MANAGEMENT OF DEMENTIA
(THIRD EDITION)

Ministry of Health
Malaysia

Malaysian Psychiatric
Association

Academy of Medicine
Malaysia

STATEMENT OF INTENT

These clinical practice guidelines (CPG) are meant to be guides for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every healthcare provider is responsible for the management of his/her unique patient based on the clinical picture presented by the patient and the management options available locally.

UPDATING THE CPG

These guidelines were issued in 2021 and will be reviewed in a minimum period of four years (2025) or sooner if new evidence becomes available. When it is due for updating, the Chairperson of the CPG or National Advisor of the related specialty will be informed about it. A discussion will be done on the need for a revision including the scope of the revised CPG. A multidisciplinary team will be formed, and the latest systematic review methodology used by MaHTAS will be employed.

Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions, corrections will be published in the web version of this document, which will be the definitive version at all time. This version can be found on the websites mentioned above.

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LEVELS OF EVIDENCE

Level	Study design
I	Evidence from at least one properly randomised controlled trial
II-1	Evidence obtained from well-designed controlled trials without randomisation
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	Evidence from multiple time series with or without intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence
III	Opinions of respected authorities based on clinical experience; descriptive studies and case reports; or reports of expert committees

SOURCE: US / CANADIAN PREVENTIVE SERVICES TASK FORCE 2001

FORMULATION OF RECOMMENDATION

In line with the current development in CPG methodology, the CPG Unit of MaHTAS is in the process of adapting **Grading Recommendations, Assessment, Development and Evaluation (GRADE)** in its work process. The quality of each retrieved evidence and its effect size are carefully assessed and reviewed by the CPG Development Group. In formulating the recommendations, overall balances of the following aspects are considered in determining the strength of the recommendations:
- overall quality of evidence
- balance of benefits versus harms
- values and preferences
- resource implications
- equity, feasibility and acceptability

KEY RECOMMENDATIONS

The following recommendations are highlighted by the CPG Development Group as the key recommendations that answer the main questions addressed in the CPG and should be prioritised for implementation.

a. Risk Reduction

- 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

b. Assessment and Diagnosis

- The diagnosis of dementia should be based on detailed history and physical examination, and supported by cognitive, functional and behavioural evaluation.
- Structural neuroimaging (computed tomography or magnetic resonance imaging) should be done in evaluation of dementia to exclude reversible causes of cognitive decline and other intracranial pathology.
- Electroencephalogram should be considered in rapidly progressive cognitive decline and atypical features of dementia.
- Diagnosis of dementia should be made based on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) or the International Classification of Diseases, Tenth Revision (ICD-10).

c. Non-Pharmacological Treatment

- To improve cognitive function in mild to moderate dementia, cognitive stimulation therapy and physical activity should be offered.
- In people with dementia having behavioural and psychological symptoms:
  - explore and address possible clinical or environmental causes/triggering factors
  - offer psychosocial and environmental interventions as initial and ongoing treatment:
    - psychological intervention for depressive symptoms and/or anxiety
    - personalised and tailored activities for agitation and aggression

d. Pharmacological Treatment

- Donepezil should be offered in Alzheimer's Disease (AD) of all severity.
  - Rivastigmine is an option in mild to moderate AD.
- Memantine may be considered in moderate to severe AD as monotherapy or in combination with acetylcholinesterase inhibitors (AChEI).
- AChEI or memantine may be considered in vascular dementia.
- Rivastigmine or donepezil may be considered for dementia with Lewy body and Parkinson's disease dementia.
- Antipsychotics may be considered for behavioural and psychological symptoms in people with dementia (PWD) where there is a risk of harming themselves or others.
- Antidepressants:

- o may be considered for PWD who have agitation
  - o may be prescribed for PWD with pre-existing severe mental health problem
- The use of anticholinergic medications in dementia should be done cautiously with regular review of indication and deprescribed whenever possible.

e. Caregiver Support

- Caregivers should be actively involved and supported in the management of dementia.
  - o This includes assessment of the burden of caregivers.

f. Legal and Ethical Issues

- If there is any doubt regarding people with dementia (PWD)'s decision-making capacity, a formal assessment of decision-making capacity should be carried out.
- A doctor should comply with a patient's unequivocal written directive to refuse a particular treatment if that decision was made while the patient had mental capacity.
- PWD (particularly moderate to severe) should be assessed for their driving ability if they still wish to drive.

g. Palliative and End-Of-Life Care

- Physical restraints should be avoided in dementia.
- Advance care planning should be considered in the management of dementia once the diagnosis is established.

h. Referral

- All patients with suspected dementia should be referred to a geriatric psychiatrist/psychiatrist, geriatrician or neurologist for assessment, diagnosis and management.

GUIDELINES DEVELOPMENT AND OBJECTIVES
GUIDELINES DEVELOPMENT

The members of the Development Group (DG) for these Clinical Practice Guidelines (CPG) were from the Ministry of Health (MoH) and Ministry of Higher Education. There was active involvement of a multidisciplinary Review Committee (RC) during the process of the CPG development.

A systematic literature search was carried out using the following electronic databases: mainly Medline via Ovid and Cochrane Database of Systemic Reviews and others e.g. PubMed and Guidelines International Network (refer to **Appendix 1** for **Example of Search Strategy**). The search was limited to literature published on humans, "all adults (19 plus years)", publication from year "2009 to Current" and English language. In addition, the reference lists of all retrieved literature and guidelines were searched and, experts in the field contacted to identify relevant studies. All searches were conducted from 19 Nov 2018 to 26 Feb 2019. Literature searches were repeated for all clinical questions at the end of the CPG development process allowing any relevant papers published before 31 January 2021 to be included. Future CPG updates will consider evidence published after this cut-off date. The details of the search strategy can be obtained upon request from the CPG Secretariat.

References were also made to other CPGs on Dementia e.g.:
- Dementia: assessment, management and support for people living with dementia and their carers [National Institute for Health and Care Excellence (NICE), 2018]
- Clinical Practice Guidelines and Principles of Care for People with Dementia [National Health and Medical Research Council (NHMRC), 2016]
- Risk Reduction of Cognitive Decline and Dementia WHO Guidelines [World Health Organization (WHO), 2019]

These CPGs were evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II prior to them being used as references.

A total of 14 clinical questions (CQ) were developed under different sections. Members of the DG were assigned individual questions within these sections (refer to **Appendix 2** for **Clinical Questions**). The DG members met 26 times throughout the development of these guidelines. All literature retrieved were appraised by at least two DG members using Critical Appraisal Skill Programme checklist, presented in evidence tables and further discussed in each DG meetings. All statements and recommendations formulated after that were agreed upon by both the DG and RC. Where evidence was insufficient, the recommendations were made by consensus of the DG and RC. This CPG is based largely on the findings of systematic reviews, meta-analyses and clinical trials, with local practices taken into consideration.

The literature used in these guidelines were graded using the US/Canadian Preventive Services Task Force Level of Evidence (2001), while the grading of recommendation was done using the principles of GRADE (refer to the preceding page). The writing of the CPG follows strictly the requirement of AGREE II.

On completion, the draft of the CPG was reviewed by external reviewers. It was also posted on the MoH Malaysia official website for feedback from any interested parties. The draft was finally presented to the Technical Advisory Committee for CPG, and the HTA and CPG Council MoH Malaysia for review and approval. Details on the CPG development methodology by MaHTAS can be obtained from Manual on Development and Implementation of Evidence-based Clinical Practice Guidelines published in 2015 (available at http://www.moh.gov.my/moh/resources/CPG_MANUAL_MAHTAS.pdf?mid=634).

OBJECTIVES

The objectives of the CPG are to provide evidence-based recommendations on the management of dementia in the following aspects:
   a. risk factors
   b. assessment and diagnosis
   c. treatment
   d. referral and follow-up

CLINICAL QUESTIONS

Refer to **Appendix 2**.

