Supercentenarian as a model of happy, healthy longevity

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Contents of the Presentation

Part 1 Brief summary of centenarian study
- ✓ Demography
- ✓ Function and medical history
- ✓ Inflammation, Frailty and aging
- ✓ Well-being

Part 2 Supercentenarian study
- ✓ Demography of SC
- ✓ Function of YC, SSC and SC

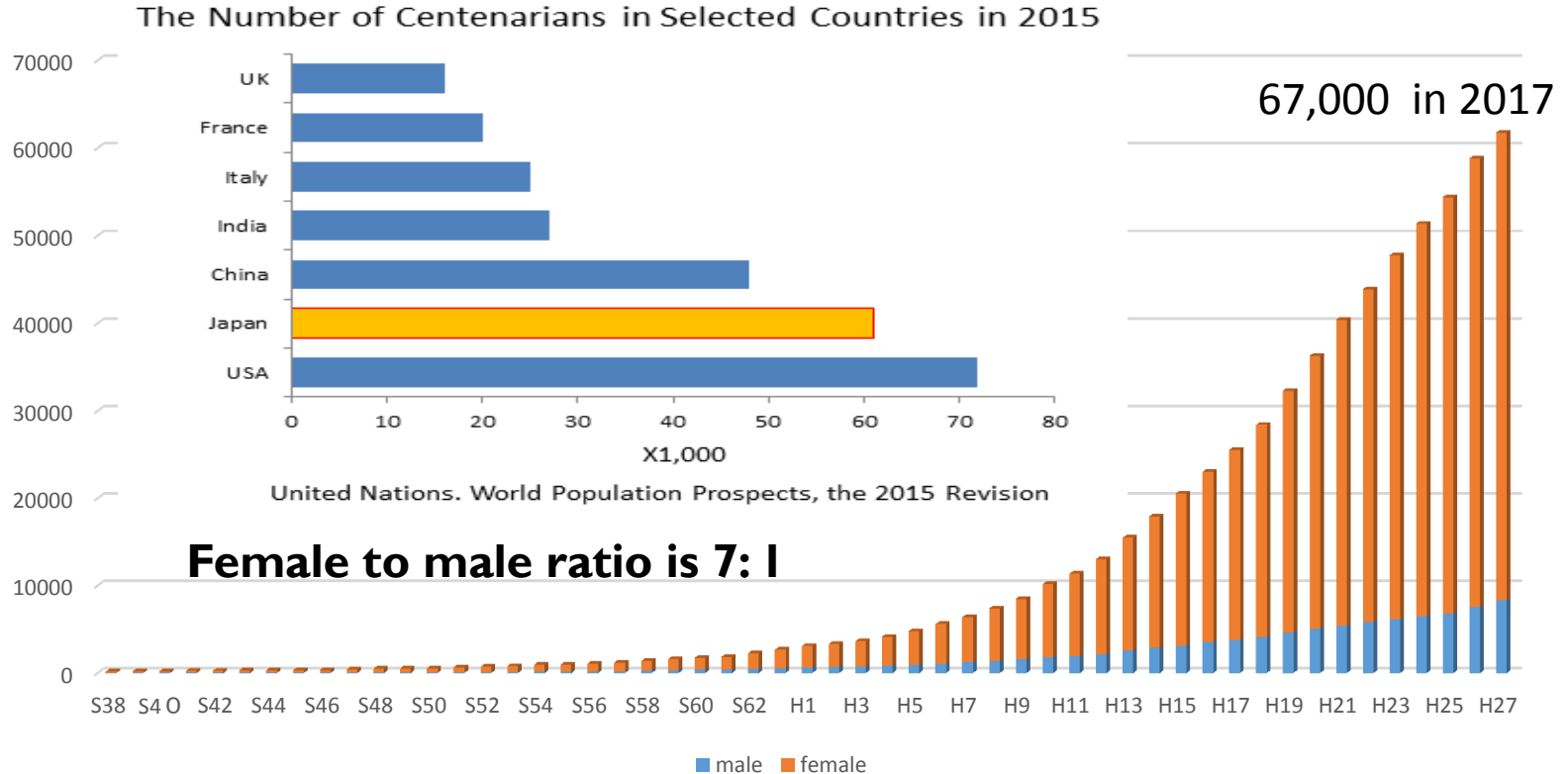Part 3 Message from the oldest man

110 years old

The map of residence of participants

Group	Age range	number of participant
Young Centenarian	100-104	**216**
SSC	105-109	**593**
SC	>110	**160**
Long-lived sibling	>90	**76** pairs
Family of centenarian	45-85	**421** families
Offspring		**421**
Spouse of offspring		**224**

