If increases in life expectancy continue, more than half of all children born today in developed countries can expect to celebrate their 100th birthdays.

Overview

I. Background of the Oldest Old and The 90+ Study

II. MCI and Dementia: Incidence and Risk Factors

III. Clinical Pathological Correlations

IV. Conclusions
Age-Specific Incidence of Dementia in Studies with Subjects Aged 90+

- Incidence (per 100 person years)
- Age (65 to 100)
- Studies: Munich, Germany, Sydney OPS, Australia, LEILAs75, Germany, CSHA, Canada, Bronx Aging, NY, Cache County, UT, ACT, Seattle WA, MoVIEs, PA, Paquid, France, Kungsholmen, Sweden, Rochester Epi Proj, MN, Rotterdam, Netherlands, Sao Paulo, Brazil
The Relative Frequency of “Dementia of Unknown Etiology” Increases With Age and Is Near 50% in Nonagenarians

- Series of 128 subjects
- Dementia of unknown etiology
  - 5% of all cases dying in their 70’s
  - 21% of all cases dying in their 80’s
  - 48% of all cases dying in their 90’s
Unknown in 90+ Year Olds

- Prevalence and Incidence of Dementia
- Risk/Protective Factors Related to MCI and Dementia
- Types of Dementia
• Insert brief 60 minute segment here
The 90+ Study

Population-based study of aging and dementia in persons aged 90 and older

Leisure World Cohort

13,978

1,931

>90 years

Alive

3,774

>90 years

Deceased

1,071

<90 years

Alive

7,202

<90 years

Deceased

Enrolled

N = 1603

83%
Assessments

- **Intake**
  - Demographics & Medical History
- **Neuropsychological Tests**
  - Memory, language, executive function
- **Neurological Examination**
- **Informant Questionnaires**
- **Genetic studies**
  - DNA and cell lines
- **Brain Donation**
# The 90+ Study Participants Baseline Results

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># of Participants</strong></td>
<td>1603</td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>College grad or more</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>77%</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>95.8</td>
<td></td>
</tr>
<tr>
<td><strong>Type of Residence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nursing or group home</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Home alone</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td><strong>Neurological Exam Cognitive Diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>33%</td>
<td>43%</td>
</tr>
<tr>
<td>Cognitively Impaired, not Demented</td>
<td>26%</td>
<td>33%</td>
</tr>
<tr>
<td>Demented</td>
<td>41%</td>
<td>24%</td>
</tr>
</tbody>
</table>
Age-Specific Incidence of Dementia in Studies with Subjects Aged 90+

Incidence (per 100 person years)

- Munich, Germany
- Sydney OPS, Australia
- LEILAV75, Germany
- CSHA, Canada
- Bronx Aging, NY
- Cache County, UT
- ACT, Seattle WA
- MoVIEWs, PA
- Paquid, France
- Kungsholmen, Sweden
- Rochester Epi Proj, MN
- Rotterdam, Netherlands
- Sao Paulo, Brazil
- 90+ Study, CA

18% per year

Baseline Cognitive Diagnoses in CIND participants of the 90+ Study

- 25% aMCI
- 25% naMCI
- 50% other cognitive impairment
  -- functional losses due to cognition
  -- MMSE < 24
Dementia Incidence in The 90+ Study by Baseline Cognitive Diagnosis follow-up 2.5 years

<table>
<thead>
<tr>
<th>Cognitive Diagnosis</th>
<th>Incidence %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AD</td>
</tr>
<tr>
<td>Normal</td>
<td>5</td>
</tr>
<tr>
<td>Amnestic MCI</td>
<td>31</td>
</tr>
<tr>
<td>Non-amnestic MCI</td>
<td>10</td>
</tr>
<tr>
<td>Other Cognitive Impairment</td>
<td>42</td>
</tr>
<tr>
<td>(MMSE &lt;24, Functional Loss)</td>
<td></td>
</tr>
</tbody>
</table>

Peltz et al. Neurology 2011
Investigations of Risk Factors and Dementia

- Vitamin E (supplementation)
- Vitamin C (diet and supplementation)
- BMI
- Alcohol
- Caffeine
- Activities
- Homocysteine levels
- Thyroid function
- ApoE E4
Vascular Risk Factors and Prevalent Dementia

