

Rates and Predictors of Progression from Mild Cognitive Impairment to Dementia: The Mayo Clinic Study of Aging

11th Annual Mild Cognitive Impairment Symposium
January 19th, 2013

Rosebud Roberts, M.B. Ch.B., M.S.
Professor of Epidemiology
College of Medicine, Mayo Clinic

Financial Disclosures

Research Funding From:

- NIH
 - U01 AG006786,
 - K01 AG028573
 - R01 AG034676
- Abbot Research Laboratories
- Driskill Foundation

Background Issues on MCI Progression

- Estimates of progression frequently based on prevalent cases
- Limited information on progression in incident cases
- Predictors of MCI progression may differ from predictors of incidence
- Limited insights on outcomes in MCI cases who revert to normal

Learning Objectives

- To understand the rates of MCI progression to dementia
- Gain insight into rates of MCI reversion to normal
- Gain insight into the predictors of progression and reversion

Mayo Clinic Study of Aging Objectives

- Estimate prevalence and incidence of MCI
- Identify risk factors for MCI
- Identify predictors of MCI progression to dementia

Mayo Clinic Study of Aging

- Prospective, population-based study
- Sampling frame: Olmsted County, MN
 - Rochester Epidemiology Project (REP)
 - 70-89 years old
 - Index Date: October 1, 2004
- Target population: 9,953
 - Randomly Selected: 5,233
- Stratified sampling by:
 - Age (70-79 years, 80-89 years)
 - Gender