Number of Centenarians in Japan from 1963 to 2017

The Number of Centenarians in Selected Countries in 2015

67,000 in 2017

Female to male ratio is 7: 1

United Nations. World Population Prospects, the 2015 Revision

Smoking and drinking behavior of Centenarians
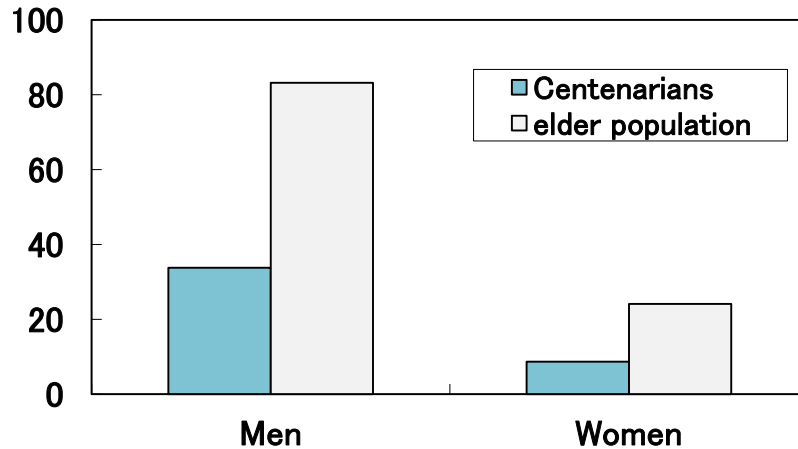
Classification of centenarian, based on function

Gondo Y,. J Gerontol A Biol Sci Med Sci. 2006; 61:305-10

30-40% of centenarians are dementia free

40% of centenarians are independent

Red : Men
Blue : Women

Number

- w
- m

4 fuctional categories

Exceptional — Normal — Frail — Fragile
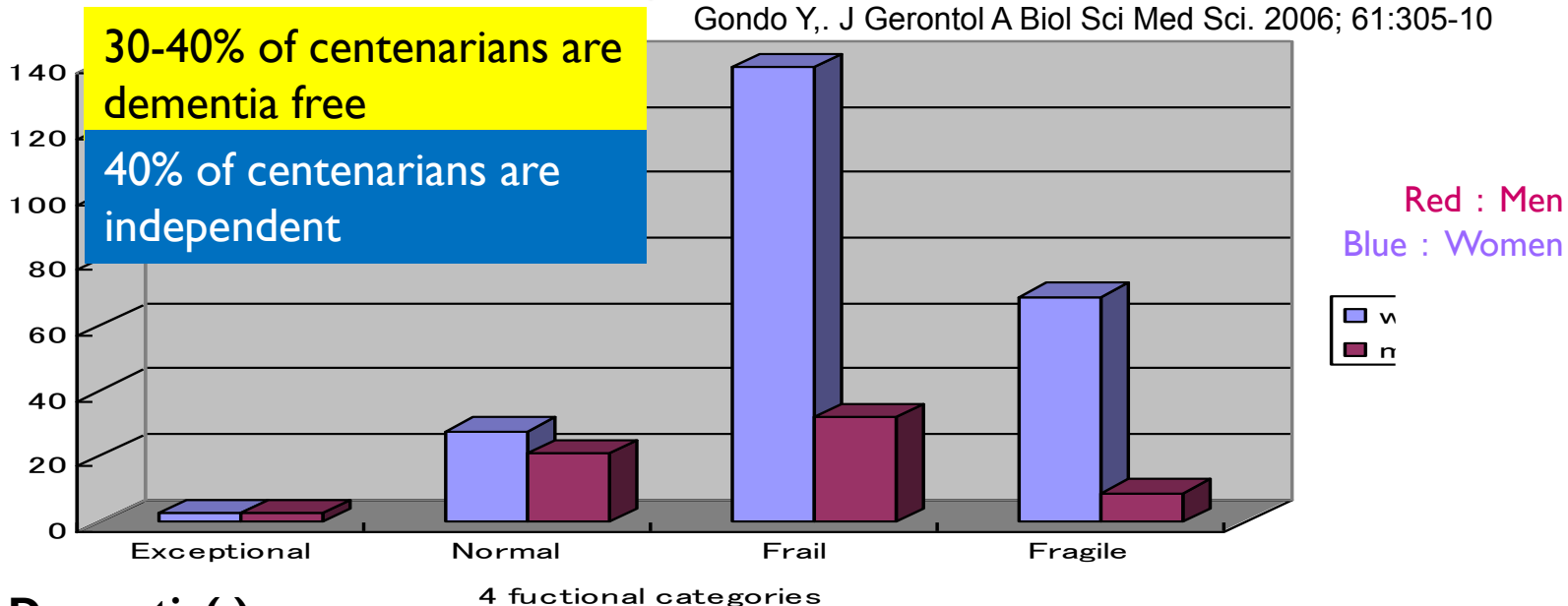
**Dementia(-),
independent,**
No impairment of vision & hearing
**4% of total
8% of men,
2% of women**

