Perché fare prevenzione

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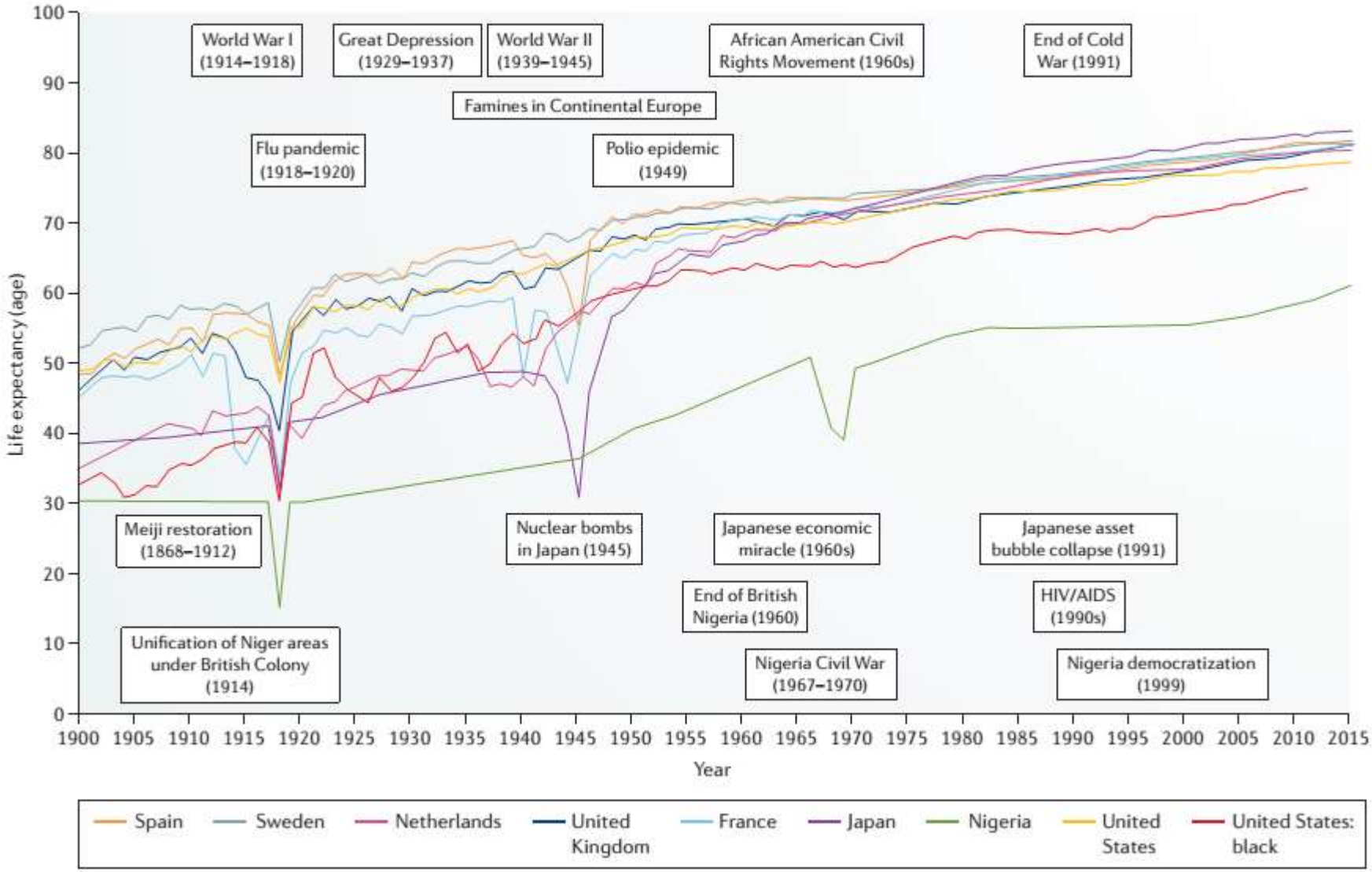

World War I (1914–1918)
Great Depression (1929–1937)
World War II (1939–1945)
African American Civil Rights Movement (1960s)
End of Cold War (1991)
Famines in Continental Europe
Flu pandemic (1918–1920)
Polio epidemic (1949)
Meiji restoration (1868–1912)
Nuclear bombs in Japan (1945)
Japanese economic miracle (1960s)
Japanese asset bubble collapse (1991)
End of British Nigeria (1960)
HIV/AIDS (1990s)
Unification of Niger areas under British Colony (1914)
Nigeria Civil War (1967–1970)
Nigeria democratization (1999)
Life expectancy (age)
Year
Spain
Sweden
Netherlands
United Kingdom
France
Japan
Nigeria
United States
United States: black

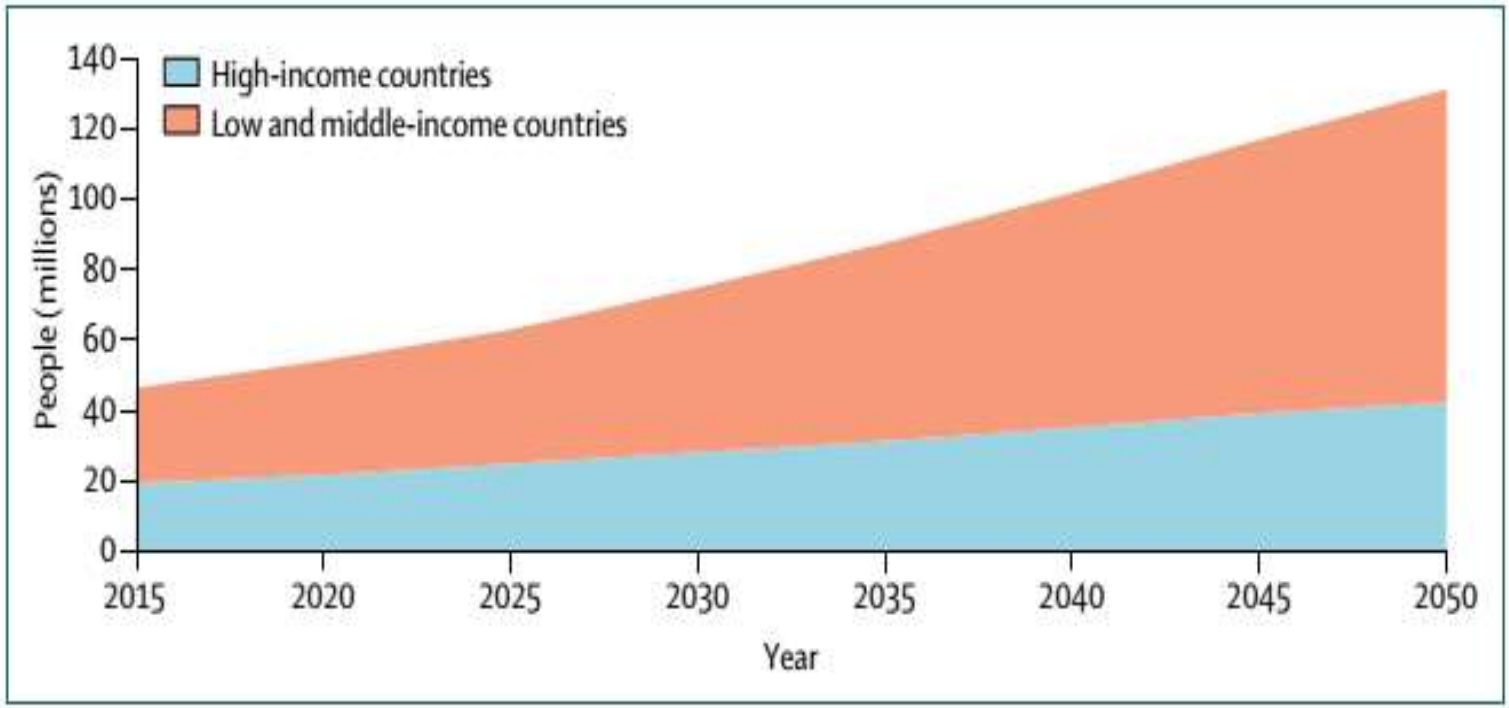


Figure 1: Growth in numbers of people with dementia in high-income and low and middle-income countries

World Alzheimer Report 2015, 46.8 million people worldwide have dementia, and this number is expected to increase to 74.7 million by 2030 and 131.5 million by 2050

