



UNIVERSITY OF GOTHENBURG

RESULTS FROM THE H70 STUDY

- I. The Flynn effect: how secular changes influence the predictive value of cognitive performance in dementia
- &
- II. The potential role of conventional CT brain imaging in prodromal dementia

Simona Sacuiu

Sahlgrenska University Hospital, Sahlgrenska Academy
Institute of Neuroscience and Physiology, University of Gothenburg
Gothenburg, Sweden

NO CONFLICTS TO DISCLOSE

The Sahlgrenska Academy

AIMS OF THE STUDIES

I. Characterize secular trends in cognitive performance across cohorts in relation to the development of dementia

II. Investigate the association of subjective cognitive symptoms with structural brain changes according to computer tomography in the preclinical stage of dementia

WE KNOW THAT...

- Successive birth cohorts improved their performance in cognitive tests over the past century

Flynn JR. *The mean IQ of Americans: Massive gains 1932 to 1978*. Psychological Bulletin 1984

Flynn JR. *The Discovery of IQ gains over time*. American Psychologist 1999

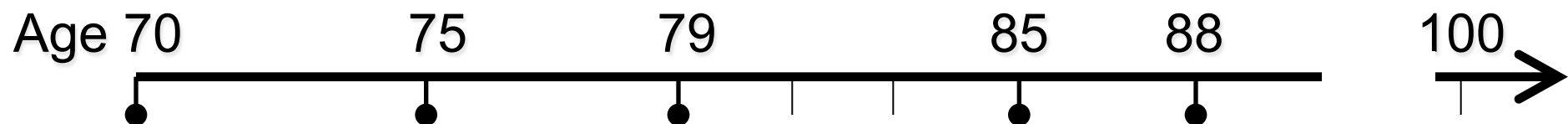
Schaie KW. *An Historical Framework for Control Differences in Intelligence*. Res. Hum Dev 2005

- The prodromal stage of dementia is characterized by mild cognitive impairments in amnestic and non-amnestic domains defined according to performance in psychometric tests

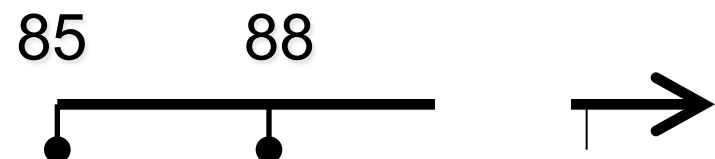
HOWEVER... It is not clear whether the secular cognitive trends influence the expression of prodromal mild cognitive impairments