**Dementia(-)
Independent**
Impairment of hearing or vision
**14% of total
26% of men
8% of women**

**Dementia,
dependent**

Totally dependent

Function of female centenarian is lower than male. Absolute number of exceptional and normal cent is same between male and female

Morbidity Spetrum of Centenarian （%）

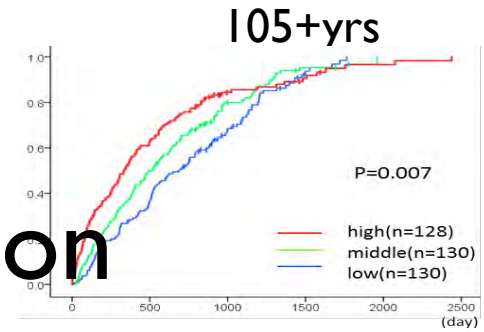| Disease	total	Men	Women
HBP	63.6	61.5	64.1
Fracture	46.4	24.6	52.3
Cataract	46.4	40.0	48.1
HeartDisease	28.8	26.2	29.5
Respiratory	20.9	24.6	19.0
Stroke	15.9	23.1	13.9
Cancer	9.9	18.5	7.6
DM	6.0	4.6	6.3

Takayama M, et al. J Gerontol Med Sci 2007；62：774-82.
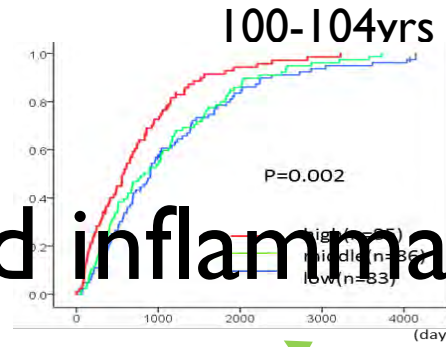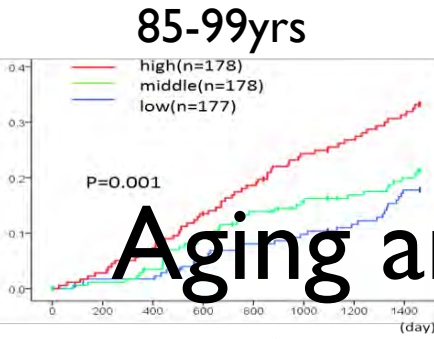
Morbidity spectrum is different between men and women
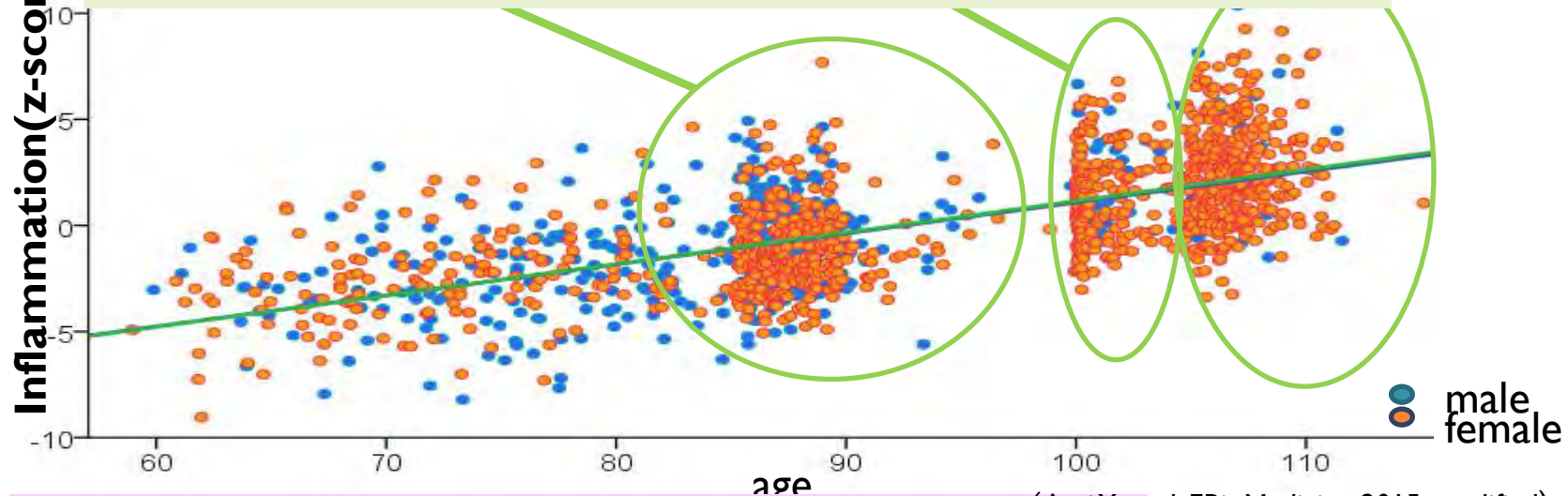
Inflammation, Frailty and Aging