Trends in prevalence and incidence of dementia

Studies that investigate changes in its prevalence or incidence over time have emerged only within the past few years

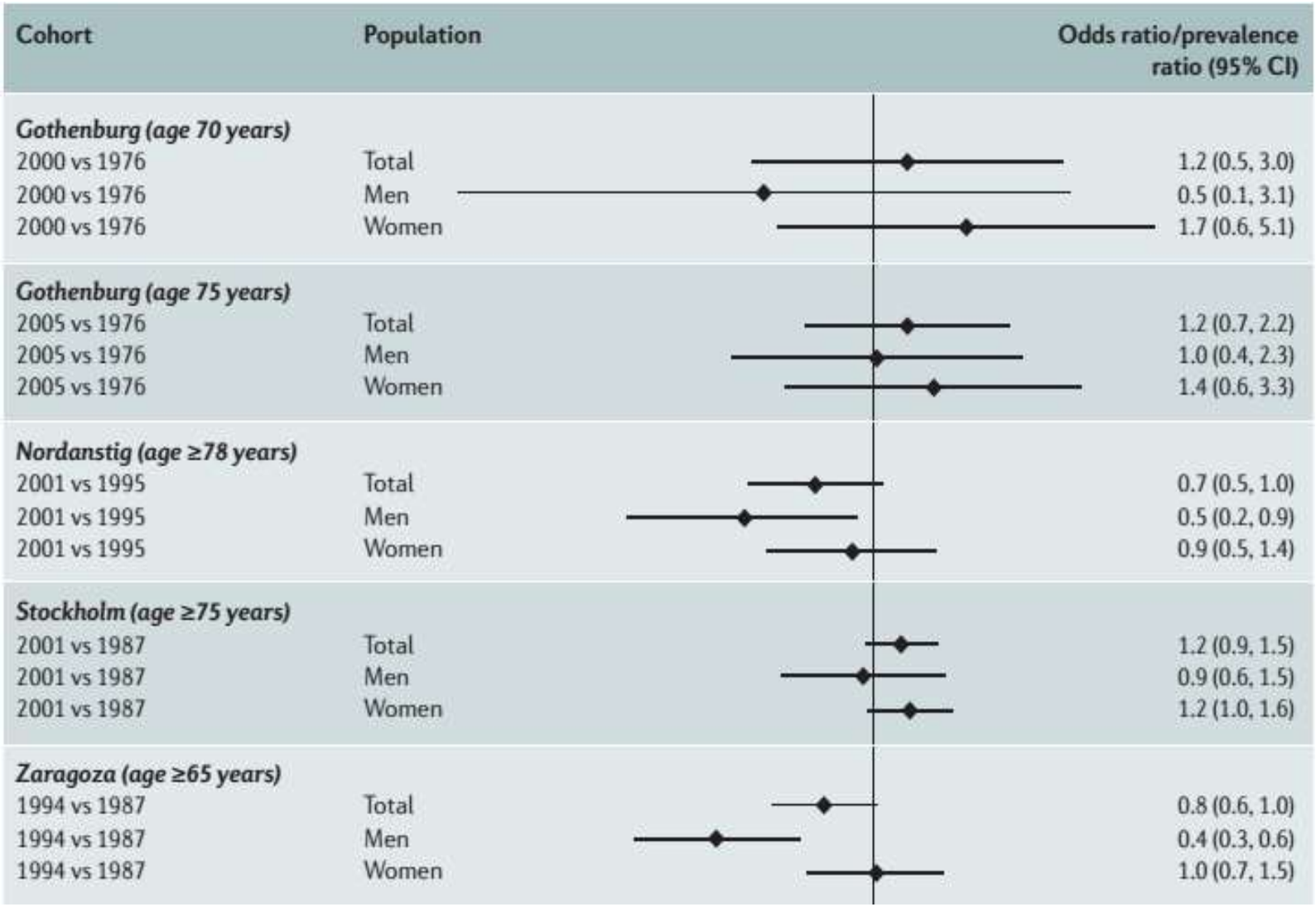
Primary evidence must be founded on population- based studies that have consistent study designs and measurement methods over time

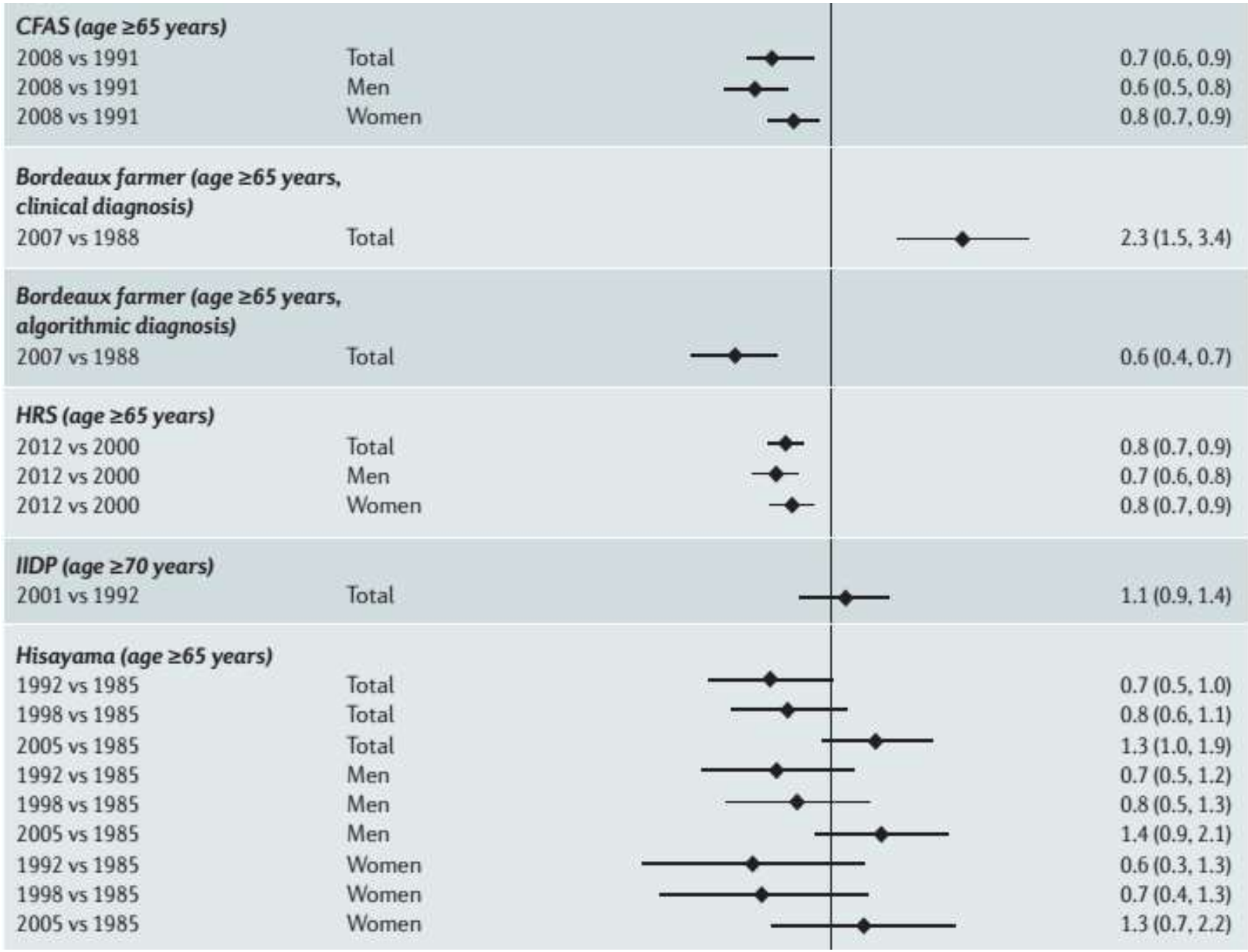
Different criteria are known to identify different groups of patients with Dementia, and any differences in the approach to diagnosis will affect estimates of prevalence and incidence.

