

Global Dementia Legacy Event Japan

Roppongi Hills, Tokyo 2014.11.6

**The role of geriatricians in
management of dementia
- from the viewpoint of life style modification -**

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Some about The Japan Geriatrics Society

- The Japan Geriatrics Society (JGS), established in 1959, is only one scientific society in Japan which organizes the research in the field of geriatric medicine, focusing mainly on the research of the diagnosis & treatment of geriatric diseases including dementia, osteoporosis, atherosclerosis, infectious diseases, and geriatric syndrome such as frailty.
- JGS also aims at conducting research toward the construction of better long-term care for the elderly.
- JGS has 6,486 members, mainly medical practitioners and investigators.
- JGS organizes an annual scientific meeting and many educational seminars for practitioners and medical students.
- JGS publishes official scientific journals, Japanese journal and English journal named *Geriatrics and Gerontology International* (2012 IF 2.167).
- JGS approves board-certified geriatricians (1,537 all over Japan at present).
- JGS is a member society of The Japan Gerontological Society.
- JGS considers that the role of geriatricians in dementia practice is the management of life style and life style-related diseases including hypertension, diabetes, and dyslipidemia which possibly accelerates the development of not only vascular dementia but also Alzheimer's disease.

Risk factors for Alzheimer's Disease

① Unpreventable risk factors ② Medical risk factors

1) Aging 2) Menopause

3) Family history

4) Genetic factors

APP gene

Presenilin gene1,2

Apo E

Life style-
related
diseases

Depression

Head trauma

hypothyroidism

hypertension

DM

dyslipidemia

③ Life style

⇒ **Diet, Smoking, Excess intake of alcohol,
exercise deficiency**

What life-style is good for preventing Alzheimer's disease?

Diet

☆ Rotterdam Study (Holland)

1. Fish intake
($\geq 18.5\text{g/day}$)
2. Vitamin C, E

Exercise

☆ Canada

Regular exercise
More than 3 times /week

Communication

☆ Sweden

Living with large family

Intellectual performances

☆ USA

Reading books, Chess,
Music play

The content of daily foods in AD (Case-control study)

Food	AD n=64	Control n=80	P value
Rice	261.9 ± 105.8	231.9 ± 94.1	NS
Potato	16.7 ± 12.2	22.6 ± 16.7	NS
Sugar	6.1 ± 15.1	5.4 ± 3.8	NS
Snack	16.1 ± 16.0	16.5 ± 13.4	NS
Beans	119.5 ± 86.9	127.8 ± 69.2	NS
Fish	40.5 ± 24.4	58.3 ± 28.2	0.0001
Meat	25.1 ± 15.4	21.0 ± 16.3	0.13
Egg	16.0 ± 15.4	13.5 ± 11.0	NS
Milk	77.2 ± 77.8	117.5 ± 99.9	0.01
Green vegetable	45.7 ± 31.7	68.9 ± 59.8	0.01
Vegetable	55.9 ± 32.2	70.6 ± 46.4	0.03
Fruits	78.9 ± 60.1	89.4 ± 54.2	NS
Fungi	4.4 ± 4.4	7.6 ± 7.7	0.004
See weeds	6.3 ± 7.3	10.7 ± 8.3	0.001
Alcohol	65.1 ± 164.4	75.5 ± 177.2	NS
Soft drink	399.7 ± 320.0	559.8 ± 381.5	NS
Spice	18.9 ± 23.1	39.4 ± 47.3	NS

