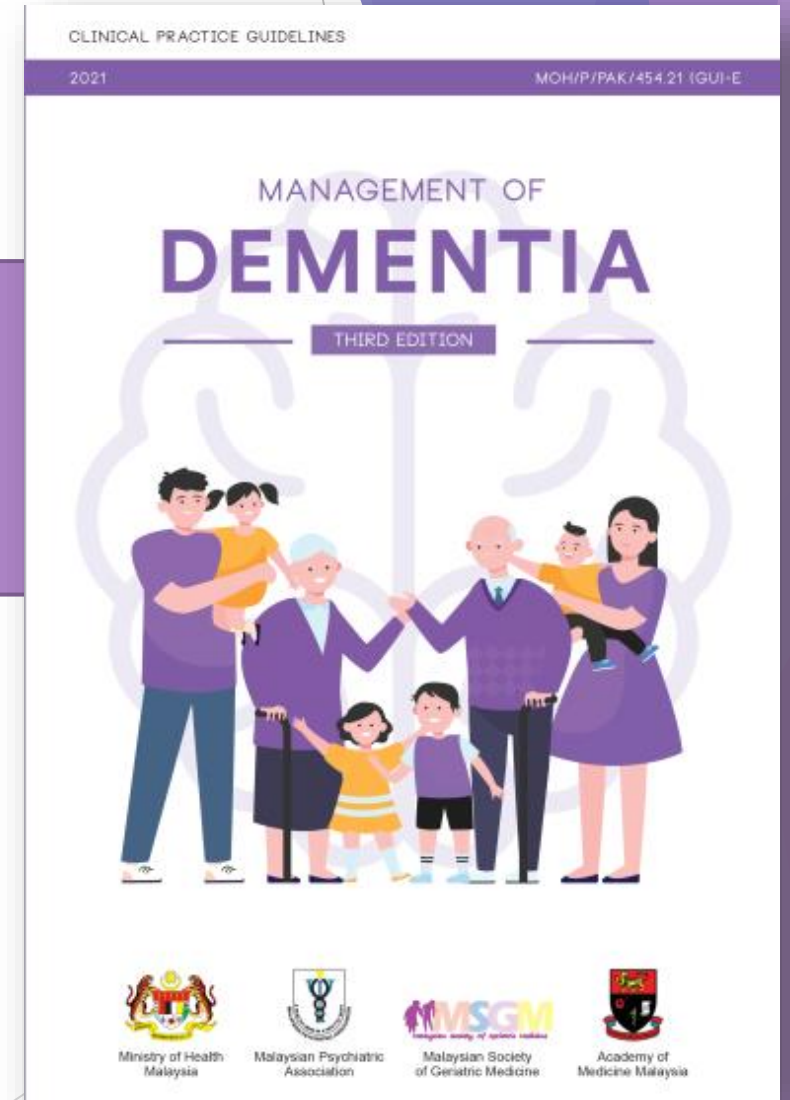


# Training of Core Trainers CPG Management of Dementia (Third Edition)

## Risk Factors & Risk Reduction Strategies

**By:**  
**Dr. Valarmathi Masilamani**  
Family Medicine Specialist  
Klinik Kesihatan Batu

**Dr. Zaleha Jusoh**  
Family Medicine Specialist  
Klinik Kesihatan Batu Rakit



# Learning Objectives

1. To identify the non-modifiable and modifiable risk factors for dementia.
2. To identify the risk reduction strategies that can be undertaken to reduce risk of dementia.



# Risk Factors For Dementia

## ► Non-modifiable risk factors:

- Advancing age
- Female Gender
- Apolipoprotein E ε4, genetic variants

## ► Modifiable risk factors:

- Cardiovascular Risk Factors
- Psychiatric illness -Depression
- Smoking
- Excessive alcohol consumption
- Physical inactivity
- Environmental elements - nitrogen oxides, ozone and particulate matter in the air
- Traumatic Brain Injury
- Lower early life education level
- Mid-life hearing impairment