110 years old

Aging and inflammation

All-cause Mortality

85-99yrs   **100-104yrs**   **105+yrs**

high(n=178)
middle(n=178)
low(n=177)

P=0.001

P=0.002

high(n=128)
middle(n=130)
low(n=130)

P=0.007

Inflammation predicts life expectancy.

Inflammation(z-score)

male
female

age

（Arai Y, et al. EBioMedicine 2015, modified)

Low-grade inflammation increases with age

WHAT IS **FRAILTY?**

commonly associated with aging. Frail older adults are weak, have a lower ability for independent living, and often require assistance for daily activities (dressing, eating, toileting, mobility)

Definition(Fried)

· **Low physical activity**

· **Muscle weakness**

· **Slowed performance**

· **Fatigue or poor endurance**

· **Unintentional weight loss**

Frailty

More than Three symptoms

Inflammation is associated with Frailty
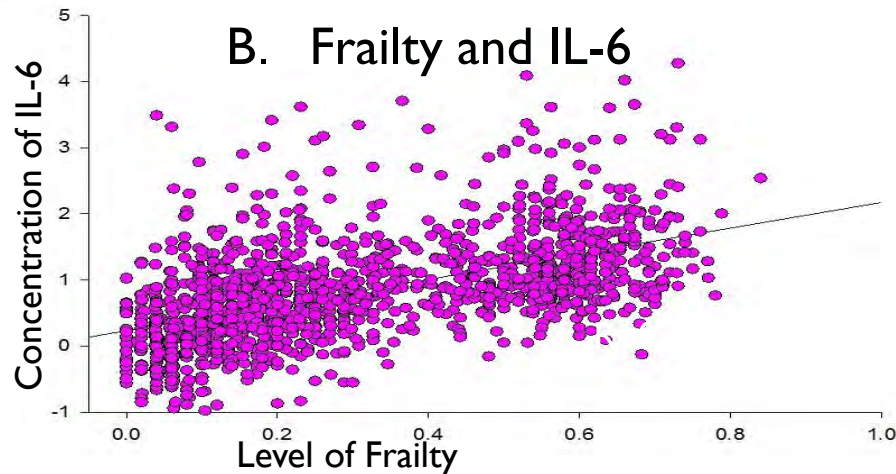
A. Frailty and TNF-α

Concentration TNF-α

Level of Frailty

The level of frailty is correlated with the concentration of TNF and IL-6.
TNF and IL-6 are cytokine causing inflammation.

B. Frailty and IL-6

Concentration of IL-6

Level of Frailty

Inflammation is one of the causes of frailty.
Other factors are associated with frailty