Dietary intervention to AD

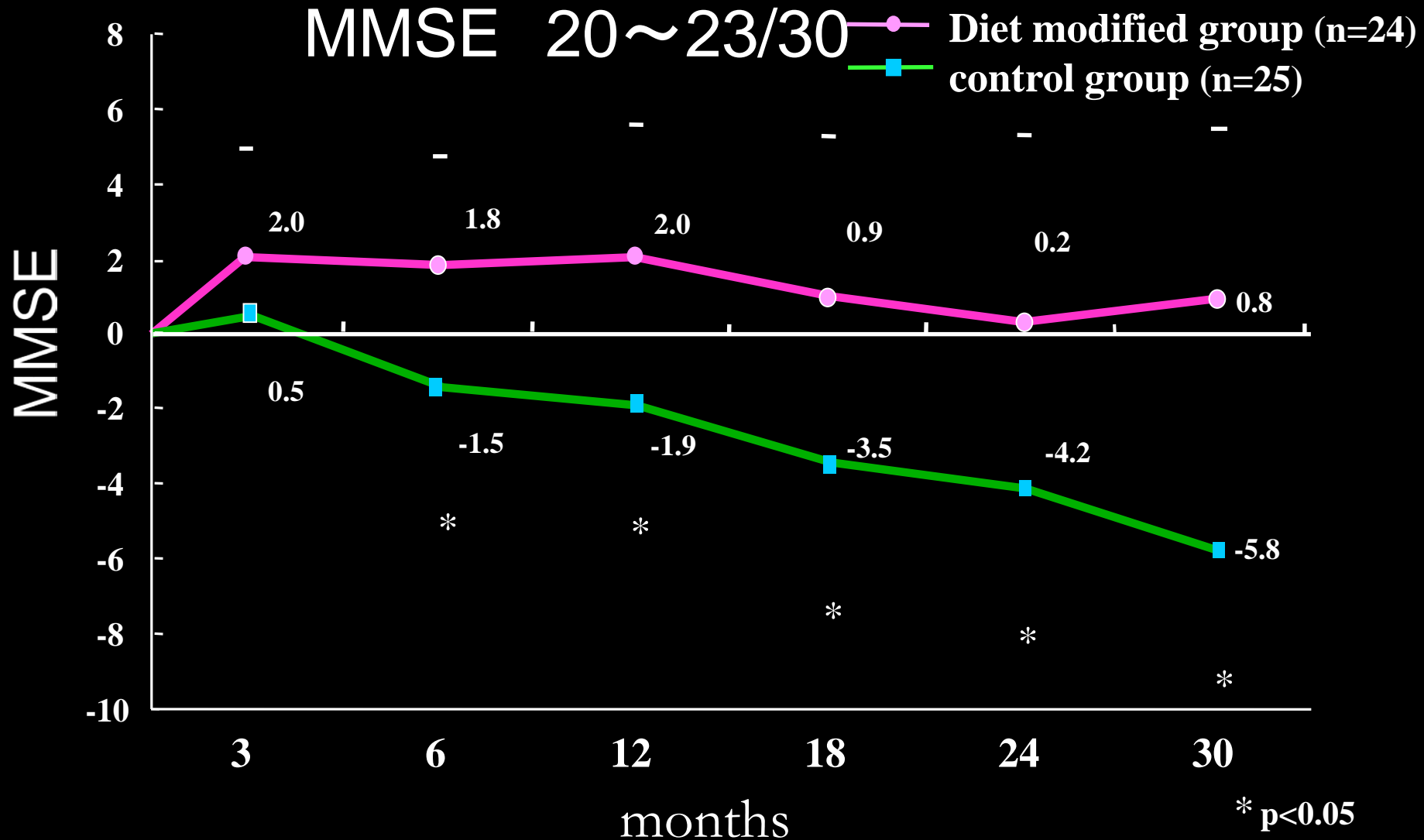
Adequate calorie intake

Sufficient vitamin & mineral intake

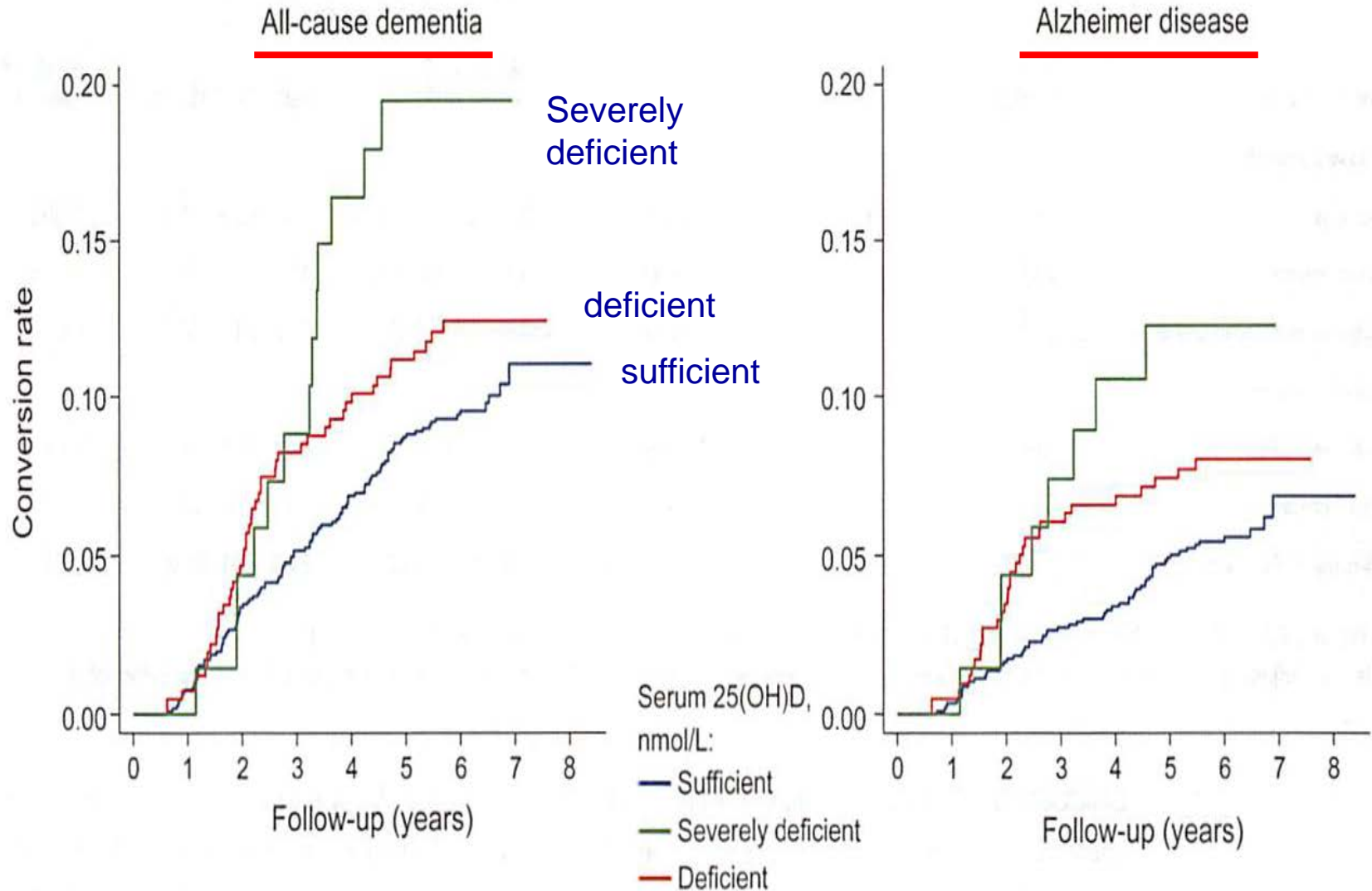
Fatty acids : n-6/n-3 = 3.0

Fish	60~90g/day
Vegetable	100g/day
Fruits	at least once a day

The effect of dietary modification on MMSE in mild to moderate AD

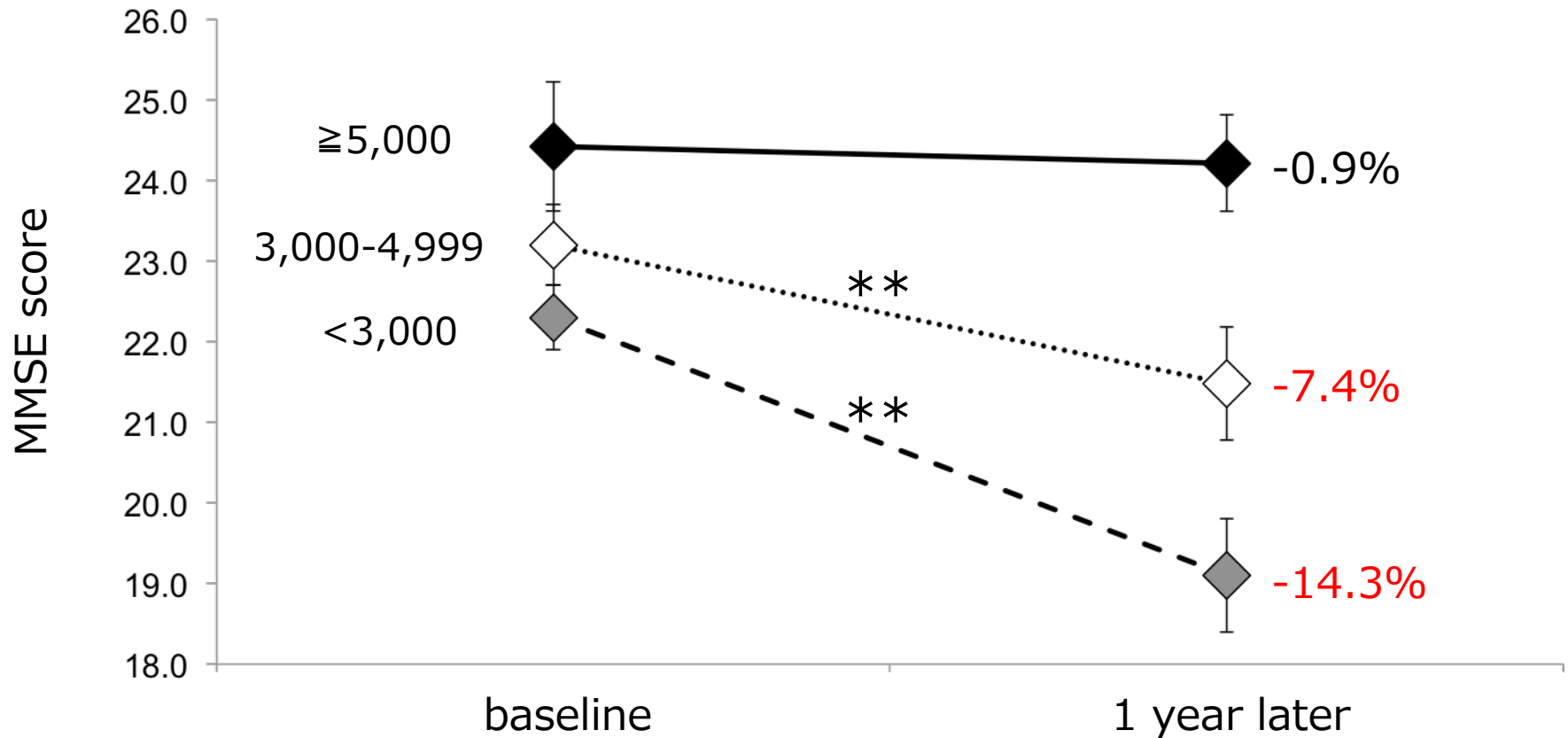


Cumulative occurrence of all-cause dementia and Alzheimer's disease when subjects were classified by serum 25(OH)D concentration



(Littlejohns TJ, et al. Neurology 2014)

The daily steps and cognitive function decline in mild to moderate AD patients