STUDY DESIGN H70 STUDY

Cohort born 1901-02



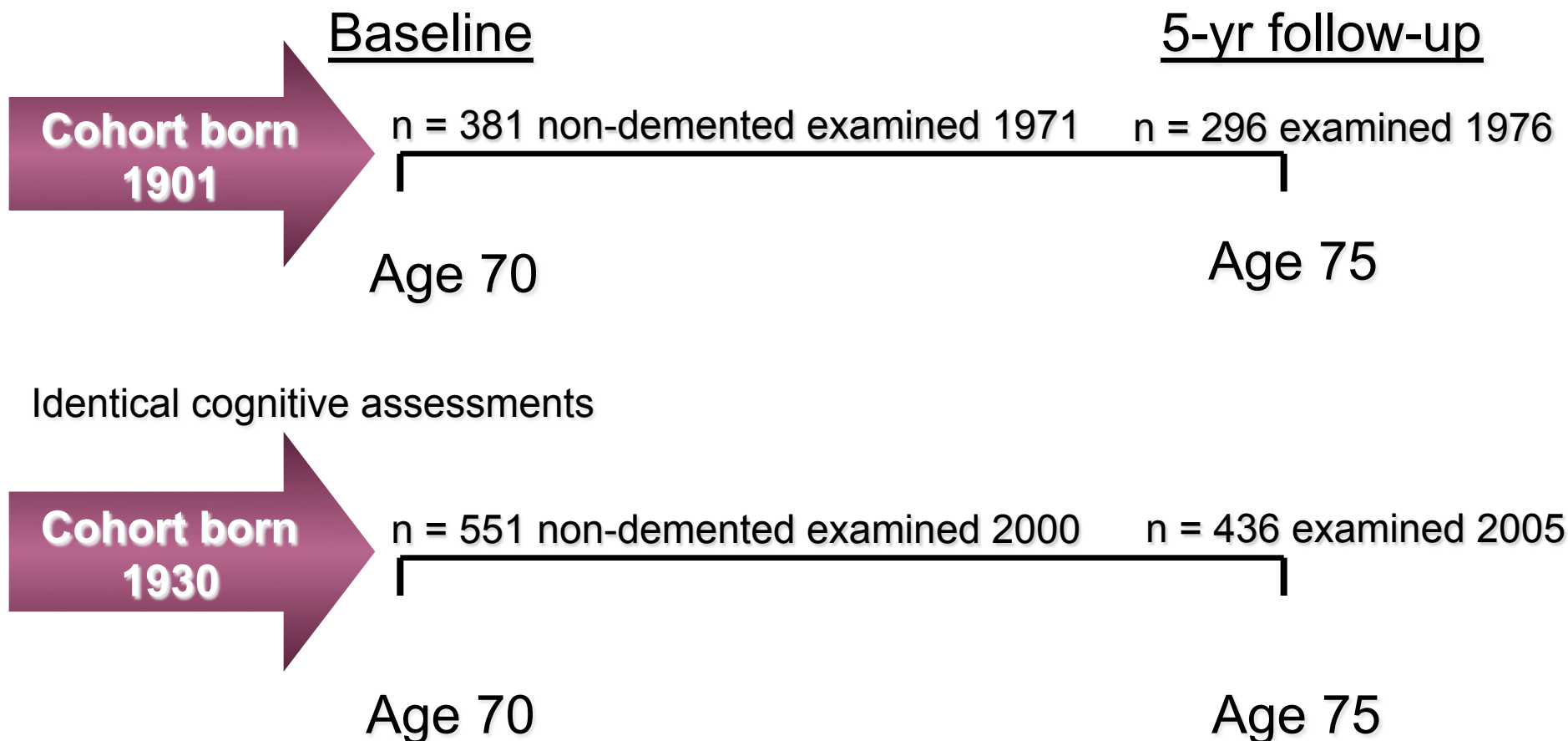
Extended cohort born 1901-02



Cohort born 1930



STUDY DESIGN I



INFORMATION ON COGNITION

● **Non-amnestic domains using psychometric tests**

Acc. Dureman and Sälde (1959) based on Thurstone's primary mental abilities; continuous scales

Synonym Test - verbal ability

Figure Classification - reasoning ability

Block Design - spatial constructional ability

Identical Forms - perceptual speed

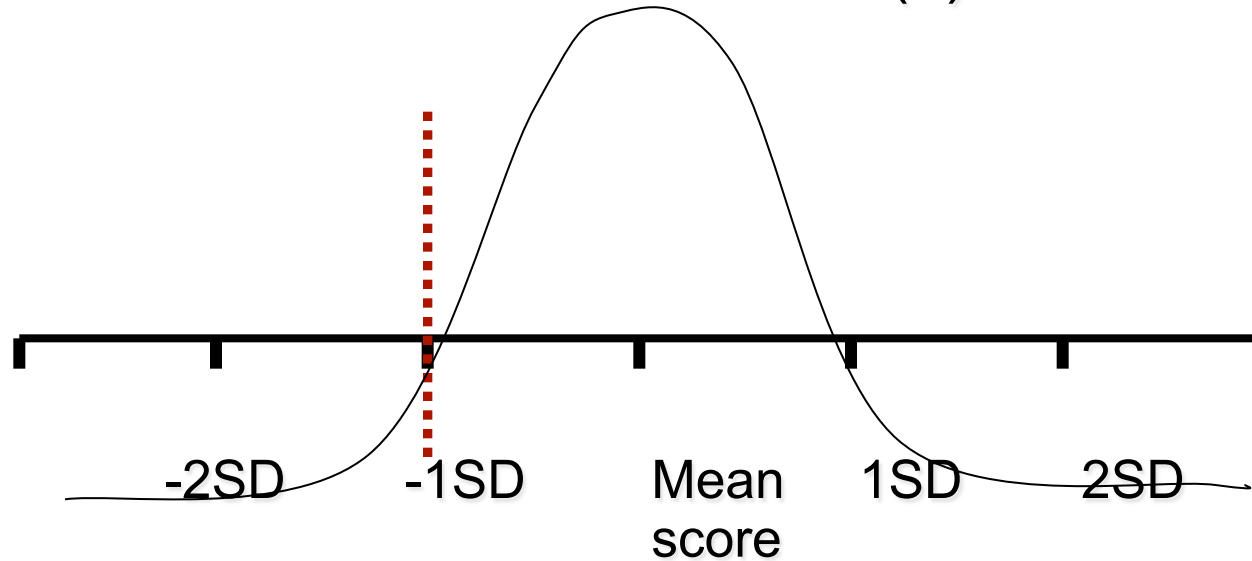
Digit Span (forward and backward) – short-term memory/ attention

● **Recent memory using psychiatric examination**

Global assessment of short-term/working memory and memory for recent events according to a comprehensive psychiatric examination rated on a symptom severity scale (nominal scale)

