for the diagnosis of future Alzheimer's type dementia in depressed subjects was 94%, sensitivity was 90%, positive predictive value was 90%, and negative predictive value was 94%. CONCLUSIONS: Depression is common in preclinical AD. Depressed subjects with preclinical AD can be accurately differentiated from subjects with depression-related cognitive impairment by age and the severity of the memory impairment. Research that aims to investigate preclinical AD should not exclude a priori subjects with depression inasmuch as preclinical AD is often accompanied by depression

11 Visser, P. J., Scheltens, P., Verhey, F. R., Schmand, B., Launer, L. J., Jolles, J. et al. (1999). Medial temporal lobe atrophy and memory dysfunction as predictors for dementia in subjects with mild cognitive impairment. *Journal of Neurology, 246,* 477-485.
Notes: Department of Psychiatry and Neuropsychology, Institute of Brain and Behavior, University of Maastricht, The Netherlands ; ABSTRACT: To determine whether the medial temporal lobe is atrophic in subjects with mild cognitive impairment, and whether atrophy of this structure is a better predictor of dementia than memory dysfunction. Forty-five noninstitutionalized subjects aged 65-85 years were randomly selected from a population based study to obtain a sample with Alzheimer's disease (AD; n = 7), and a clinically nondemented sample (n = 38). Twenty of the latter subjects displayed some cognitive impairment and fulfilled CAMDEX criteria for "minimal dementia." Coronal T1-weighted magnetic resonance imaging was used to visualize the medial temporal lobe. The volume of the parahippocampal gyrus and hippocampus was measured, and medial temporal lobe atrophy was assessed qualitatively. The memory subscore from the CAMCOG was used as a measure of memory functioning. The follow-up period was 3 years. Nine subjects who were diagnosed as being minimally demented at baseline met the criteria for AD during follow-up. At baseline the volume of the parahippocampal gyrus of these subjects was smaller than that of the other subjects with minimal dementia. The memory score was the best predictor of clinical outcome. All medial temporal lobe measures increased the accuracy of prediction compared with only the memory score, by reducing the number of false-negative classifications of dementia. Severe medial temporal lobe atrophy is present even in some subjects with mild cognitive impairment and is an indicator of subsequent AD. The absence of medial temporal lobe atrophy, however, does not exclude the development of dementia. In the majority of subjects memory impairment was a better predictor of dementia than atrophy

of the medial temporal lobe. The combination of the two increased predictive accuracy. Nondemented subjects with severe atrophy of the medial temporal lobe could be enrolled in drug trials aimed at slowing the progression of AD