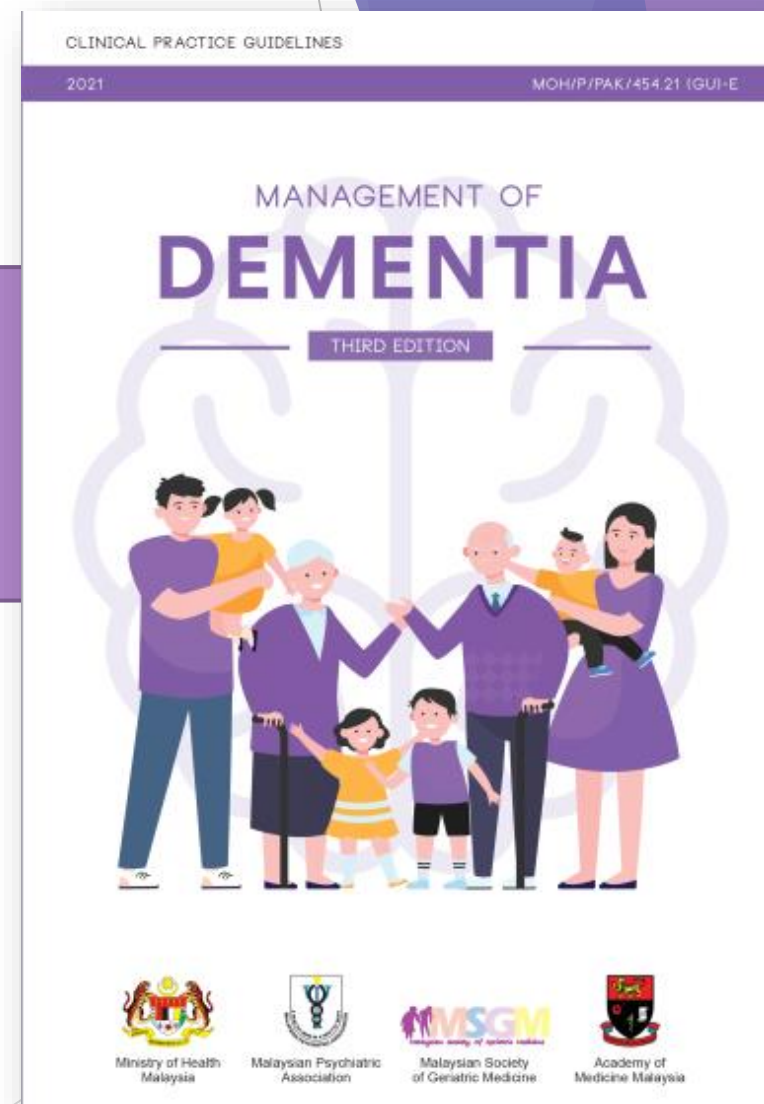


Training of Core Trainers CPG Management of Dementia (Third Edition)

SPECIAL POPULATION

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Learning Objectives

1. To provide current evidence-based management approach to populations with acquired brain injury, alcohol-related dementia (ARD) and HIV-associated neurocognitive disorders (HANDs)



Special Population

- ▶ The management of certain populations with early-onset cognitive impairment is aimed at preventing further deterioration or sequelae of the cognitive function.
 - This is done with AChEI or specific pharmacological intervention specific to the causes as well as non-pharmacological measures.
 - These populations include those with acquired brain injury, alcohol-related dementia (ARD) and HIV-associated neurocognitive disorders (HANDs).



Acquired Brain Injury

- ▶ In a Cochrane systematic review on chronic cognitive impairment (≥ 12 months post-injury) in traumatic brain injury (TBI):¹¹³
 - rivastigmine significantly improved only one primary measure i.e. verbal memory functioning compared with placebo;
 - there was no significant difference in safety profile

113. Dougall D, Poole N, Agrawal N. Pharmacotherapy for chronic cognitive impairment in traumatic brain injury. The Cochrane database of systematic reviews. 2015(12):Cd009221.



Acquired Brain Injury-2

- ▶ Two Cochrane systematic reviews on non-pharmacological interventions in acquired brain injury showed:¹¹⁴
 - cognitive rehabilitation was not effective compared to no intervention or conventional rehabilitation in improving:
 - return to work
 - independence in activities of daily living (ADL)
 - community integration or
 - quality of life for adults with TBI

114. Kumar KS, Samuelkamaleshkumar S, Viswanathan A, et al. Cognitive rehabilitation for adults with traumatic brain injury to improve occupational outcomes. The Cochrane database of systematic reviews. 2017;6(6):Cd007935.



Acquired Brain Injury-3

- ▶ Two Cochrane systematic reviews on non-pharmacological interventions in acquired brain injury showed:¹¹⁵
 - music interventions may be beneficial on
 - communication (SMD=0.75, 95% CI 0.11 to 1.39), naming (MD=9.79, 95% CI 1.37 to 18.21) and speech repetition (MD=8.90, 95% CI 3.25 to 14.55) in persons with post-stroke aphasia compared with control;
 - however, these findings were based on a small number of studies with small sample sizes.

115. Magee WL, Clark I, Tamplin J, et al. Music interventions for acquired brain injury. The Cochrane database of systematic reviews. 2017;1(1):Cd006787.



Alcohol-related Dementia

- ▶ The prevalence of ARD ranges from 0.12% to 25.6% with more males being affected.
- ▶ It occurs more consistently at approximately 10% in early-onset dementia compared with the scarce data in late-onset dementia.¹¹⁶

116. Cheng C, Huang CL, Tsai CJ, et al. Alcohol-Related Dementia: A Systemic Review of Epidemiological Studies. Psychosomatics. 2017;58(4):331-42.