Cognitive function was preserved in AD patients who walk $\geq 5,000$ steps/day.

(Yamada A, Arai H, Kyoto University, unpublished data)

Smoking and Smoking cessation vs. the risk of dementia

Smoking Status	Non-smoker	Ex-smoker	Current Smoker	< 20 /day	> 20 /day
<Total dementia>					
Age-,sex-, survey year-matched OR	1.0	1.4 (0.6-2.8)	2.2 (1.1-4.4)	2.1 (1.1-4.3)	2.6 (0.9-7.3)
Multivariable OR	1.0	1.5 (0.7-3.3)	2.3 (1.1-4.7)	2.2 (1.1-4.7)	2.7 (0.9-8.2)
<Dementia with history of stroke>					
Age-,sex-, survey year-matched OR	1.0	1.4 (0.4-4.5)	2.4 (0.8-7.1)	2.4 (0.8-7.2)	2.5 (0.5-11.9)
Multivariable OR	1.0	1.7 (0.5-5.9)	2.4 (0.8-7.7)	2.4 (0.7-7.9)	2.5 (0.4-14.4)
<Dementia without history of stroke>					
Age-,sex-, survey year-matched OR	1.0	1.3 (0.5-3.5)	2.0 (0.8-5.0)	2.0 (0.8-4.9)	2.6 (0.6-11.1)
Multivariable OR	1.0	1.5 (0.6-4.3)	2.3 (0.9-6.0)	2.2 (0.8-5.9)	3.0 (0.7-13.8)

(Adjusted for body mass index, alcohol use, serum total cholesterol, systolic blood pressure, use of antihypertensive medication, diabetes mellitus, atrial fibrillation and ST-T abnormality)

(Ikeda A, et al.: Cerebrovascular Diseases 2008)

AD and life style-related diseases

Well-known risk factors for atherosclerosis . . .