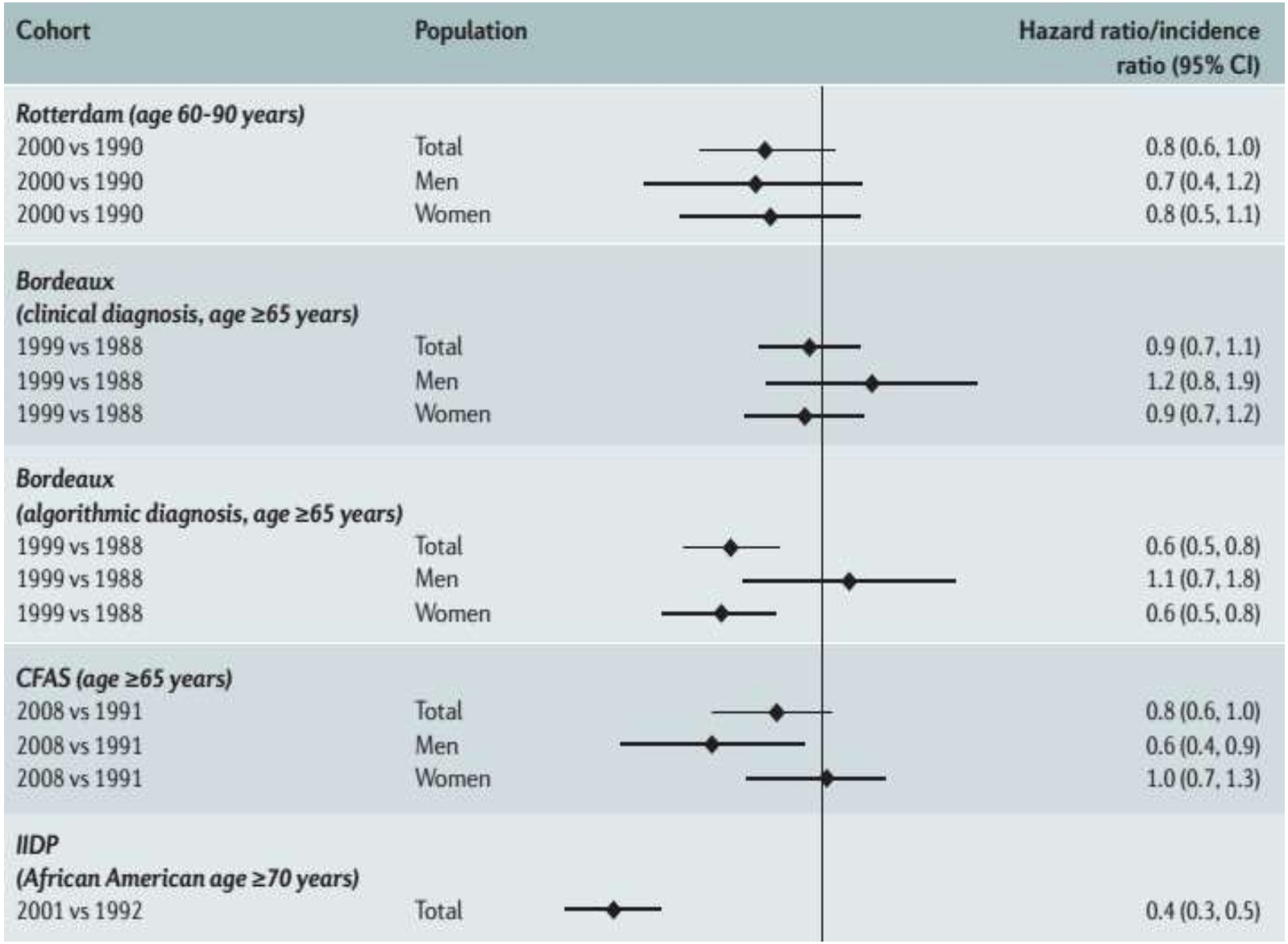
Wu et al. NATURE REVIEWS NEUROLOGY 2017

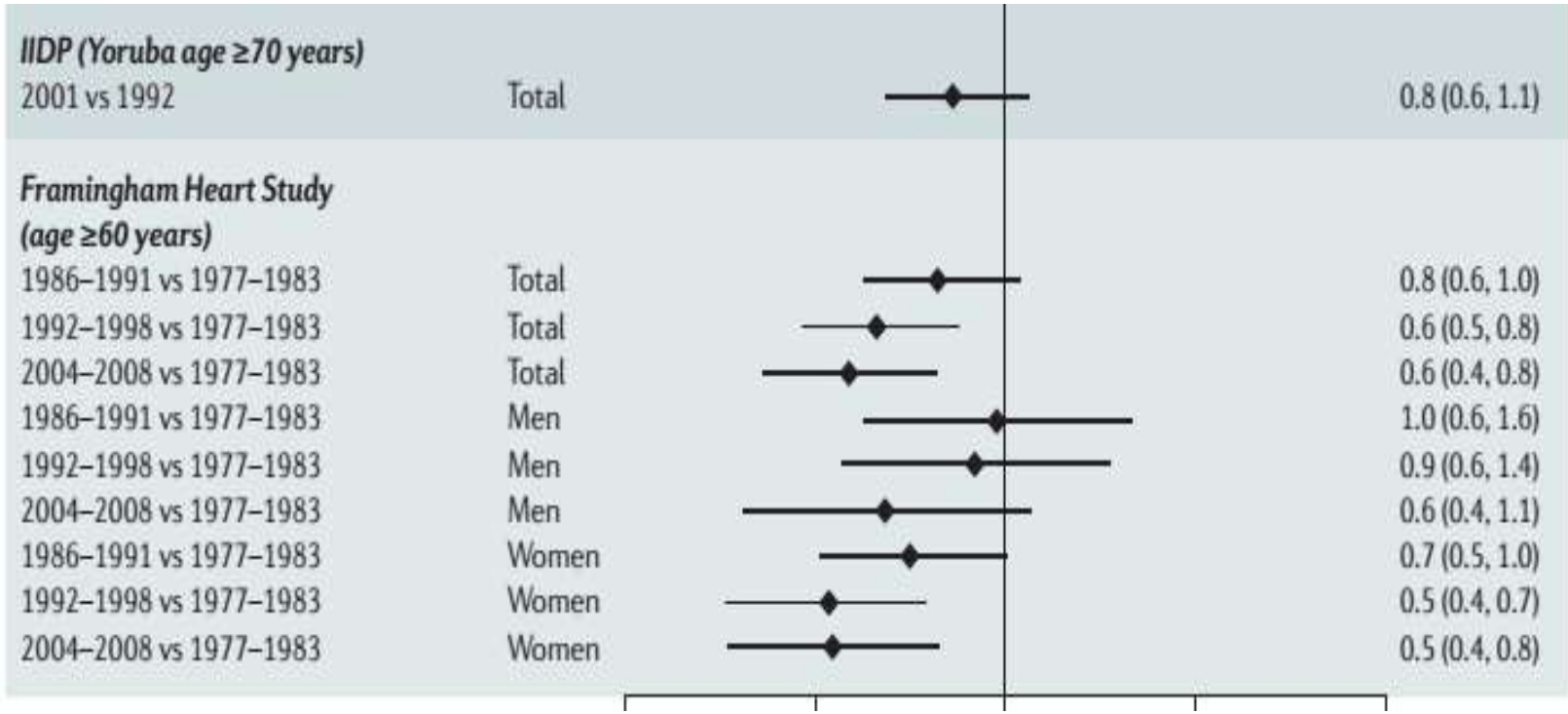
14 population-based studies in which the study methods used at all time points were sufficiently similar and in which the geographical areas were sufficiently well-defined to enable a meaningful comparison.