Alcohol-related Dementia-2

- ▶ Heavy alcohol use could cause ARD from:¹¹⁷
 - direct neurotoxic effect with permanent structural and functional brain damage
 - thiamine deficiency leading to Wernicke-Korsakoff syndrome
 - risk factor for other conditions that could also damage the brain (e.g. hepatic encephalopathy in patients with cirrhotic liver disease)
 - cardiovascular diseases resulting indirectly in vascular dementia

117. Rehm J, Hasan OSM, Black SE, et al. Alcohol use and dementia: a systematic scoping review. *Alzheimer's research & therapy*. 2019;11(1):1.



Alcohol-related Dementia-3

- ▶ Two systematic reviews on the treatment of ARD showed:
 - for persons with alcohol dependence and Wernicke-Korsakoff syndrome with no triad of acute symptoms,
 - intramuscular (IM) thiamine at 200 mg/day for two consecutive days was more effective than 5 mg/day on working memory performance using the delayed alternation test (MD= -17.90, 95% CI -35.4 to -0.40)¹¹⁸

118. Day E, Bentham PW, Callaghan R, et al. Thiamine for prevention and treatment of Wernicke-Korsakoff Syndrome in people who abuse alcohol. The Cochrane database of systematic reviews. 2013;2013(7):Cd004033.



Alcohol-related Dementia-4

- ▶ Two systematic reviews on the treatment of ARD showed:
 - persons with Korsakoff's syndrome performed similarly to healthy population on associative verbal learning procedure¹¹⁹
 - with the use of extra processing time, explicit encouragement to generate associations and extra retrieval time
- ▶ However, the primary papers used in the two reviews had some methodological limitations.

119. Svanberg J, Evans JJ. Neuropsychological rehabilitation in alcohol-related brain damage: a systematic review. Alcohol and alcoholism (Oxford, Oxfordshire). 2013;48(6):704-11.



HIV-Associated Neurocognitive Disorders

- ▶ There are different diagnostic approaches for HANDs e.g. 2007 Frascati criteria, Global Deficit Score and Clinical Mental State Examinations.
- ▶ Among all, the 2007 Frascati criteria is the most widely used diagnostic criteria for HANDs¹²⁰ and it consists of three categories:¹²¹
 - Asymptomatic Neurocognitive Impairment (ANI) – mild neurocognitive impairment in at least two cognitive domains but not affecting daily functions
 - Mild Neurocognitive Disorder (MND) – mild neurocognitive impairment in at least two cognitive domains and has mild interference with daily functions
 - HIV-associated Dementia (HAD) – severe neurocognitive impairment in at least two cognitive domains and has marked difficulty with daily functions

120. Wang Y, Liu M, Lu Q, et al. Global prevalence and burden of HIV-associated neurocognitive disorder: A meta-analysis. *Neurology*. 2020;95(19):e2610-e21.

121. Antinori A, Arendt G, Becker JT, et al. Updated research nosology for HIV-associated neurocognitive disorders. *Neurology*. 2007;69(18):1789-99.



HIV-Associated Neurocognitive Disorders-2

- ▶ The prevalence of HANDs ranged from 39.1% to 44.4% according to a meta-analysis on global disease burden of it.
- ▶ MND and HAD were shown to be lower in patients with higher level of income, current CD4 count and proportion on Anti-Retroviral Therapy (ART).
- ▶ These findings suggested that early ART initiation to maintain a high level of CD4 cell count and prevent severe immunosuppression was likely to reduce the prevalence and severity of HANDs.¹²⁰



HIV-Associated Neurocognitive Disorders-3

- ▶ A meta-analysis on cognitive screening tools to diagnose HANDs showed that HIV Dementia Scale and International HIV Dementia Scale had generally poor (0.48) and moderate (0.62) pooled sensitivities.
 - Thus, both were not ideal tools for identifying a range of neurocognitive impairment in HIV patients.¹²²
 - Apart from that, the primary papers were of moderate quality and the heterogeneity was significant.

122. Zipursky AR, Gogolishvili D, Rueda S, et al. Evaluation of brief screening tools for neurocognitive impairment in HIV/AIDS: a systematic review of the literature. AIDS (London, England). 2013;27(15):2385-401.



HIV-Associated Neurocognitive Disorders-4

- ▶ Every ART agent has different CPE (Central Nervous System [CNS] Penetration Effectiveness) score and use of combined agents with higher CPE score may be associated with better neurocognitive outcome.
- ▶ An RCT showed that one unit increase in the CPE score was associated with an increase in the Composite Neuropsychology Z Score (NPZ3) score among HANDs patients with >3 antiretroviral drugs in the regimen (change in NPZ3 score=0.07, 95% CI 0.02 to 0.12).¹²³

123. Smurzynski M, Wu K, Letendre S, et al. Effects of central nervous system antiretroviral penetration on cognitive functioning in the ALLRT cohort. AIDS (London, England). 2011;25(3):357-65.

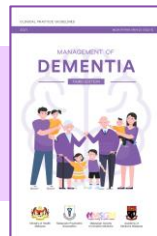


Take Home Message

- ▶ In these special populations, the causes of cognitive impairment should be managed accordingly to prevent further complications.
- ▶ As such cases occur more often in those younger than 65 years old, apart from addressing the cognitive issues, greater psychological and social support are needed for them in terms of employment, finances and social life.
- ▶ There is insufficient evidence on the effectiveness of AChEI or memantine in these special populations



Thank You



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