Association between plasma 25-hydroxyvitamin D concentration and incident disabling dementia risk in Japan: a case-cohort study

Yukai Lu

Division of Cohort Research, Institute for Cancer Control,

National Cancer Center Japan

I have no conflict of interest to report in relation to this presentation.

September 26, 2024

WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024

国立研究開発法人
国立がん研究センター
National Cancer Center Japan

PHC STUDY

Backgrounds

- Vitamin D may play a **neuroactive** role, possibly involved in the **pathogenesis of Alzheimer's disease**.
- **Lower** circulating 25-hydroxyvitamin D (25[OH]D) concentration (indicator of vitamin D level) is associated with dementia risk factors, such as **hypertension, stroke, and diabetes.**
- Previous cohort studies have shown **mixed results** regarding 25(OH)D and dementia risk.

Aim: To investigate the association between **plasma 25(OH)D concentration and incident dementia risk** among Japanese adults

国立研究開発法人
国立がん研究センター
National Cancer Center Japan

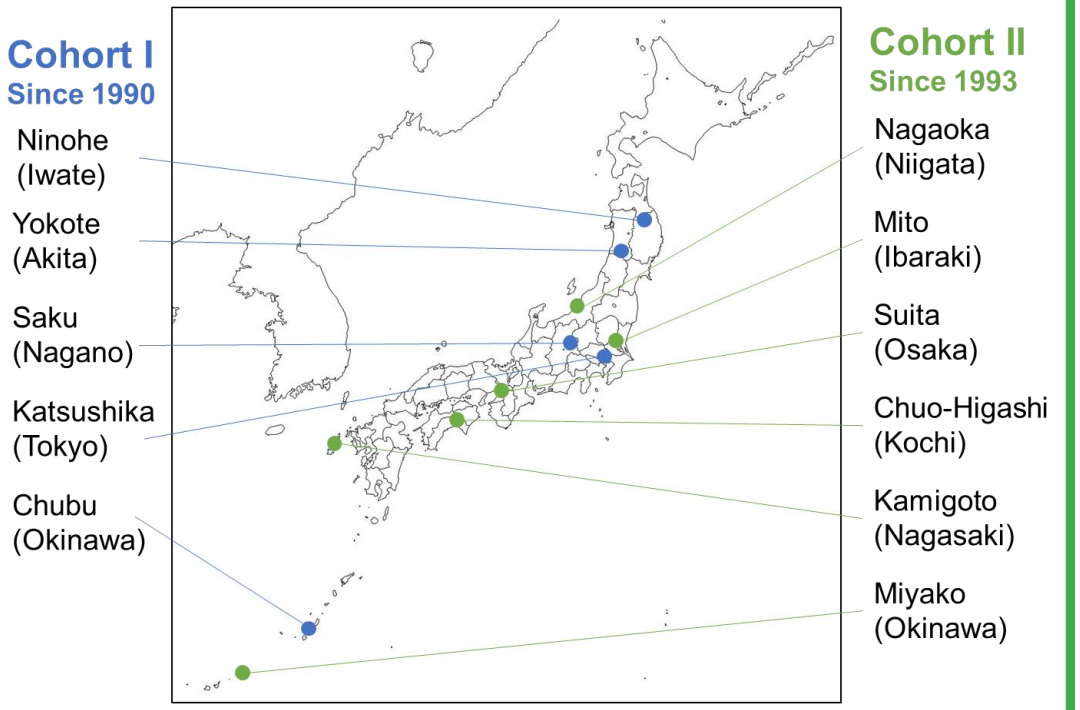
PHC STUDY

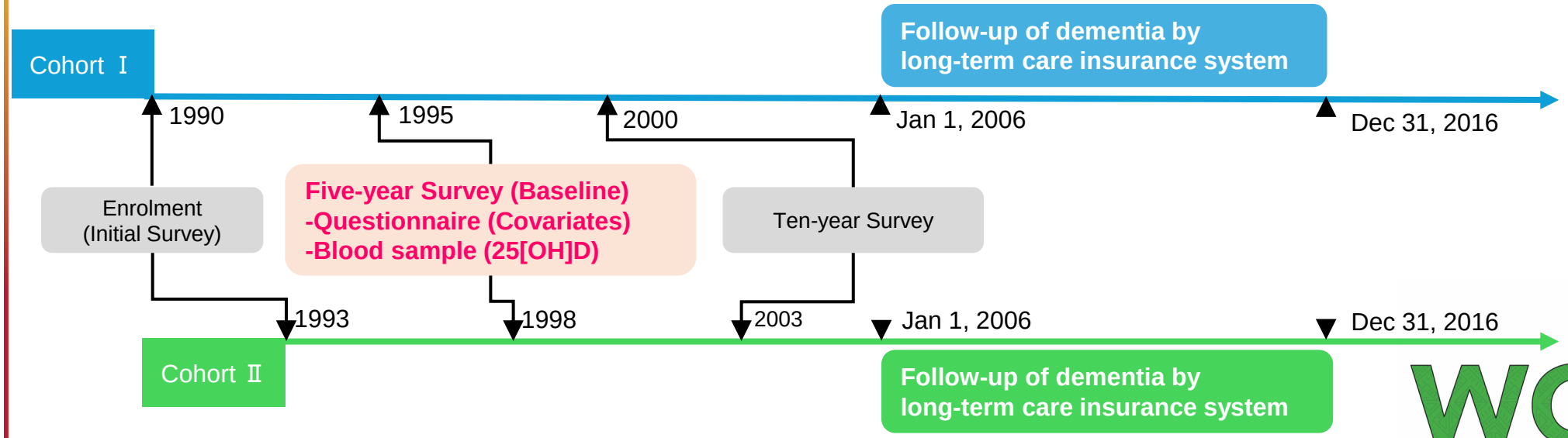
Methods: Study design

JPHC Study

Japan Public Health Center-based prospective Study

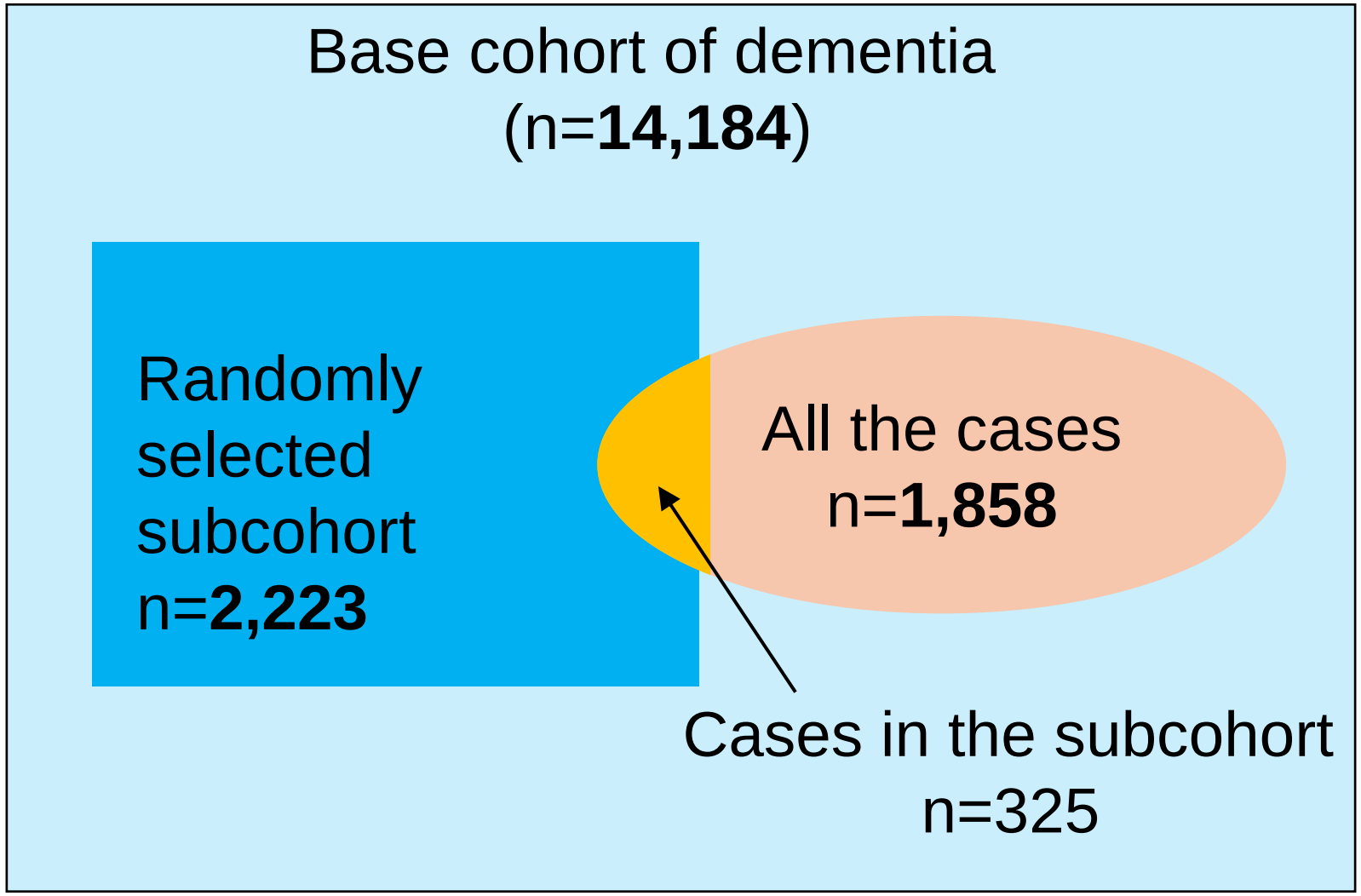
Subjects (n = 140,420)
Cohort Ⅰ (1990-):61,595 (40-59y)
Cohort Ⅱ (1993-):78,825 (40-69y)





WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024

Methods: Case-cohort study



Methods

- **Exposure**: Plasma 25(OH)D concentration categorized in **sex- and season-specific quartiles**
- **Outcome**: Incident disabling dementia, defined as **functional disability with dementia** according to the Long-term Care Insurance certification records
- **Follow-up**: January 1, 2006 ~ December 31, 2016
- **Covariates**: Age, sex, study areas, occupation, BMI, smoking status, alcohol drinking, physical activities, living alone, history of diabetes, and history of hypertension
- **Statistical analyses:**
  - Weighted Cox proportional hazards models
  - Subgroup analysis by age
  - Restricted cubic spline analyses

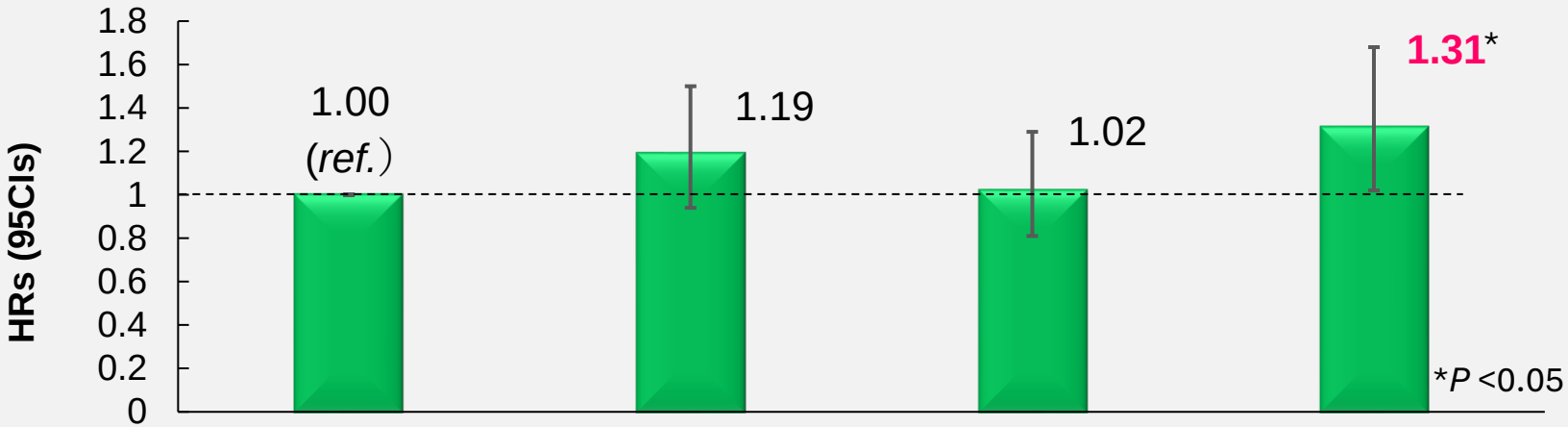
Results: Characteristics of subcohort

Characteristics	Quartiles of sex and season-specific plasma 25(OH)D concentration			
	Q1 (lowest) (n=544)	Q2 (n=561)	Q3 (n=559)	Q4 (highest) (n=559)
25(OH)D, median (IQR), ng/mL	17.5 (5.0)	21.7 (3.5)	25.2 (4.3)	31.9 (6.5)
Age, mean (SD), year	59.0 (8.3)	58.6 (7.7)	58.7 (7.4)	57.7 (6.7)
Male, %	36.2	36.4	36.1	36.3
BMI, mean (SD), kg/m^2	23.5 (3.0)	23.6 (2.8)	23.5 (2.8)	23.4 (2.9)
Never smokers	65.8	70.1	71.0	73.7
Non-drinkers	61.6	60.8	58.5	58.1
Physical activities, mean (SD), MeT-h/d	25.2 (9.3)	26.4 (9.3)	27.5 (10.1)	28.7 (9.4)
Living alone, %	4.8	3.7	3.9	1.6
History of diabetes, %	7.2	5.9	6.3	2.9
History of hypertension,%	21.7	25.0	24.3	22.5

25(OH)D= 25-hydroxyvitamin D;SD= standard deviation; IQR=interquartile range; BMI= body mass index;
MeT-h/d=metabolic equivalents of task hours per day

Participants in the **highest** quartile of 25(OH)D concentration tended to be older, never smokers, physically active, live alone, and have a history of diabetes.