Hypertension have been reported to be risk factors
Diabetes also for AD

Dyslipidemia

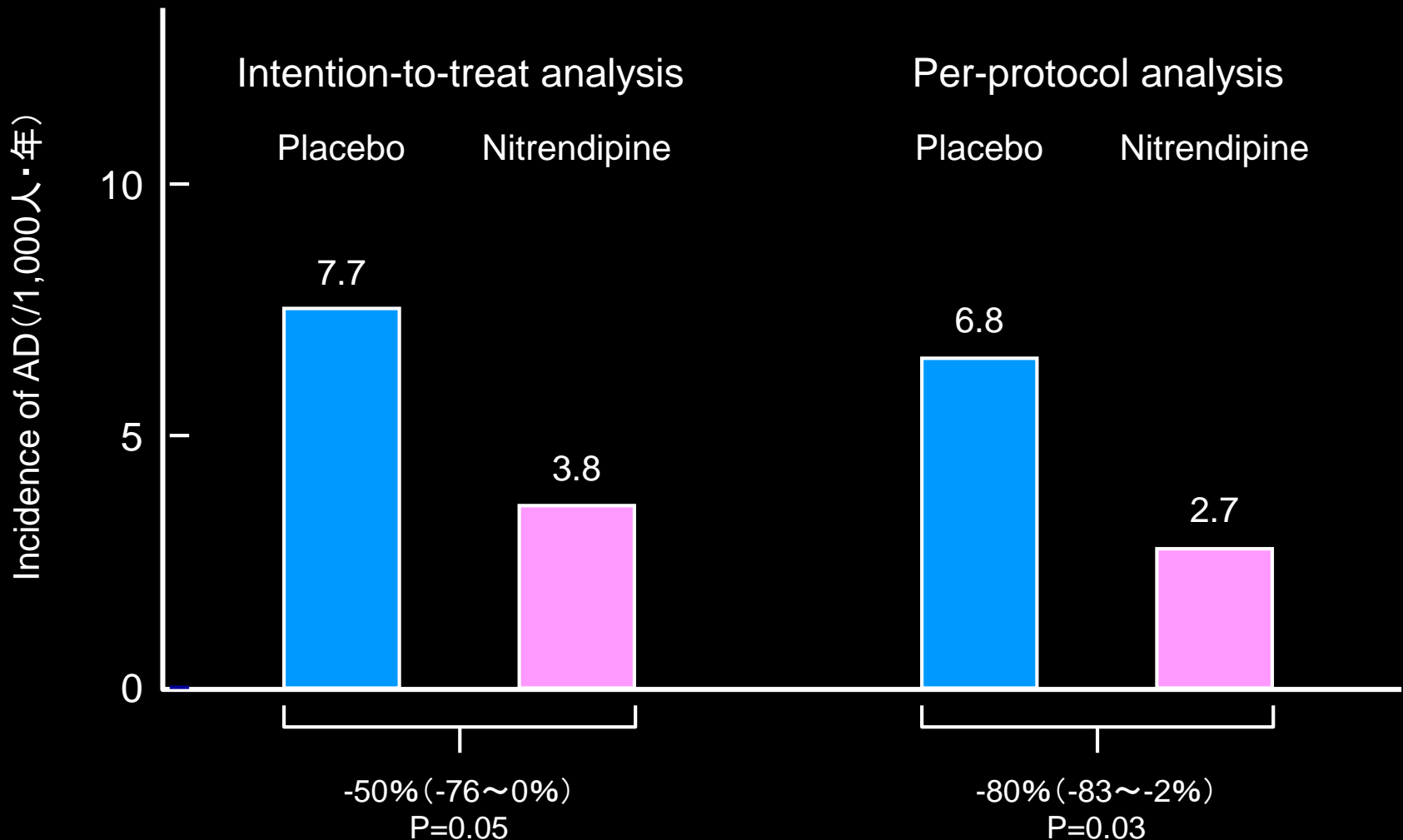
Obesity

Smoking

Also, treatment of life style-related diseases has been reported to decrease the incidence of AD.

