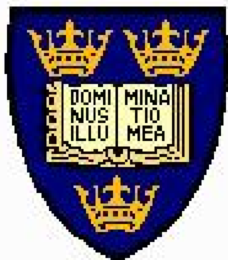
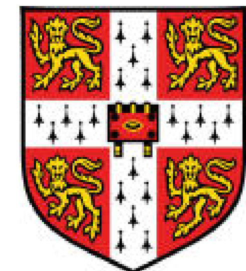
Loughborough University
Leicestershire, UK, LE11 3TU
Tel: +44 (0) 1509 263171

Dementia prevention in LMIC case study Indonesia

Eef Hogervorst, Tri Budi Rahardjo, Yvonne Handajani
Yuda Turana, Philip Kreager, Elisabeth Schroeder-Butterfill

Loughborough University
Respati University
Atma Jaya Indonesia
Universitas Indonesia
Oxford University
Southampton University



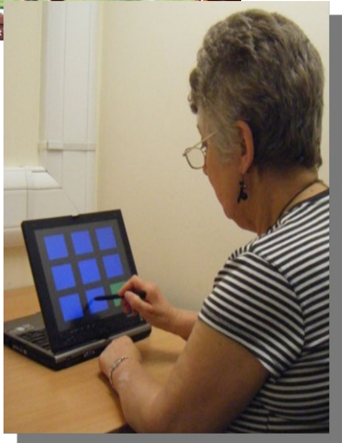


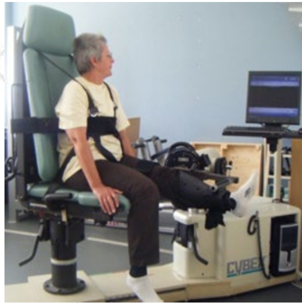
- Author discloses a food supplement review for Proctor& Gamble in 2019

Loughborough University

Best university in the world for sports-related subjects for the fifth year running

QS World University Rankings by Subject 2017, 2018, 2019, 2020, 2021





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TOP 10 FOR SEVEN CONSECUTIVE YEARS

COMPLETE UNIVERSITY GUIDE 2023

#LboroFamily

Dementia is a huge problem worldwide

There is no current treatment

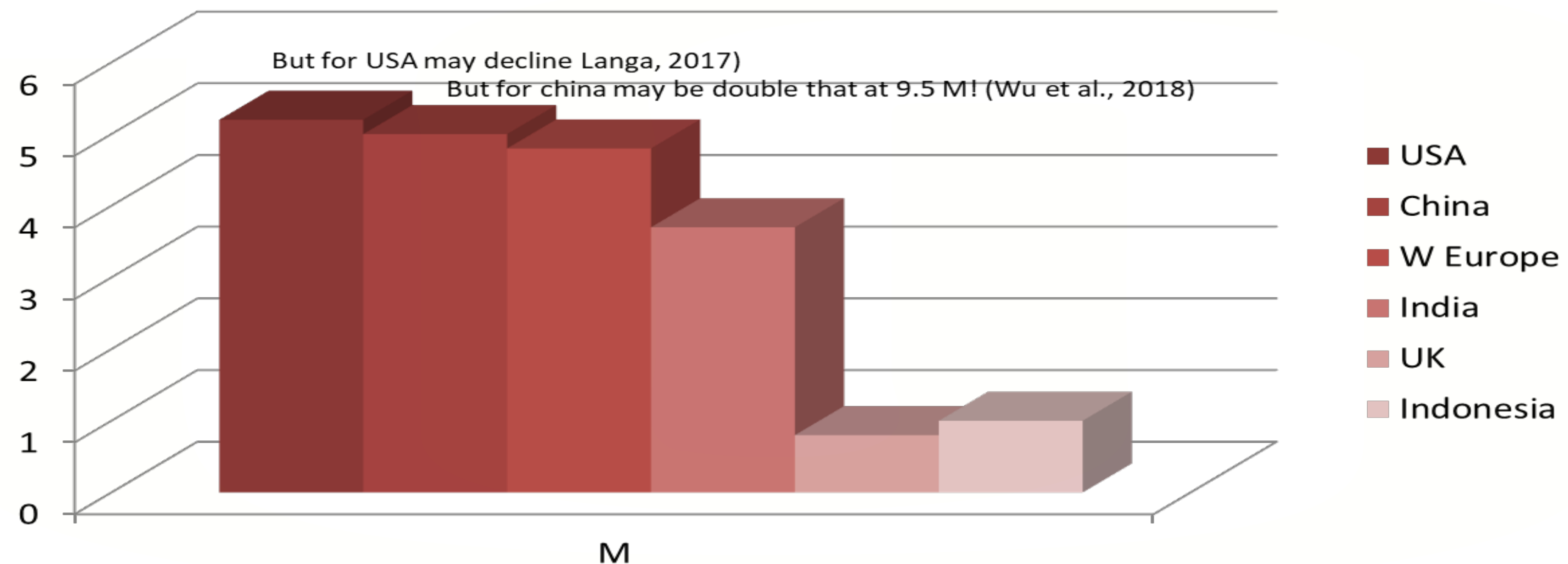
58% live in LMIC: deprivation and low education

2015: 47 million worldwide afflicted with dementia

2030: 75 million

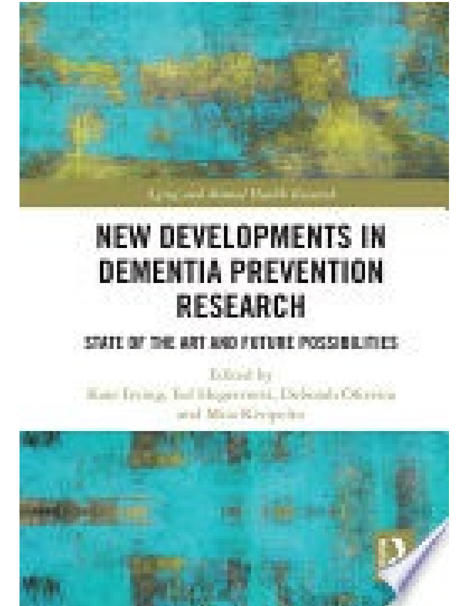
2050: 132 million

Costs: **£1 trillion** in 2018



Dementia prevention (Irving et al., 2018; Livingston et al., 2020) could reduce numbers by 40%

1. Primary: over the lifespan, to prevent pathology
2. Secondary: in prodromal phase: Mild Cognitive Impairment (MCI) to prevent dementia onset
3. Tertiary: once people have dementia, to reduce rate worsening of symptoms (mild/mod->severe)



Changaris 2017

Risk factors for dementia

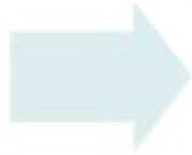
Things we cannot change:

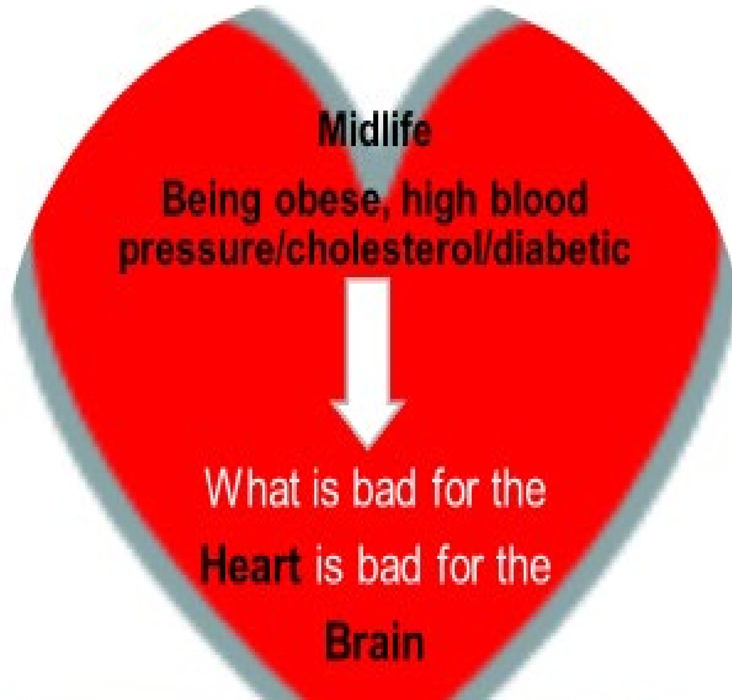
Getting older, gender, having little education, genetics

+

Things we can change:

smoking, diet, exercise





Percentage reduction in dementia prevalence if this risk factor is eliminated

Early life

Less education 7%

Cognitive reserve

Life course approach

Midlife

8% Hearing loss

3% Traumatic brain injury

2% Hypertension

1% Alcohol >21 units per week

1% Obesity

Later life

5% Smoking

4% Depression

4% Social isolation

2% Physical inactivity

2% Air pollution

1% Diabetes

Diet, other CVD risk var (Hearing/TBI)

Activities (Diabetes?)

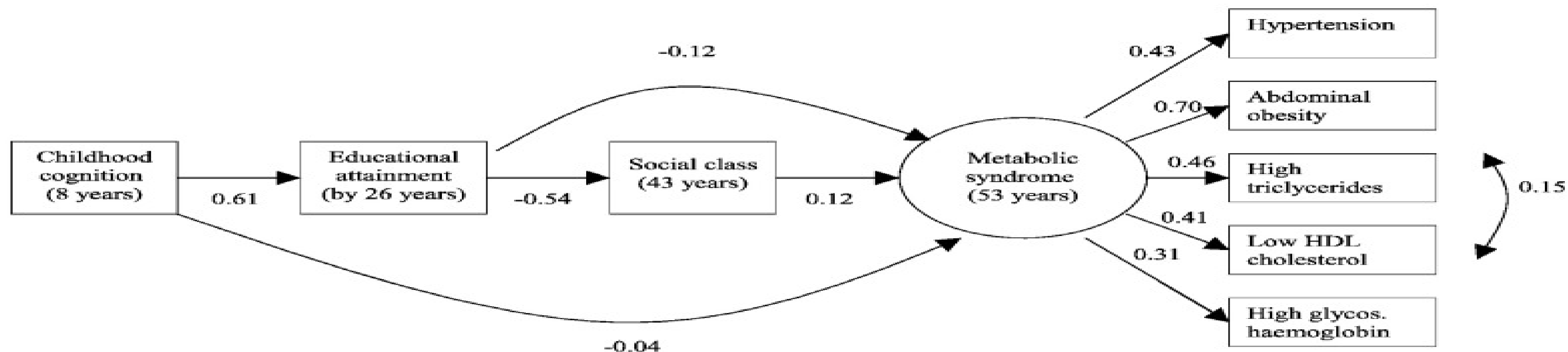
Potentially modifiable 40%

Risk unknown 60%

Livingston et al., 2017/2020

Primary prevention
Changes in cardiovascular/dementia risk factors over lifetime

- High blood pressure in midlife in UK was associated with childhood IQ (Hart, 2004; Richards 2009; Hogervorst 2012)= **cognitive reserve-> optimal environment**: better education-higher socioeconomic class-fewer MeTS, stressors/pollutants etc
- High blood pressure >130 mmHg risk factor (40%) for dementia in UK at age 50, not age 60 or 70



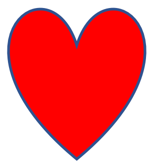
- High blood pressure was seen in Scandinavian cohort 15 years before onset of dementia (in *midlife in 1901 cohort-but not anymore in 1930 cohort- their average BP was lower*), BUT a *decrease* in blood pressure was seen 1-2 years < onset dementia *(Skoog, 2003; 2018;2022).* Same for cholesterol decline over 32 years *(Mielke, 2010)* and lower body weight in AD. Forget to eat? Sarcopenia, loss muscle mass, frailty: immune system?

Modifiable factors-reviews: mixed evidence for individual nutrients, vs. Mediterranean (and similar e.g. DASH) diets

are associated with better cognitive function, lower rates of cognitive decline and a reduced risk of dementia in later life, with follow-up (FU) < 6 years (but usually not found with longer FU)

(Lourida, 2013 Hogervorst, 2020, FU et al., 2022)

Meta-analyses *(Limongi 2020) :* 7 RCT, 38 Longitudinal studies showed reduced risk global cognitive decline in middle-aged/older people with this diet for secondary/primary prevention mainly BUT not in dementia= so probably not for tertiary prevention



Risk factors also often occur together

<u>Meta-analyses</u> n=40,000, 18 studies *(Siervo, 2014, JAD)*

Smoking, low physical activity, , excess alcohol, and poor diet (lifestyle)

hypertension, hypercholesterolaemia, diabetes, high body mass index :

were associated with cognitive impairment *(<u>BUT mainly in < 70 years of age</u>)*