TARGET POPULATION

1. Inclusion Criteria
Adults with:
   • dementia
   • mild cognitive impairment

2. Exclusion Criteria
Adults with:
   • learning disabilities who develop dementia

TARGET GROUP/USERS

This document is intended to guide those involved in the management of dementia at any healthcare level including:
   i. doctors
   ii. allied health professionals
   iii. trainees and medical students
   iv. patients and their caregivers/advocates
   v. professional organisations

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Primary, secondary and tertiary care settings

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ALGORITHM 1: EARLY DETECTION OF DEMENTIA

Presence of symptoms suggestive of dementia (including subjective memory complaint, changes in activity of daily living and/or caregivers concerns), clinician suspicion and patients at increased risk of dementia

Perform clinical assessment:
- History from patients and/or caregivers
- Examination
  - Physical including cardiovascular and neurological systems
  - Mental state and cognition (e.g. mini-Cog/AMTS/MMSE)

Abnormalities detected on clinical assessment — NO → Provide reassurance

YES

Perform laboratory tests*

Any abnormalities present — YES → Treat and reassess

NO

Findings meet criteria for dementia — YES → Refer to specialist services/memory clinic

Symptoms remain — YES

Symptoms remain — NO → Provide reassurance

NO (Findings meet criteria for dementia)

Patient is cognitively impaired but not demented — YES → Consider referral to a specialist and/or reassess in six months → Refer to specialist services/memory clinic

NO

Provide reassurance or referral as appropriate

*Refer to **Chapter 3** on **Diagnosis and Assessment**

AMTS = Abbreviated Mental Test Score
MMSE = Mini Mental State Examination

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ALGORITHM 2: DIAGNOSIS OF DEMENTIA

Referral on possible diagnosis of dementia

Perform clinical assessment:
- history from patients and/or caregivers
- examination
  - o physical
  - o cognition (e.g. MMSE, MoCA)
  - o mental state (e.g. CSDD, NPI)
  - o function (e.g. IADL/ADL)
  - o others - caregivers burden (e.g. ZBI)

Reassess after 6 months

Patient is cognitively impaired — NO → Consider other diagnosis

YES

- Laboratory tests for dementia screening to exclude potentially reversible causes (full blood count, biochemistry tests, thyroid function test, serum vitamin B12 and folate levels, VDRL and HIV tests)

Dementia or mild cognitive impairment — NO → Consider other diagnosis

YES

- Perform MRI/CT brain
- EEG if indicated

DEMENTIA — NO → MCI

YES

Determine type of dementia

| Alzheimer's disease | Vascular Dementia | Dementia with Lewy Body/Parkinson's Disease Dementia | Fronto-temporal Dementia | Other types of dementia
• Mixed dementia
• Related to medical conditions
• HIV/TBI/alcohol-related dementia |

MMSE = Mini Mental State Examination
MoCA = Montreal Cognitive Assessment
CSDD = Cornell Scale for Depression in Dementia
NPI = Neuropsychiatric Inventory
IADL = Instrumental Activity of Daily Living
ZBI = Zarit Burden Interview

VDRL = Venereal Disease Research Laboratory test
HIV = Human Immunodeficiency Virus
MRI = Magnetic Resonance Imaging
CT = Computed Tomography
EEG = Electroencephalogram
TBI = Traumatic Brain Injury

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ALGORITHM 3: TREATMENT OF DEMENTIA

DEMENTIA

Non-pharmacological intervention

Pharmacological Intervention

Psychosocial Intervention (tailored to individual's needs)

Alzheimer's disease

Vascular dementia

Dementia with Lewy Body/Parkinson's Disease Dementia

Frontotemporal Dementia

Multidisciplinary team Involvement (multicomponent intervention for patients and care givers)

Treat vascular risk factors

Maintenance of cognitive function and encouragement of independence

Mild

Moderate to severe

Consider AChEI or memantine

Consider rivastigmine or donepezil

AChEI

Donepezil and/or memantine

Improvement of quality of life

Behavioural and Psychological Symptoms of Dementia

Co-morbid emotional disorders

• Agitation
• Aggression
• Psychosis

• Depression
• Anxiety

• Assess and address clinical or environmental causes
• Offer psychosocial and environmental intervention
• Consider antipsychotics or antidepressants

• Assess and address clinical or environmental causes
• Offer psychosocial and environmental intervention
• Consider antidepressant in pre-existing condition

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AChEI = acetylcholinesterase inhibitors

1.   INTRODUCTION

Dementia is a syndrome in which cognitive function (i.e. ability to process thought) deteriorates progressively. It is not part of a normal ageing process. It affects memory, thinking, orientation, calculation, learning capacity, language, judgement, emotional control, social behaviour, or motivation (refer to **Appendix 3** on **10 Warning Signs of Dementia**). However, consciousness is not affected. Dementia can lead to disability and dependency among people with dementia (PWD). It is commonly associated with behavioural and psychological symptoms which can lead to increased dependency on caregivers and subsequent nursing home admission. The lack of awareness and understanding of dementia can lead to stigmatisation and, delay in diagnosis and care. The physical, psychological, social and economic impact of dementia on caregivers, family and society is tremendous and often overlooked.

There are estimated 50 million PWD worldwide and 60% of them live in low- or middle-income countries. There are nearly 10 million new cases every year.[WHO factsheet, 2020] According to Alzheimer's disease International, the estimated number of PWD in Malaysia was 123,000 in 2015. This number was projected to be 261,000 by 2030 and further increase to 590,000 by 2050.[ADI, 2014] Based on the Malaysian National Health and Morbidity Survey 2018: Elderly Health, the overall prevalence of probable dementia was 8.5% (95% CI 6.97 to 10.22).[NHMS, 2018]

Alzheimer's disease (AD) is the commonest type of dementia (60 - 70%), followed by vascular dementia (VaD), mixed dementia, frontotemporal dementia (FTD), Dementia with Lewy bodies (DLB), Parkinson's disease dementia (PDD) and others. People with AD often present initially with gradual episodic memory impairment. However, in early-onset AD (less than 65 years old), patients may present with behavioural (frontal), visual (posterior cortical atrophy) or language (logopenic) variants with relatively well-preserved memory until the later stages of the disease.[Ryan NS et al., 2010] VaD is associated with cardiovascular risk factors, and often present with impaired executive function, slowed processing speed and memory retrieval difficulties.[Karantzoulis S et al., 2011] Mixed dementia is a combination of two or more dementia types, most frequently AD with vascular pathology.[Boyle PA et al., 2018] In cases of behavioural variant frontotemporal dementia, the early manifestations tend to be changes in the personality with executive dysfunction prior to memory issues.[Warren JD et al., 2013] People with DLB often experience fluctuating cognitive decline with prominent visual hallucinations and spontaneous motor parkinsonism. Dementia occurs at least a year after the onset of motor symptoms in people with PDD.[Jellinger KA, 2018]

As Malaysia is moving towards an ageing nation, the country must prepare itself to address health issues pertaining to the older people e.g. non-communicable diseases (NCDs) including dementia. The second edition of clinical practice guidelines (CPG) on management of dementia was published in 2009. Since then, diagnostic criteria on dementia have been revised and become more comprehensive. There have been minor advancements in the treatment of PWD. These are addressed in the new edition of the CPG. Apart from that, new sections on risk reduction strategies and special populations are added. This third edition aims to update on the management of dementia and eventually improve the quality of care for PWD.

2.   RISK FACTORS AND RISK REDUCTION STRATEGIES

2.1   Risk Factors
Dementia is caused by a combination of genetic and environmental factors.[Husain M et al., 2016] Risk factors for dementia can be divided into modifiable and non-modifiable risk.

Non-modifiable risk factors are:
- Advancing age: age ≥ 65 years is a risk factor for any dementia[MoH, 2009]
- Sex: Female has higher risk of dementia especially in AD[MoH, 2009]
- Genetic:
  - Early-onset AD accounts for 6 - 7% of all AD cases. Of this group, only 13% exhibit autosomal dominant transmission. Three causative gene mutations have been identified; amyloid β-protein precursor on chromosome 21, presenilin 1 on chromosome 14 and presenilin 2 on chromosome 1.[MoH, 2009]
  - Late-onset AD (age of >65 years old) is considered to be multifactorial but involves a strong genetic predisposition.[Van Cauwenberghe C et al., 2015, level III] The genetic component itself is complex and heterogeneous.[MoH, 2009]
  - The presence of the ε4 variant of the APOE gene (APOE4) may contribute to the development of late-onset AD and sporadic early-onset AD. However, presence of APOE ε4 itself is neither necessary nor sufficient to cause the disease. The APOE ε2 allele is thought to have a protective effect. Large-scale genome-wide association studies have identified at least 20 loci associated with disease risk. None of these risk loci has an effect comparable to APOE ε4, with OR ranging from 1.1 to 2.0.[Van Cauwenberghe C et al., 2015, level III]

Modifiable risk factors can be divided into:

a.   Cardiovascular
Major cardiovascular risk factors e.g. hypertension, diabetes mellitus, hyperlipidaemia, obesity and smoking are independent risk factors for the development of atherosclerosis VaD.
- Hypertension occurring at mid-life (40 to 60 years old) is a risk factor for dementia and should be appropriately treated.[MoH, 2009] A systematic review showed that treatment of elderly patients with hypertension improved cognitive function especially for those on angiotensin II receptor blockers (ARB).[Stuchec M et al., 2017, level I]
- Diabetes mellitus (DM) is a modifiable risk factor for the development of dementia and should be appropriately treated.[MoH, 2009] A meta-analysis showed DM was a risk factor for all types of dementia (RR=1.73, 95% CI 1.65 to 1.82), Whereas It was also a risk for AD (RR=1.56, 95% CI 1.41 to 1.73) and VaD (RR=2.27, 95% CI 1.94 to 2.66). However, there were methodological issues noted in the primary papers.[Gudala K et al., 2013, level II-2]
- High total serum cholesterol (TC) is a risk factor for developing late-life dementia:[Anstey KJ et al., 2017, level II-2]
  - 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).
  - 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)
- In a meta-analysis, serum LDL-C level was higher in AD patients compared with healthy control (OR=2.55, 95% CI 1.25 to 5.22). The quality of primary papers was good although there was high heterogeneity and confounders were not fully explained.[Sáiz-Vazquez O et al., 2020, level II-2]
- Obesity is a modifiable risk factor and maintenance of normal body mass index (BMI) is recommended.[MoH, 2009] This is supported by two meta-analyses showing that:
  - mid-life (age 35 to 65 years) BMI ≥30 and BMI ≤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[Albanese E et al., 2017, level II-2]
  - obesity (BMI ≥30) 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[Anstey KJ et al., 2011, level II-2]

b.   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).[Cherbuin N et al., 2015, level II-2]

c. Lifestyle

- **Smoking**

Tobacco smoking is a risk factor for cognitive impairment and dementia.[WHO, 2019]

- **Excessive alcohol consumption**

Heavy (>12 and ≤24 g/d) and very heavy (>24 g/d) alcohol consumption is a 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.[Handing EP et al., 2015, level II-2] One unit is equivalent to 8 g of alcohol.