46%  Hypertension
12%  Coronary Artery Disease
12%  Myocardial Infarction
17%  Congestive Heart Failure
22%  Atrial Fibrillation

Vascular risk factors did not distinguish demented and non-demented participants – except HTN
325 non-demented participants
- 70% women
- Mean age = 94 (90 – 103)
- 137 incident cases

History of hypertension at baseline
- 53% reported a history

Corrada, et al, ICAD 2010
Hypotension and Increased Risk of Dementia

- Gothenburg H-70 & Rotterdam
  - Ruitenberge et al., *Ann Neurol*, 2001

- East Boston Study
  - Morris et al., *Arch Neurol*, 2001

- Bronx Aging Study

- OCTO-Twin Study
Risk of Dementia in Relation to Age of Onset of Hypertension

Adjusted for age & education

M Corrada, et al. AAIC 2014
Blood Pressure & Dementia
Potential Interpretations

1. “Normal” blood pressure may be different for 90+ year olds

2. Elderly torturous cerebral vessels may require increased pressure for adequate perfusion

3. Low blood pressure may be a marker for other diseases

4. Medication effects – ACE-inhibitors, Ca-channel blockers, others

5. Differential medical care
What is Related to Dementia in Oldest-Old?

- \(O_2\) Saturation <93%  
  \[\text{OR}\] 2.3

- Performance Based Physical Function
  - Walk Speed 11.8
  - Hand Grip 5.3

- History of HTN 0.7
The 90+ Autopsy Study

- 342 people enrolled
- 233 have come to autopsy
- Brain sections are both fixed and frozen
- Mean Post-Mortem Interval 4.9 hours
Pathological Diagnoses by Dementia Status

No Dementia (N=76)
- AD Pathology: 42%
- None or Insufficient Pathology: 58%

Dementia (N=90)
- AD Pathology: 60%
- None or Insufficient Pathology: 40%

AD = Intermediate/High NIA Reagan Criteria
The Effect of Multiple Pathologies
Brain Pathologies

Alzheimer’s Plaques & Tangles

Hippocampal Sclerosis

Microinfarct

White Matter Disease
Pathological Diagnoses

- Alzheimer’s (NIA Reagan No-Low vs Interm-High)
- Microinfarcts (0-2 vs 3+)
- Hippocampal Sclerosis (No vs Yes)
- Amyloid Angiopathy (no-mild vs mod-severe)
- Subcortical Arteriosclerotic Leukoencephalopathy (No vs Yes)
- Lewy Bodies (No-brainstem vs limbic-neocortical)
- Macroinfarcts-large & lacunes (0-1 vs 2+)
- Other pathologies (CBD & glioblastoma)
Odds of Dementia For Different Pathologies (vs not having that pathology)

<table>
<thead>
<tr>
<th>Neuropathologies</th>
<th>Odds Ratio (95% CI)</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alzheimer's</td>
<td>2.2</td>
<td>50%</td>
</tr>
<tr>
<td>Microinfarcts</td>
<td>3.7</td>
<td>17%</td>
</tr>
<tr>
<td>Hippocampal Sclerosis</td>
<td>10.7</td>
<td>17%</td>
</tr>
<tr>
<td>Leukoencephalopathy</td>
<td>13.3</td>
<td>8%</td>
</tr>
<tr>
<td>Amyloid Angiopathy</td>
<td>1.9</td>
<td>13%</td>
</tr>
<tr>
<td>Large Infarcts</td>
<td>4.5</td>
<td>4%</td>
</tr>
<tr>
<td>Lewy Body Disease</td>
<td>6.3</td>
<td>4%</td>
</tr>
</tbody>
</table>

N=183 From logistic regression adjusting for age at death and sex
Frequency of Dementia by Number of Pathologies (N=183)

- 0 pathologies: 41%
- 1 pathology: 62%
- 2 pathologies: 93%
- 3 pathologies: 100%

Corrada M (unpub. data)
MMSE Score by Number of Pathologies in people with Dementia

From multiple linear regression adjusting for age at death, sex, and duration of dementia

N=94
Summary

- Remarkable increase in longevity and numbers of oldest-old world-wide
- Risk of MCI and dementia is exceptionally high in these individuals, most likely due to multiple pathologies
- We know little about other pathologies or their risk and protective factors
- Old people are not bad versions of younger people
- More research is needed!
Did you hear? 95 is the new 65!
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