So treat/tackle in midlife

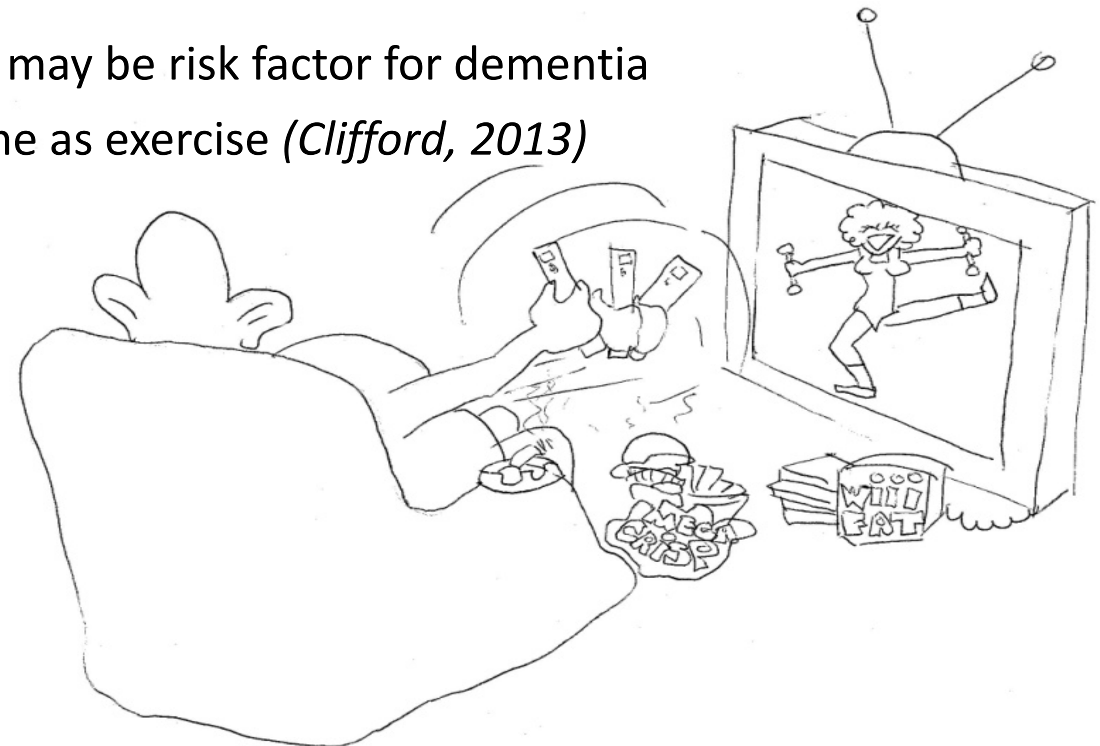
Cohort effects, but also **gender** effects: e.g. hypertension may be risk factor for dementia in <u>women</u>, but not men *(Blanken, 2020; Gong, 2021),* same as exercise *(Clifford, 2013)*

<u>Socioeconomic effects:</u>

Population based observed risk factor **clusters** typically include

- Smoking/ Excess alcohol intake
- Poor diet (fruit/veg)
- Low levels of exercise/sedentary

Peters, 2019 (BMJ open)



Secondary Prevention FINGER study: too late?

Kivipelto et al. Lancet 2013

2 year trial, n=1260 Finnish aged 60-77 years at risk for dementia.

Treatment: advice healthy diet, and medical management of heart disease risk factors, exercise (muscle and cardiovascular training) & brain training

Control group: received health advice

After two years, study better cognition global score intervention group **25**% higher. Planning: **83**% higher. Processing speed **150**% higher after intervention. Risk CAIDE score reduced by 6%, small effects *(Jonsson, 2022)*

https://alz-journals.onlinelibrary.wiley.com/doi/full/10.1002/alz.12123

Similar studies (MAPT France, PreDIVA Netherlands): No effect on primary outcomes, but better for those with increased risk scores *(Kivipelto et al, 2020)*

SINGER (FINGER in Singapore) outcome pilot (n=76, over 65 years of age, average 74 years of age): no difference in cognitive outcomes but trend for blood pressure to be better after 6 months *(Chew, 2021)*

SEMAR: Study of Elderly, Memory decline and Associated Risk factors since 2005

- N=702 participants, multiethnic from rural and urban Java
- Aged 60 to 99 years of age, 68% women

>100 publications with 15 joint PhD In Indonesia with Prof Tri Budi Rahardjo

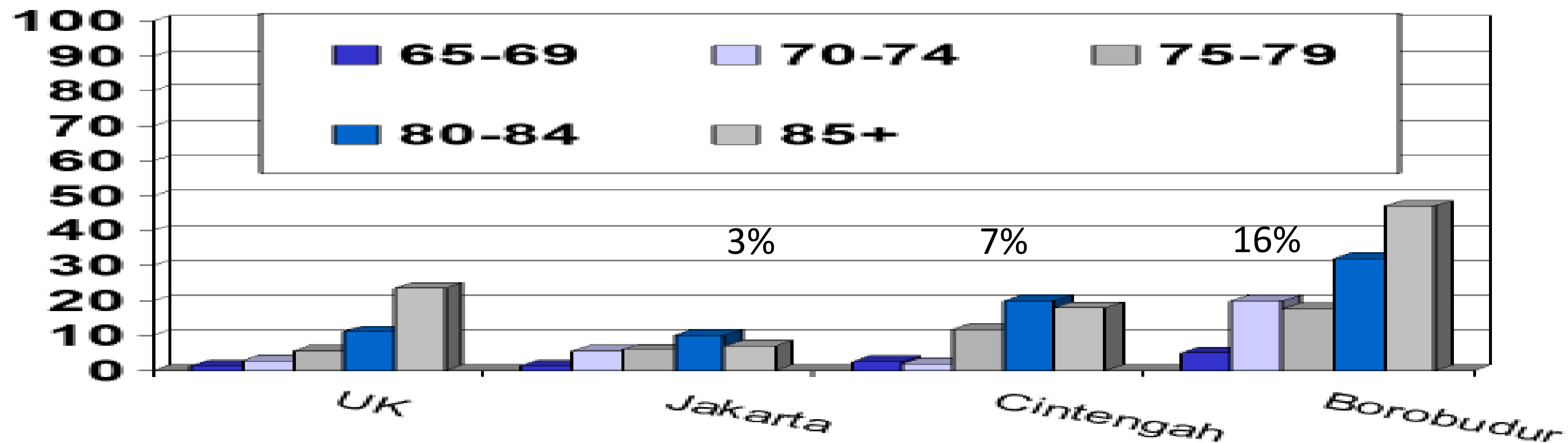
Ageing in Indonesia

Indonesia 2020: 270.2 M-> 9.8% (26.5 M) is 60+,
In 2025 60+= 13.5% (35 M) to 80 M in 2050

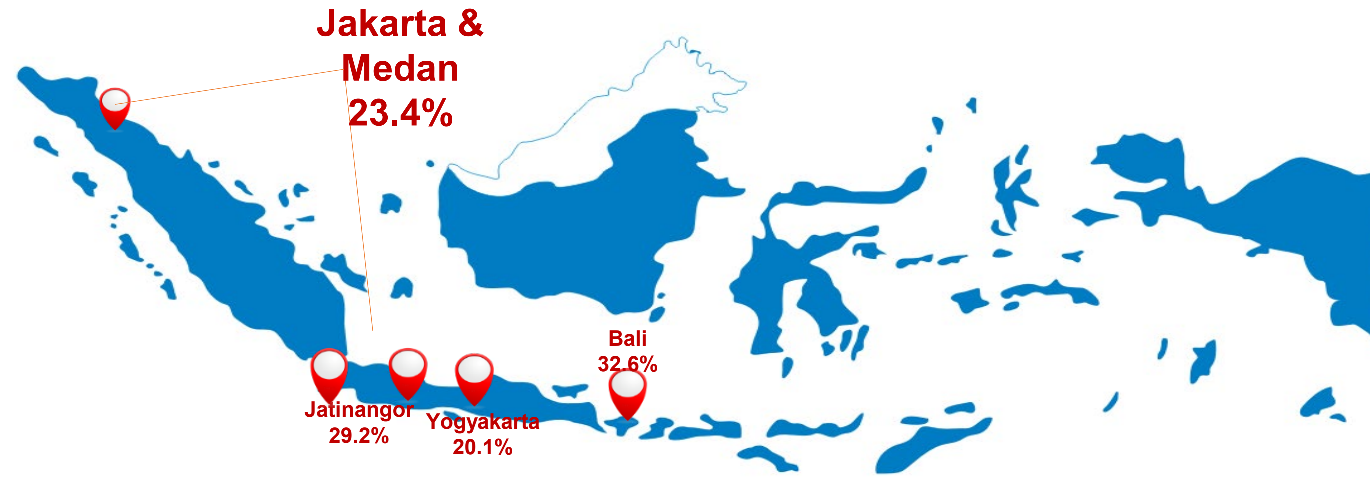
Dementia 5-9% in 2005/6=1.3 M-> 4 M in 2050