Prevention of Frailty

Some physical activity (such as walking) in each day

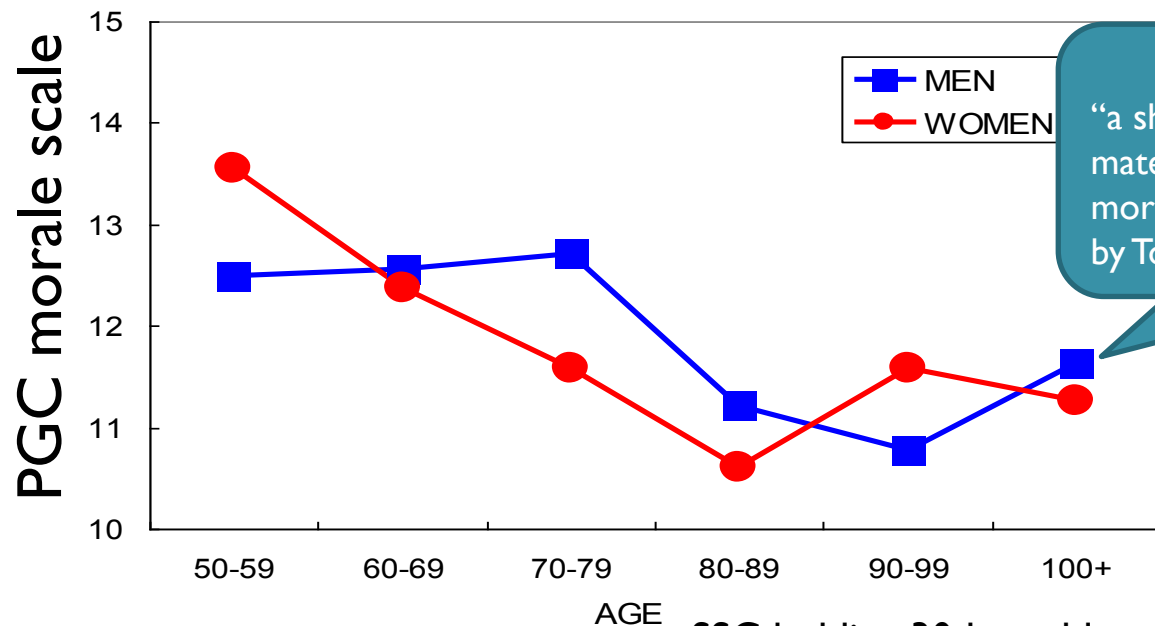**Keeping the mind active**

Recognize and treat depression

Recognize and treat medical problems

Maintain good nutrition with a balanced diet including enough protein

JAMA 2006; 296: 2280

Are they really happy?
Wellbeing of Older Adults and Centenarians

Gondo Y & Masui Y. presented in 20th Anniversary of Georgia Centenarian Study

Gerotranscendence
"a shift in meta-perspective, from a materialistic and rational vision to a more cosmic and transcendence one."
by Tornstam

SSC holding 30days old great granddaughter.
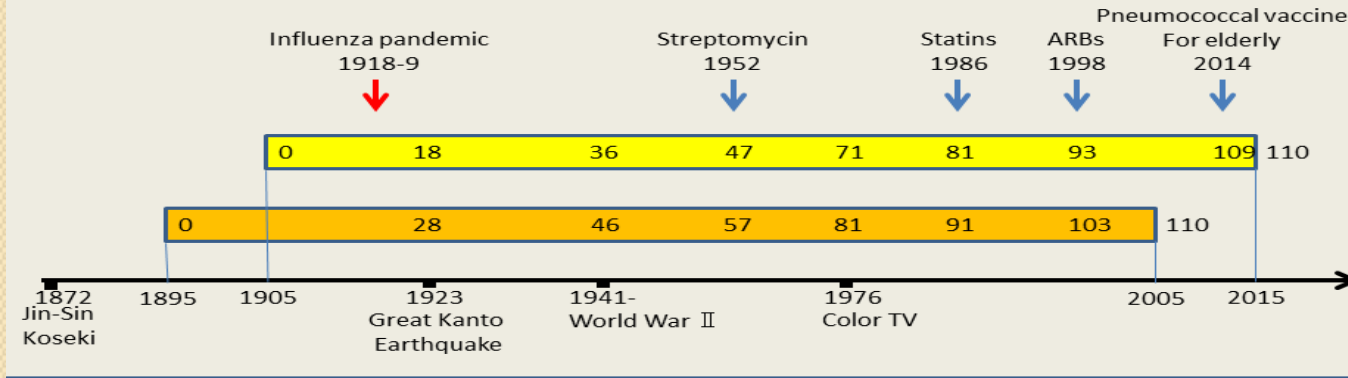He looks so happy.

Part 2 Preliminary results of supercentenarian

- Demography and Characteristics of supercentenarian
- Autopy of SC

Number of SC from 1991 to 2015

Life Event of Supercentenarians

the year of national census.

Influenza pandemic 1918-9 · Streptomycin 1952 · Statins 1986 · ARBs 1998 · Pneumococcal vaccine For elderly 2014