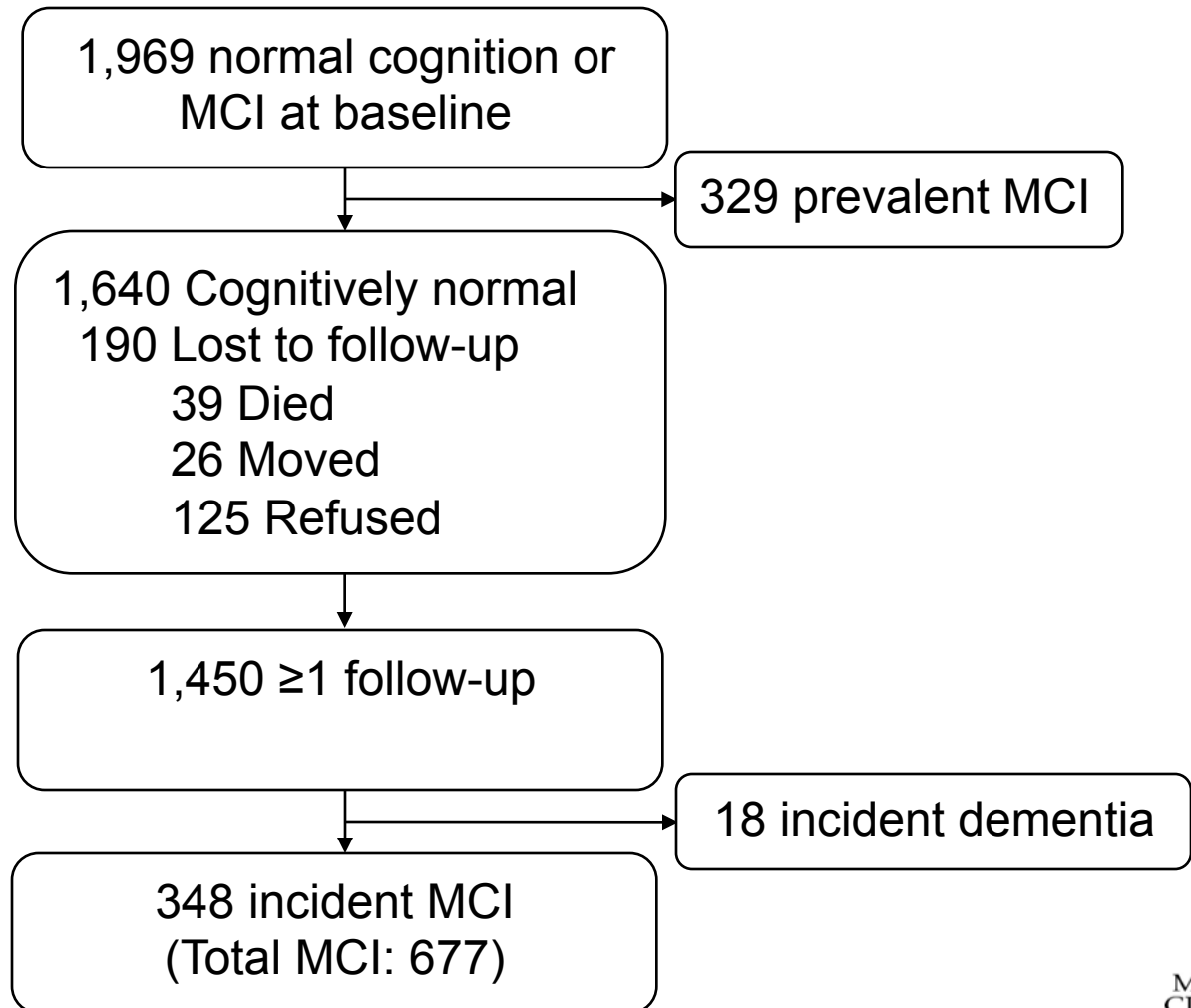
Study Protocol

- Nurse interview
 - Memory questions
 - Clinical Dementia Rating
 - Medications
 - Comorbid medical conditions
- Neurological evaluation by physician
- Cognitive testing battery
 - Memory
 - Language
 - Executive Function
 - Visuospatial (WAIS-R)