# Non-modifiable Risk Factors

- ▶ Advancing age: age  $\geq$  65 years<sup>10</sup>
- ▶ Gender: Female higher risk especially in AD
- ▶ Genetic:
  - Early-onset AD - 13% exhibit autosomal dominant transmission. Three causative gene mutations identified; amyloid precursor protein (APP) gene, presenilin 1 (PSEN1) gene & presenilin 2 (PSEN2) gene<sup>10</sup>

# Non-modifiable Risk Factors-2

## ► Genetic:

- Late-onset AD – multifactorial with more complex genetic basis<sup>11</sup>
- $\epsilon 4$  variant of the APOE gene (APOE4) increases risk for AD<sup>10</sup>
- Presence of APOE4 itself is neither necessary nor sufficient to cause AD<sup>11</sup>

11. Van Cauwenberghe C, Van Broeckhoven C, Sleegers K. The genetic landscape of Alzheimer disease: Clinical implications and perspectives. Genetics in medicine: official journal of the American College of Medical Genetics. 2015;18.



# Modifiable Risk Factors: Cardiovascular

- ▶ Hypertension at midlife should be appropriately treated.<sup>10</sup>
  - ARBs have the most positive effect on cognition in elderly patients with hypertension without apparent prior cerebrovascular disease.<sup>12</sup>

12. Stuhec M, Keuschler J, Serra-Mestres J, et al. Effects of different antihypertensive medication groups on cognitive function in older patients: A systematic review. *European psychiatry: the journal of the Association of European Psychiatrists*. 2017;46:1-15



# Modifiable Risk Factors: Cardiovascular-2

- ▶ Diabetes mellitus (DM) - should be appropriately treated.<sup>10</sup>
  - DM was a risk factor for all types of dementia (RR=1.73, 95% CI 1.65 to 1.82), AD (RR=1.56, 95% CI 1.41 to 1.73) and VaD (RR=2.27, 95% CI 1.94 to 2.66).<sup>13</sup>

13. Gudala K, Bansal D, Schifano F, et al. Diabetes mellitus and risk of dementia: A meta-analysis of prospective observational studies. Journal of diabetes investigation. 2013;4(6):640-50.



# Modifiable Risk Factors: Cardiovascular-3

- Diabetes mellitus (DM) - should be appropriately treated.

**Table 2** | Pooled risk ratios of all type dementia, Alzheimer's disease and vascular dementia

Type of dementia	No. studies pooled	Pooled estimate		Level of significance of pooled RR	Tests of heterogeneity			Tests of publication bias
		RR	95% CI		Q value (d.f.)	P-value	I <sup>2</sup> (%)	
All type dementia	20	1.73	1.65–1.82	<0.001	76.5 (22)	<0.01	71.25	0.12
Alzheimer's disease	20	1.56	1.41–1.73	<0.001	23.3 (21)	0.32	9.8	0.93
Vascular dementia	13	2.27	1.94–2.66	<0.001	12.0 (12)	0.52	0	0.41

CI, confidence interval; d.f., degrees of freedom; RR, relative risk.

- Gudala K, Bansal D, Schifano F, et al. Diabetes mellitus and risk of dementia: A meta-analysis of prospective observational studies. *Journal of diabetes investigation*. 2013;4(6):640-50.





# Modifiable Risk Factors: Cardiovascular-4

- ▶ High total serum cholesterol (TC) - risk factor for developing late life dementia.<sup>14</sup>
- ▶ High TC in mid-life compared with non-high TC is associated with risk of late-life AD (RR=2.14, 95% CI 1.33 to 3.44).<sup>14</sup>
- ▶ High TC in late-life is not associated with any cognitive or dementia outcome in late-life (RR=1.02, 95% CI 0.88 to 1.87).<sup>14</sup>

14. Anstey KJ, Ashby-Mitchell K, Peters R. Updating the Evidence on the Association between Serum Cholesterol and Risk of Late-Life Dementia: Review and Meta-Analysis. Journal of Alzheimer's disease : JAD. 2017;56(1):215-28