CUT-OFF USING PSYCHOMETRIC TESTS

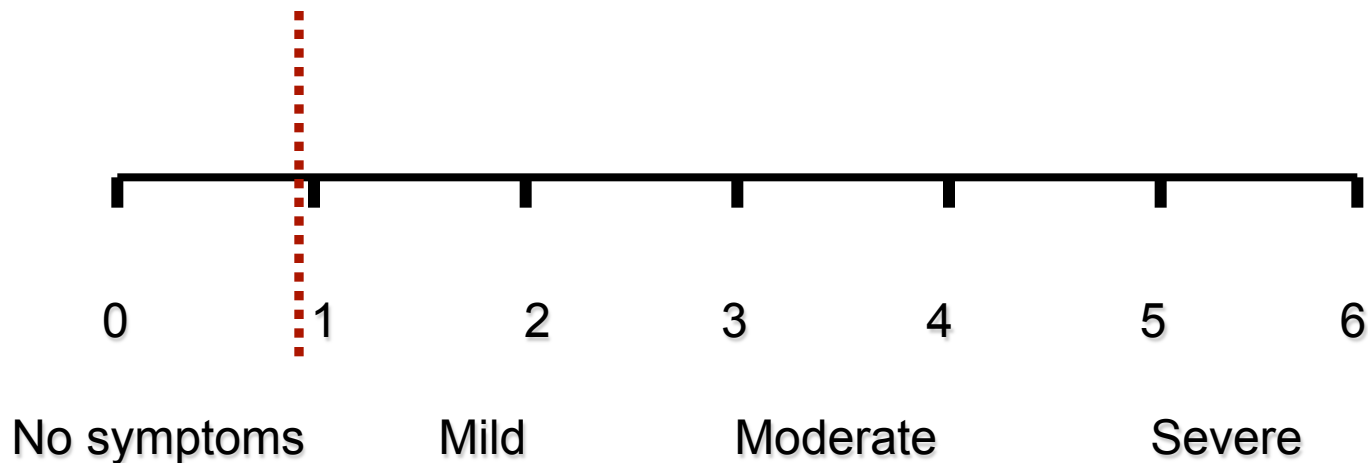
CONTINUOUS SCORE minimum (0) to maximum



LOW PERFORMANCE

CUT-OFF USING OBSERVED RECENT MEMORY ACCORDING TO THE PSYCHIATRIC EXAM.

SYMPTOM SEVERITY SCALE



LOW PERFORMANCE

DEMENTIA DIAGNOSIS

In participants

- COHORT 1901 dementia was defined as severe disorientation for time and place or severe memory impairment (Kay, Roth & Beamish 1964)
- COHORT 1930 dementia was diagnosed according to both the historical criteria and the DSM-III-R: observed agreement kappa 0.807

In those lost to follow-up

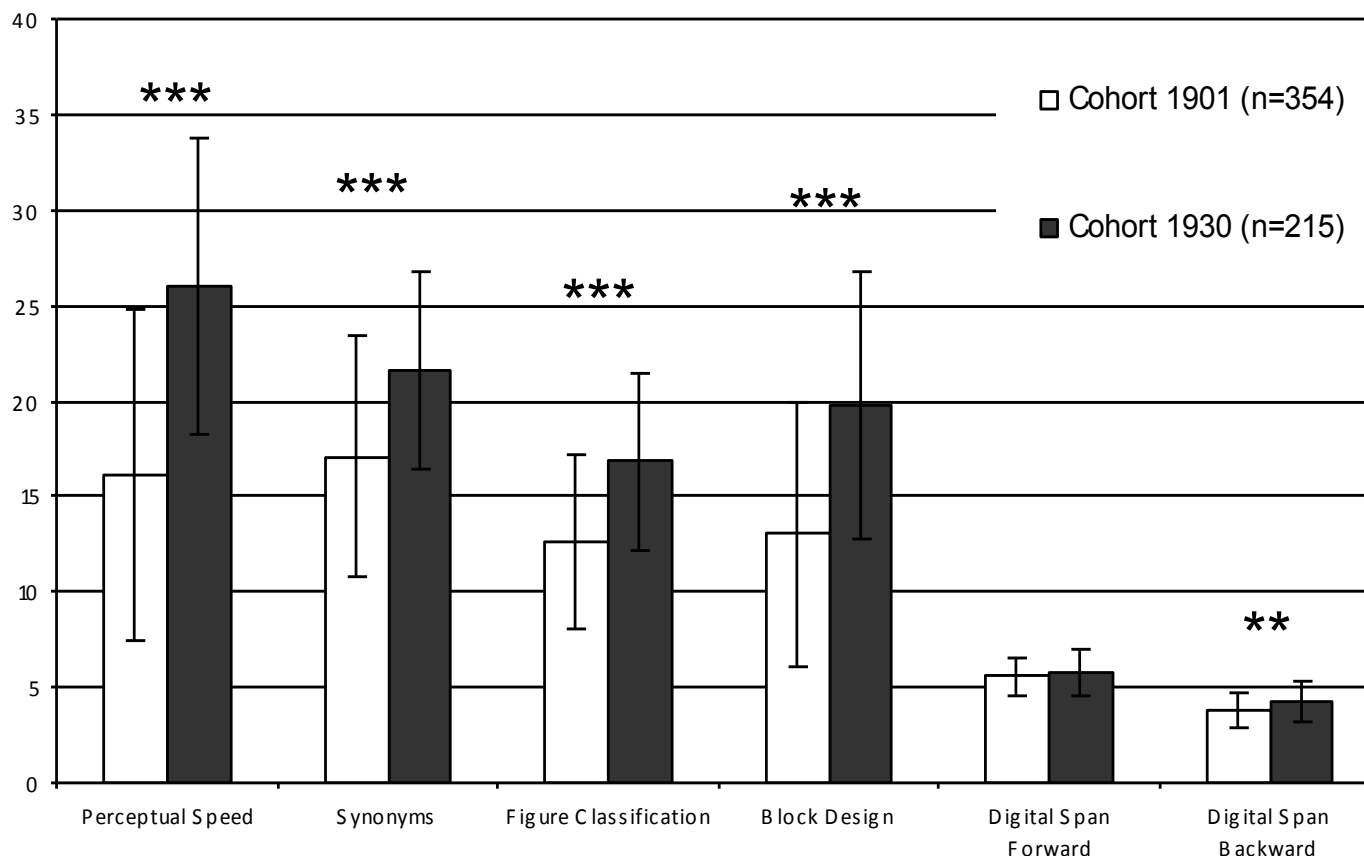
- Medical records had to reveal cognitive impairment at a level that affected ADL