- **Physical inactivity**

A meta-analysis showed that physical inactivity 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). When reverse causation was minimised by assessing physical activity ≥10 years before all-cause dementia and AD onset, no difference in dementia risk between physically active and inactive participants was found for the two outcomes.[Kivimäki M, et al. 2019; level II-2] However, there was no standard definition of self-reported physical inactivity and quality assessment in the primary papers used in the meta-analysis.

- **Social relationship**

A meta-analysis of 19 cohort studies showed that 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. However, there were variations in social relationship factor measurements, adjustment of potential confounders and substantial dropout in the primary studies.[Kuiper JS et al., 2015, level II-2]

d. Environment

A systematic review showed different strengths of evidence on the association between environmental elements and dementia.[Killin LOJ et al., 2016, level II-2]
  - Strong evidence (reported association with dementia in the majority of published papers) was seen in nitrogen oxide, ozone and particulate matter in the air.
  - Environmental tobacco smoke showed dose-response based on cumulative dose score (calculated as level years of exposure based on setting, level and duration of exposure) as shown below.

Level years of exposure	aHR
>0 - 24	0.99, 95% CI 0.76 to 1.28
25 - 49	1.15, 95% CI 0.93 to 1.42
50 - 74	1.18, 95% CI 0.87 to 1.59
75 - 99	1.39, 95% CI 1.03 to 1.84
≥100	1.95, 95% CI 1.34 to 2.83

e. Others

The Lancet Commission (2020) found several risk factors associated with dementia e.g.:[Livingston G et al., 2020, level III]
  - 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 (TBI) (RR=1.8, 95% CI 1.5 to 2.2)

f. Co-occurrence of modifiable risk factors

Exposure to additional modifiable risk factors of dementia should be kept to the minimum. A meta-analysis on dementia outcomes revealed a pooled RR for dementia of 1.20 (95% CI 1.04 to 1.39) for one risk factor, 1.65 (95% CI 1.40 to 1.94) for two risk factors and 2.21 (95% CI 1.78 to 2.73) for three or more compared with no risk factor.[Peters R. et. al., 2019, level II-2]

2.2 Risk Reduction Strategies

WHO recommends strategies to reduce the risk of cognitive decline and/or dementia in adults with normal cognition which include:[WHO, 2019]
- physical activity
- tobacco cessation
- interventions for alcohol use disorders
- management of hypertension
- management of diabetes

Other interventions that may be considered are:[WHO, 2019; Livingston G et al., 2020, level III]
- weight management
- management of dyslipidaemia
- nutritional interventions
- social activities
- cognitive interventions
- management of depression
- management of hearing loss

Tobacco cessation
- Smoking of tobacco and tobacco products (cigarette, electronic cigarette/vape, shisha, pipe, cigar etc.) can lead to various non-communicable diseases (NCDs). Worldwide, more than eight million people die every year because of this habit.[WHO Tobacco Fact Sheet, 2020]

- Hence, the decision to integrate smoking treatment with NCDs is important to reduce the prevalence of NCDs and their complications. This decision was made during the World Health Organization Framework Convention on Tobacco Control (WHO FCTC) Steering Committee Meeting in December 2019 chaired by the Honourable Health Minister of Malaysia.
- The treatment for smoking should be initiated by the treating doctor based on the assessment and treatment of tobacco use disorder as in Table 1. Details on this can be found in the CPG on Treatment of Tobacco Use Disorder 2016, available at:
- https://www.moh.gov.my/moh/resources/Penerbitan/CPG/Respiratory/CPG_TobacoDisorder.pdf

Table 1: Assessment and treatment of tobacco use disorder

ASSESSMENT AND TREATMENT	
1.	Ask and document smoking status for all patients.
2.	Provide brief advice on quit smoking at every visit to all smokers.
3.	Assess level of nicotine addiction using Modified Fagerström Test for Cigarette Dependence Questionnaire (**COMPULSORY**) and verify smoking status using carbon monoxide breath analyser (**IF AVAILABLE**).
4.	Offer pharmacotherapy to all smokers who are attempting to quit, unless contraindicated.
5.	If selected, use nicotine replacement therapy (NRT) for at least eight to twelve weeks, whereas varenicline should be used for at least twelve weeks.
6.	Combination therapy (e.g. two NRTs, a non-NRT, e.g. bupropion with an NRT) is better than monotherapy in smoking cessation treatment and may be most useful for those smokers at highest risk of relapse.

7.	Use smoking cessation medications with caution in special populations (e.g. children and adolescents, pregnant, breastfeeding women, psychiatric and substance abuse disorder patients).
8.	Arrange a minimum of six to eight face to face follow-up sessions for smoking cessation interventions in six months through counselling support team (health education officer, pharmacists or any officer trained for quit smoking services).

Medication and Supplement

In a Cochrane systematic review of 28 RCTs with low risk of bias, vitamins (folic acid, vitamin B6 and B12, antioxidant vitamins [vitamin A, C and E] and vitamin D) and mineral supplementation (zinc and copper) did not maintain cognitive function in cognitively healthy people in mid (<70 years old) and late life at 5 - 10 years follow-up.[Rutjes AWS et al., 2018, level I]

Another three Cochrane systematic review studying on the association of supplements and medication with dementia found:
- no benefits or harms from vitamin E supplements in dementia[Farina N et al., 2017, level I]
- no evidence to support the use of either aspirin or other NSAIDs for prevention of dementia[Jordan F et al., 2020, level I]
- statins given to people at risk of vascular disease did not prevent cognitive decline or dementia compared with placebo[McGuinness B et al., 2016, level I]

- There is insufficient evidence to support the use of medication (aspirin and statins), vitamins and supplements to prevent 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

3. ASSESSMENT AND DIAGNOSIS

The evaluation of dementia should be targeted at patients who present with memory complaints (by patients themselves and/or carer), have clinical suspicion of cognitive impairment or are at increased risk for dementia as well as elderly patients who have questionable mental capacity.[SMOH, 2013] The evidence on routine screening for cognitive impairment among asymptomatic community-dwelling adults age 65 and older is insufficient to determine the balance of its benefits and harms.[USPSTF, 2020]

Initial assessment may be performed using various cognitive assessment tools. If dementia is suspected on clinical assessment, laboratory tests for basic dementia screening should be performed that include full blood count, biochemistry tests (glucose, lipid, electrolytes, renal and liver function tests, and calcium level), thyroid function test and, serum vitamin B12 and folate levels, to exclude potentially reversible causes as shown in **Table 2** and to identify risk factors for dementia. When the initial evaluation is suggestive of dementia, patients need to be referred to specialist services (e.g. geriatrics/psychiatry/neurology) for further assessment and confirmation of diagnosis. Refer to **Algorithm 1** on **Early Detection of Dementia.**

Table 2: Some dementia-mimicking conditions

Conditions that can be excluded by laboratory tests
Hypothyroidism Vitamin B12 deficiency Folate deficiency Hypercalcaemia Neurosyphilis HIV-related dementia
Conditions that can be excluded by imaging/EEG
Normal pressure hydrocephalus Subdural haemorrhage Brain tumour Creutzfeldt-Jakob disease Autoimmune/limbic encephalitis

- Laboratory tests for basic dementia screening are indicated to exclude dementia-mimicking conditions.

3.1 Assessment
3.1.1 Clinical Assessment
A detailed history from patient and reliable informants, and a comprehensive physical examination are the basis of clinical evaluation for dementia. Clinical assessment should include cognitive domain and non-cognitive domain as well. During clinical assessment, clinicians should exclude delirium and other mental disorders before diagnosing dementia.

- **Cognitive domain**

There are many cognitive assessment tools available to support the diagnosis of dementia. It can be divided into informant-rated instruments and direct patient assessment instruments. Summary of the commonly used cognitive assessment tools are shown in **Table 3**.