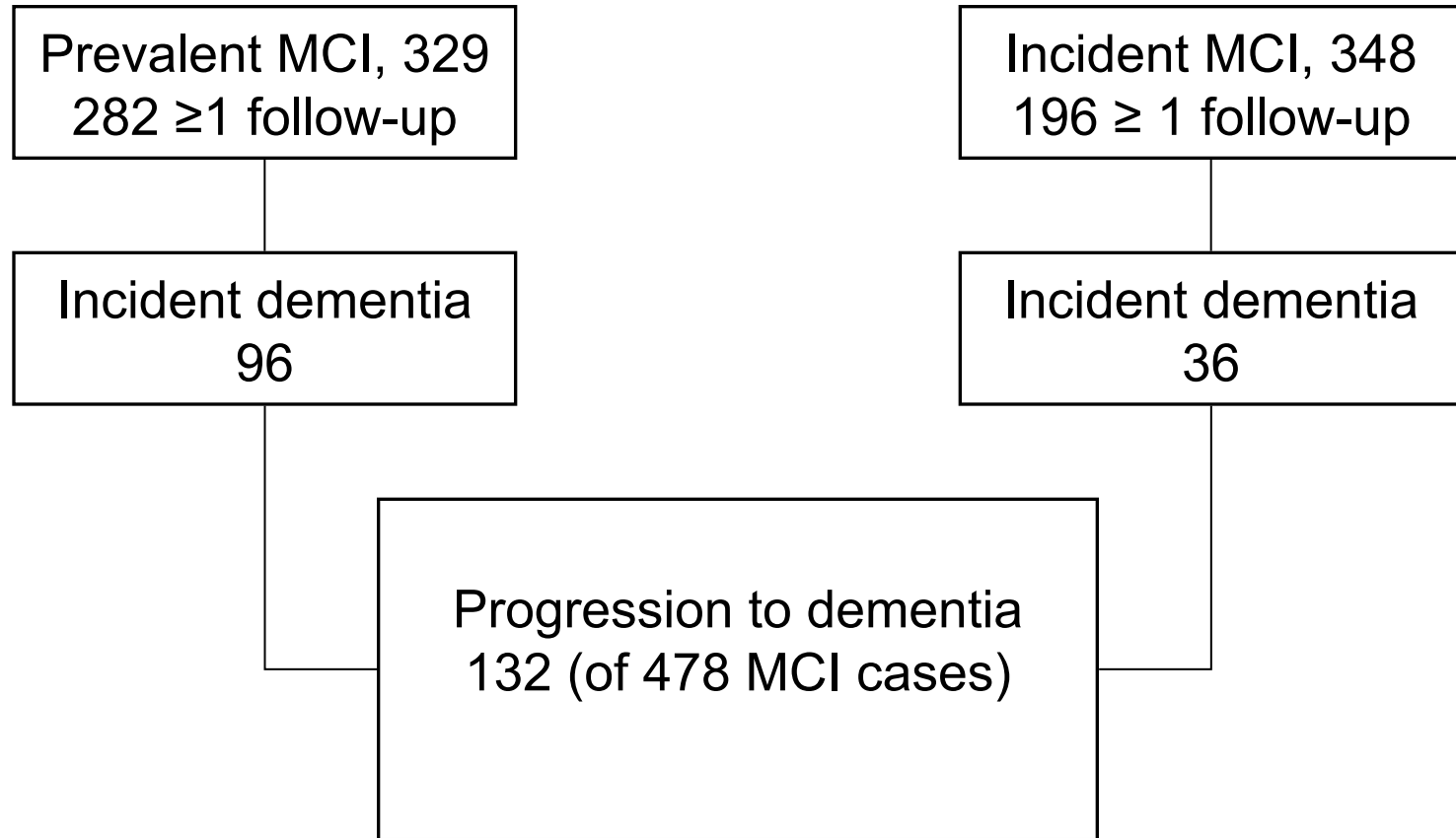
Diagnosis by Consensus

- MCI: Clinical Criteria
 - Cognitive decline or impairment
 - Impairment in ≥ 1 cognitive domains
 - Essentially normal functional activities
 - Absence of dementia
- MCI
 - amnestic vs. non-amnestic
 - Single vs. multiple domain

Study Flow Chart



MCI Progression to Dementia



Characteristics of MCI Subjects*

Characteristics	Prevalent	Incident	Both
N	282	196	478
% ≥ 80, yr	66	72	68
% Men	57	58	58
Education, ≤ 12 yrs	58	55	57
APOE ε4	31	29	30
Moderate exercise [†]	47	58	51
Mean follow-up, yrs	2.8	2.5	2.7