DEMOGRAPHIC CHARACTERISTICS

	COHORT 1901-02	COHORT 1930	P-value
<i>AGE 70 YRS BASELINE</i>	n=381	n=564	
Women n (%)	221 (58.0)	337 (59.8)	0.637
More than compulsory education n (%)	53 (14.1)	218 (39.1)	<0.001
Depression n (%)	22 (5.8)	50 (8.9)	0.082
<i>AGE 75 YRS FOLLOW-UP</i>			
Participants	296 (77.7)	436 (77.3)	0.937
Women	183 (61.8)	274 (62.8)	0.816
More than compulsory education n (%)	44 (15.1)	183 (42.2)	<0.001
Deceased	60 (15.7)	24 (4.3)	<0.001
Refusals	25 (6.6)	91 (16.1)	<0.001
Moved		13 (2.3)	
Incident dementias	19 (5.0)	24 (4.4)	0.751

Sacuiu et al. Neurology 2010

Secular changes in mean scores in psychometric tests in non-demented 70-year-olds born 30 years apart



***P < 0.001, ** P < 0.01 using ANCOVA with sex and education as covariates

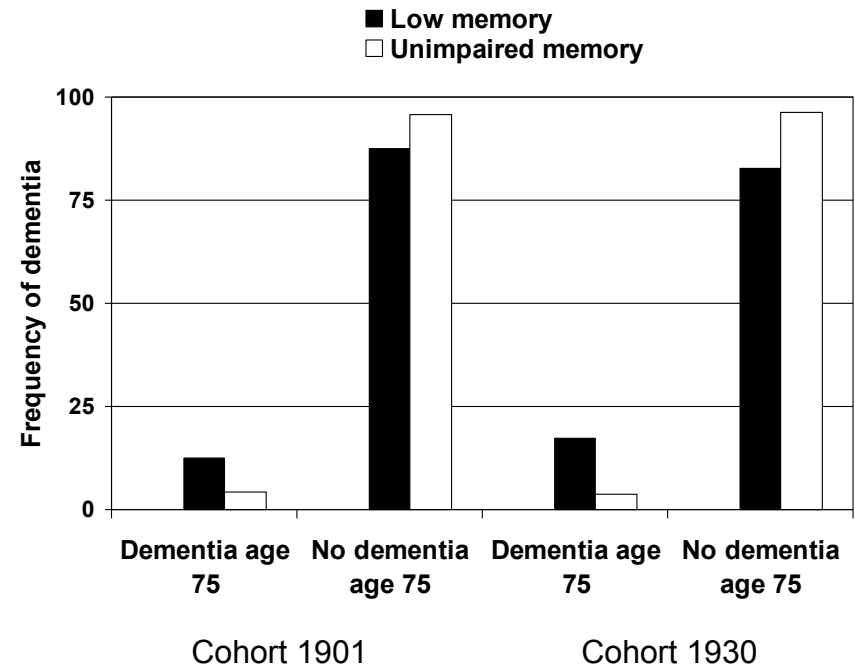
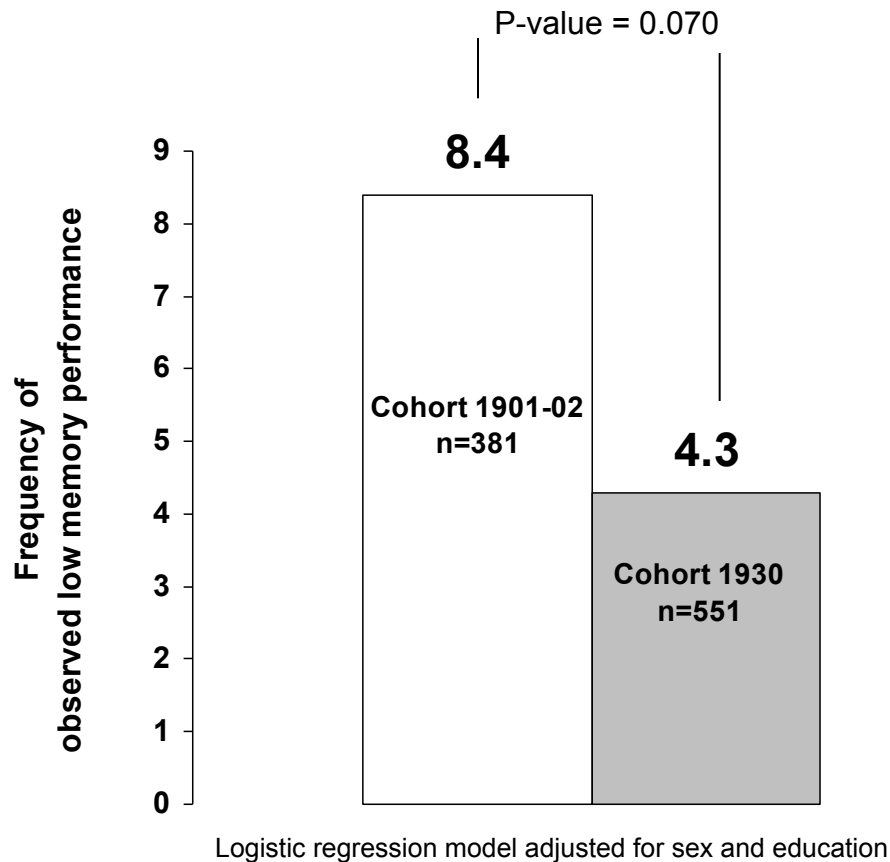
COGNITIVE PERFORMANCE AT AGE 70 RELATED TO DEVELOPMENT OF DEMENTIA BY AGE 75

Psychometric test age 70	COHORT 1901		COHORT 1930	
	No dementia age 75	Dementia age 75 (n=18)	No dementia age 75	Dementia age 75 (n=12)
	mean \pm SD	mean \pm SD	mean \pm SD	mean \pm SD
Perceptual speed	16.5 \pm 8.6	11.3 \pm 8.1*	26.3 \pm 7.6	23.7 \pm 8.8
Synonyms	17.2 \pm 6.3	14.9 \pm 7.8	21.8 \pm 5.1	18.8 \pm 7.1
Figure Classification	12.7 \pm 4.6	10.7 \pm 4.4*	17.1 \pm 4.5	16.7 \pm 4.6
