Secular trends in dementia and its risk factors in a Japanese Community: the Hisayama Study

Toshiharu Ninomiya\textsuperscript{a)}, Yutaka Kiyohara\textsuperscript{b)}

\textsuperscript{a)}Center for Cohort Studies, Graduate School of Medical Sciences, Kyushu University
\textsuperscript{b)}Department of Environmental Medicine, Graduate School of Medical Sciences, Kyushu University
Population of Hisayama town

**Location of Hisayama town**

- Kyushu university
- Hisayama town
- Fukuoka city
- Tokyo
- Osaka
- Fukuoka

**Population of Hisayama town**

<table>
<thead>
<tr>
<th>Year</th>
<th>1960</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hisayama town</td>
<td>6,500</td>
<td>8,400</td>
</tr>
<tr>
<td>Japan</td>
<td>93 million</td>
<td>128 million</td>
</tr>
</tbody>
</table>

**Age-distribution**

- **Japan vs. Hisayama town, in 1960 and 2010**
- **Proportions of the residents aged ≥40 years**
  - Japan: 28%
  - Hisayama: 28%
- **Populations of residents aged 40 years**
  - Japan: 57%
  - Hisayama: 55%

**Proportions of labor population by industry**

- **Japan vs. Hisayama town, in 2010**
- **Primary sector**
- **Secondary sector**
- **Tertiary sector**
The Hisayama Study

- Population-based prospective cohort study
- Target population, all residents aged ≥40 years
- Detailed evaluation of all cases of cardiovascular disease, dementia and death
- High participation rate (80%)
- High follow-up rate (over 99%)
- High autopsy rate (75%)

N of Hisayama residents

- 1961 cohort (n=1,618)
- 1974 cohort (n=2,038)
- 1983 cohort (n=2,459)
- 1993 cohort (n=1,983)
- 2002 cohort (n=1,983)
- 2012 cohort (n=3,167)

Survey year

- 1961
- 1974
- 1983
- 1993
- 2002
- 2012

N of Hisayama residents:
- 6,500
- 7,700
- 7,600
- 7,600
- 7,800
- 8,300
Cross-sectional and follow-up surveys of dementia in the Hisayama Study
Hisayama residents, aged ≥65 years

Follow-up surveys: Annual regular health check-ups, medical records, information from local physicians or members of the town’s Health and Welfare office, and autopsy findings.
Trend in prevalence of total dementia
Hisayama residents, aged ≥65 years, unadjusted

Prevalence of total dementia increased with time.

* p for trend < 0.01

Survey year

Prevalence (%)


6.7 5.7 7.1 12.5 17.9

*
**Prevalence of Alzheimer’s disease increased with time.**

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<th></th>
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<tbody>
<tr>
<td>Vascular dementia</td>
<td>2.4%</td>
<td>1.9%</td>
<td>1.7%</td>
<td>3.3%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>1.4%</td>
<td>1.8%</td>
<td>3.4%</td>
<td>6.1%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Other dementia</td>
<td>2.9%</td>
<td>2.1%</td>
<td>1.9%</td>
<td>3.1%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

* P for trend < 0.01

**Subtype of dementia**

- Vascular dementia
- Alzheimer’s disease
- Other dementia
Risks of dementia subtypes in people with late-life or midlife hypertension
Hisayama 668 residents aged 65-79 years (1988-2005) and 534 residents aged 50-64 years (1973-2005), multivariable-adjusted

Hypertension, especially from midlife, is a risk factor for vascular dementia.

Alzheimer’s disease

<table>
<thead>
<tr>
<th>Blood pressure level</th>
<th>Normal</th>
<th>PreHT</th>
<th>Stage 1 HT</th>
<th>Stage 2 HT</th>
</tr>
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<tbody>
<tr>
<td>PreHT: prehypertension, HT: hypertension</td>
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Vascular dementia

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<td>*p&lt;0.05 vs. Normal. **p&lt;0.01 vs. Normal.</td>
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<td></td>
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</tr>
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PreHT: prehypertension, HT: hypertension

Adjusted for age, sex, education level, antihypertensive agent use, diabetes, chronic kidney disease, serum total cholesterol, body mass index, history of stroke, smoking habits, and alcohol intake

Ninomiya T, et. al. Hypertension 58: 22, 2011
Diabetes is a risk factor for Alzheimer's disease.

**Risks of dementia subtypes in people with diabetes**

Hisayama 1,017 residents aged ≥60 years (1988-2003), multivariable-adjusted

Diabetes is a risk factor for Alzheimer's disease.

**Alzheimer’s disease**

<table>
<thead>
<tr>
<th>Glucose tolerance status</th>
<th>Normal</th>
<th>IFG</th>
<th>IGT</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>(559)</td>
<td>(73)</td>
<td>(235)</td>
<td>(150)</td>
</tr>
<tr>
<td>Hazard ratio</td>
<td>1.0</td>
<td>0.6</td>
<td>1.6</td>
<td>2.1</td>
</tr>
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* p<0.05 vs. normal

**Vascular dementia**

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<td>1.4</td>
<td>1.8</td>
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IFG: impaired fasting glycemia, IGT: impaired glucose tolerance

Adjusted for age, sex, education level, hypertension, total cholesterol, body mass index, waist to hip ratio, electrocardiogram abnormalities, history of stroke, smoking habits, alcohol intakes, and physical activity

*Ohara T, et. al. Neurology 77:1126, 2011*
Risk factors and protective factors for dementia
Summaries of the results from the Hisayama Study

**Risk factors**

- Hypertension (from Midlife)
  - *Hypertension* 2011; 58: 22-28
- Diabetes (postprandial hyperglycemia)
  - *Neurology* 2011; 77: 1126-1134
- Smoking *(Submitting)*
- Genetic factors (APOE-ɛ4, PICALM)
  - *Psychiatr Genet* 2012; 22: 290-293

**Protective factors**

- Japanese diet + Milk (or dairy consumption)
- Exercise *(Submitting)*
Elucidating the etiology of dementia and establishing its preventive strategies

Establishing a large scale, multisite cohort study for dementia in Japan

Target population: 10,000 community-dwelling residents aged ≥65 years

Baseline survey (in 5-6 sites)

- Screening of dementia and depression
  - First: Neuropsychological tests
  - Second: Diagnosis by psychiatrists
- Questionnaires
  - Medical history, family history, medication, smoking, drinking, diet, exercise, etc.
- Physical examinations
  - Height, weight, blood pressure, etc.
- Blood tests
  - Lipid, kidney function, blood sugar, etc.
- Blood samples
  - Serum, DNA
- Imaging
  - Brain MRI/CT

Follow-up survey

Outcomes
- Dementia, depression, cardiovascular disease and death

Omics data
- Genome
- Metabolome

Elucidating the etiology of dementia and establishing its preventive strategies
Age-specific prevalence of Alzheimer’s disease increased with time in individuals aged 75-79 years and 80 years or older.

Trends in age-specific prevalence of total dementia and Alzheimer's disease
Hisayama residents, aged ≥65 years, unadjusted