Results: 25(OH)D and risk of disabling dementia

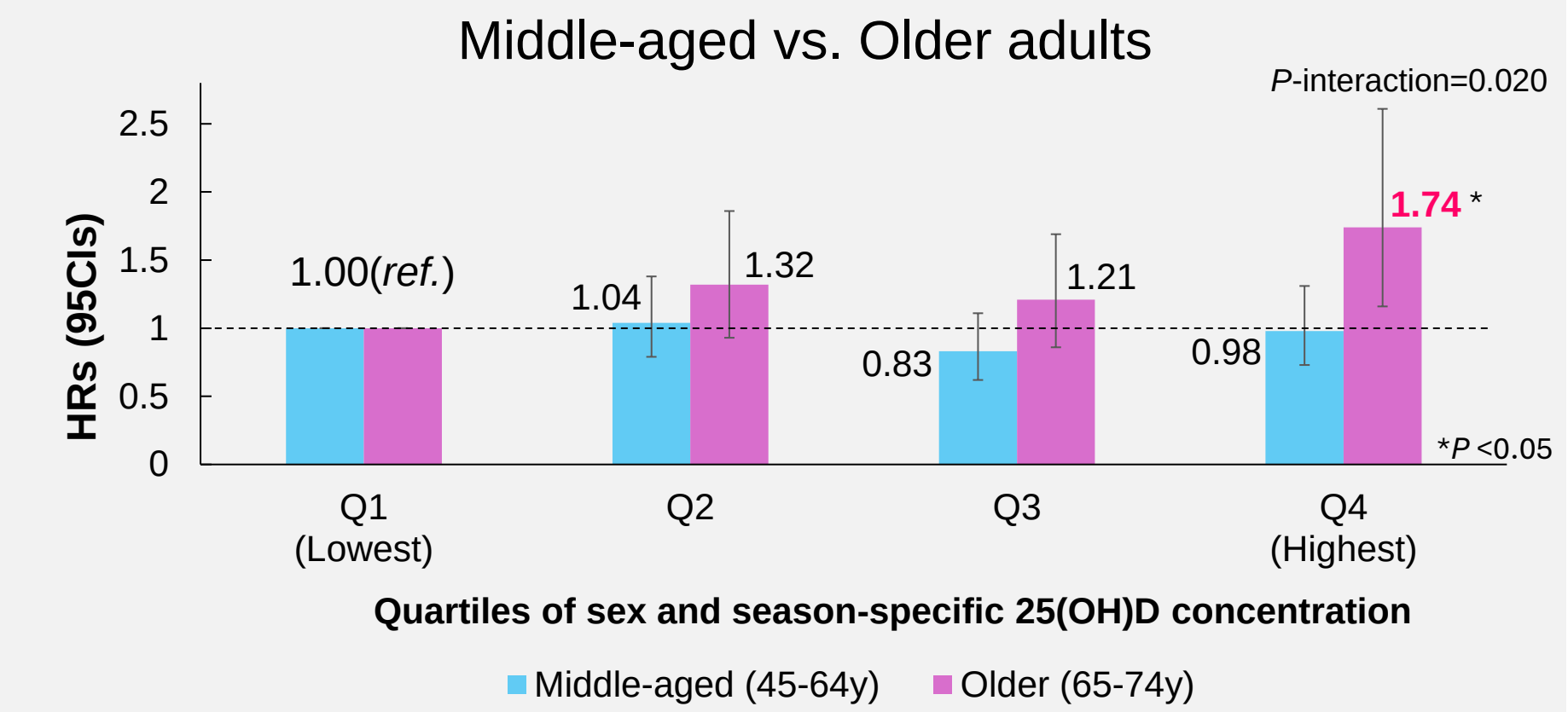


No. of subcohort participants	544	561	559	559
No. of cases	432	509	461	456

Adjusted for sex, age, public health centers, occupation, BMI, smoking status, alcohol, physical activities, living alone, history of diabetes, and history of hypertension.

Participants in the **highest quartile** of 25(OH)D concentration showed an **increased** risk of incident disabling dementia.