Block Design	13.3 \pm 6.9	9.3 \pm 7.5*	19.9 \pm 7.0	19.2 \pm 6.6
Digits Forward	5.6 \pm 1.0	5.7 \pm 1.0	5.9 \pm 1.2	5.2 \pm 1.0
Digits Backward	3.8 \pm 1.0	3.7 \pm 0.6	4.3 \pm 1.1	3.8 \pm 1.2

Mean score differences between those who did or did not develop dementia within each cohort were tested with ANCOVA (covariates sex and education) * $p < 0.05$

Sacuiu et al. Neurology 2010

Secular changes in low performance in recent memory according to the psychiatric examination



Sacuiu et al. Neurology 2010

BIRTH COHORT DIFFERENCES IN COGNITIVE PERFORMANCE AT AGE 70 RELATED TO DEVELOPMENT OF DEMENTIA BY AGE 75

	COHORT 1901			COHORT 1930		
	Unimpaired Total n (dementia)	Low performance Total n (dementia)	Adjusted OR (95% CI)	Unimpaired Total n (dementia)	Low performance Total n (dementia)	Adjusted OR (95% CI)
<u>Psychometric tests age 70</u>						
Perceptual speed	148 (6)	32 (5)	4.4 (1.2 – 15.6)	179 (9)	34 (3)	1.7 (0.4 – 7.0)
Synonyms	293 (12)	59 (6)	3.1 (1.1 - 9.0)	162 (9)	33 (3)	1.2 (0.3 – 4.9)
Figure Classification	286 (11)	68 (7)	3.4 (1.2 - 9.7)	177 (11)	35 (1)	0.3 (0.04-2.7)
Block Design	138 (6)	39 (5)	3.8 (1.03 - 13.8)	177 (9)	37 (3)	1.3 (0.3 – 5.1)
<u>Psychiatric exam age 70</u>						
Observed recent memory	348 (15)	32 (4)	3.5 (1.1-11.8)	527 (19)	24 (5)	6.7 (2.2-20.3)