| 0 | 18 | 36 | 47 | 71 | 81 | 93 | 109 | 110 |

| 0 | 28 | 46 | 57 | 81 | 91 | 103 | 110 |

1872 Jin-Sin Koseki · 1895 · 1905 · 1923 Great Kanto Earthquake · 1941- World War II · 1976 Color TV · 2005 · 2015

146

2015

2010

78

Female to male ratio is 15 to1

Long term care insurerance
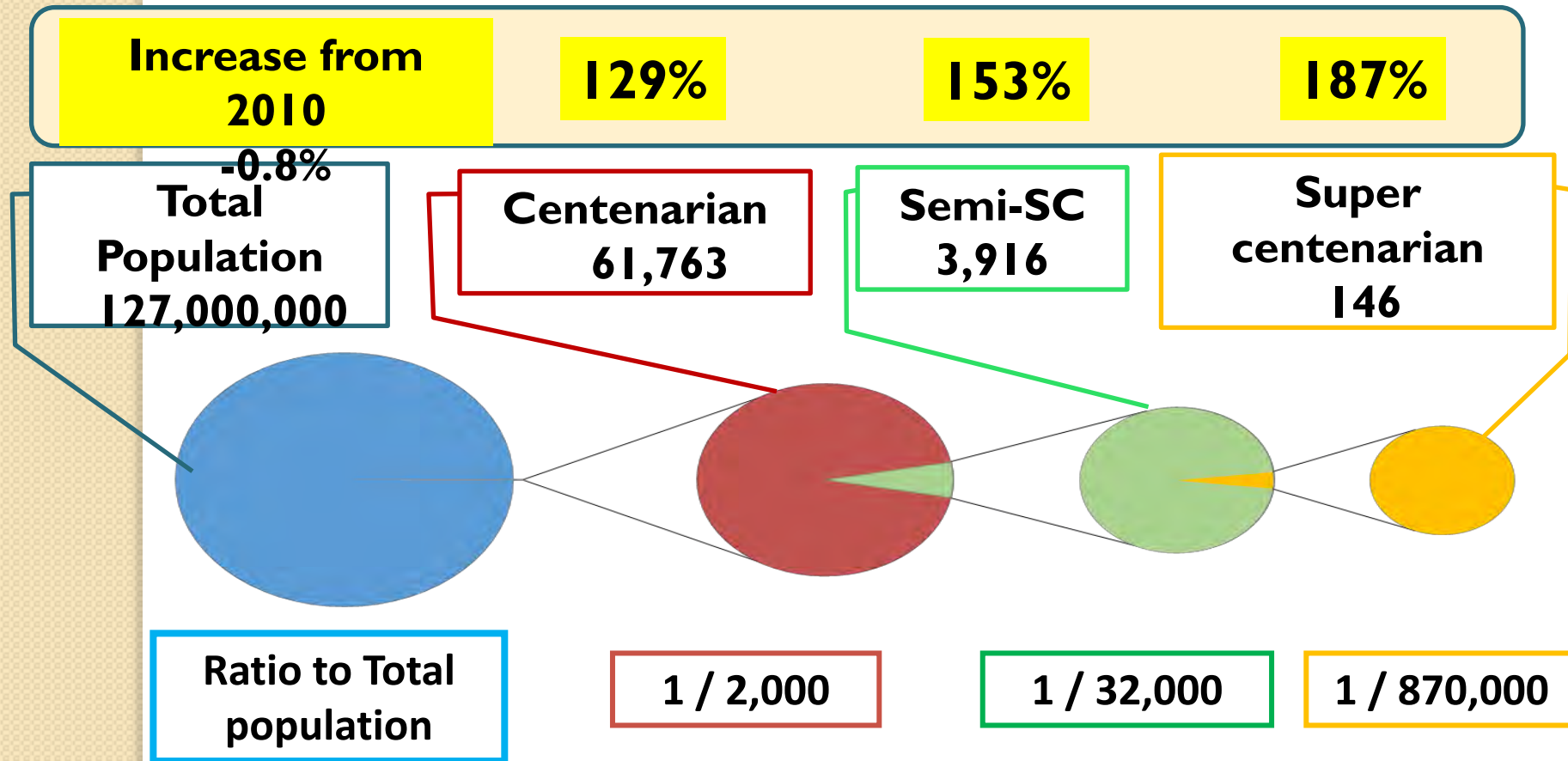
H3(1991…) H6(1994) H7(1995) H8(1996) H9(1997) H10(1998) H11(1999) H12(2000) H13(2001) H14(2002) H15(2003) H16(2004) H17(2005) H18(2006) H22(2010) H27(2015)