* At diagnosis of MCI

[†] Moderate exercise at least once a week; p < .05

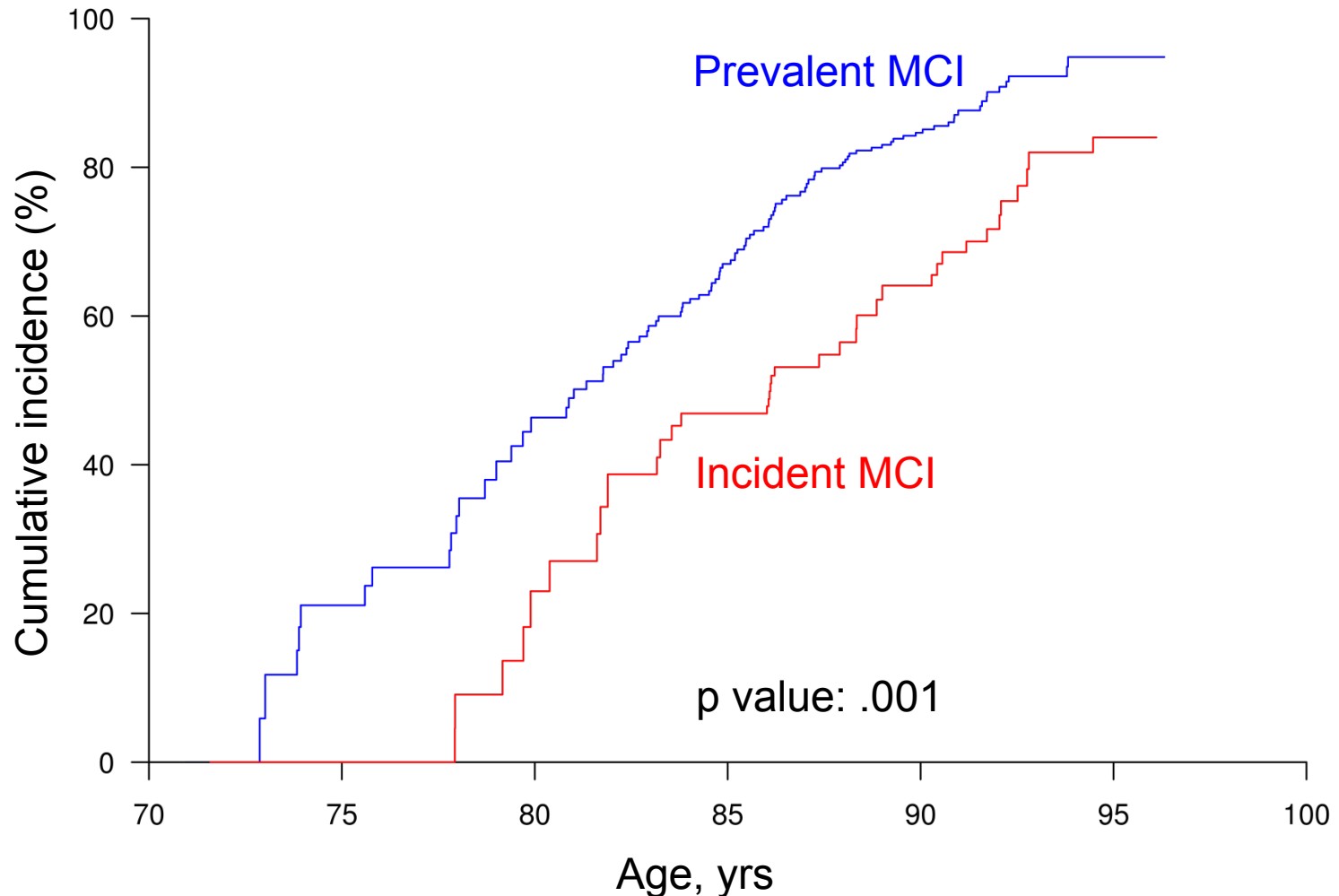
Results

MCI Progression to Dementia

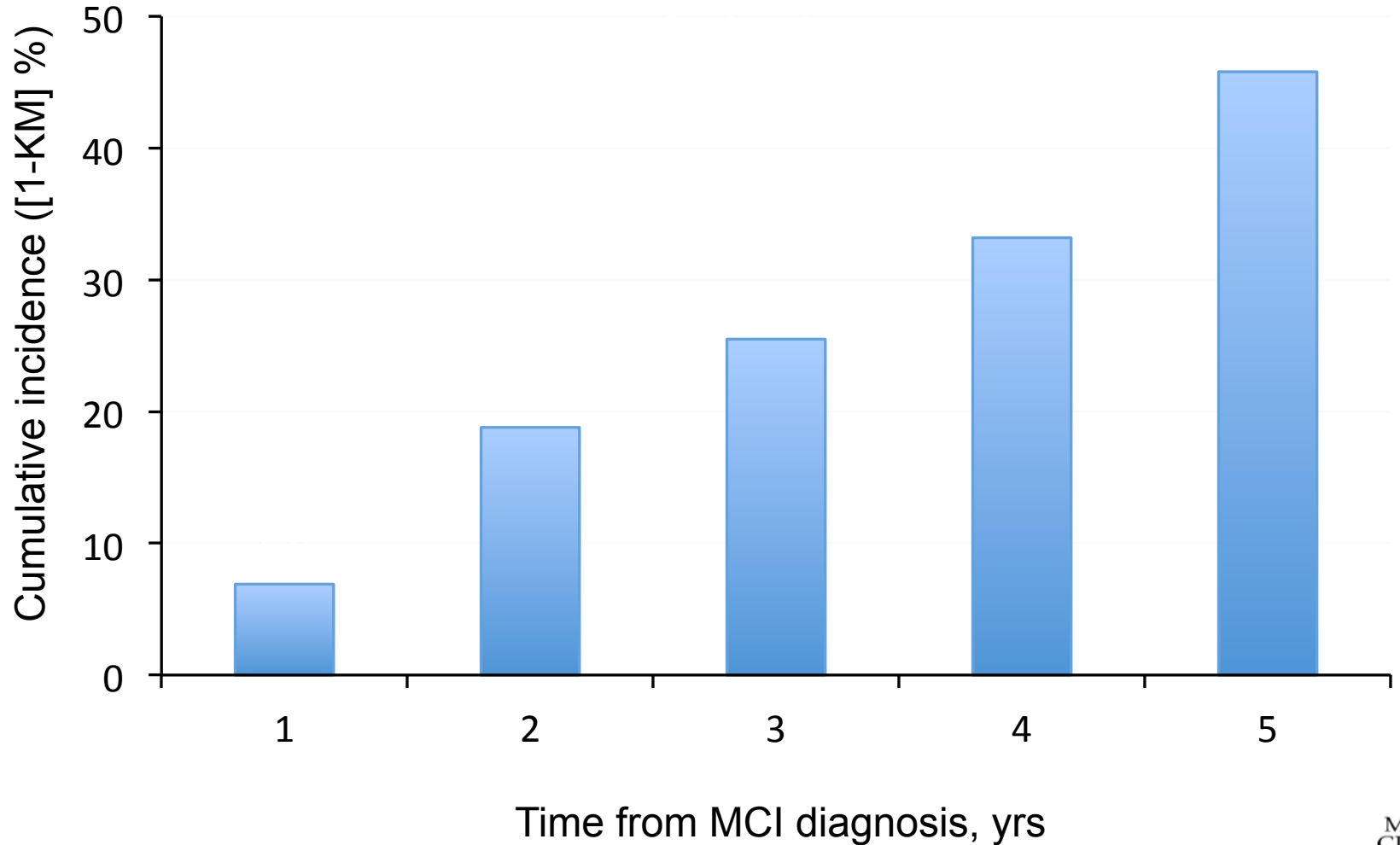