Dependency: needs help with activities daily life

1: 5 in rural Borobudur, 1: 10 Citengah/Jakarta



Dementia Prevalence Indonesia in recent years

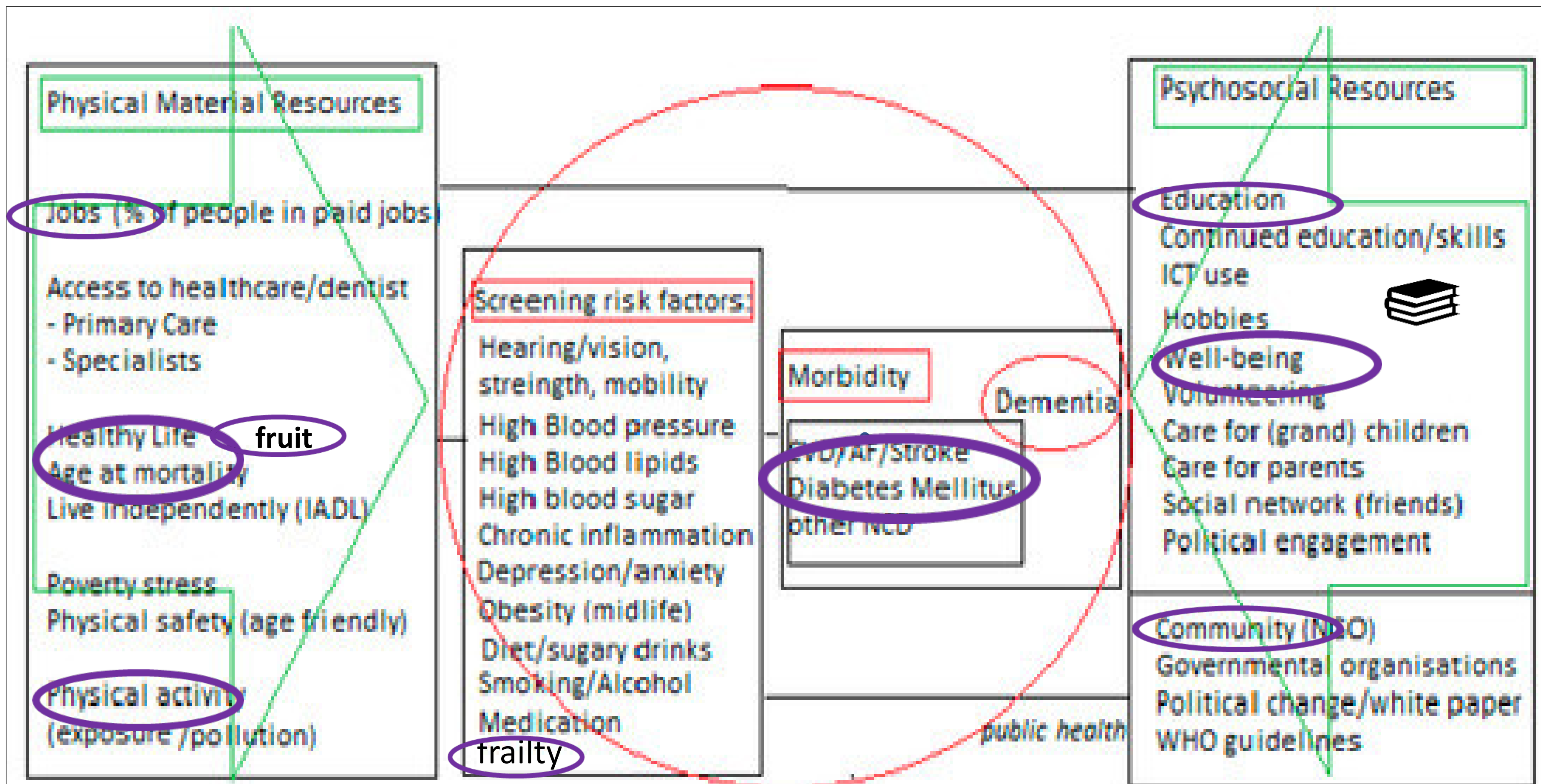


Is dementia prevalence increasing in Indonesia?

Site	Stride Jakarta	Stride North Sumatra	Yogyakarta	Jatinangor	Bali
Number (N)	1100	1100	1976	686	1400
Instrument	Short 10/66	Short 10/66	MMSE/ AD8/ ADL/IADL	AMT / AD8	MMSE/ AD 8/ ADL / IADL
Prevalence(%): Male/ Female	21.2 / 27.6	18.2 /24.3	17.9/22.0	10.8/34.9	25.7/38.6
Level of Education	Not gone to school: 37.7 Senior High School>: 10.3	Not gone to school: 39.2 Senior High School>: 11.1	Not attending >11 years: 9.7	3.6 ± 3.4 years	Not gone to school:48.2 >11 years: 9.2
Mean Age (SD)	69.9 ± 4.7 y.o	72.3 ± 5.9 y.o	71.0±8.3 y.o	72.99 ± 7.21	70.4± 7.9
Prevalence dementia	**24.8**	**22.0**	**20.1**	**29.2**	**32.6**

Risk and protective factors in different Indonesian cohort studies

Hogervorst	Handajani	Ong	Suriastini
2006/2021	2015/in prep	2013/2021	2015/2020
SEMAR n=702	IFLS n=4320	n=686	n=1976
Jakarta Sum Yogya	Indonesia	Sumedang	Yogya
3% 7% 16%	33%	29%	20%
		(22%urban/39% urban)	(14% urban,17-29%)
MMSE/HVLT/IADL/carer	MMSE<21	AMT/AD8/IADL	MMSE/IADL/AD8
Age, education, rural	idem	idem, no job	idem, no job, gender
Subjective health	**idem, falls, morbidity**	**(Stroke/Diabetes)**	**Stroke**
Exercise, Community activities	**idem**	**idem, marriage**	
Eating fruit (and tempe)	**BMI (UW)**	**BMI (UW) fruit**	
(depression)	**insomnia/depression**	**(depression)**	