Of these 14 studies, nine investigated prevalence and five investigated incidence


Cohort
Population
Odds ratio/prevalence ratio (95% CI)
Gothenburg (age 70 years)
2000 vs 1976
Total
1.2 (0.5, 3.0)
2000 vs 1976
Men
0.5 (0.1, 3.1)
2000 vs 1976
Women
1.7 (0.6, 5.1)
Gothenburg (age 75 years)
2005 vs 1976
Total
1.2 (0.7, 2.2)
2005 vs 1976
Men
1.0 (0.4, 2.3)
2005 vs 1976
Women
1.4 (0.6, 3.3)
Nordanstig (age ≥78 years)
2001 vs 1995
Total
0.7 (0.5, 1.0)
2001 vs 1995
Men
0.5 (0.2, 0.9)
2001 vs 1995
Women
0.9 (0.5, 1.4)
Stockholm (age ≥75 years)
2001 vs 1987
Total
1.2 (0.9, 1.5)
2001 vs 1987
Men
0.9 (0.6, 1.5)
2001 vs 1987
Women
1.2 (1.0, 1.6)
Zaragoza (age ≥65 years)
1994 vs 1987
Total
0.8 (0.6, 1.0)
1994 vs 1987
Men
0.4 (0.3, 0.6)
1994 vs 1987
Women
1.0 (0.7, 1.5)


CFAS (age ≥65 years)
2008 vs 1991 Total 0.7 (0.6, 0.9)
2008 vs 1991 Men 0.6 (0.5, 0.8)
2008 vs 1991 Women 0.8 (0.7, 0.9)
Bordeaux farmer (age ≥65 years, clinical diagnosis)
2007 vs 1988 Total 2.3 (1.5, 3.4)
Bordeaux farmer (age ≥65 years, algorithmic diagnosis)
2007 vs 1988 Total 0.6 (0.4, 0.7)
HRS (age ≥65 years)
2012 vs 2000 Total 0.8 (0.7, 0.9)
2012 vs 2000 Men 0.7 (0.6, 0.8)
2012 vs 2000 Women 0.8 (0.7, 0.9)
IIDP (age ≥70 years)
2001 vs 1992 Total 1.1 (0.9, 1.4)
Hisayama (age ≥65 years)
1992 vs 1985 Total 0.7 (0.5, 1.0)
1998 vs 1985 Total 0.8 (0.6, 1.1)
2005 vs 1985 Total 1.3 (1.0, 1.9)
1992 vs 1985 Men 0.7 (0.5, 1.2)
1998 vs 1985 Men 0.8 (0.5, 1.3)
2005 vs 1985 Men 1.4 (0.9, 2.1)
1992 vs 1985 Women 0.6 (0.3, 1.3)
1998 vs 1985 Women 0.7 (0.4, 1.3)
2005 vs 1985 Women 1.3 (0.7, 2.2)


Cohort
Population
Hazard ratio/incidence ratio (95% CI)
Rotterdam (age 60-90 years)
2000 vs 1990
Total
0.8 (0.6, 1.0)
2000 vs 1990
Men
0.7 (0.4, 1.2)
2000 vs 1990
Women
0.8 (0.5, 1.1)
Bordeaux
(clinical diagnosis, age ≥65 years)
1999 vs 1988
Total
0.9 (0.7, 1.1)
1999 vs 1988
Men
1.2 (0.8, 1.9)
1999 vs 1988
Women
0.9 (0.7, 1.2)
Bordeaux
(algorithmic diagnosis, age ≥65 years)
1999 vs 1988
Total
0.6 (0.5, 0.8)
1999 vs 1988
Men
1.1 (0.7, 1.8)
1999 vs 1988
Women
0.6 (0.5, 0.8)
CFAS (age ≥65 years)
2008 vs 1991
Total
0.8 (0.6, 1.0)
2008 vs 1991
Men
0.6 (0.4, 0.9)
2008 vs 1991
Women
1.0 (0.7, 1.3)
IIDP
(African American age ≥70 years)
2001 vs 1992
Total
0.4 (0.3, 0.5)



all five studies suggest a decrease in the incidence of dementia in the total population across cohorts and time periods

Explanations

The Rotterdam study, improvement of brain health — as indicated by larger brain volume, less brain atrophy and less cerebral small vessel disease — was reported in the most recent cohort

Educational level

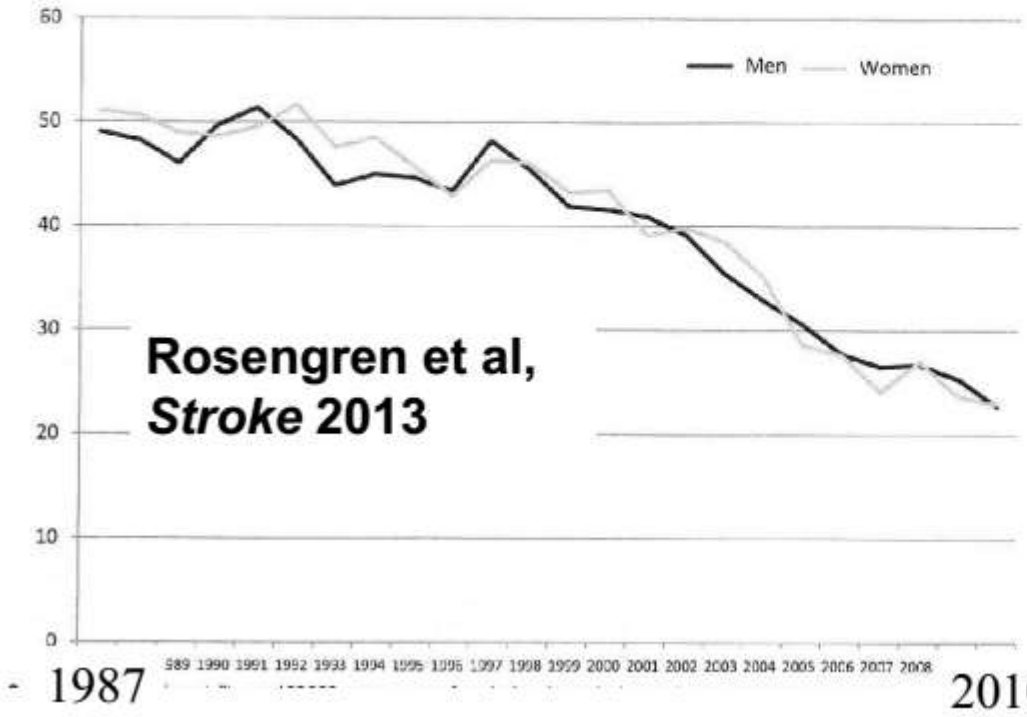
Cessation of smoking

Changing prevalence of several chronic diseases, improvements in the treatments for chronic conditions in the future

Changes in diet and physical activity

A single risk factor is unlikely to be responsible. Changes in Western societies and improvements in living conditions since the two World Wars have led to improvements in overall health and in cognitive development and reserve throughout the life-course

Decreased incidence and mortality of major cardiovascular diseases in high-income countries since the 1980s



Di Cesare et al, *Int J Epidemiol* 2013

Nichols et al, *Eur Heart J* 2013

‘A predominantly reductionist approach that focuses on single mechanisms does not suffice to provide an understanding of the full spectrum of dementia in the general population and to identify risk factors across different populations and life Courses’

Brayne&Davis

The concept of population-based studies — that is, recruiting participants from community-based contexts to ensure representations of the whole population — should be incorporated into future neurobiological and neuropathological research in dementia. Results from small, clinic-based samples, which include only patients from memory clinics or other medical services, have inherently limited generalizability and considerable potential for bias owing to highly selective recruitment.

In particular, people who are socially disadvantaged are less likely to take part in such research.

20 years: major results

1. **The majority of persons affected by AD are very old people**
2. **Marked inter-individual differences in cognitive health in late-life are observed at a population-level**
3. **Several cases present mixed pathologies**
4. **Importance of life-long exposure to multiple factors**
5. **Three possible preventive strategies**