MCI Outcomes

- Transitions
 - 121 (25.3%) progression to dementia without reversion
 - 189 (39.5%) stable MCI
 - 168 (35.2%) ≥ 1 reversion to normal
- Annual progression rates
 - ~10.2% per year in MCI cases
 - < 1% in cognitively normal
- Progression to dementia: MCI vs. normal
 - HR: 21.3 (95% CI, 12.9, 35.2)

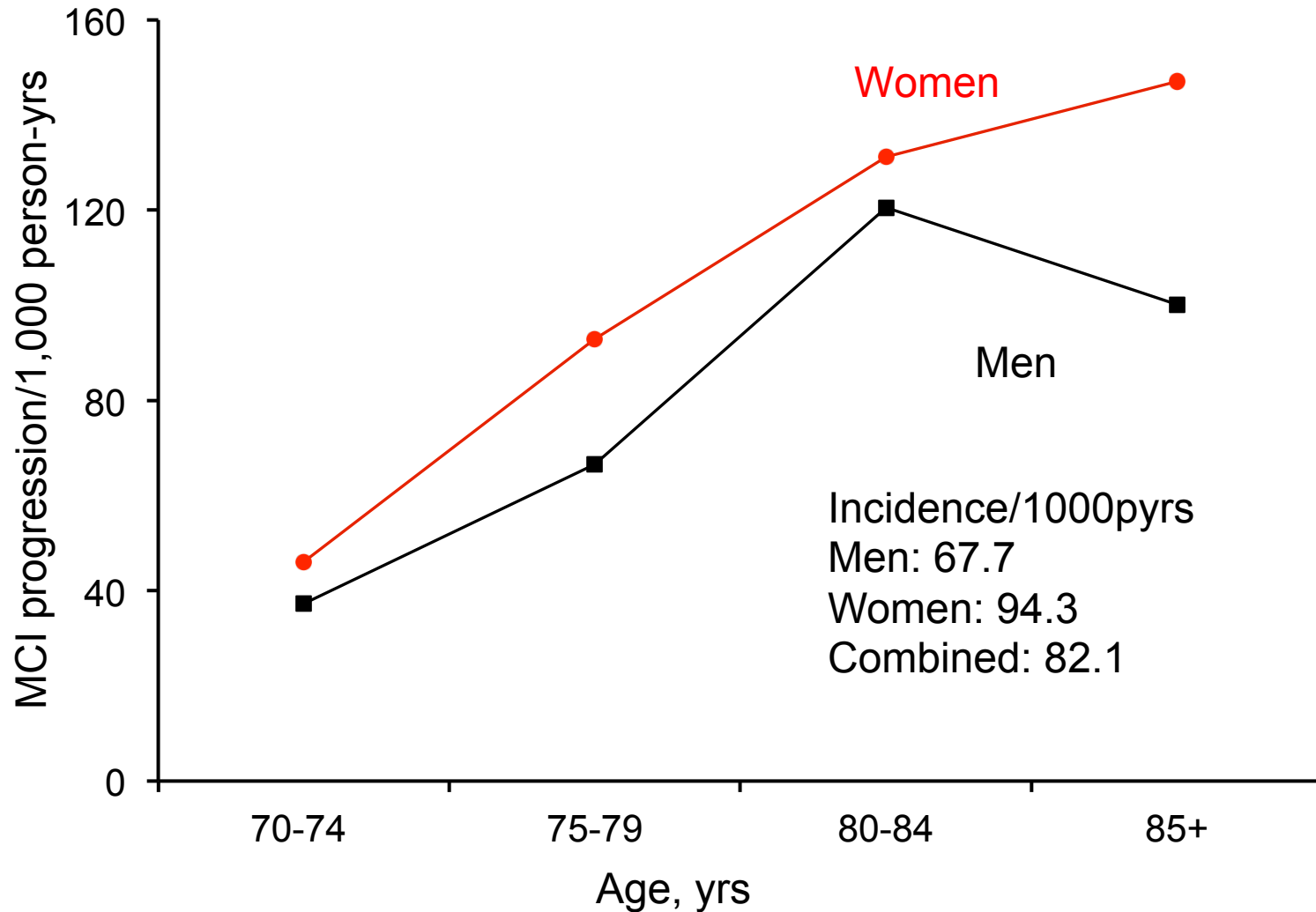
Progression to Dementia: Prevalent and Incident MCI