Logistic regression models adjusted for sex and education

Sacuiu et al. Neurology 2010

SUMMARY

1. Incidence of dementia over a 5-yr period was similar in both cohorts of 70-year-olds
2. Non-amnestic psychometric tests predicted dementia in the cohort born 1901-02 but not in the cohort born 30 years later
3. Recent memory observed using psychiatric examination predicted dementia across cohorts

POSSIBLE EXPLANATIONS

1. Changes in the structure of the population with more elderly who survive into their 70s in the later born cohort may explain similar incidence of dementia in the two cohorts
2. Qualitatively better education programs and cognitively demanding occupations in the later born cohort may explain improved cognitive performance compared to the earlier born cohort
3. A larger cognitive reserve in the later born cohort may sustain brain activities in the normal range for a longer period of time. Thus the prodromal stage of dementia may appear compressed and more sensitive tests have to be used

LIMITATIONS STUDY I

1. Small sample size
2. Restricted range of psychometric tests available
3. Low incidence of dementia between ages 70-75 years
4. Methodological issues (differences in education level and drop-out rate between cohorts; quality of the medical records regarding information on dementia between 1970s and 2000s)

Sacuiu et al. Neurology 2010

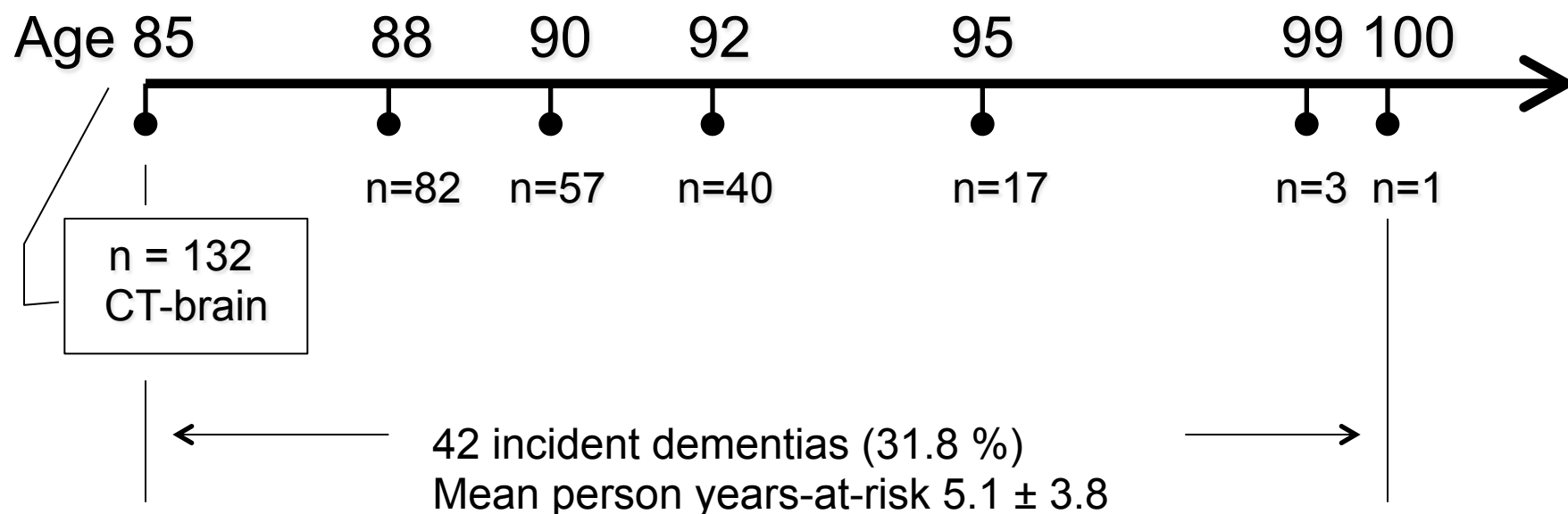
AIMS OF THE STUDIES

I. Characterize secular trends in cognitive performance across cohorts in relation to the development of dementia

II. Investigate the association of subjective cognitive symptoms with structural brain changes according to computer tomography in the preclinical stage of dementia

STUDY DESIGN II

Cohort born 1901-02



INFORMATION ON COGNITION

- **Using self-reports** symptom severity scales (nominal scales)