Solomon A, et al. *J Intern Med* 2014; 275(3): 229-50

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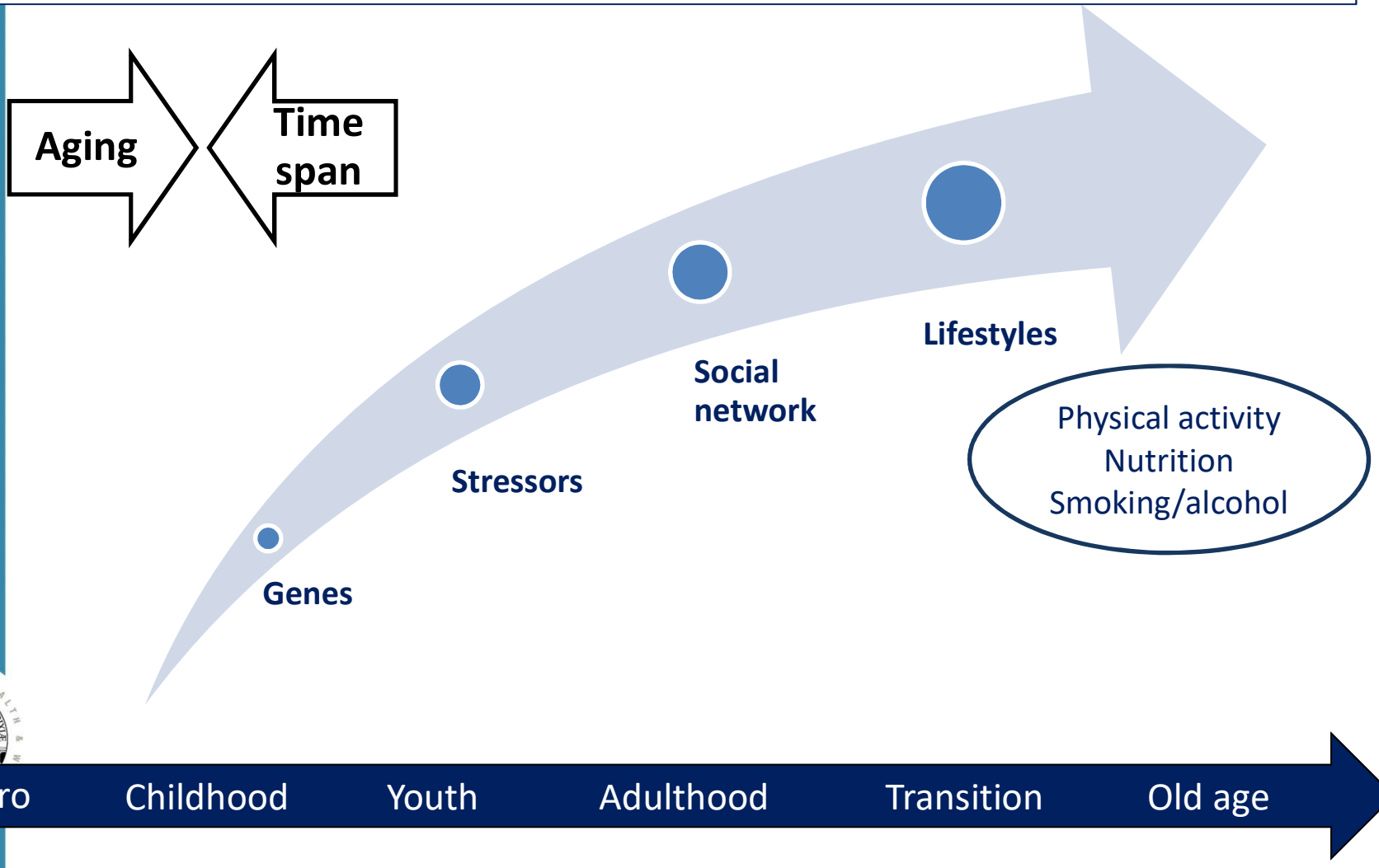
Un complesso di fattori protettivi (o di rischio) durante l'arco della vita agisce come determinante di un invecchiamento di successo (o di fragilità)

BIOLOGY



Characteristics of risk and protective factors

- Non-modifiable risk factors (age, gender, genes)
- Modifiable risk factors

- Increase or decrease the likelihood of developing AD
- Advance or delay the clinical onset

Timing of Exposure

Early life

Mid life

Late life

Whole life

- For developing brain pathology
- For development of symptoms (counteracting the effects of brain pathology)

- Transient
- Persistent

Reverse causality

Developmental factors

Psychological factors

Lifestyle factors

Cardiovascular factors

Education Why?

Proxy of a third variable: intelligence

Ascertainment bias: those with low education perform worse at neuropsychological tests

The brain-battering hypothesis: higher SES, healthier lifestyles, better health literacy, better healthcare

The use-it-or-loose-it hypothesis: intellectual stimulation during life

Cognitive reserve: higher education – greater complexity and/or efficiency of neural networks

In Utero and Early-Life Conditions and Adult Health and Disease

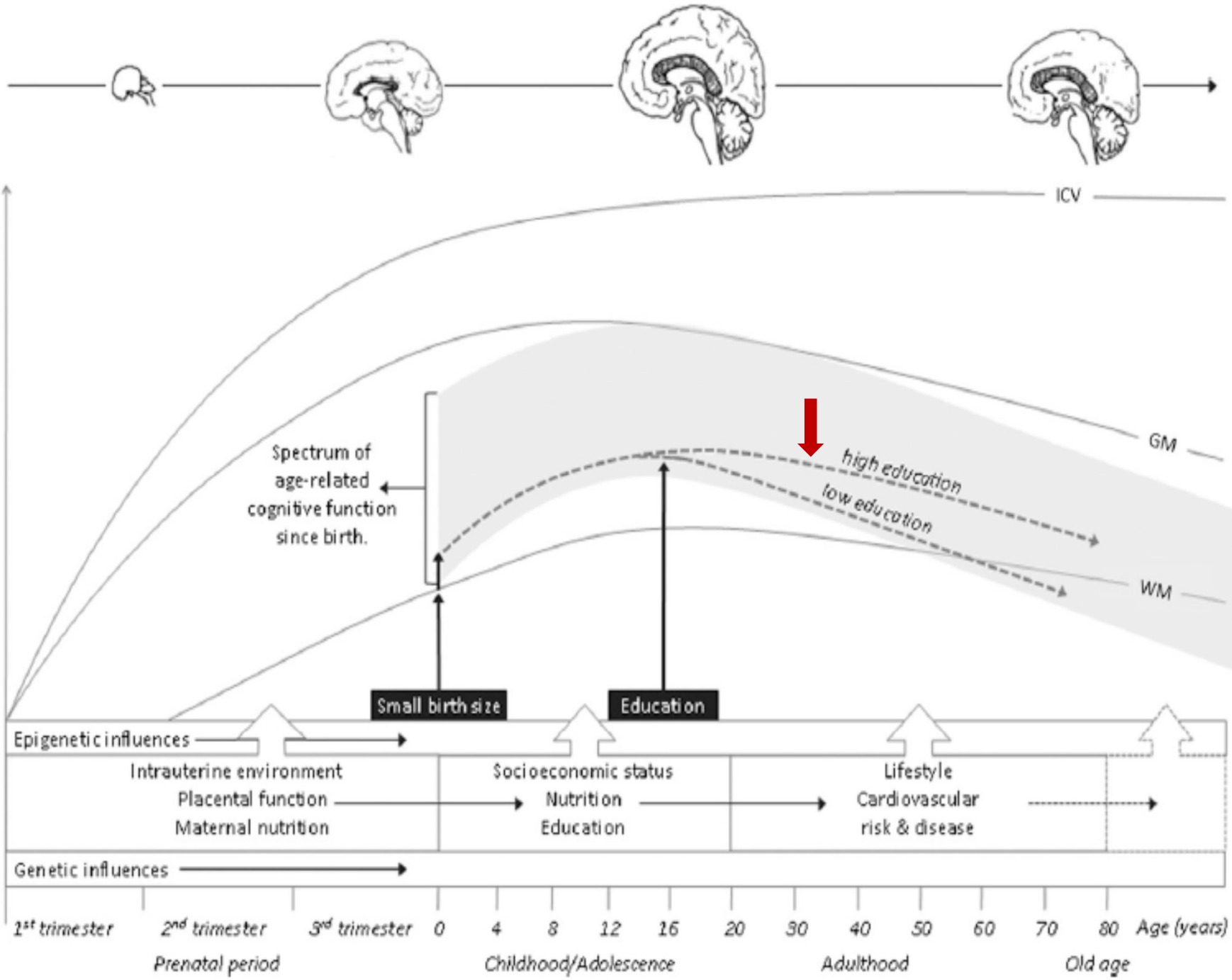
Gluckman et al. 2008 NEJM

TO THE EDITOR:

'…Considering the aging of the worldwide population and the associated increase in the prevalence of chronic diseases, research on the initiating events of such diseases is valuable and necessary, but research on possible synergism or antagonism between in utero and childhood or adulthood conditions on elderly health could be as important for future public health policies. For example, the interaction between education – which has been found to be inversely associated with both multiple chronic conditions and Alzheimer's disease in the elderly population – and in utero environment might be a pioneering project in this growing research field.'

Marengoni et al. 2008 NEJM

Muller et al. Pediatrics 2014



CHARACTERISTICS OF LIFESTYLES

- Modifiable

- Typical targets of preventive programs and interventions

BUT: They cluster

Smoking and alcohol consumption.

Low physical activity level and poorer diet, smaller social network and fewer social interactions.

This means that separating out the potential effect on health of a specific lifestyle is challenging.