Table 3. Common cognitive assessment tools in clinical practice

Cognitive assessment tools	Accuracy		Validation in local languages
	Sensitivity (95% CI)	Specificity (95% CI)	
Informant-rated			
1. AD8 Dementia Screening Interview[Hendry K et al, 2019, level II-2]	Cut-off point of 2:		No
	0.92 (0.86 - 0.96)	0.64 (0.39 - 0.82)	
	Cut-off point of 3:		
	0.91 (0.80 - 0.96)	0.76 (0.57 - 0.89)	
2. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)[Harrison JK et al., 2016, level III]	Cut-off point >3.0 - 3.3:		Yes: Malay
	Range 0.75 - 0.86	Range 0.38 - 0.90	
Direct patient assessment			
1. Mini-Cog[Tsoi KK et al., 2015, level I]	0.91 (0.80 - 0.96)	0.86 (0.74 - 0.93)	No
2. Abbreviated Mental Test Score (AMTS)[Jackson TA et al., 2013, level III]	Cut-off point <7:		No
	0.81 (0.76 - 0.86)	0.84 (0.83–0.85)	

3.	Mini–Mental State Examination (MMSE)*[Tsoi KK et al., 2015, level I]	0.81 (0.78 - 0.84)	0.89 (0.87 - 0.91)	Yes: Malay, Mandarin
4.	Montreal Cognitive Assessment (MoCA)[Davis DH et al., 2015, level III]	Cut-off points 18 - 26: Range 0.77 - 1.00	Range 0.51 - 0.87	Yes: Malay, Mandarin
5.	Addenbrooke's Cognitive Examination-III (ACE-III)*[Matias-Guiu JA et al., 2017, level III]	0.96	0.68	Yes: Malay, Mandarin
6.	Visual Cognitive Assessment Test (VCAT)[Lim L et al., 2018, level II-2]	0.92	0.74	Yes No language bias
7.	Saint Louis University Mental Status (SLUMS)[Cummings-Vaughn LA et al., 2014, level III]	0.93	0.96	No

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A systematic review on Cognitive Assessment Tools in Asia showed that educational bias was present in 74% of the studies with wide range of sensitivity and specificity which may lead to over estimation of dementia prevalence.[Rosli R et al., 2016, level II-3] Hence, diagnosis of dementia should not be made based on cognitive assessment score solely. The assessment score can be used to support the diagnosis of dementia and to monitor the disease progress. The choice of cognitive assessment tool depends on the clinical setting and the experience of the clinician. Refer to **Appendix 4** on **Initial Assessment Tools in Dementia**

Further evaluation with detailed neuropsychological tests can be considered if the diagnosis of dementia is still doubtful after initial assessment or to determine the subtype of dementia.[NICE, 2018]

- **Non-cognitive domain**

Two systematic reviews on the Neuropsychiatric Inventory (NPI) showed that:
  - o it was able to identify behavioural and psychological symptoms in persons with Alzheimer's dementia[Canevelli M et al., 2012, level III]
  - o the items on irritability, agitation, anxiety, apathy, sleep disturbances and delusion exerted the most impact on caregiver for PWD[Terum TM et al., 2017, level III]

The NPI and Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) were utilised:
  - o to assess the presence and severity of behavioural and psychological symptoms in PWD with proven good psychometric properties, sensitivity to pharmacological and non-pharmacological interventions, and applicability to various institutional, outpatient and community settings[Jeon YH et al., 2011, level III]
  - o in particular, to identify delusions and hallucinations in PWD among the nursing home residents[Cohen-Mansfield J et al., 2011, level III]

A cut-off score ≤5 and ≤7 for Cornell Scale for Depression in Dementia (CSDD) and Montgomery-Asberg Depression Rating Scale (MADRS) respectively give a 100% sensitivity in the screening of depression in nursing home residents with dementia when the source of information is from the professional caregivers.[Leontjevas R et al., 2012, level III]

A systematic review on instrumental activities of daily living (IADL) showed that Disability Assessment for Dementia (DAD) and Bristol Activities of Daily Living Scale (Bristol ADL) had the best ratings among 12 questionnaires despite lack of psychometric properties.[Sikkes SAM et al., 2008, level III]

In another systematic review on caregiver burden, the Zarit Burden Interview (ZBI, 22-item version) had strong psychometric properties [reliability (Cronbach's alpha ranging from 0.70 to 0.93) and validity] and had been used for caregivers in the care of PWD.[Whalen KJ & Buchholz SW, 2009, level III]

> **Recommendation 2**
> - The diagnosis of dementia should be based on detailed history and physical examination, and supported by cognitive, functional and behavioural evaluation.

3.1.2 Imaging and Biomarkers
- **Structural neuroimaging**

Structural neuroimaging with computed tomography (CT) or magnetic resonance imaging (MRI) is usually offered in the assessment of people with suspected dementia to exclude reversible causes of cognitive decline and other cerebral pathologies, and to assist in subtype diagnosis.[NICE 2018, Australian guideline 2016] The second edition of this CPG recommends structural neuroimaging e.g. CT and MRI brain to be done where available in the evaluation of dementia to exclude intracranial pathology.[MoH, 2009]

Some conditions that mimic dementia can be detected and excluded by structural neuroimaging are listed in **Table 2**.

A narrative review of structural MRI on patients with AD revealed cerebral atrophy. The progression of atrophy follows Braak staging and is first observed at medial temporal lobe structures, including hippocampus and entorhinal cortex with a reduction of 26% and 40% respectively compared with controls. Other limbic structures including amygdala, olfactory bulb tract, cingulate gyrus, and thalamus are involved later. As the disease progresses, the atrophy spreads to cortical regions causing volume reduction.[Chandra A et al., 2019, level III] Visual rating scales for medial temporal lobe may be useful to grade the degree of medial temporal atrophy on CT or MRI.[Harper L et al., 2015, level III]

MRI is recommended if dementia subtype is uncertain and VaD is suspected. CT can be used if MRI is unavailable or contraindicated. It is readily available and better tolerated. However, VaD should not be diagnosed based solely on vascular lesion burden on imaging because the extent of vascular damage required to impair a person's cognitive function is still unclear.[NICE, 2018]

- **Functional neuroimaging**

NICE recommends further testing with functional neuroimaging should only be considered if it helps to diagnose a dementia subtype and change the patient's subsequent management.[NICE, 2018]

Fluorodeoxyglucose-positron emission tomography (FDG-PET) or perfusion single-photon emission CT (SPECT) can be considered if the dementia diagnosis is uncertain and AD or FTD is suspected. Iodine 123-radiolabeled 2β-carbomethoxy-3β-(4-iodophenyl)-N-(3-fluoropropyl) nortropane (^{123}I-FP-CIT) SPECT or ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) cardiac scintigraphy can be considered if the dementia diagnosis is uncertain and DLB is suspected.[NICE, 2018] A Cochrane systematic review showed that dopamine transporter (DAT)

imaging is a promising test for diagnosing DLB, though the evidence was derived from only one small study. A normal DAT imaging may be an accurate means to exclude the diagnosis of DLB.[McCleery J et al., 2015, level III]

Two Cochrane systematic reviews did not support routine use of FDG-PET and ^{11}C-labeled Pittsburgh compound B-positron emission tomography (^{11}C-PIB-PET) scans for the early diagnosis of AD and other dementia subtypes in people with Mild Cognitive Impairment (MCI).[Smailagic N et al., 2015, level III; Zhang S et al., 2014, level III] In fact, an Australian guideline recommends that SPECT should not be used to differentiate MCI from dementia.[Australian guideline, 2016]

- **Electroencephalogram**

Electroencephalogram (EEG) is not routinely used in the investigation of dementia.[NICE 2018, Australian guideline 2016] It should be considered when there is rapidly progressive cognitive decline and atypical features of dementia e.g. CJD, autoimmune/limbic encephalitis.

A systematic review of dementia subtypes showed that a normal EEG result rendered a diagnosis of DLB very unlikely. Non-specific slowing of background rhythm on EEG was seen in >90% of DLB cases as opposed to an estimated 10% of AD cases.[Law ZK et al., 2020, level III]

- **Cerebrospinal fluid biomarkers**

After clinical assessment and structural neuroimaging, if the diagnosis remains uncertain and AD is suspected, lumbar puncture may be considered to examine the cerebrospinal fluid (CSF) for total tau or total tau and phosphorylated-tau 181, and amyloid beta 1-42 or amyloid beta 1-42 and amyloid beta 1-40.[NICE, 2018]

In view of insufficient and heterogeneity of evidence, a Cochrane systematic review did not recommend the use of CSF tau and CSF tau/amyloid beta ratio to identify people with MCI who would clinically convert to AD later.[Ritchie C et al., 2017, level I]

Recommendation 3
- Structural neuroimaging (computed tomography or magnetic resonance imaging) should be done in evaluation of dementia to exclude reversible causes of cognitive decline and other intracranial pathology.
- Functional neuroimaging may be considered if the diagnosis of dementia is uncertain.
- Electroencephalogram should be considered in rapidly progressive cognitive decline and atypical features of dementia.