M   F

Number of SC was stable till 2006. In 2010 suddenly number became 78, and after 5years, number doubled .Effective standard medical intervention was not available to present SC.
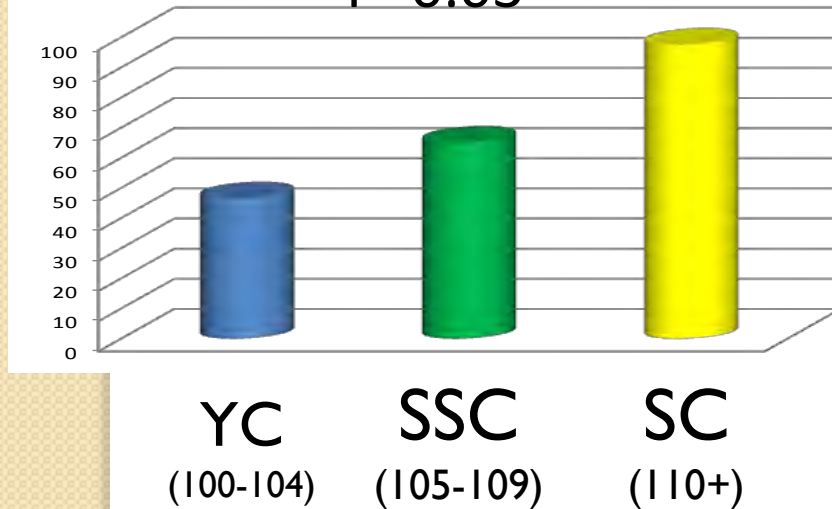
Number & ratio of Cent. , SSC and SC in Japan in 2015

| Increase from 2010 | 129% | 153% | 187% |

-0.8%

Total Population 127,000,000

Centenarian 61,763

Semi-SC 3,916

Super centenarian 146

Ratio to Total population

1 / 2,000

1 / 32,000

1 / 870,000
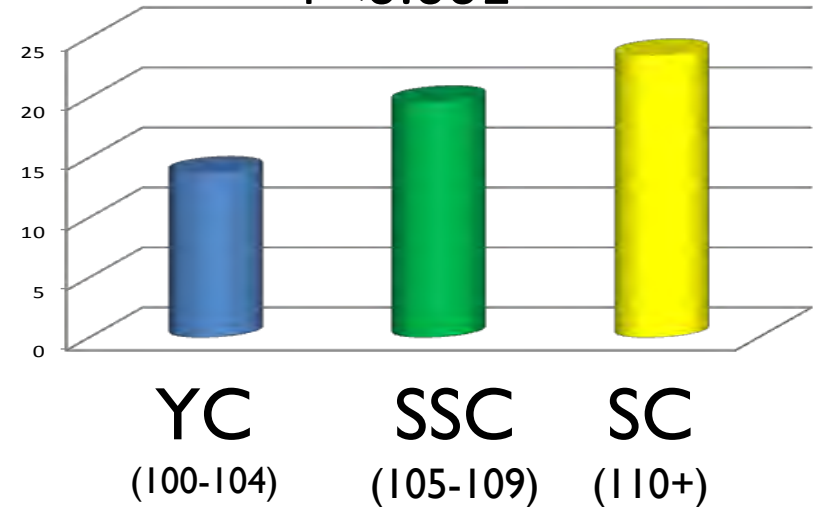
Physical and Cognitive Function of YC, SSC and SC at the age of 100 y/o

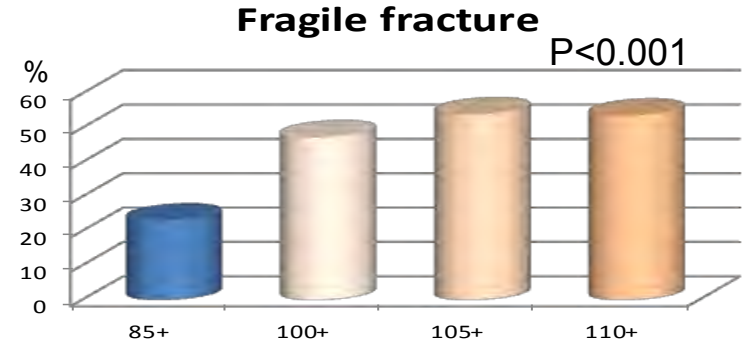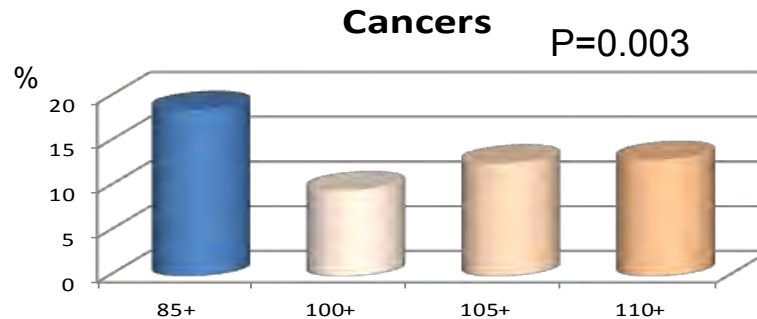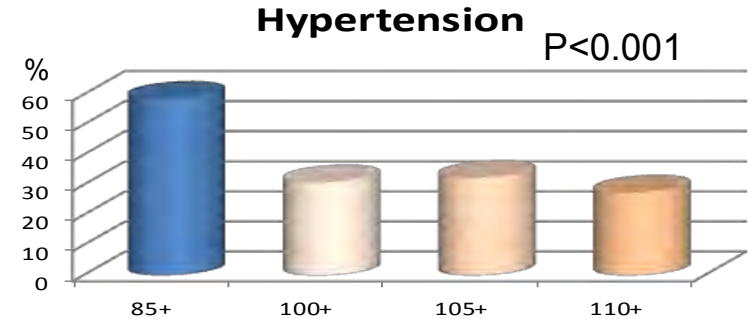Physical function (BADL)