HEARING LOSS

Mechanism not clear

Hearing aid? Not known, many people not treated

Social disengagement and depression

Accelereted atrophy

Central hearing loss maybe a prodromal symptom of AD (but rare)

Language importance in brain evolution and social interaction

3 preventive strategies against dementia

- **Decreasing vascular burden**

  - hypertension - heart failure – atrial fibrillation

  - diabetes - stroke

- **Promoting healthy lifestyles**

  - non-smoking

  - moderate alcohol intake

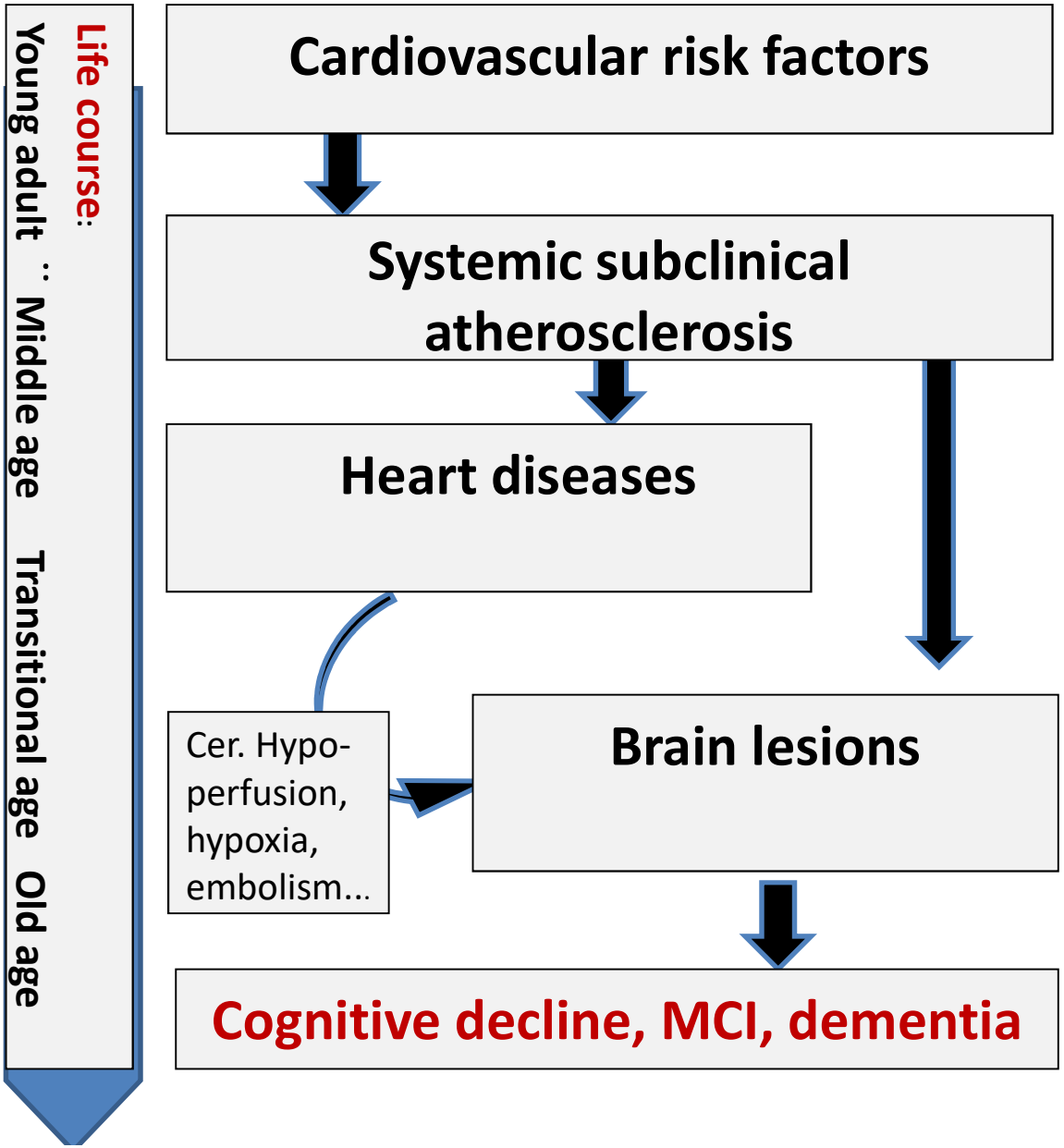
  - physical activity

- **Increasing cognitive reserve**

Courtesy from Laura Fratiglioni

Heart-brain connection in aging

Qiu & Fratiglioni. Nat Rev Cardiol 2015



Brain Plasticity

Van Praag et al. (2006) *Nat Rev Neurosci*

Draganski et al. (2006) *J Neurosci*

Draganski et al. (2004) *Nature*

Gaser & Schlaug (2003) *J Neurosci*

Woollett & Maguire 2006; (2011) *Curr Biol*

J Frisen, 2013: "a large subpopulation of hippocampal neurons constituting one-third of the neurons is subject to exchange. "

Courtesy from Laura Fratiglioni

Brain Plasticity

Is it possible to use brain plasticity to increase cognitive reserve?

Mental stimulation & training

Education

Mentally complex job

Leisure activities

Physical activities

Social network

Other psychosocial factors

Fratiglioni & Wang. Brain reserve hypothesis in dementia. *J Alzheimers Dis* 2007; 12: 11-22.

Draganski et al. (2004)
Nature

CALL FOR ACTION

- Regarding the first two strategies: promoting healthy lifestyle and decreasing vascular burden------starting in middle age
- We need studies to find better strategies to implement these preventive actions
- Brain health promotion messages should be integrated in public health promotion

Regarding the third strategy ”increasing cognitive reserve”: only large intervention studies can answer still open questions:

- **Relevance of cognitive training?**
- **Type of cognitive activity ?**
- **Psychological component? Social engagement?**
- **Is it never too late?**
- **Added value *vs* the first 2 strategies?**
- **Computer based cognitive activities programs?**

THE LANCET Neurology

Fratiglioni & Qiu, 2011 **Time for intervention**

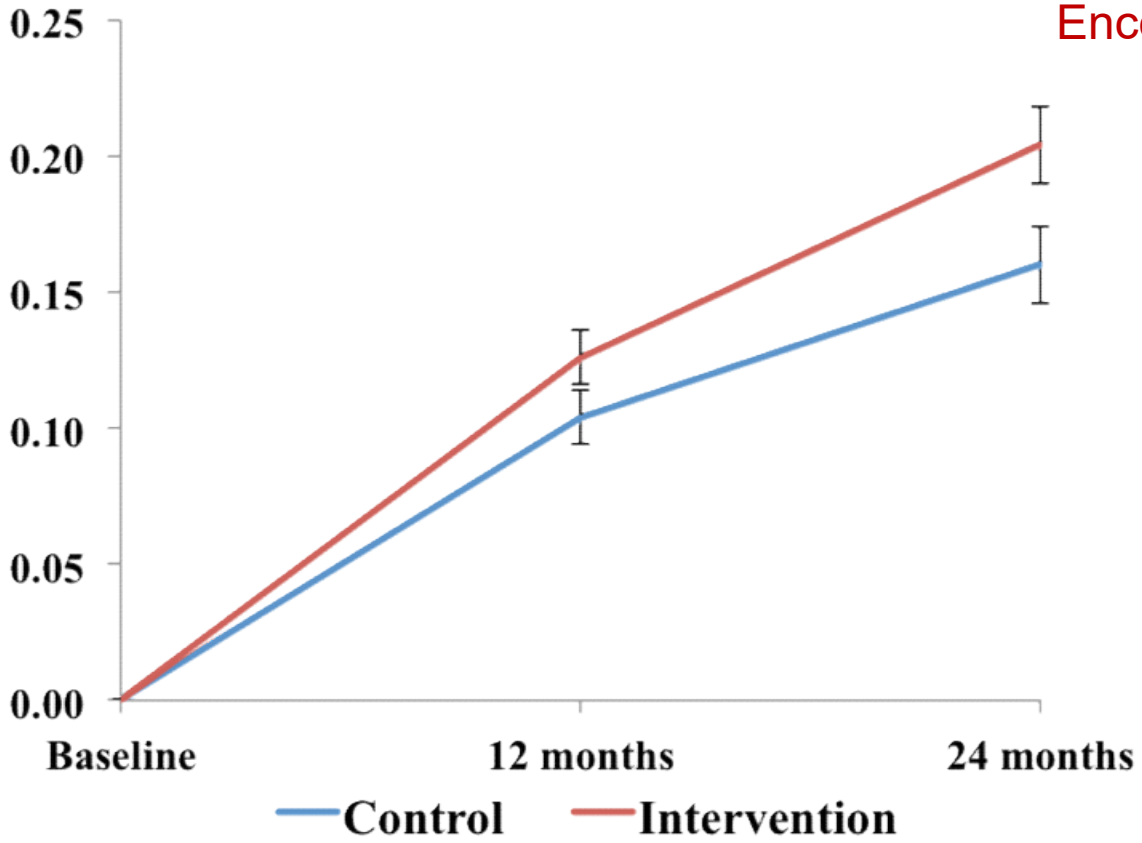
- **FINGER** Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability
- **Pre-DIVA** Prevention of Dementia by Intensive Vascular Care
- **MAPT** Multidomain Alzheimer Preventive Trial