3.2 Diagnostic Criteria

There are a few diagnostic criteria available for each subtypes of dementia, the majority are for clinical use and some are for research purpose (refer to **Table 4**). Major changes have been made to diagnostic criteria for dementia in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) published in 2013. Major neurocognitive disorder is used to replace dementia while mild neurocognitive disorder is introduced for MCI. It only requires decline in one or more of the cognitive domains, which is severe enough to interfere with daily activities, to diagnose major neurocognitive disorder. The latest edition of DSM-5 helps clinicians to diagnose different types of dementia more easily. Another diagnostic criteria that can be used in the diagnosis of dementia is the International Classification of Diseases, Tenth Revision (ICD-10). Refer to **Appendix 5** on **DSM-5** and **Appendix 6** on **ICD-10**

Table 4. Diagnostic Criteria for Subtypes of Dementia

Dementia Subtypes	Diagnostic Criteria	
Alzheimer's Disease	DSM-5 or ICD-10	• National Institute on Aging and Alzheimer's Association (NIA-AA)
Vascular Dementia		• National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) • Alzheimer's Disease Diagnostic and Treatment Centers (ADDTC)
Mixed Dementia		-
Parkinson's Disease Dementia (PDD)		• Movement Disorder Society (MDS) guidelines for diagnosis of PDD
Dementia of Lewy Body (DLB)		• Fourth consensus report of the DLB Consortium
Frontotemporal Dementia (FTD)		• International consensus criteria for behavioural variant FTD

> **Recommendation 4**
> • Diagnosis of dementia should be made based on Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) or the International Classification of Diseases, Tenth Revision (ICD-10)

Refer to **Algorithm 2** on **Diagnosis of Dementia.**

3.3   Stages

The severity of dementia can be staged according to functional status as stated in DSM-5 as shown below.[DSM-5]

Severity	Functional status
Mild	Difficulties with instrumental activities of daily living (e.g. housework, managing money).
Moderate	Difficulties with basic activities of daily living (e.g. feeding, dressing).
Severe	Fully dependent

In addition, severity of dementia can also be assessed using the Global Deterioration Scale for Assessment of Primary Degenerative Dementia and Functional Assessment Staging (FAST). FAST is especially useful for grading severity in more advanced stages of dementia (FAST stage 6 and 7). Refer to **Appendix 7a** and **7b** for the mentioned scales.

4.   TREATMENT

Specialists in the care of dementia (psychiatrists/geriatric-psychiatrists/neuropsychiatrists, neurologists/geriatricians and physicians or family medicine specialists with special interest training in geriatric care) should initiate treatment in PWD. Once treatment is initiated, PWD should be regularly reviewed to assess cognition, behavioural and psychological symptoms of dementia (BPSD), global functioning and potential side effects. Management of dementia can be divided into non-pharmacological and pharmacological approach. Non-pharmacological

interventions should be the mainstay of treatment in PWD throughout all stages of the condition.

- For those who require regular medication, the '3T' approach is a good practice:[MoH, 2009]
  - treatments should have a specific target symptom
  - the starting dose should be low and then titrated upwards
  - treatments should be time limited

4.1 Non-pharmacological Interventions

Non-pharmacological interventions attempt to promote positive effects on cognition, quality of life, mood and, other behavioural and psychological symptoms of dementia. They have shown to have potential benefits in the management of dementia.

- **Cognition and Quality of life**

A meta-analysis showed that physical activity interventions improved cognitive function (SMD=0.42, 95% 0.23 to 0.62) compared with control in PWD. In terms of type of intervention, positive results were seen in combined exercise interventions (SMD=0.59, 95% CI 0.32 to 0.86) and aerobic-only exercise interventions (SMD=0.41, 95% CI 0.05 to 0.76) only. Both high and low frequency interventions were also effective.[Groot C et al., 2016, level I]

There are three major types of cognitive approaches:
  - cognitive stimulation - entails exposure to and engagement with activities and materials involving some degree of cognitive processing
  - cognitive training - a specific training exercise geared to specific cognitive functions and, includes practice and repetition which may be computer-assisted
  - cognitive rehabilitation - include working on personal goals, often using external cognitive aids and with some use of learning strategies

In two Cochrane systematic reviews on mild to moderate dementia:
  - moderate quality evidence showed that cognitive stimulation therapy given either through specific manual or general activities improved cognitive function (SMD=0.41, 95% CI 0.25 to 0.57); it can be carried out at patient's own home, day care, outpatient or at residential setting by caregiver with minimal training[Woods B et al., 2012, level I]
  - low to moderate quality evidence demonstrated that cognitive training was not associated with improvement in global measure of cognition (SMD=0.10, 95% CI -0.21 to 0.40)[Bahar-Fuchs A et al., 2013, level I]

NICE recommends group cognitive stimulation therapy to people with mild to moderate dementia. It also recommends cognitive rehabilitation or occupational therapy to support functional ability in the same group of PWD.[NICE, 2018]

In a Cochrane systematic review, reminiscence therapy (RT) showed no improvement in self-rated quality of life (QoL) compared with no treatment in PWD (SMD=0.11, 95% CI -0.12 to 0.33). The quality of evidence was moderate based on GRADE.[Woods B et al., 2018, level I] However, NICE recommends group RT to promote cognition, independence and well-being of PWD.[NICE, 2018]

In another systematic review on cognition and quality of life, spirituality and religious activities delayed cognitive decline and improve QoL of PWD.[Agli O et al., 2014, level II-2]

> **Recommendation 5**
> - To improve cognitive function in mild to moderate dementia, cognitive stimulation therapy and physical activity can be offered

- **Behaviour and Psychological symptoms**

Before starting non-pharmacological or pharmacological treatment for distress or BPSD in PWD, NICE recommends structured assessment exploring and addressing possible reasons for their distress including clinical or environmental causes e.g. pain, delirium or inappropriate care. Psychosocial and environmental interventions should be offered as initial and ongoing management, to reduce distress in PWD.[NICE, 2018]

Anxiety and depression are very common in PWD. Psychological interventions have been suggested as a potential treatment for this population.

In a Cochrane systematic review, psychological interventions, e.g. cognitive behavioural therapy (CBT) and, multifaceted and semi-tailored interventions (e.g. counselling sessions, education and outreach support to patients and carers) reduced depressive symptoms (SMD= -0.22, 95% CI -0.41 to -0.03) and clinician-rated anxiety (MD= -4.57, 95% CI -7.81 to -1.32) compared with treatment as usual in dementia. The primary papers were of low to moderate quality.[Orgeta V et al., 2014, level I]

PWD who are being cared in long-term care settings are often not involved in meaningful activities. Offering them activities may improve their quality of life and reduce challenging behaviour. Nevertheless, in a Cochrane systematic review, personally-tailored activities showed no significant reduction in challenging behaviour and improvement in self-rated QoL among PWD in long-term care setting. However, the evidence is of low quality.[Mohler R et al., 2018, level I] On the other hand, NICE recommends to offer personalised activities in PWD with agitation or aggression to promote engagement, pleasure and interest.[NICE, 2018]

In a meta-analysis of three high-quality RCTs, multicomponent interventions for caregivers showed 33% less institutionalisation after 6 - 12 months (RR=0.67, 95% CI 0.49 to 0.92) compared with minimal support or usual care in mild to moderately severe AD. The intervention were long-term programmes comprised of education and support for caregivers plus other components e.g. respite care and support groups, tailored to the needs of PWD.[Olazaran J et al., 2010, level I]

Other non-pharmacological interventions on PWD addressed in systematic reviews/meta-analysis are shown in **Table 5**.

Table 5: Other non-pharmacological interventions on PWD

Interventions	Effectiveness	Quality of evidence
Music-based therapy vs usual care[van der Steen JT et al., 2018, level I]	- Reduced depressive symptoms (SMD= -0.27, 95% CI -0.45 to -0.09) - Reduced overall behaviour problems (SMD= -0.23, 95% CI -0.46 to -0.01)	Moderate
Aromatherapy vs placebo[Forrester LT et al., 2014, level I]	- Equivocal findings on agitation and behavioural symptoms	Very low (GRADE)
Massage and touch vs daily routine care or being accompanied[Wu J et al., 2017, level I]	Improved: - behavioural problems (SMD= -0.39, 95% CI -0.53 to -0.25) - negative emotions (SMD= -0.60, 95% CI -1.14 to -0.06)	Low to moderate (GRADE)

Validation therapy vs usual care[Neal M et al., 2009, level I]	• Insufficient evidence on behaviour and emotional state	Low
Light therapy vs usual care[Forbes D et al., 2014, level I]	• No effect on sleep, challenging behaviour or psychiatric symptoms	Moderate
Simulated presence therapy vs usual care[Abraha I et al., 2017, level I]	• Inconclusive efficacy on behavioural and psychological symptoms, and QoL	Very low (GRADE)
Snoezelen vs control[Vilela VC et al, 2017, level I]	• No effect on mood, behaviour, communication and cognition	Low

> **Recommendation 6**
> • In people with dementia having behavioural and psychological symptoms:
>   o explore and address possible clinical or environmental causes/triggering factors
>   o offer psychosocial and environmental interventions as initial and ongoing treatment:
>   - psychological intervention for depressive symptoms and/or anxiety
>   - personalised and tailored activities for agitation and aggression

Refer to **Algorithm 3** on **Treatment of Dementia**.