# Modifiable Risk Factors: Cardiovascular-5

- ▶ Obesity - maintenance of normal body mass index (BMI) is recommended.<sup>10</sup>
  - obesity (BMI  $\geq 30$  kg/m<sup>2</sup>) in mid-life were associated with risk of developing AD (RR=2.04, 95% CI 1.59 to 2.62) and any dementia (RR=1.64, 95% CI 1.34 to 2.00) compared with normal BMI.<sup>17</sup>
  - mid-life (aged 35 to 65 years) BMI  $\geq 30$  and BMI  $\leq 18.5$  were associated with late-life dementia with risk of 1.33 (95% CI 1.08 to 1.63) and 1.39 (95% CI 1.13 to 1.70) respectively.<sup>16</sup>

17. Anstey KJ, Cherbuin N, Budge M, et al. Body mass index in midlife and late-life as a risk factor for dementia: a meta-analysis of prospective studies. *Obesity reviews* : an official journal of the International Association for the Study of Obesity. 2011;12(5):e426-37

16. Albanese E, Launer LJ, Egger M, et al. Body mass index in midlife and dementia: Systematic review and meta-regression analysis of 589,649 men and women followed in longitudinal studies. *Alzheimer's & dementia* (Amsterdam, Netherlands). 2017;8:165-78



# Modifiable Risk Factors: Psychiatric illness

- ▶ Late-life depression is associated with a two-fold increased risk of dementia (RR=1.98, 95% CI 1.50 to 2.63) and AD (RR=2.04, 95% CI 1.40 to 2.98).<sup>18</sup>

18. Cherbuin N, Kim S, Anstey KJ. Dementia risk estimates associated with measures of depression: a systematic review and meta-analysis. *BMJ open*. 2015;5(12):e008853.



# Modifiable Risk Factors: Lifestyle

- ▶ Tobacco smoking.<sup>19</sup>
- ▶ Excessive alcohol consumption
  - Heavy ( $>12$  and  $\leq 24$  g/d) & very heavy ( $>24$  g/d) alcohol consumption - risk factor for incident dementia with HR of 1.10 (95% CI 1.01 to 1.19) and 1.18 (95% CI 1.01 to 1.36) respectively.<sup>20</sup>

19. World Health Organization. Risk Reduction of Cognitive Decline and Dementia: WHO Guidelines. Geneva: World Health Organization;2019

20. Handing EP, Andel R, Kadlecova P, et al. Midlife Alcohol Consumption and Risk of Dementia Over 43 Years of Follow-Up: A Population-Based Study From the Swedish Twin Registry. The journals of gerontology Series A, Biological sciences and medical sciences. 2015;70(10):1248-54



# Modifiable Risk Factors: Lifestyle-2

## ► Physical Inactivity<sup>21</sup>

- measured <10 years before dementia diagnosis was associated with increased incidence of all-cause dementia (HR=1.40, 95% CI 1.23 to 1.71) and AD (HR=1.36, 95% CI 1.12 to 1.65)
- reverse causation was minimised - assessed physical activity ≥10 years before dementia onset - no difference in dementia risk between physically active and inactive participants.
- signal of elevated risk for dementia observed in physically inactive adults who developed cardiometabolic disease (hazard ratio for physical activity assessed >10 years before dementia onset 1.30, 0.79 to 2.14)

21. Kivimäki M, Singh-Manoux A, Pentti J, et al. Physical inactivity, cardiometabolic disease, and risk of dementia: an individual-participant meta-analysis. *BMJ (Clinical research ed)*. 2019;365:l1495.



# Modifiable Risk Factors: Lifestyle-3

## ► Social relationship<sup>22</sup>

- low social participation (RR=1.41, 95% CI 1.13 to 1.75), less frequent social contact (RR=1.57, 95% CI 1.32 to 1.85) and more loneliness (RR=1.58, 95% CI 1.19 to 2.09) were associated with incident dementia.
- primary papers in the meta-analysis – there were variations in social relationship factor measurements, adjustment of potential confounders and substantial dropout

22. Kuiper JS, Zuidersma M, Oude Voshaar RC, et al. Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. *Ageing research reviews*. 2015;22:39-57.