FINGER

A 2-year multi-domain life-style intervention

Difference between intervention and control groups per year in global cognition score---------p=0.03

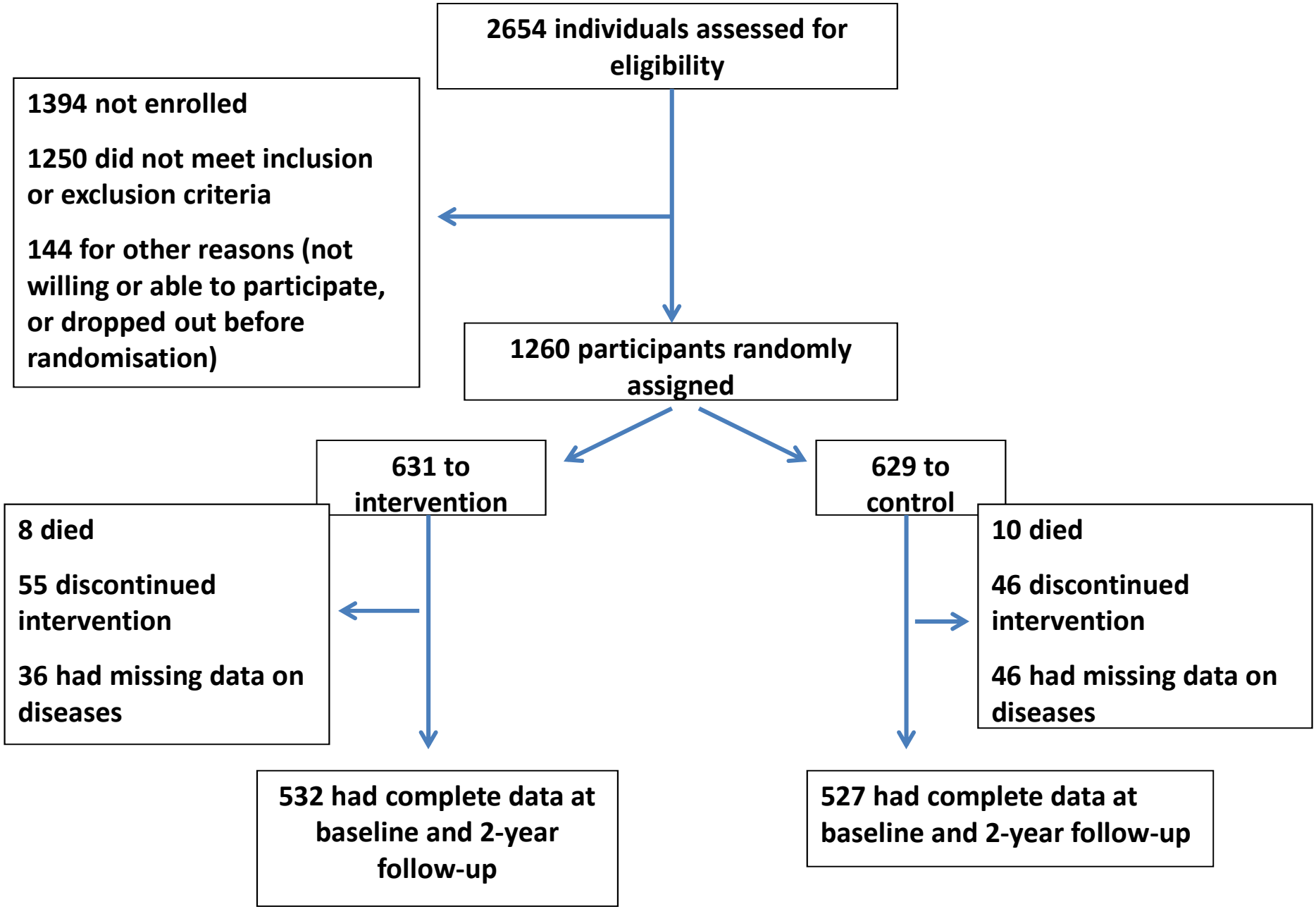
Encouraging results



Kivipelto et al, Lancet 2015

CAIDE RISK SCORE

The CAIDE dementia score uses age, years of formal education, sex, systolic blood pressure, body mass index, total cholesterol, and physical activity to determine an individual's likelihood of developing dementia within 20 years. (See table.) The risk of dementia was found to be 1% for patients with a score of 0–5; 1.9% for patients with a score of 6–7; 4.2% for those with a score of 8–9; 7.4% for a score of 10–11; and 16.4% for patients with a score of 12–15 (Lancet Neurol. 2006;5:735–41).



TRIAL PROFILE

MULTIDOMAIN INTERVENTION

- **Nutritional guidance**
- **Physical exercise**
- **Cognitive training**
- **Management of vascular risk factors**

General advices on health

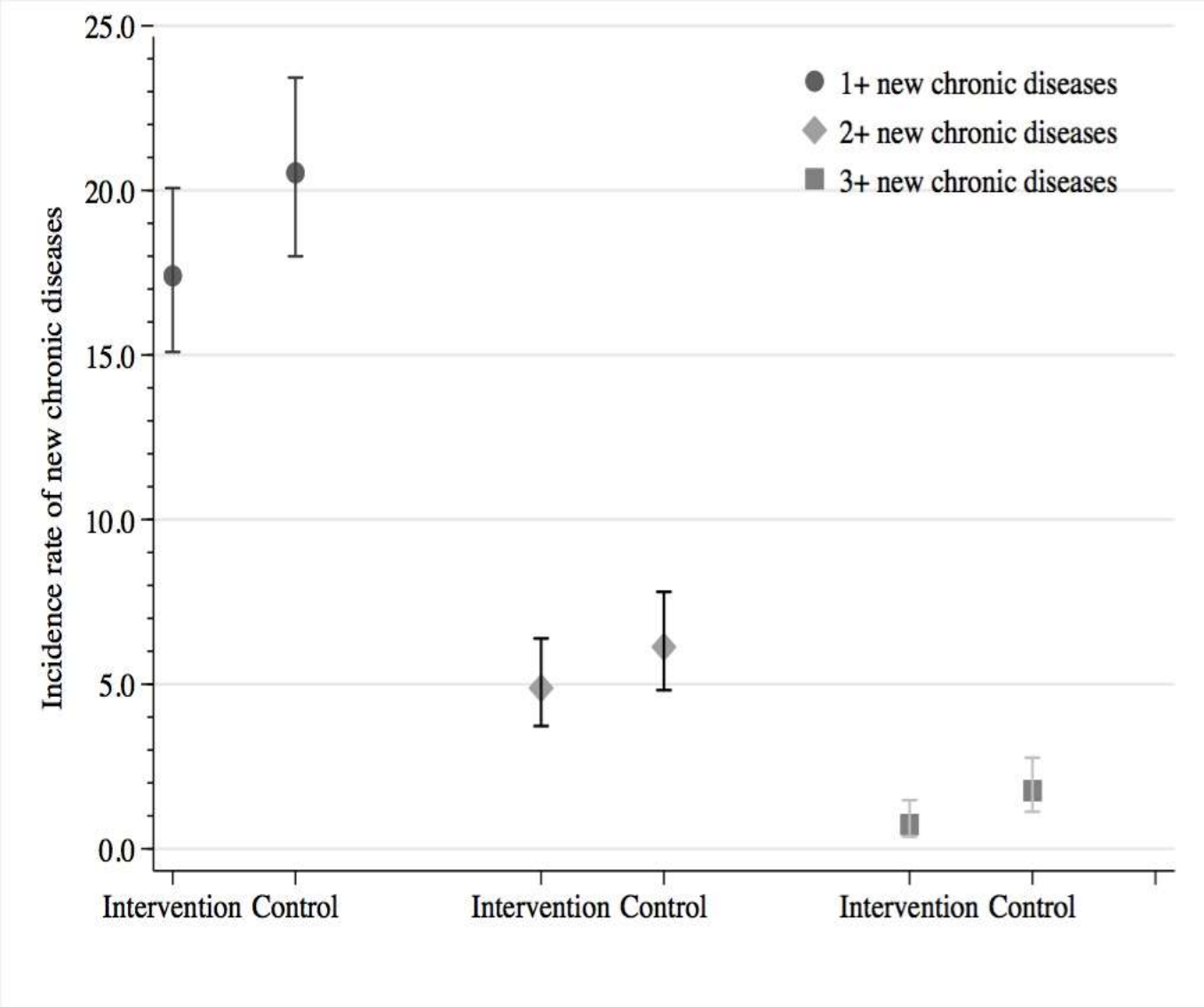
Kivipelto et al., Alzheimer's & Dementia, 2013;9:657-665