4.2 Pharmacological Interventions

No new drug has been licensed for the treatment of dementia since the previous edition of the CPG published in 2009.

The three acetylcholinesterase inhibitors (AChEI) (donepezil, galantamine and rivastigmine) as well as the N-methyl-D-aspartate (NMDA) receptor antagonist (memantine) are still the mainstay treatment in managing PWD.

AChEI works by augmenting the levels of acetylcholine in the brain to compensate for the losses of cholinergic function. Additionally, galantamine also modulates activity at nicotinic receptors.

Memantine is a voltage-dependent, moderate-affinity, uncompetitive NMDA receptor antagonist that inhibits the effects of pathologically elevated tonic levels of glutamate that may lead to neuronal dysfunction.[Bond M, 2012]

> • Available pharmacological treatment for dementia is not curative; however they are aimed at managing symptoms (cognitive, non-cognitive and behavioural), improve independence and preserve function.[NICE, 2018]

Currently under the MoH Medicines Formulary, donepezil, rivastigmine and memantine are listed and indicated for use in AD while only rivastigmine is indicated for PDD. Refer to **Appendix 8** on **Pharmacological Treatment of Dementia**.

4.2.1 Alzheimer's Disease
Donepezil
a.   Cognition
i.   All disease severity

In a Cochrane systematic review of moderate quality RCTs, donepezil 10 mg was more effective than placebo at 24 - 26 weeks in AD across all severity based on MMSE (MD=1.05, 95% CI 0.73 to 1.37).[Birks JS et al., 2018, level I]

ii.   Mild to moderate severity
Donepezil 10 mg/day was more effective than placebo in mild to moderate AD at 24 - 26 weeks based on Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) (MD= -2.67, 95% CI -3.31 to -2.02).[Birks JS et al., 2018, level I]

Donepezil 5 mg/day was more effective than placebo in moderate AD at 12 - 24 weeks based on MMSE (MD=1.22, 95% CI 0.54 to 1.90).[Birks JS et al., 2018, level I]

iii.   Severe
Benefit in cognitive function was seen with donepezil 10 mg/day compared with placebo in severe AD based on Severe Impairment Battery (SIB) (MD=5.92, 95% CI 4.53 to 7.31).[Birks JS et al., 2018, level I]

There was no difference in the outcome between donepezil 5 mg/day and 10 mg/day at 24 weeks based on MMSE or SIB. However, the outcome was in favour for 10 mg/day for ADAS-Cog at 24 weeks (MD= -1.05, 95% CI -1.80 to -0.30).[Birks JS et al., 2018, level I]

b.   Safety
Mild adverse events (AEs), namely nausea, vomiting and diarrhoea, were higher in PWD on donepezil 10 mg/day:[Birks JS et al., 2018, level I]
- compared with 5 mg/day at 26 weeks (OR=1.56, 95% CI 1.07 to 2.28)
- compared with placebo at 24 weeks (OR=1.59, 95% CI 1.23 to 2.05)

There was no difference seen between donepezil 5 mg/day and placebo at 24 weeks.

Rivastigmine
a.   Cognition
In another Cochrane systematic review of moderate quality evidence, rivastigmine 6 to 12 mg/day twice daily or 9.5 mg/day patch improved cognition in mild to moderate AD at 26 weeks compared with placebo based on:[Birks JS et al., 2015, level I]
- MMSE (WMD=0.74, 95% CI 0.52 to 0.97)
- ADAS-Cog test score (WMD= -1.79, 95%CI -2.21 to -1.37)

MMSE results were in favour of rivastigmine (twice daily capsules) compared with placebo at 26 weeks at the following dosages:[Birks JS et al., 2015, level I]
- 1 - 4 mg/day (WMD=0.43, 95% CI 0.08 to 0.78)
- 6 - 12 mg/day (WMD=0.82, 95% CI 0.56 to 1.08)

Benefit was also seen in MMSE for rivastigmine patch compared with placebo in AD at 24 weeks for different dosages:[Birks JS et al., 2015, level I]
- 20 cm^2 (17.4 mg/day) patch (MD=0.90, 95% CI 0.32 to 1.48)
- 10 cm^2 (9.5 mg/day) patch (WMD=0.64, 95% CI 0.26 to 1.02)

However, no difference was seen in MMSE in similar comparison using rivastigmine 5 cm^2 (4.6 mg/day) patch.

Rivastigmine 10 cm^2 (9.5 mg/day) patch vs 6 to 12 mg/day twice daily capsules showed no difference in MMSE for AD at 24 weeks. [Birks JS et al., 2015, level I]

In an RCT comparing rivastigmine 13.3 mg/ 24 h patch vs 4.6 mg/24 h patch in severe AD, the higher dose patch was superior to lower dose in terms of:[Farlow MR et al., 2013, level I]
- cognition by SIB at 16 weeks (p<0.0001) and 24 weeks (p<0.0001)

- global function by Alzheimer's Disease Cooperative Study – Clinical Global Impression of Change (ADCS-CGIC) (p=0.0023)

However, there was no difference in behaviour using NPI-12.

b. Safety

In terms of tolerability, rivastigmine 6 to 12 mg/day twice daily capsules or 9.5 mg/day patch had at least one AE compared with placebo at 26 weeks (OR=2.16, 95% CI 1.82 to 2.57). At these doses, the transdermal patch may have fewer side effects than the capsules but comparable effectiveness.[Birks JS et al., 2015, level I]

Apart from that, 20 cm^2 (17.4 mg/24 h) patch had higher incidence of at least one AE (OR=2.28, 95% CI 1.64, 3.16) than 10 cm^2 (9.5 mg/24 h) patch (OR=1.63, 95% CI 1.29 to 2.06) when they were compared with placebo.[Birks JS et al., 2015, level I]

The incidence of AEs is greater with 13.3 mg/24 h (15 cm^2) patch than 9.5 mg/24 h (10 cm^2) patch (75.0% vs 68.2% respectively). Most of the AEs are mild and decrease over time.[Grossberg G et al., 2013, level I]

Galantamine

An HTA of variable quality evidence showed a benefit in ADAS-Cog from galantamine compared with placebo at:[Bond M et al., 2012, level I]
- 12 - 16 weeks (WMD= -2.39, 95% CI -2.80 to -1.97)
- 21 - 26 weeks (WMD= -2.96, 95% CI -3.41 to -2.51)

Benefit was also seen in behaviour based on NPI at 21 - 26 weeks (WMD= -1.46, 95% CI -2.59 to -0.34). There were higher percentage of AEs in galantamine compared with placebo which were mainly gastrointestinal.

A network meta-analysis of moderate quality studies found superior effectiveness of galantamine 24 mg daily compared with placebo in mild to moderate AD (SMD= -0.50, 95% CI -0.61 to -0.40).[Dou KX et al., 2018, level I]

NICE recommends the three AChEIs (donepezil, galantamine and rivastigmine) as monotherapy options for managing mild to moderate AD.[NICE, 2018]

Memantine

a. Cognition

i. Mild

A Cochrane systematic review found no difference between memantine and placebo based on ADAS-Cog (SMD= -0.03, 95% CI -0.19 to 0.13) and Clinician's Interview-Based Impression of Change (CIBIC+) (SMD= -0.08, 95% CI -0.27 to 0.12).[McShane R et al., 2019, level I]

ii. Moderate to Severe

In the same review as above, moderate- to low-certainty evidence showed that memantine was more effective than placebo based on SIB (SMD= -0.27, 95% CI -0.34 to -0.21) and CIBIC+ (SMD= -0.20, 95% CI -0.28 to -0.13).[McShane R et al., 2019, level I]

iii. Moderate to Severe ± AChEI

Sub-analysis based on AChEI use showed that memantine was also effective against placebo based on:[McShane R et al., 2019, level I]
- SIB
  - with AChEI (SMD= -0.24, 95% CI -0.33 to -0.14)
  - without AChEI (SMD= -0.33, 95% CI -0.43 to -0.23)
- CIBIC+
  - with AChEI (SMD= -0.21, 95% CI -0.32 to -0.09)

- without AChEI (SMD= -0.20, 95% CI -0.30 to -0.10)

b. Safety

The same Cochrane systematic review found no difference between memantine and placebo in the number of people with at least one AE, regardless of dementia aetiology or severity (RR=1.03, 95% CI 1.00 to 1.06).[McShane R et al., 2019, level I]

Another meta-analysis showed no difference between memantine and placebo in AD based on:[Blanco-Silvente L et al., 2018, level I]

- AEs (OR=1.05, 95% CI 0.88 to 1.25)
- serious AEs (OR=0.89, 95% CI 0.70 to 1.13)
- mortality (OR=1.03, 95% CI 0.74 to 1.44)

NICE recommends memantine monotherapy as an option in:
- moderate AD where there is intolerance or contraindication to AChEI
- severe AD

Recommendation 7
- Donepezil should be offered in Alzheimer's Disease (AD) of all severity.
  - Rivastigmine is an option in mild to moderate AD.
- Memantine may be considered in moderate to severe AD as monotherapy or in combination with acetylcholinesterase inhibitors.