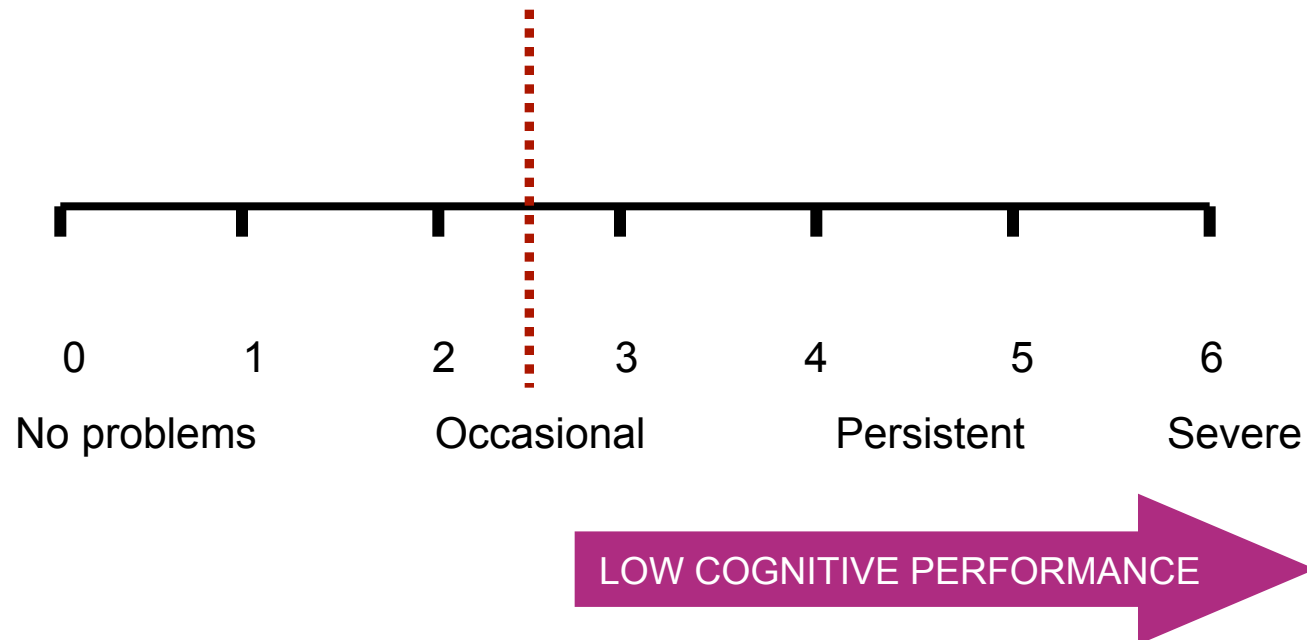
- Memory

“Do you feel your memory is worse compared to earlier in life/compared to your peers?”

- Executive function - concentration, planning, decision making

CLASSIFICATION OF COGNITIVE PERFORMANCE USING SELF-REPORTS

- SELF-REPORTED SYMPTOMS
(memory and executive functions)



BRAIN COMPUTED TOMOGRAPHIES (CT)

- Conventional, structural CT scans w/o contrast enhancement (n=132)
- Classification of structural brain changes (nominal scales)
 - Cortical regional atrophy (frontal, temporal, parietal & occipital)
 - normal
 - mild, moderate or severe
 - White matter lesions (WML) (subcortical and periventricular)
 - no signal attenuation
 - mild, moderate or severe signal attenuation
- Total intracranial volume (TICV) was based on digitized hard copies of the original CT scans analyzed using the US National Institute of Health NIH-IMAGE J program with manual pre-processing