Probability of Progression Over Time



MCI Progression to Dementia by Age and Sex



Predictors of MCI Progression to Dementia

	HR	95% CI	<i>p</i>
Risk factors			
Slow gait	1.59	1.05, 2.39	.03
Stroke	1.54	1.03, 2.31	.04
Parkinsonism	1.77	1.24, 2.53	.002
APOE ε4	1.38	0.95, 1.98	.09
Subjective memory complaint	1.88	0.92, 3.86	.09
Protective factors			
Moderate exercise	0.66	0.45, 0.97	.04
No association			
Female sex	1.17	0.83, 1.67	0.37

Adjusted for gender and education, age as the time variable

Predictors of MCI Progression by Subtype and Domains

	HR	95% CI	<i>p</i>
MCI Subtype			
aMCI vs. naMCI	1.24	0.83, 1.86	.30
Multi- vs. single domain	1.64	1.15, 2.34	.007

Predictors of MCI Progression to Dementia by Sex

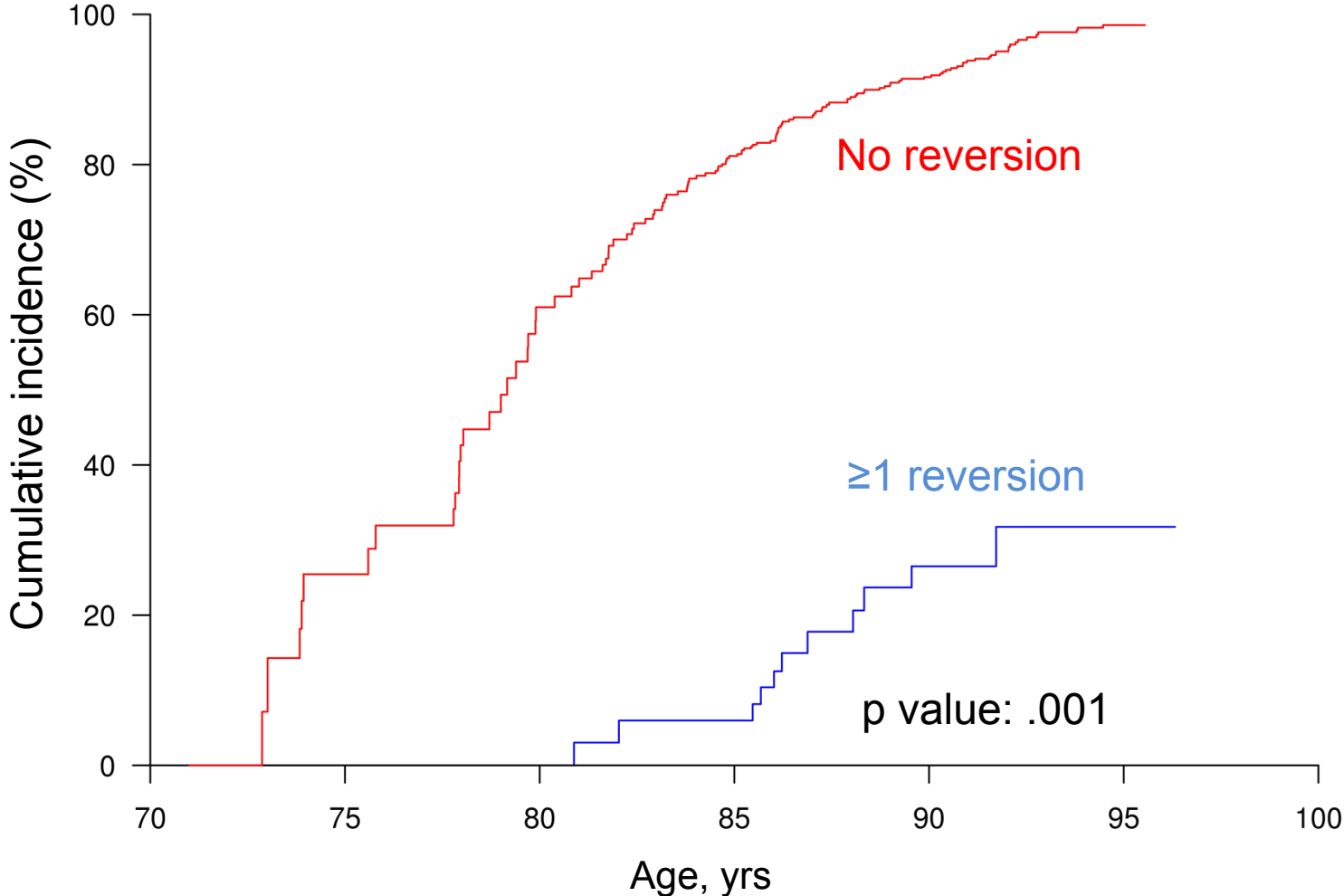
	Men	Women
Factor	HR (95% CI)	HR (95% CI)
Stroke	1.00 (0.54, 1.87)	2.39 (1.38, 4.16)
Slow gait speed	1.43 (0.82, 2.49)	1.87 (0.97, 3.61)
Parkinsonism	1.57 (0.97, 2.54)	1.98 (1.18, 3.32)
FAQ score \geq 10	4.63 (2.20, 9.74)	1.72 (0.77, 3.86)
Moderate exercise	0.55 (0.33, 0.92)	0.88 (0.48, 1.59)
Not married	1.11 (0.66, 1.87)	0.55 (0.32, 0.93)