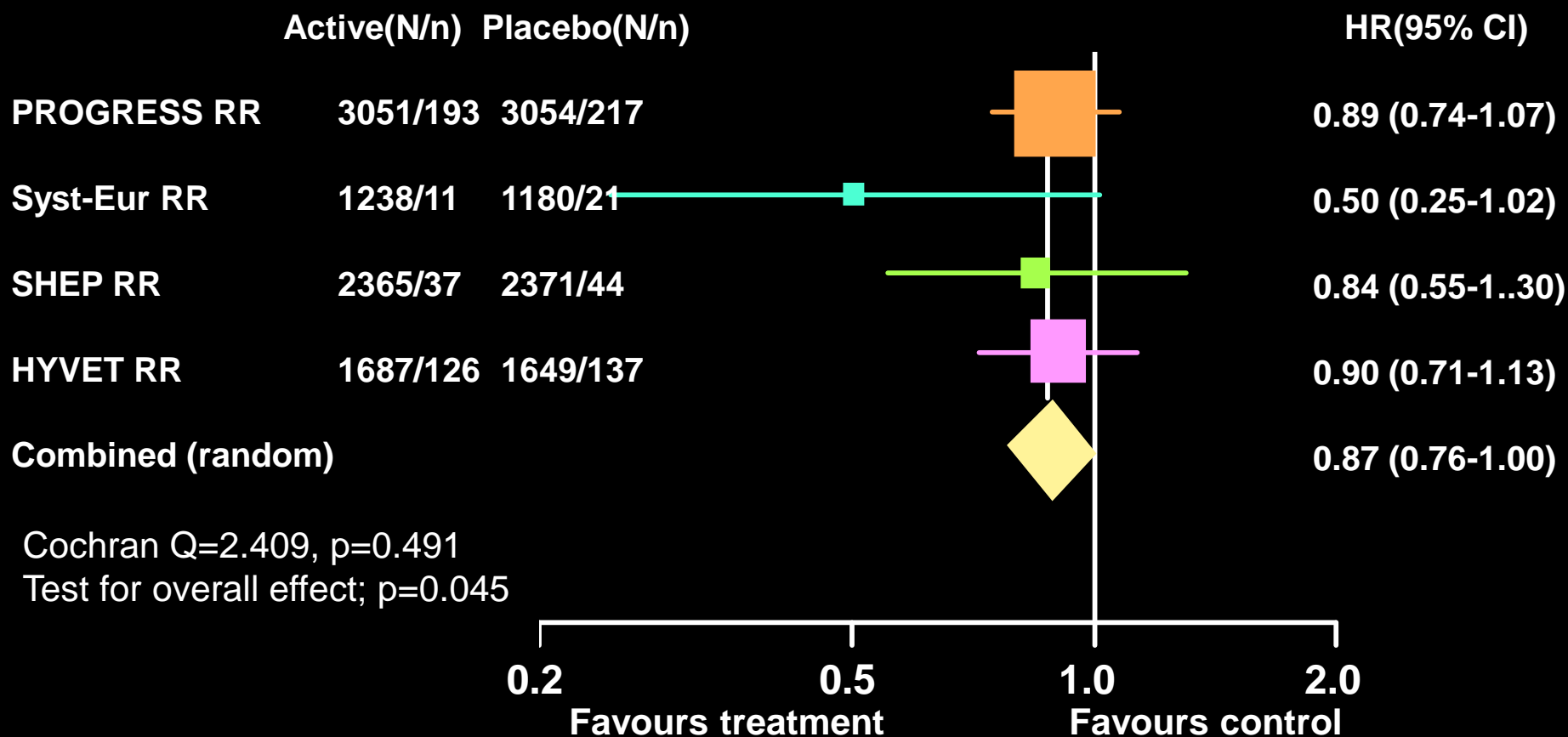
The incidence of AD in Syst-Eur Trial

Possibility : Treatment of life style-related disease reduces the risk of AD Diabetes, HT.....



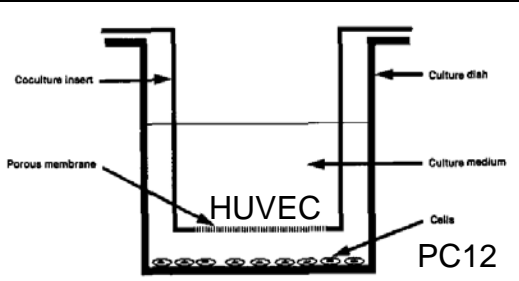
The effect of anti-hypertensive treatment on the occurrence of dementia

-Meta-analysis-



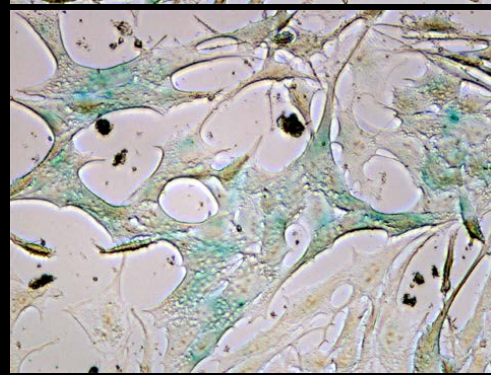
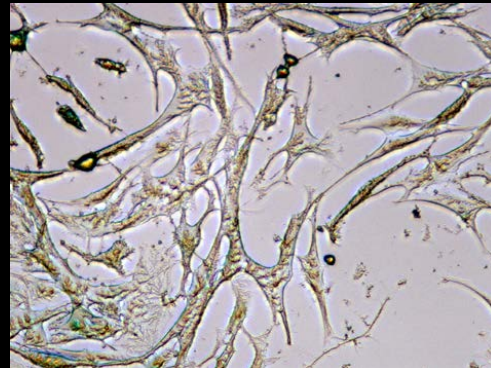
N=total participants, n=number with dementia

(Peters R., et al., 2008)

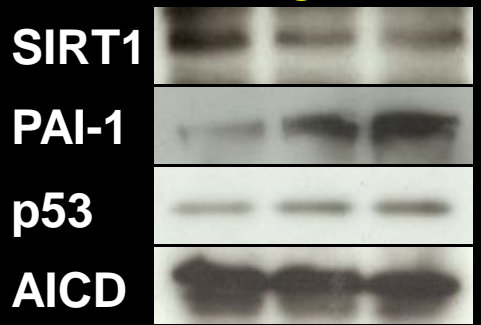


Co-culture system
(size; 0.4µm micro pore)