Compression of needs related to Dementia through Active Ageing Index Indicators

Hogervorst 2021 https://www.mdpi.com/1660-4601/18/16/8235

Study of Elderly, Memory impairment and Associated Risk Factors (n=719)

Clifford, 2010; Hogervorst 2018

Engaging in sport is associated with better memory (HVLT) and global cognition (MMSE) in Indonesian older people

Engaging in sport halves dementia risk

	Stand. Beta	t	*p*	R^2 change	*p*	Exp(B)	*p*
HVLT	.136	3.308	.001	.012	.001	.449	.076
MMSE	.174	4.248	.000	.020	.000		

Pride
Promoting independence in dementia

Primary prevention

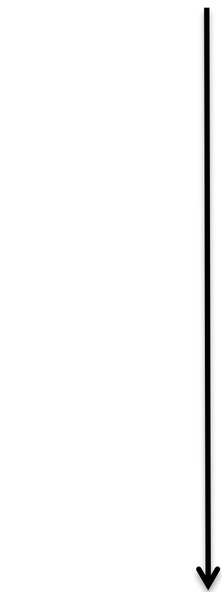
ELSA data UK

Physical activity (PA) reduces dementia risk in a dose dependent manner (Soni, 2017)

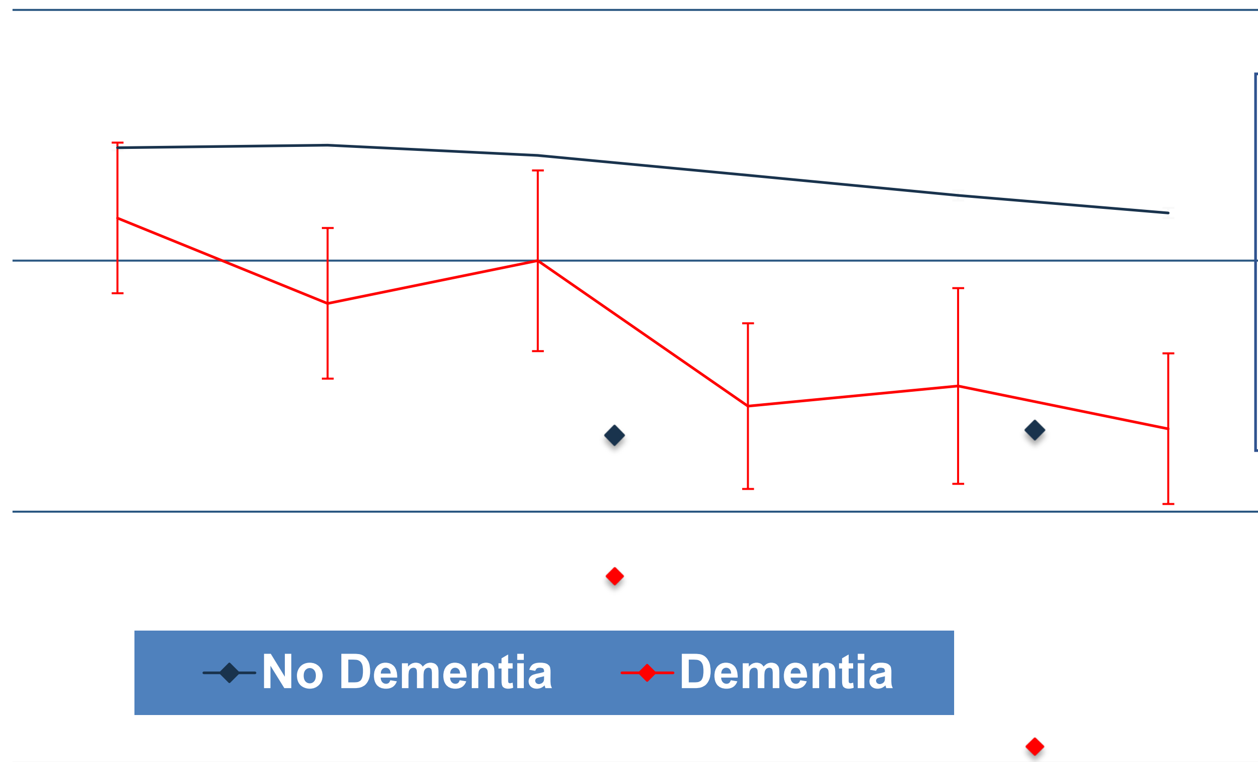
Improving Dementia Care
ESRC·NIHR

Using Cox Proportional Hazard analyses, higher average physical activity (PA) levels across the 10 year follow-up lowered the HR for dementia (full multivariate adjusted HR=0.79, 95%CI=0.69–0.91, p=0.001)

Highest PA levels



Lowest PA levels



Once people have dementia but continue to exercise: their memory (word list recall/verbal fluency) remains better

Walking

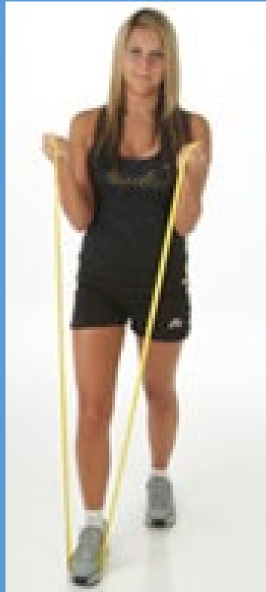
- Dementia risk 50% reduced with 9800 steps a day BUT
- Benefit is already seen with 3800 steps a day
- Brisk walking is better
- Data UK biobank 7 year follow-up, n=78430

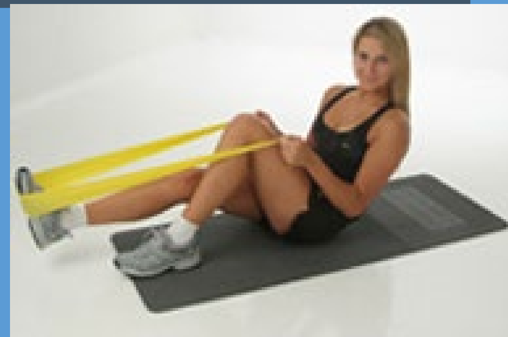
Del Pozo Cruz 2022

Exercise to improve memory in people with(out) dementia (Hogervorst, 2017)