# Modifiable Risk Factors: Environment

## ► Environmental Risk Factors<sup>23</sup>

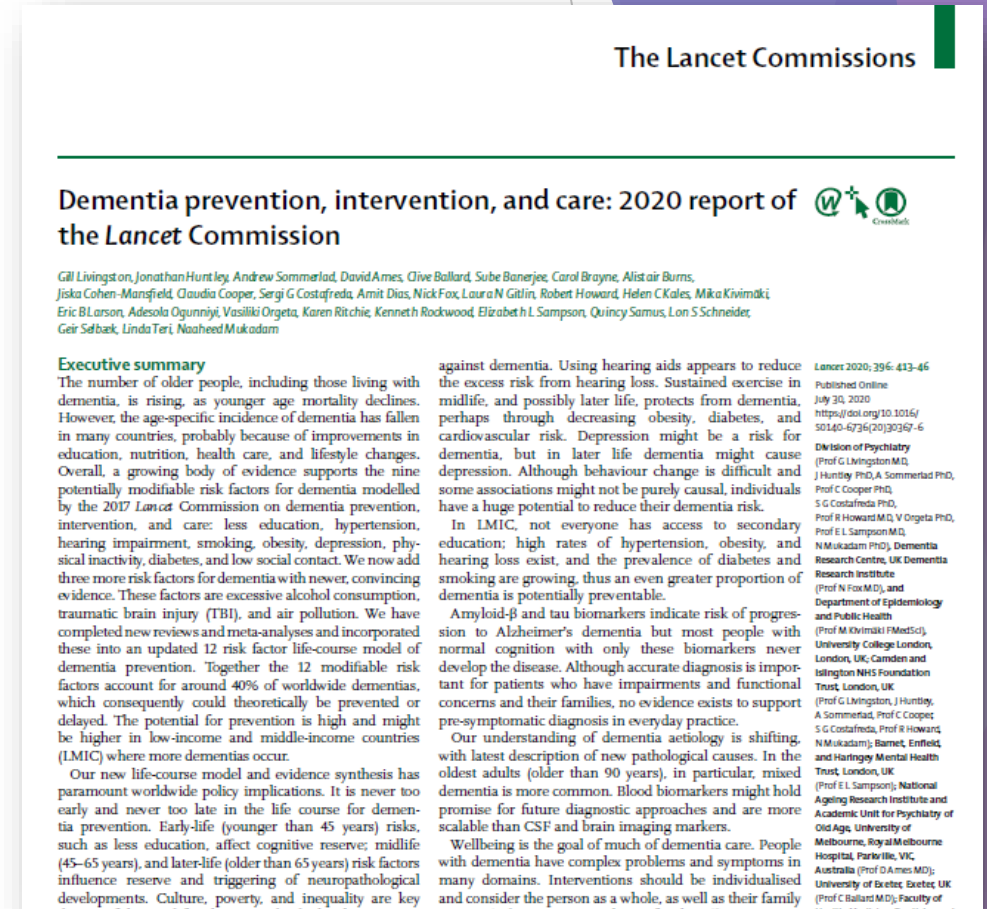
- moderate evidence for air pollution exposures - particularly nitrogen oxides, particulate matter, and ozone
- Environmental tobacco smoke - associated with dementia risk - showed a dose-response association

23. Killin LO, Starr JM, Shiue IJ, et al. Environmental risk factors for dementia: a systematic review. BMC geriatrics. 2016;16(1):175.



# Modifiable Risk Factors: Others

- ▶ Several other risk factors associated with dementia include:<sup>24</sup>
  - lower early life education level (RR=1.6, 95% CI 1.3 to 2.0)
  - mid-life hearing impairment (RR=1.9, 95% CI 1.4 to 2.7)
  - mid-life traumatic brain injury (RR=1.8, 95% CI 1.5 to 2.2)