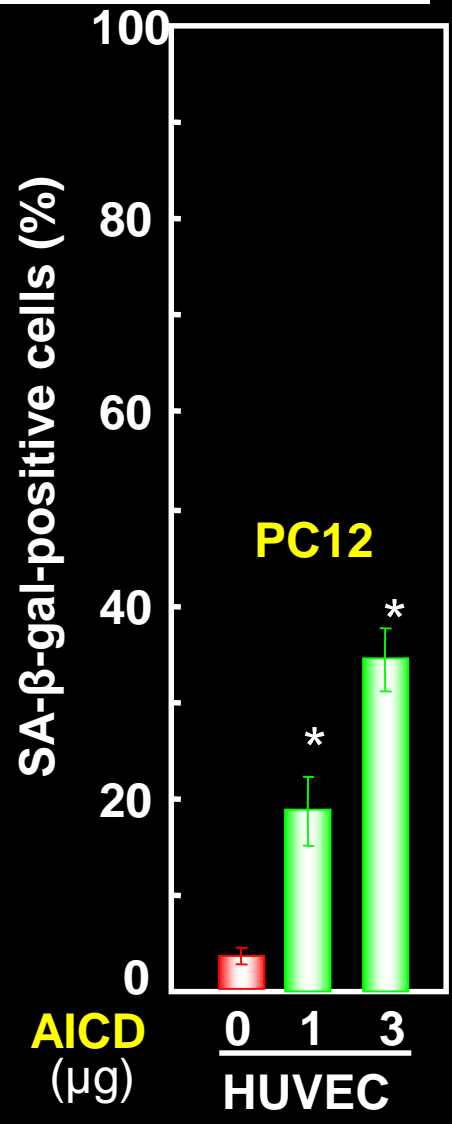
PC12



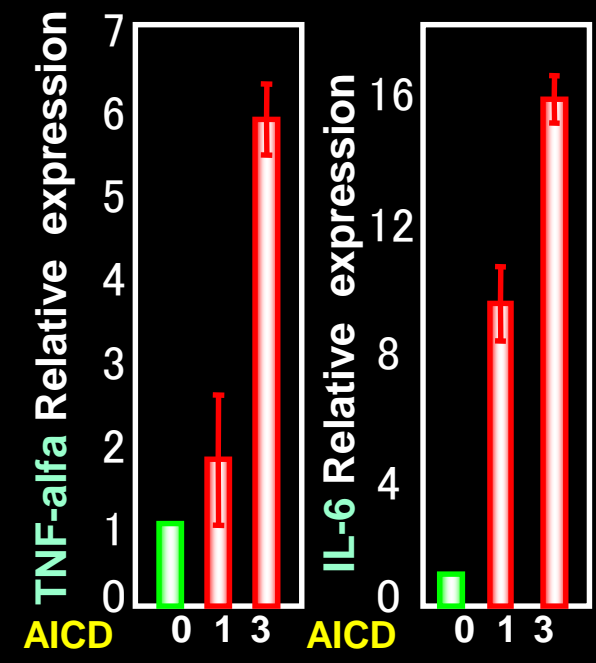
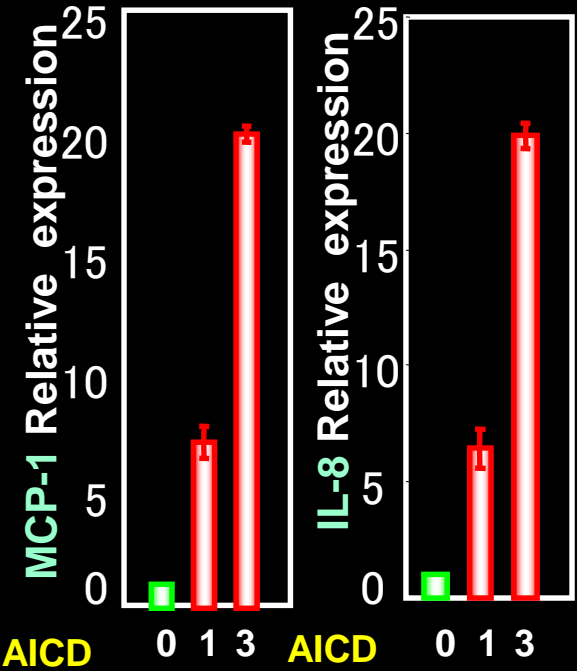
PC12