4.2.2 Vascular Dementia
Donepezil
a. Cognition

In vascular dementia, donepezil is significantly more effective than placebo based on:[Román GC et al., 2010, level I]

- V-ADAS-cog at 12, 18 and 24 weeks (p<0.05)
- MMSE at 24 weeks (p=0.0301)

c. Safety

Donepezil is well tolerated; most adverse events are transient and mild to moderate in severity.[Román GC et al., 2010, level I]

Rivastigmine
a. Cognition

A Cochrane systematic review found benefit in MMSE (MD=0.60, 95% CI 0.11 to 1.09) with rivastigmine (3 - 12 mg/day) compared with placebo in probable vascular dementia at 24 weeks. There was no significant difference between:[Birks J et al., 2013, level I]
- rivastigmine 6 mg/day and placebo in MMSE for subcortical vascular dementia
- rivastigmine 3 - 9 mg/day and placebo in ADAS-Cog for MCI and cognitive impairment no dementia (CIND)

b. Safety

There were significantly higher rates of vomiting, nausea, diarrhoea and anorexia in rivastigmine compared with placebo.[Birks J et al., 2013, level I]

Memantine
a. Cognition

A Cochrane systematic review found probable small benefit favouring memantine against placebo based on ADAS-Cog (MD= -2.15, 95% CI -3.25 to -1.05).[McShane R et al., 2019, level I]

b.   Behaviour
The same review showed low certainty evidence favouring memantine against placebo based on Nurses' Observation Scale for Geriatric Patients (NOSGER) (SMD= -0.20, 95% CI -0.37 to -0.03).[McShane R et al., 2019, level I]

c.   Safety
Refer to **Subchapter 4.2 A (Memantine - Tolerability)**.

Donepezil, rivastigmine, galantamine and memantine comparison
a.   Cognition
In a network meta-analysis on vascular cognitive impairment, donepezil 10 mg/day and rivastigmine 6 mg/day were superior than placebo based on MMSE with MD of 0.84 (95% CI 0.14 to 1.57) and 1.37 (95% CI 0.22 to 2.53) respectively. The derived dose-based hierarchy of the cognitive enhancers' efficacy was as follows: rivastigmine 6 mg > donepezil 10 mg > donepezil 5 mg > rivastigmine 12 mg > memantine 20 mg > placebo. Meanwhile the derived dose-based hierarchy based on ADAS-cog were: memantine 20 mg > galantamine 24 mg > donepezil 10 mg > donepezil 5 mg > rivastigmine 12 mg > placebo > rivastigmine 9 mg.[Jin BR et al., 2019, level I]

b.   Safety
The derived hierarchy of the risk of total AEs was donepezil 10 mg > galantamine > donepezil 5 mg > memantine > placebo > rivastigmine.[Jin BR et al., 2019, level I]

NICE recommends only to consider AChEI or memantine for people with vascular dementia if they have suspected co-morbid Alzheimer's disease, Parkinson's disease dementia or dementia with Lewy bodies.[NICE, 2018]

> - Patients with vascular dementia with concurrent vascular risk factors should be treated with recommended drugs for the management of the medical problems.[MoH, 2009]

> **Recommendation 8**
> - Acetylcholinesterase inhibitors or memantine may be considered in vascular dementia.

4.2.3 Lewy Body Disease (Dementia with Lewy Body/Parkinson's Disease Dementia)
Acetylcholinesterase inhibitors
a.   Cognition
A Cochrane systematic review of six moderate quality RCTs showed an improvement in the MMSE favouring treatment with AChEI (rivastigmine and donepezil) compared with control in DLB, PDD and cognitive impairment in Parkinson's disease (CIND-PD) (WMD=1.08, 95% CI 0.50 to 1.66). However, subgroup analysis showed:[Rolinski M et al., 2012, level I]
- positive effect in PDD (WMD=1.09, 95% CI 0.45 to 1.73) and, PDD and CIND-PD (WMD=1.05, 95% CI 0.42 to 1.68)
- no difference in DLB (WMD=1.24, 95% CI 0.28 to 2.76)

A recent meta-analysis found that results on MMSE and MoCA favoured AChEI (rivastigmine and donepezil) and memantine compared with control in PDD and DLB (SMD=0.46, 95% CI 0.36 to 0.55).[Meng YH et al., 2019, level I] The 15 studies used in the meta-analysis were small and short duration but of good quality.

b.   Behaviour
Two meta-analyses showed improvement in behaviour outcomes with:

- AChEI compared with control in DLB, PDD and CIND-PD (SMD=-0.20, 95%CI -0.36 to -0.04); the effect was only seen in RCTs using rivastigmine and lasting ≥18 weeks[Rolinski M et al., 2012, level I]

- AChEI and memantine compared with control in PDD and DLB (MD= -1.73, 95% CI -2.84 to -0.62)[Meng YH et al., 2019, level I]

c. Safety
In the two meta-analyses mentioned above, treatment groups experienced more adverse events than control groups with:
- OR=1.64, 95% CI 1.26 to 2.15; there was no difference in severe adverse events[Rolinski M et al., 2012, level I]
- RR=1.09, 95% CI 1.04 to 1.16[Meng YH et al., 2019, level I]

Rivastigmine was also found to be less tolerable than donepezil and memantine.

Memantine
a. Cognition
A Cochrane systematic review found very low certainty evidence that memantine had no difference with placebo based on MMSE.[McShane R et al., 2019, level I]

b. Behaviour
There was no difference between memantine with placebo based on NPI in the same review.[McShane R et al., 2019, level I]

c. Safety
Refer to **Subchapter 4.2 A (Memantine - Tolerability)**.

> **Recommendation 9**
> - Rivastigmine or donepezil may be considered for dementia with Lewy body and Parkinson's disease dementia.

4.2.4 Frontotemporal Dementia
Donepezil
A systematic review found low level evidence on discontinuation of donepezil resulting in reduction in NPI total and ZBI scores after two weeks of the discontinuation in FTD.[Bouli M et al., 2017, level I]

Rivastigmine
In the same review as above, an open-label study demonstrated amelioration of behavioural changes after 12 months treatment with rivastigmine in patients with a probable diagnosis of FTD.[Bouli et al., 2017, level I]

Galantamine
A systematic review found that galantamine was not effective based on Frontal Behavioural Inventory (FBI), Western Aphasia Battery (WAB), Clinical Global Impressions-severity (CGI-S) and Clinical Global Impressions-improvement (CGI-I) in behavioural variant of FTD (bvFTD).[Nardell M et al., 2014, level I] Another systematic review showed that it was also not associated with improvement of psychiatric symptoms in FTD.[Bouli M et al., 2017, level I] However, galantamine was found to be well tolerated.[Nardell M et al., 2014, level I]

Memantine
A meta-analysis and two systematic review of RCTs showed that memantine had no significant difference with placebo based on:
- CGI, MMSE, NPI and ZBI[Kishi T et al,, 2015, level I]

- CGIC, CIBIC+, MMSE, NPI, MDRS, ZBI and DAD[Nardell M et al., 2014, level I]
- NPI[Bouli M et al., 2017, level I]

Memantine was also found to be well tolerated.[McShane R et al., 2019, level I; Kishi T et al., 2015, level I; Nardell M et al, 2014, level I]

The lack of effectiveness of memantine discussed above were supported by a later Cochrane systematic review based on MMSE and NPI.[McShane R et al., 2019, level I]

> - There is insufficient evidence to support the use of ACheI or memantine to patients with FTD.

4.2.5 Behavioural and Psychological Symptoms
a.   Effectiveness
Antipsychotics
A systematic review found that antipsychotics (APs) had small but significant effect in reducing BPSD in PWD compared to placebo (SMD= -0.13, 95% CI -0.21 to -0.06).[Dyer SM et.al., 2017, level I]

A network meta-analysis found that risperidone was more effective than placebo in reducing agitation based on agitation rating scale of Cohen-Mansfield Agitation Inventory (CMAI), NPI-A, BEHAVE-AD-A and Neurobehavioral Rating Scale-Agitation (NBRS-A) in PWD (OR=1.96, 95% CI 1.49 to 2.59) but haloperidol appeared less effective compared with nearly all comparators.[Kongpakwattana K et al., 2018, level I]

Another network meta-analysis on PWD with BPSD compared APs with placebo and showed:[Yunusa I et.al., 2019, level I]
- aripiprazole improved outcomes on NPI (SMD= -0.17, 95% CI -0.31 to -0.02)
- risperidone improved outcomes on CMAI (SMD= -0.26, 95% CI -0.37 to -0.15)

There were no significant differences on effectiveness between the APs.