P=0.03

Cognitive function (MMSE)

P<0.001

Arai Y, et al. J Gerontol Med Sci 2014, modified

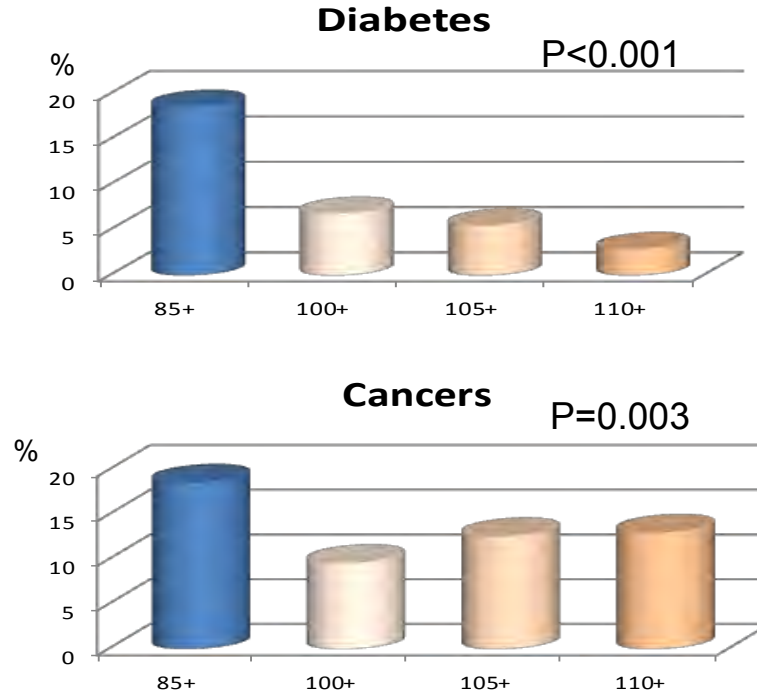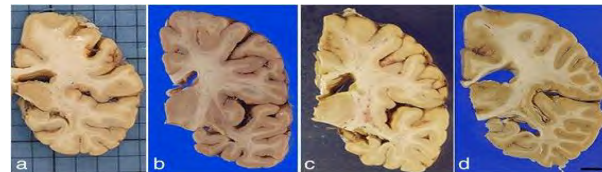# Medical history of centenarians and oldest old

Arai Y, et al. J Gerontol Med Sci 2014, modified

Risk factors of atherosclerosis are low in SSC and SC.

Four Brain Autopsy Cases of Supercentenarians

Neuropathological diagnosis following international criteria(NIA-AA)

	Case 1 (111 yo)	Case 2 (111 yo)	Case 3 (114 yo)	Case 4 (110 yo)
Past medical history	HT−, DM−	HT−, DM−	HT−, DM−	HT+, DM−
Apo E	2/3	2/3	3/3	3/3
Atrophy	F, T	F, T	F, T	T
AD pathological changes (NIA-Reagan)	Intermediate	Intermediate	Unclassified	Intermediate
AD pathological changes (NIA-AA)	Intermediate	Intermediate	Low PART possible	Intermediate
Hippocampal Sclerosis	None	None	None	None
Vascular injury	Multiple cortical infartcs	None	None	None
Arteriolosclerosis	Mild to moderate	Mild to moderate	Mild to moderate	Mild to moderate

Brain of SC shows intermediate AD changes and mild atherosclerosis, suggesting SC has neuroprotective and anti-

Are you happy now?
I am very happy for everything and everyday. I want to become acquainted with many people
I want to express appreciation. Without the support I cannot survive to 115.
Recently I become forgetful.
I always forget and recall.
So I do not want to become old.
Many old people also forget and recall.
I think that forgetfulness is nature of old people.