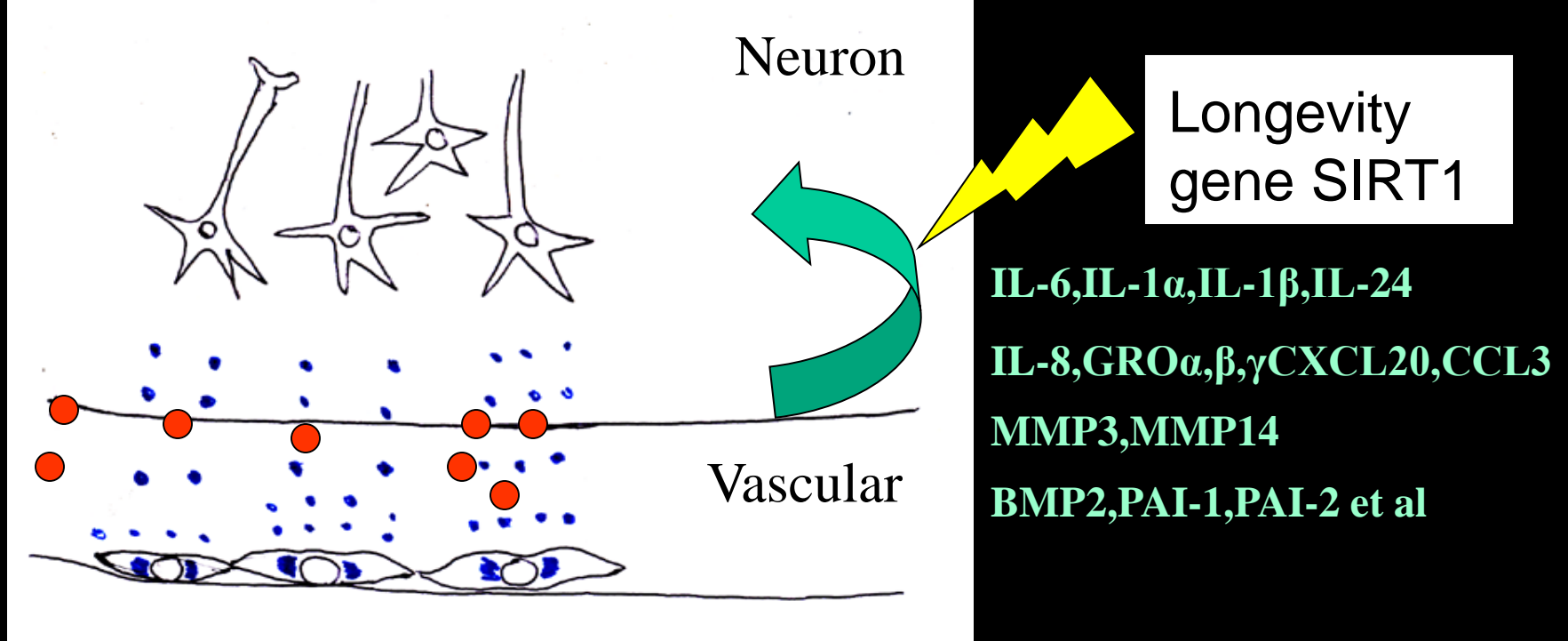
AICD 0 1 3 (µg)
HUVEC



HUVEC (RT-PCR mRNA)



Hypothesis: Vascular senescence/damage promotes neuronal senescence/damage by secretion of inflammatory cytokines



SASP (Senescence-associated secretory phenotype)

1. Progression or inhibition of tumor
2. Induction of inflammation
3. Progression of Cellular Senescence

Messages from JGS

- Life style modification is important for the prevention of both vascular and Alzheimer's types of dementia.
- Although evidence is not concrete, life style-related diseases, especially diabetes and hypertension, should be well treated for the prevention of both types of dementia.
- The basic research on the mechanism underlying the effect of life style modification or treatment of life style-related diseases may provide a new preventive and therapeutic approach for AD.

The perspective of dementia practice from the geriatric point of view

1. Seamless coordination :
 - ◉ Prevention→diagnosis & treatment at early stage→care
2. Insight **from whole body to brain**
 - ◉ Control of vascular risk factors
3. Insight **from brain to whole body**
 - ◉ Treatment and care for **geriatric syndrome** including aspiration pneumonia, osteoporosis and frailty
 - ◉ Treatment and care of **complicated diseases** in demented patients
4. Coordination : **Geriatricians – Neurologists - Psychiatrists**
5. Coordination : **Medical - Care & Social welfare**

Thank you very much for your attention



New Toranomon Hospital
(completed 2018)



Toranomon Hospital
since 1958