# Co-occurrence of modifiable risk factors

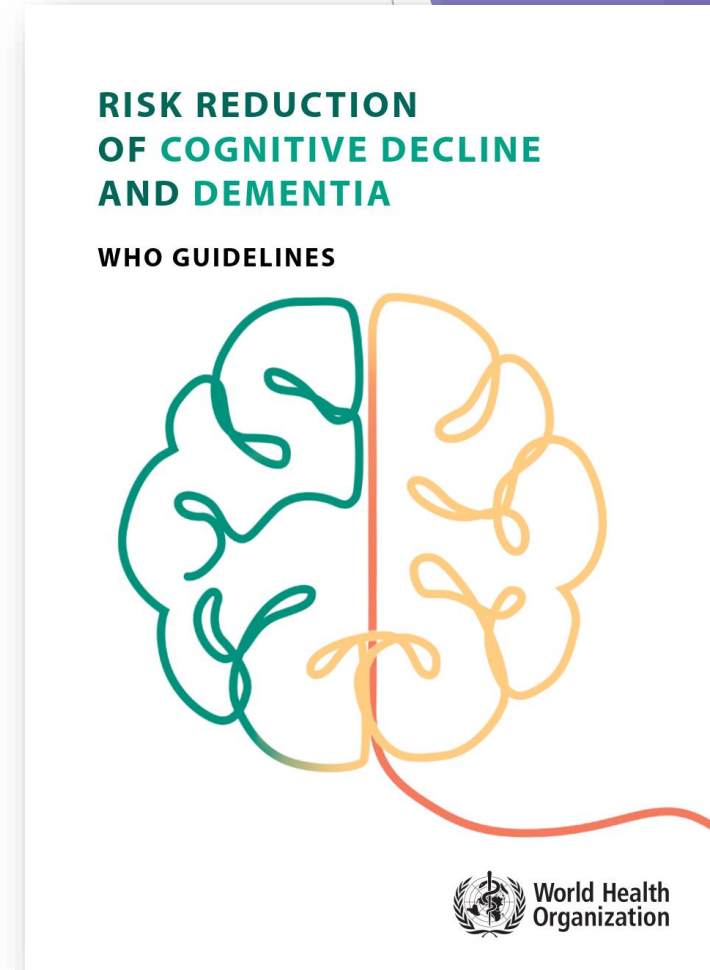
- ▶ Exposure to additional modifiable risk factors of dementia should be kept to the minimum<sup>25</sup>
  - 1 risk factor: RR for dementia of 1.20 (95% CI 1.04 to 1.39)
  - 2 risk factors: RR=1.65 (95% CI 1.40 to 1.94)
  - 3 or more risk factors: RR=2.21 (95% CI 1.78 to 2.73)compared with no risk factor.

25. Peters R, Booth A, Rockwood K, et al. Combining modifiable risk factors and risk of dementia: a systematic review and meta-analysis. *BMJ open*.2019;9(1):e022846.



# Risk Reduction Strategies

- ▶ WHO recommended strategies:<sup>19</sup>
  - Physical activity
  - Tobacco cessation interventions
  - Interventions for alcohol use disorders
  - Management of hypertension
  - Management of diabetes
  - Weight management



19. World Health Organization. Risk Reduction of Cognitive Decline and Dementia: WHO Guidelines. Geneva: World Health Organization;2019.



# Risk Reduction Strategies-2

- ▶ Other strategies:<sup>19, 24</sup>
  - management of dyslipidaemia
  - nutritional interventions
  - social activities
  - cognitive interventions
  - management of depression
  - management of hearing loss

19. World Health Organization. Risk Reduction of Cognitive Decline and Dementia: WHO Guidelines. Geneva: World Health Organization;2019.

24. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet (London, England). 2020;396(10248):413-46.



# Take Home Message

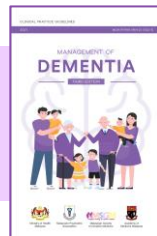
- ▶ The risk factors for dementia can be divided into modifiable and non-modifiable risks.
- ▶ There should be awareness regarding modifiable risk factors and risk reduction strategies should be advocated to reduce the risk of developing dementia.

## Recommendation 1

- Risk reduction strategies should be advocated to reduce the risk of developing cognitive decline and/or dementia. These include:
  - physical activity
  - tobacco cessation
  - interventions for alcohol use disorders
  - management of hypertension
  - management of diabetes



# Thank You



**Training of Core Trainers on  
CPG Management of Dementia  
(Third Edition)**