Progressive resistance training:
Programme of 6 exercises using resistance bands

Flexibility training:
Programme of 7 yoga exercises



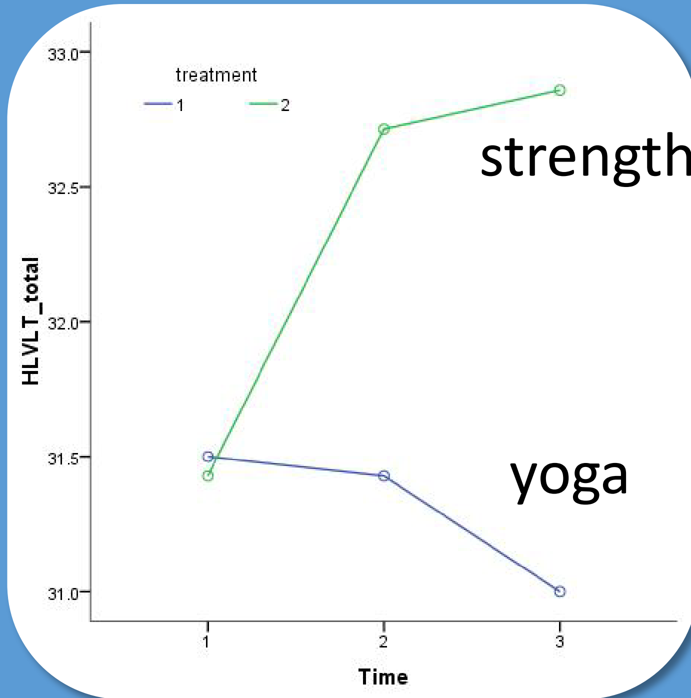


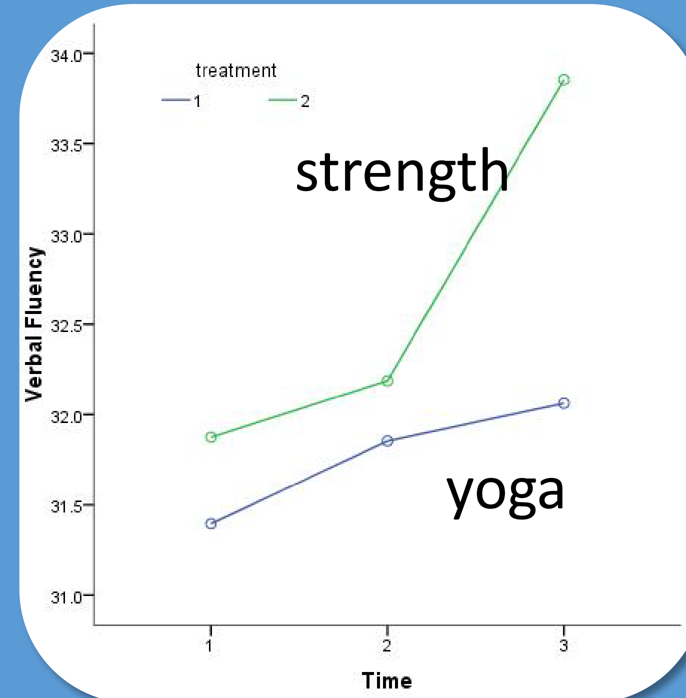
*Team Colours

*10-minute Yoga workouts (Barbara Currie)

Strength training: 6 and 12 weeks improvements in memory performance in middle-aged & older people

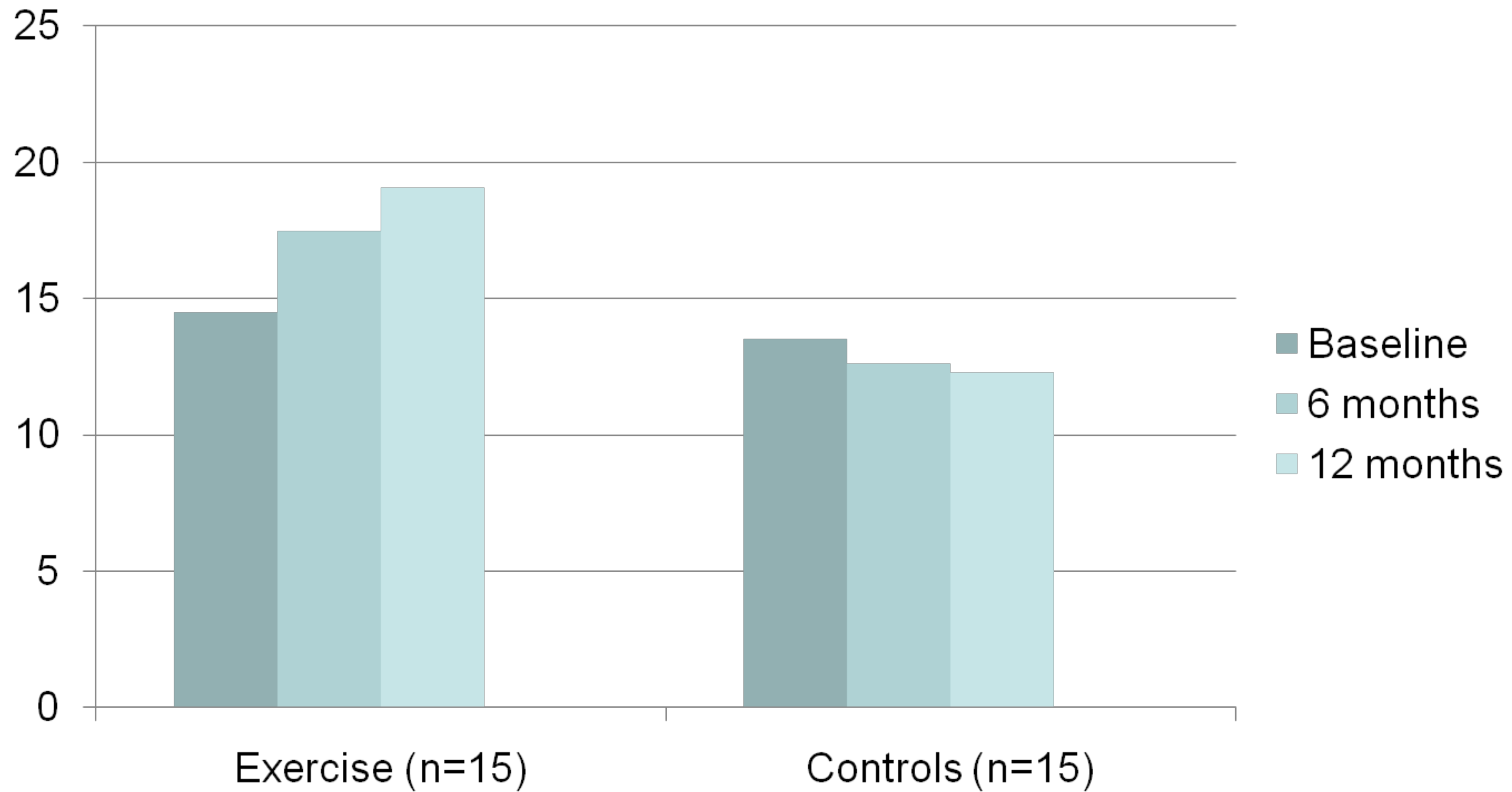
- Resistance (strength) training led to improvements on memory (HVLT and VF)





These are tests which are sensitive to dementia

Tertiary prevention
Mixed stretching/strength (60% VO2max)



MMSE performance in 60+ elderly with dementia

Kwak 2008

Tertiary prevention
RCT in people with dementia

Review of reviews: in 3:7 studies (**walking**) + 4:5 studies (**timed get up & go test**) showed benefit on physical ability in dementia (McDermott et al., 2017) .

Majority reviews: also benefit physical activity on global cognitive function.