Progression of MCI to Dementia Neuropsychological Factors

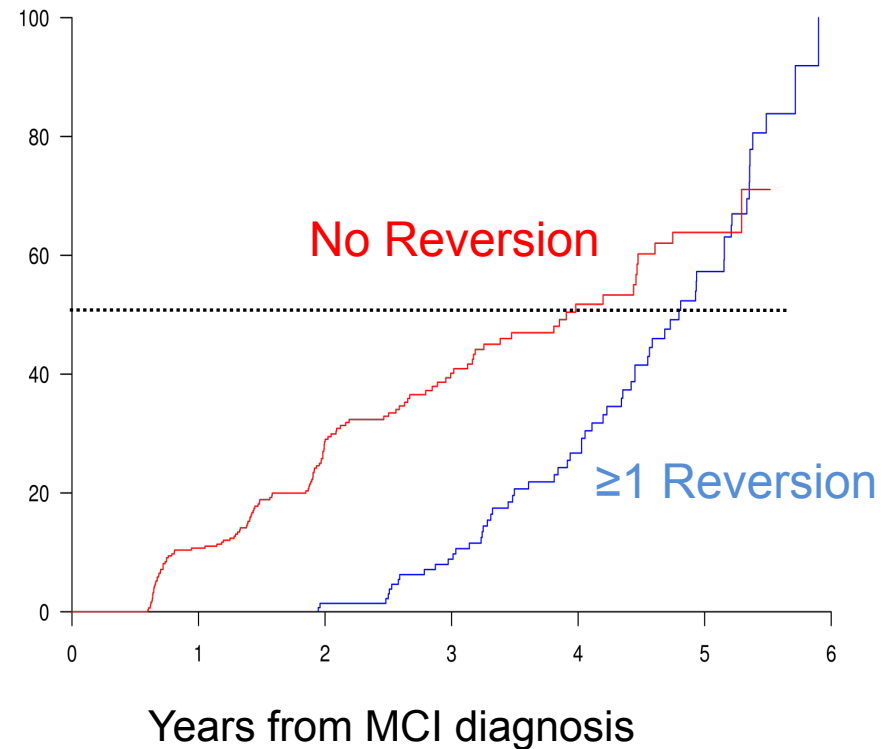
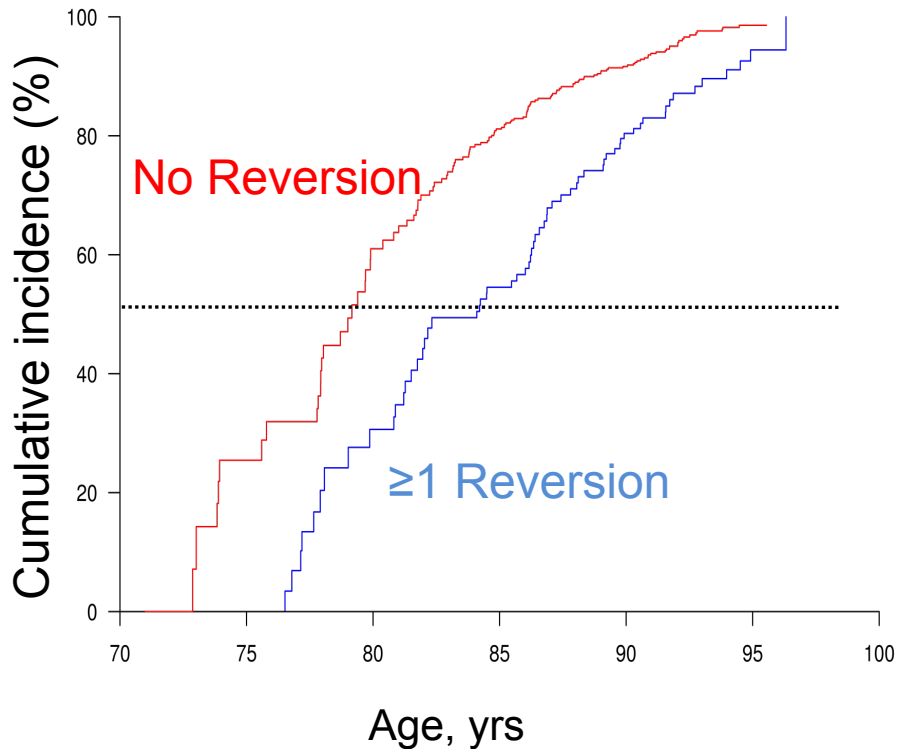
Domain z Scores	HR	95% CI	<i>p</i>
Global domain score \leq -1 SD	2.65	1.69-4.16	<.0001
Language \leq -1 SD	2.20	1.51-3.19	<.0001
Executive function \leq -1 SD	1.76	1.18-2.62	.005
Memory \leq -1 SD	1.74	1.20-2.52	.004
Visuospatial \leq -1 SD	1.74	1.18-2.57	.005

Outcomes Following MCI Reversion to Normal

Progression to Dementia



Outcomes* by Age and Time



No Reversion: outcome is dementia

≥ 1 Reversion: outcome is MCI or dementia

Predictors of Reversion to Normal

	HR	95% CI	<i>p</i>
Increased reversion			
Moderate exercise	1.45	1.03, 2.03	.03
Reduced reversion			
APOE ϵ 4	0.57	0.39, 0.83	.004
Not married	0.69	0.48, 0.99	.04
FAQ score \geq 10	0.24	0.06, 0.98	.05
Depressive symptoms	0.40	0.26, 0.63	<.001
Female sex	0.87	0.63, 1.21	.42
Stroke	0.70	0.45, 1.10	.13
Coronary artery disease	0.80	0.59, 1.10	.17

Reversion by Subtype and Domains

	HR	95% CI	<i>p</i>
Reduced reversion			
aMCI vs naMCI	0.63	0.45, 0.87	.005
Multiple vs. single domain	0.58	0.40, 0.83	.003

Conclusions

- Progression from MCI to dementia is much higher than from normal cognition
- Predictors of MCI progression differ from predictors of incidence
- Multi-domain MCI:
 - Higher risk of progression and lower reversion
 - Suggests greater brain pathology
- Predictors of progression differ from predictor for MCI incidence
- Subjects who revert to normal progress to MCI or dementia in 4-5 years

Acknowledgements

- Dr. Ronald Petersen, PI
- Dr. David Knopman
- Dr. Michele Mielke
- Dr. Yonas Geda
- Dr. Eric Tangalos
- Dr. Bradley Boeve
- Dr. Robert Ivnik
- Ms. Dana Swenson-Dravis
- Alzheimer's Disease Patient Registry Staff
- Study Participants
- National Institute on Aging
- Robert H. & Clarice Smith
- Abigail van Buren Alzheimer's Disease Research Program