SUBJECTIVE SIGNS ASSOCIATED WITH CT-BRAIN CHANGES

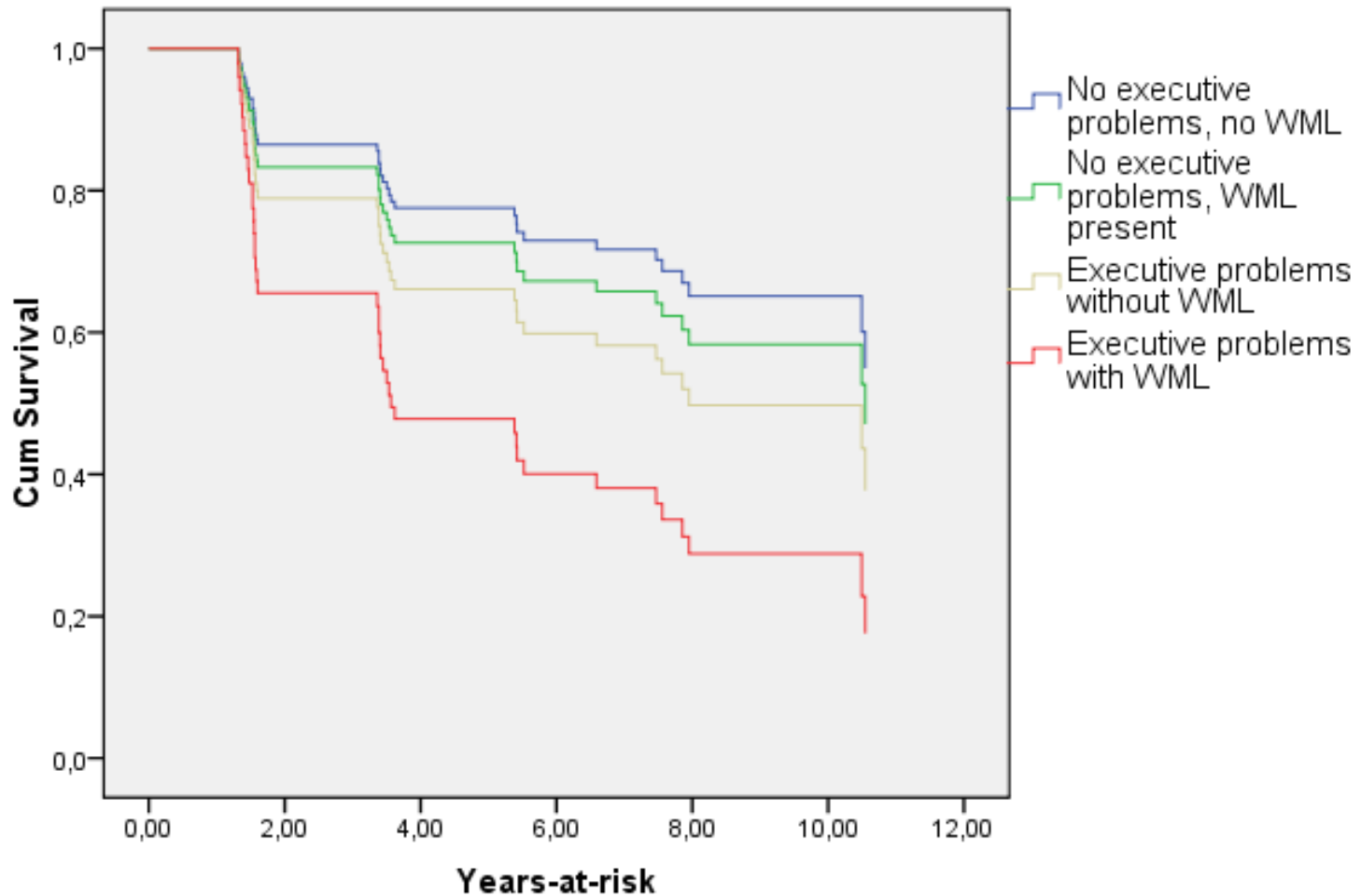
Self-report *OR (95% Confidence Interval)*

	Memory	Executive functions
WML	non-significant	3.2 (1.1-9.4)
Cortical atrophy	non-significant	non-significant

Forward stepwise LR adjusted for total intracranial volume, education, sex and mood disorders

Sacuiu et al. Manuscript

Survival Function for different groups based on self-reported executive functions and WML in relation to dementia at follow-up



Cox regression model adjusted for total intracranial volume, education, sex and mood disorders

Sacuiu et al. Manuscript



UNIVERSITY OF GOTHENBURG

SUMMARY STUDY II

- Preliminary results in a cohort of 85-year-olds show an association between self-reported cognitive symptomatology and white matter lesions detectable by visual inspection of CT brain scans
- There was a trend for increased risk of dementia in individuals reporting cognitive symptoms and having white matter lesions on brain CT
- These findings may contribute to increase the validity of CT brain scans in early detection of dementia in the very old

Neuropsychiatric Epidemiology Unit Institute of Neuroscience and Physiology University of Gothenburg, Sweden

Ingmar Skoog

Margda Waern

Tore Hällström

Deborah Gustafson

Anne Börjesson

Xinxin Guo

Svante Östling

Pia Gudmundsson

Lena Johansson

Stefan Wiktorsson

Madeleine Mellqvist Fässberg

Nils Beckman

Thorsteinn Gislason

Robert Sigström

Helena Hörder

Björn Karlsson

Tina Jacobsson

Kristoffer Bäckman

Eric Joas

Thomas Marlow

Valter Sundh

Margareta Lewander

Helen Lidén

Maria Staaf

Maria Larsson

Birgitta Tengelin Widepalm

Mats Andersson

Vincent Lak

Johan Nilsson

Johan Skoog

Cecilia Mellqvist

Collaborators

Boo Johansson, *Inst. of Psychology,
Univ of Gothenburg, Sweden*

Eric Bigler, *Department of Psychology,
Brigham Young University, Provo, Utah,
USA*