- Increased blood pressure/hypertension
- heart failure
- angina pectoris
- cancer
- asthma
- pulmonary emphysema/chronic bronchitis
- gallstones/gall bladder inflammation
- rheumatoid arthritis
- other articular disease
- degenerative arthritis of the back/other illness of the back
- chronic urethritis/nephritis
- cerebrovascular disease
- coronary by-pass, angioplasty
- diabetes
- depression
- and other psychological illness

Baseline characteristics of the intervention and control groups

Characteristics at baseline	Intervention (n=532)	Control (n=527)	p-value
Age, mean years of (n; SD)	69.3 (4.6)	68.9 (4.7)	0.176
Women (n; %)	239 (44.9)	260 (49.3)	0.150
Education, mean years of (n; SD)	9.9 (3.4)	9.9 (3.4)	0.891
Current smokers (n; %)	47 (8.9)	42 (8.0)	0.612
Alcohol, at least once per week (n; %)	236 (44.5)	232 (44.4)	0.978
Number of chronic diseases, mean (n; SD)	1.8 (1.4)	1.8 (1.3)	0.645
None (n; %)	93 (17.5)	97 (18.4)	0.980
One (n; %)	151 (28.4)	148 (28.1)	
Two (n; %)	145 (27.3)	144 (27.3)	
Three or more (n; %)	143 (27.0)	138 (26.2)	

Incidence rates per 100 person-years of 1+, 2+, and 3+ new chronic diseases in the intervention and control group



Adjusted* Hazard ratios (aHR) and 95% confidence intervals (95% CI) from Cox regression models testing the effect of the intervention on the development of 1+, 2+, and 3+ new chronic diseases at follow-up

	Number of persons		aHR	95% CI
	Intervention	Control		
Development of 1+ chronic disease(s)	189	221	0.80	0.66 - 0.98
Development of 2+ chronic disease	53	66	0.74	0.51 - 1.06
Development of 3+ chronic disease	8	19	0.38	0.16 - 0.88

*Models were adjusted for age, sex, education, smoking status, alcohol consumption, and number of chronic diseases at baseline

Adjusted* Hazard ratios (aHR) and 95% confidence intervals (95% CI) from Cox regression models testing the effect of the intervention on the development of 1+, 2+, and 3+ new chronic diseases at follow-up stratified by baseline number of diseases

	Subpopulation with no chronic diseases		Subpopulation with 1+ chronic disease(s)	
Intervention vs. control group	aHR	95% CI	aHR	95% CI
Development of 1+ chronic disease(s)	0.64	0.10 - 3.86	0.33	0.13 - 0 .87
Development of 2+ chronic diseases	0.57	0.26 - 1.27	0.79	0.52 - 1.19
Development of 3+ chronic diseases	0.64	0.10 - 3.87	0.33	0.13 - 0 .87

REMARKS

A multidomain intervention may reduce the risk of cumulating new chronic diseases in older people. The effect is greater in participants who already are affected by at least one chronic disorder

Non-pharmacological trials may be feasible also in persons affected by multiple diseases at baseline.

FINGER provides a pragmatic model for future trials and integrated intervention programs that could be extended beyond prevention of cognitive impairment to prevention of multiple chronic diseases in various settings and populations

LIMITATIONS

1. FINGER was designed to prevent cognitive impairment and disability. Participants were selected for specific characteristics; i.e., cognitive performance and dementia risk.

2. The assessment of chronic diseases was done by a physician through a medical questionnaire, so recall bias may have affected participants' answers. Though, it is unlikely that recall bias differed between the intervention and control group.

3. Because of the design of the study, we cannot ascertain the effect of single domains of the intervention on the development of chronic diseases or evaluate the contribution of each component to the overall effect.

4. The follow-up period was short, so we cannot rule out the possibility that new diseases were only delayed by the intervention. However, delaying the onset of chronic diseases in old age may translate into a compression of morbidity in late life

Pre-DIVA: aimed to reduce vascular risk factors to prevent dementia

Over 6 years dementia incidence did not differ between intervention and usual care

10% more of the intervention group were initiated with anti hyperthensive drugs and in those the risk of dementia was lower

MAPT tested omega 3 and multidomain intervention; no differences

HATICE ongoing e-health intervention

http://www.hatice.eu/

Posta in arrivo - alessandra.ma... | Alessandra Marengoni - Outlo... | bsic88200t Argomenti di lezion... | Home - HATICE.EU

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HATICE

Healthy Aging Through Internet Counselling in the Elderly

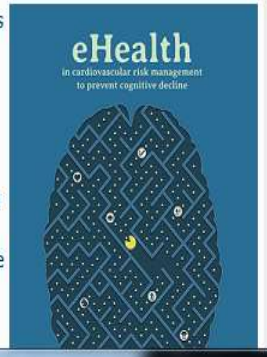
Collaborative project co-funded by the European Unions' Seventh Framework Programme (FP7, 2007-2013) under grant agreement No 305374.

HATICE is the first major research project following the launch of the European Dementia Prevention Initiative (EDPI) in 2011. Cardiovascular risk factors including hypertension, diabetes, obesity, smoking and lack of physical exercise are common in the elderly and increase the risk of myocardial infarction, stroke and dementia.

Main aims of HATICE:

1. Develop an innovative, interactive internet intervention platform to optimise treatment of cardiovascular disease in the elderly
2. Test this new intervention in a randomised controlled trial to investigate whether new cardiovascular disease and cognitive decline can be prevented

First HATICE PhD defense by Susan Jongstra



On 22 September 2017 Susan Jongstra will be the first to obtain a PhD degree based on the HATICE project. As a PhD student Susan was involved in the ongoing trials evaluation, the design of the generic intervention, and the controlled trial itself.

Her thesis covers a broad spectrum of issues involving eHealth in cardiovascular risk management to prevent cognitive decline. Not only the rationale and design of the HATICE trial is presented, but also the extensive, profound and time-consuming process of developing an internet platform for the prevention of cardiovascular disease in older adults. Based on data from the preDIVA trial, the added predictive value of a neuropsychological test of visual memory (Visual Association Test, VAT) over and above a cognitive screening instrument (Mini Mental State Examination, MMSE) was assessed. It seemed that such a short, simple test as the VAT has substantial incremental value for distinguishing older individuals that are at increased risk of developing dementia. For more information, or a copy of the thesis, please contact Susan: s.jongstra[at]amc.uva.nl

In January 2017, Susan has started her training to become a neurologist at the Academic Medical Center in Amsterdam, the Netherlands

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World Wide FINGERS

World Wide FINGERS based on a multidomain lifestyle model which is is going to be tested in different populations and settings across the world, with studies starting recruitment in 2018.

The US study to protect brain health through lifestyle intervention to reduce risk (**US POINTER**) is a 2-year trial testing the multidomain intervention in 2500 adults aged 60–79 years who are at high risk for cognitive decline.

The multimodal intervention to delay dementia and disability in rural China (**MIND-CHINA**) study will recruit 2500 elderly people at risk of developing AD in a 2-year trial in the Shandong province, China.

The Singapore intervention study to prevent cognitive impairment and disability (**SINGER**) is a 6-month feasibility study adapting and testing the FINGER multidomain model to 150 participants with mild cognitive impairment in Singapore.

UK-FINGER is being planned and other countries, including Canada, Germany, Japan, and Spain, are joining WW-FINGERS and planning trials for dementia prevention.

The key feature common to all these trials is the multidomain approach.