Meta-analyses: optimal benefits of **multicomponent exercise** for a minimum of 12 weeks, 3 times a week for 45-60 minutes, including **resistance exercise** (Begde et al., 2021; McDermott et al., 2017; Huang et al., 2022)

ELSEVIER

JAMDA

journal homepage: www.jamda.com

Review Article

Physical Activity and Exercise in Mild Cognitive Impairment and Dementia: An Umbrella Review of Intervention and Observational Studies

Demurtas et al., 2020, n=28205

Table 2
Summary of the Main Findings Regarding Cognitive Function of the Meta-analyses Included in the Umbrella Review

	Global Cognition	Attention	Executive Function	Memory	Motor Speed	Language
MCI	*Mind-body intervention* Small effect Low certainty *Mixed physical activity intervention* Small effect Moderate certainty *Resistance training intervention* Large effect Very low certainty	*Mind-body intervention for visuospatial executive function* Small effect Low certainty *Mind-body intervention* Small effect Low certainty	*Mind-body intervention* Small effect Low certainty	*Mind-body intervention* Medium effect Low certainty *Tai Chi intervention* Medium effect Low certainty *Aerobic exercise intervention for delayed memory* Small effect Moderate certainty	No statistically significant effect	No statistically significant effect
Dementia	*Mixed physical activity intervention in AD* Large effect Very low certainty *Mixed physical activity intervention in all dementias* Medium effect Low certainty	No statistically significant effect	No statistically significant effect	No statistically significant effect	No statistically significant effect	No statistically significant effect

AD, Alzheimer's disease.

Tertiary prevention with exercise: mixed findings

Forbes 2015 (Cochrane) no benefit of exercise on cognition in dementia
Including 3 later trials of high intensity exercise vs control: no benefit on global cognition either *(Toots, 2017 Hoffman, 2016; Lamb, 2018)*

e.g. Lamb et al.(2018) N=500 people with dementia -> n=329 strenuous exercise, 4 months, 2x/week 60-90 min cycling on stationary bike, weights + 1 hr exercise at home (phew!): worse cognition (very small effect) but they were fitter.
Was it too much? (no adherence, was good)

Swedish study, 11 healthy volunteers too much High Intensity Interval Training (HIIT 5x/wk) : mitochondria (energy factories in cell) reduced function, had only 60% of energy production compared to before HIIT -> blood sugar dysregulated (Flockhart, 2021 Cell Metabolism).

Another earlier study showed HIIT 3x per week for 6 weeks did not improve blood pressure or body fat as much as moderate exercise (5x week).
Is less more?

Cognitive Stimulation Therapy

(Spector and Orrell, UCL/Nottingham)

may be as effective as dementia drugs

http://www.cstdementia.com/

<u>Quotes from people with dementia participating included</u>:
"I noticed people becoming more fluent .. trying to express themselves more".
"We just enjoyed ourselves; there's an awful lot of laughter".
"It helped all of us know we were in the same boat".

Tertiary Prevention

Sun (2021): Review of 17 studies: group and maintenance CST are better than individual CST for cognition and quality of life .

Hogervorst 2021 Regional differences in risk

- urban **Jakarta** affluent:

Exercise, reading (proxy of lifelong learning) better *diets, access to care homes, hospitals*

- In rural **Borobudur**:

insufficient access and/or uptake *medical care*. Less likely to do *exercise*. More likely to live with *relatives,* BUT do IADL by themselves (cook alone etc)=cultural aspect

- rural **Citengah:**

heavy labour may impact on health in ageing (people complain, but are objectively healthy). Are more likely to live with *spouse, get help from neighbours:* less impact?

Case study Jakarta 2021 district

for dependency (25%, in high density mixed urban area)
14% dementia MMSE (19%)/HVLT/IADL
Handajani et al. (2022) n=126, 60+

Age (OR=1.10, p<0.001)

Gender (OR=4.06, P<0.0o1)

Possible dementia in

12% men vs. 33% **women**

(fruit consumption trend)

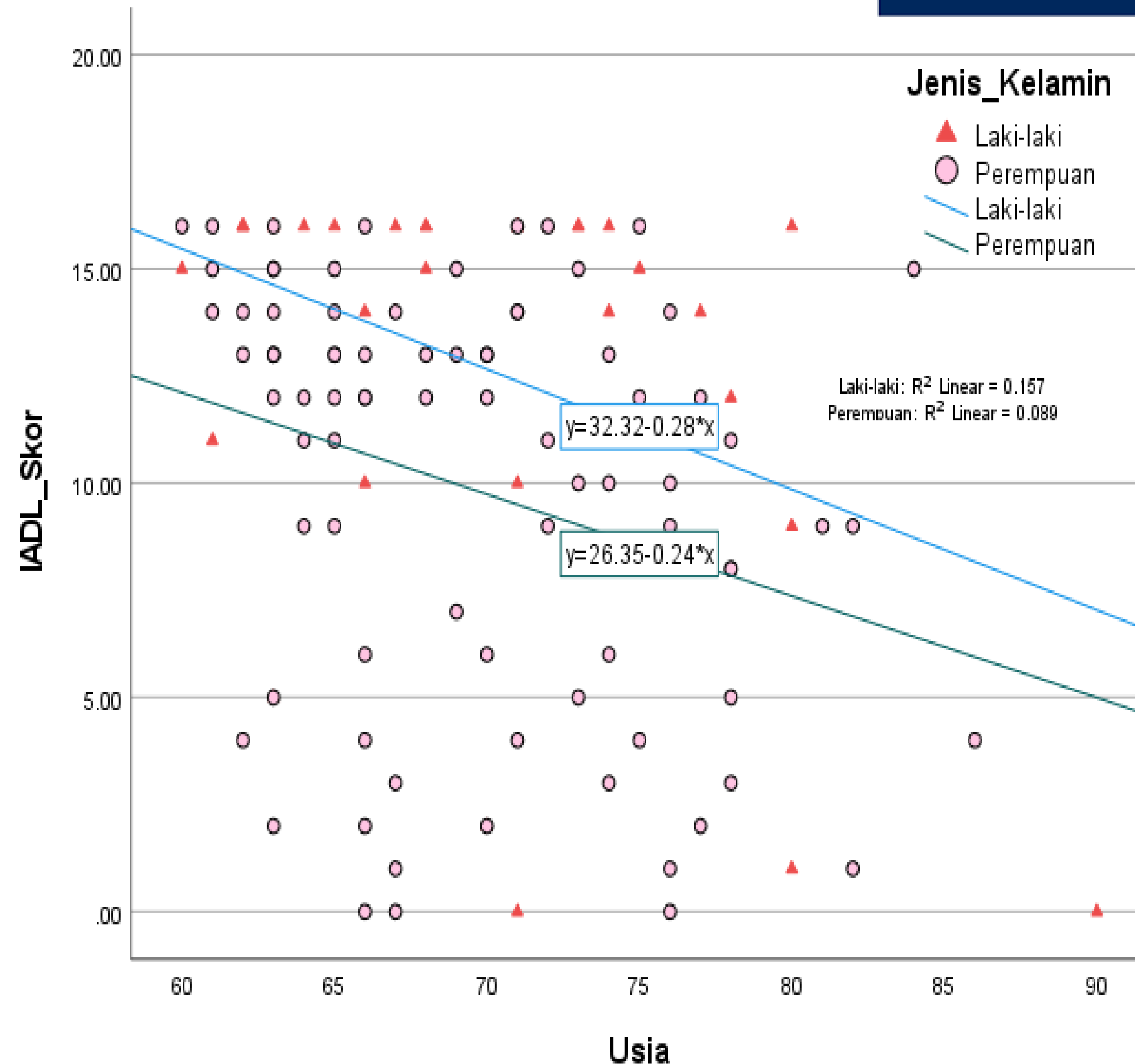
Not significant in the model were

SES: education, job, food security,

Health and **co-morbidity**

Active Ageing components

but sample was small



Older women in this district

had a

- 1.8x more risk of dementia
- 2.8x more risk of dependency
- 1.5x higher risk of falls