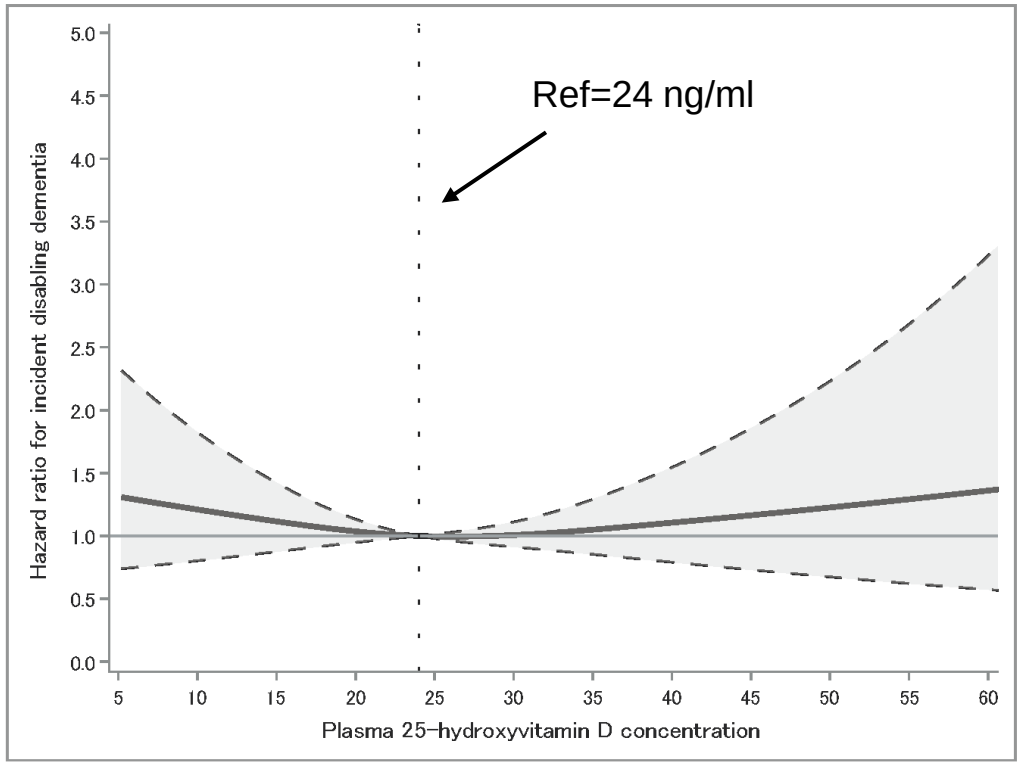
Results: Subgroups by age groups



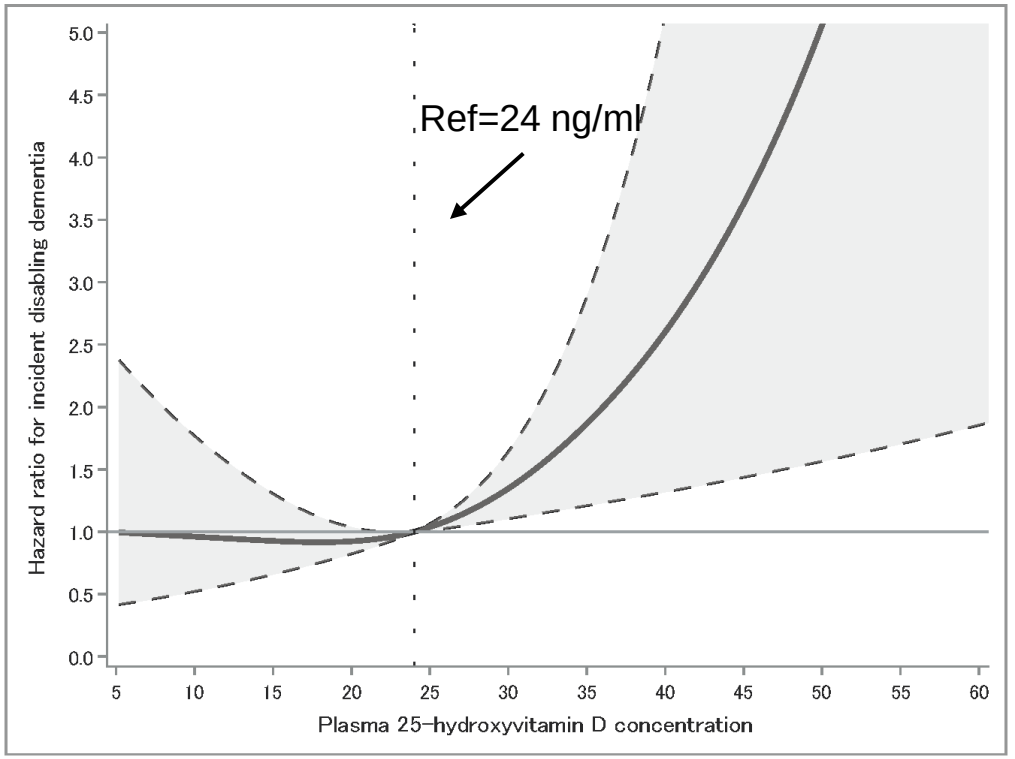
- **Middle-aged** adults: **No association**
- **Older** adults in the **highest quartile**: **Increased risk**

Results: RCS analyses by age groups

Middle-aged (45-64y)



Older (65-74y)



- **Middle-aged** adults : **No association**
- **Older** adults with a concentration **over 25 ng/ml: Increased risk**

国立研究開発法人
国立がん研究センター
National Cancer Center Japan

PHC STUDY

Discussion

■Interpretation of the increased risk

- ➢Higher vitamin D levels may contribute to **atherosclerosis** in older adults, potentially increase dementia risk.
- ➢**Survival bias**: Older adults with low vitamin D might have died earlier, lowering dementia incidence in this group.

■Strengths

- ■Large number of dementia cases (over 1,800 cases)
- ■Subgroup analysis by life stages (midlife vs. later life)

■Limitations

- ■No data on specific dementia subtypes
- ■Vitamin D level measured only once

国立研究開発法人
国立がん研究センター
National Cancer Center Japan

PHC STUDY

Conclusion

Our study **did not find a protective effect** of vitamin D levels against dementia risk among Japanese adults.

Thank you!

yriku@ncc.go.jp

WCE
WORLD CONGRESS OF EPIDEMIOLOGY 2024