No differences in age or health related factors (disease, depression, frailty etc)

BUT women were more likely to

- Have obtained less education (>9 years :1% vs 23% of men)
- Did not have a job: 20% vs 53% men
- Did not live alone (2% vs 7%) or with spouse (2.4% vs 7%):
- Most lived with family (children)

Arifin et al., 2012 - Systematic inequality

SUPAS 2005 data, survey all Indonesia included, data of older people

- 42% of men were healthy, but only 36% of women
- Most older people needed no ADL help, but more women did: 2-20%
- Women lived with children more, relied on children's income more
- Women had obtained less education, did fewer protective activities
  - have a job: 24 vs 53% of men
  - read: 4 vs 7% of men
  - do exercise: 1 vs 2% of men
  - spending time outdoors (gardening/fishing)
  - same percentage engaged in social activities (18/17%)

Discussion

- Cardiovascular risk factors (obesity, smoking, high cholesterol/blood pressure etc) treat in midlife latest to reduce the risk of dementia in later life, probably same as nutrition/diet: best used as primary prevention
- In MCI (secondary) and AD/dementia (tertiary prevention): group-based CST and community activities and possible beneficial effects of *moderate* strength and walking exercise on global cognition, falls, psychiatric symptoms, carer burden
- Gender inequality: women (in rural/deprived areas) had less education, were less likely to be able to support themselves: no job, dependency on children + higher risk of dementia
- Government policies:
  - education for deprived, rural women to support active ageing, including having a job to support themselves
  - Support community activities: help people to stay active (exercise, psychosocial), maintain a healthy weight and eating well (tempe, fruit) for independence in ageing, to prevent dementia
- These activities are done in Indonesian Posyandu by trained cadres (volunteers): how effective are these (tempe)?

Different types of soy (Indonesia) and dementia risk

In those over 68 years of age in rural Borobudur :

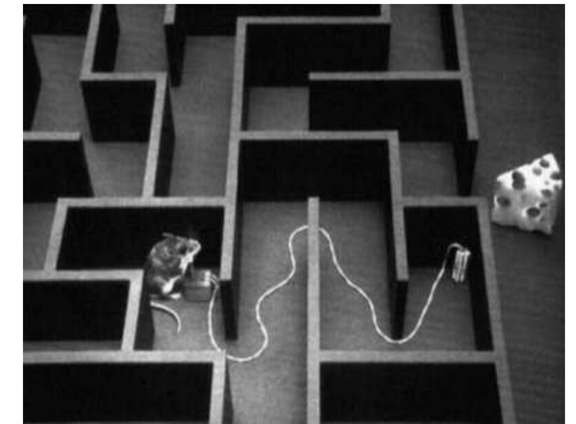
- Tofu intake (total/wk) increased risk by 30%
- Tempe intake (total/wk) reduced risk by 20%

Controlled for age, sex, and education, and other foods (fruit intake was significant, green vegetables NEG!) (Hogervorst, 2007)

When Posyandu advised older people to eat more tempe, less tofu: association between tofu disappeared @>2 year FU (Hogervorst, 2011)

Mice studies showed benefits of tempe on maze memory and Abeta42 (Kridawati, 2010)

Recent tempe RCT benefits in older women with/without dementia (Handajani, 2019; 2021)



Further research

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

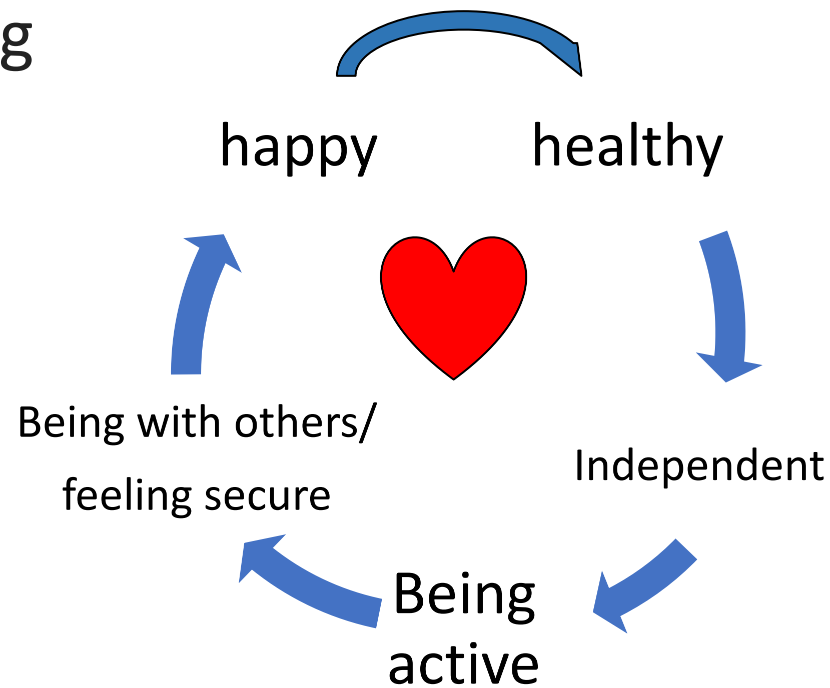
- Are dementia screening test culturally applicable (vs carer report 3-7% vs asking communities 6%)
- Reverse causality: Do people stop engaging with jobs/activities, because they have dementia (embarrassment, inability) ?
- Selection/survivor bias: did men with dementia/poor health not attend research surveys, was that out of choice and/or did they die earlier (like in UK) ?
- Why do women live with children: necessity and/or rural/urban traditions: cultural attitude towards care (filial respect and duty of care vs abuse/neglect)
- Areas with low access to health care/medication: do women suffer more, is the risk dementia higher? Vs.
- Where community centres are active incl. volunteers, is there less dementia (e.g. better cardiovascular risk reduction, activities, e.g. tempe example)?

Active Ageing Components

Well-being: what makes people happy ?

Role for community centres

- Feeling secure
- Being socially active
- Playing sports
- Walking



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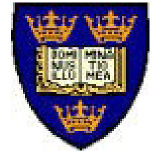

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Alzheimer's Research UK

The Power to Defeat Dementia