Two RCTs assessed the effectiveness and safety of brexpiprazole (fixed and flexible doses) compared with placebo on agitation in patients with AD. The first RCT (NCT01862640) showed brexpiprazole 2 mg/day had greater improvement in CMAI Total score at week 12 than placebo (adjusted MD= -3.77, 95% CI -7.38 to -0.17). The second RCT (NCT01922258) on brexpiprazole 0.5 - 2 mg showed no difference in the CMAI Total score at week 12 (adjusted MD= -2.34, 95% CI -5.49 to 0.82). However post-hoc analysis on patients titrated to maximum brexpiprazole dose (2 mg) at week 4 showed improvement in in the score at week 12 (adjusted MD= -5.06, 95% CI -8.99 to -1.13).[Grossberg GT et al., 2019, level I]

Antidepressants
A systematic review found very low-quality evidence that sertraline did not have significant effect on global BPSD outcomes based on NPI compared with placebo in PWD and concomitant depression.[Dyer SM et al., 2017, level I]

The above network meta-analysis also showed that selective serotonin reuptake inhibitors as a class reduced BPSD in PWD who developed agitation based on CMAI, NPI-A, BEHAVE-AD-A and NBRS-A (OR=1.61, 95% CI 1.02 to 2.53) compared with placebo.[Kongpakwattana K et al., 2018, level I]

NICE recommends not to offer antidepressants in mild to moderate depression for people with mild to moderate dementia unless they have pre-existing severe mental health problem.[NICE, 2018]

Mood stabilisers

A meta-analysis on mood stabilisers as an adjunct to conventional anti-dementia drugs on BPSD in AD suggested a significant effect in favour of placebo over valproate on NPI total (WMD=3.71, 95% CIs 0.15 to 7.26).[Xiao H et al., 2010, level I]

A Cochrane meta-analysis of moderate-quality evidence of two studies showed no difference between valproate and placebo in total Brief Psychiatric Rating Scale (BPRS) (measuring agitation) in PWD after six weeks of treatment.[Baillon SF et al., 2018, level I]

Others

In a systematic review, a low quality RCT showed that pain management with analgesics reduced global BPSD in PWD (SMD= -0.24, 95% CI -0.47 to -0.01).[Dyer SM et al., 2017, level I]

A Cochrane systematic review of small trials found some beneficial effects on sleep from trazodone and orexin antagonist with no harmful effects.[McCleery J et al., 2020, level I]

A systematic review concluded that benzodiazepine use to be avoided in the elderly based on results from a meta-analysis of 45 RCTs and review of 24 RCTs.[Schroeck JL et al., 2016, level I]

b.   Safety

Non-significant differences in treatment acceptability were observed for nearly all medications when compared with placebo except for oxcarbazepine.[Kongpakwattana K et al., 2018, level I]

The network meta-analysis which used SUCRAs in its analysis showed:[Yunusa I et al., 2019, level I]
- for somnolence or sedation: placebo was ranked as the safest, followed by risperidone, aripiprazole and olanzapine while quetiapine was the least safe
- for EPSs: quetiapine and aripiprazole ranked as the safest agents, followed by olanzapine while risperidone was ranked the worst
- for cerebrovascular adverse event: aripiprazole had highest probability of safety among the drugs, followed by quetiapine, risperidone and olanzapine
- for falls, fracture or injury: risperidone and quetiapine ranked in the top two positions for safety, followed by aripiprazole, placebo and olanzapine

The Cochrane meta-analysis of low-quality evidence showed a higher rate of adverse effects among valproate-treated participants compared with controls (OR=2.02, 95% CI 1.30 to 3.14).[Baillon SF et al., 2018, level I]

Two RCTs found no notable difference in the treatment-emergent adverse events (TEAEs) between brexipiprazole and placebo. The majority of the TEAE were mild or moderate in severity.[Grossberg GT et al., 2019, level I]

- United States Food and Drug Administration (US FDA) issued a warning regarding increased mortality associated with the use of AP in elderly patients with dementia-related psychosis in response to emerging evidence since 2005.[Rubino A et al, 2020, level III]
- NICE recommends AP to be offered to PWD who are either at risk of harming themselves or others, or experiencing symptoms that are causing them severe distress.[NICE, 2018]
- NICE recommends on AP in PWD:[NICE, 2018]
  - the lowest effective dose should be used and for the shortest possible duration
  - should be reassessed regularly and wean off if it is not needed

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Recommendation 10
- Antipsychotics may be considered for behavioural and psychological symptoms in people with dementia (PWD) where there is a risk of harming themselves or others.

- Antidepressants:
  - may be considered for PWD who have agitation
  - may be prescribed for PWD with pre-existing severe mental health problem

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- There is insufficient evidence to support the use of mood stabilisers to treat agitation in PWD

4.2.6 Anticholinergic Concerns
PWD often have multiple co-morbidities and require multiple pharmacotherapies. Examples of commonly used medications include benzodiazepines, APs and antihistamines. These medications have high anticholinergic burden (ACB) which causes negative outcomes in the patients. Therefore, careful consideration is needed before initiating such medications and, active monitoring and deprescribing should be carried out whenever possible. Refer to **Appendix 9** on **Anticholinergic Burden Score.**

American Geriatric Society on Beer's criteria consider potentially inappropriate prescription (PIP) as an explicit list of drugs that are best avoided by older adults in most circumstances or under specific situations e.g. in certain diseases or conditions.[By the 2019 American Geriatrics Society, 2019. level III]

Examples of PIP/psychotropics are:
- first-generation antihistamines (e.g. chlorpheniramine, hydroxyzine)
- antispasmodics (e.g. atropine, hyoscine)
- antipsychotics
- antidepressants
- benzodiazepines
- gastrointestinal medication (e.g. metoclopramide, proton pump inhibitors)
- non-steroidal anti-inflammatory drugs

A systematic review of 26 studies found prevalence of PIP in the range of 13 - 74% for PWD.[Hukin D et al., 2019, level II-2]

In a meta-analysis, the prevalence of PIP was lower in PWD living in the community compared with those in nursing homes and specialised care homes [31% (95% CI 9 to 52) vs 42% (95% CI 30 to 55)].[Delgado J et al., 2020, level II-2]

A cross-sectional study showed that an average ACB score >3 during the first three months initiation of AChEI in PWD increased the risk of:[Ah YM et al., 2019, level III]
- treatment modification at one year (HR=1.12, 95% CI 1.02 to 1.24)
- delirium at one year (HR=1.52, CI 1.17 to 1.96)
- mortality at two years (HR=1.23, CI 1.06 to 1.41)

NICE recommends to consider minimising the use of medicines associated with increased ACB and look for alternatives wherever possible.[NICE, 2018]

Recommendation 11
- The use of anticholinergic medications in dementia should be done cautiously with regular review of indication and deprescribed whenever possible.

Refer to **Algorithm 3** on **Treatment of Dementia**.

Refer to **Appendix 10** on **Suggested Guide to Review and Deprescribe (PIP/Psychotropic) in Dementia.**

5.   TRADITIONAL AND COMPLEMENTARY MEDICINE

There is no strong evidence on the effectiveness and safety of Traditional and Complementary Medicine (TCM) in the treatment of dementia.

In a meta-analysis on PWD, extract of *Ginkgo biloba* (EGb761) of 240 mg/day improved:[Tan MS et al., 2015, level I]

- cognitive function (WMD= -3.19, 95% CI -3.56 to -2.83)
- ADL (SMD= -0.45, 95% CI -0.55 to -0.36)
- global assessment of change (OR=2.47, 95% CI 1.91 to 3.20)
- behavioural symptoms (WMD= -4.82, 95% CI -5.44 to -4.20)

However, there was significant heterogeneity among the primary papers. On safety, there were no significant differences between EGb761 and placebo in the proportion of participants experiencing any adverse events or serious adverse events for whole group and subgroup analysis.

Another meta-analysis did not indicate a higher bleeding risk associated with standardised ginkgo biloba extract compared with placebo. However, the study population was not entirely on dementia and the primary papers were mostly of moderate/high risk of bias.[Kellermann AJ et al., 2015, level I]

A Cochrane systematic review found low-certainty evidence that melatonin doses up to 10 mg may have little or no effect on any major sleep outcome over eight to 10 weeks in people with AD and sleep disturbances.[McCleery J et al., 2020, level I] Another meta-analysis of seven RCTs (mainly moderate quality primary papers) showed melatonin prolonged total sleep time at night (SMD=0.26, 95% CI 0.01 to 0.51) compared with placebo in AD patients. However, there was no significant difference in sleep efficacy between melatonin and placebo (SMD= 0.14, 95% CI -0.17 to 0.44).[Wang YY et al., 2017, level I]

A Cochrane review could not conclude on the effectiveness and safety of traditional chinese herbal medicine for VaD due to poor reporting and trial methodology of the primary papers.[Chan ESY et al., 2018, level I]

There is insufficient evidence to support curcumin supplementation as an effective means of both preventing and treating dementia and symptoms of cognitive decline.[Seddon N et al., 2019, level I]

- There is insufficient evidence to recommend the use of TCM in the treatment of dementia.

6.   MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment (MCI) is a condition in which individuals present with cognitive impairment but minimal impairment of instrumental activities of daily living (IADL). Those with MCI/CIND have greater risk of developing all types of dementia (RR=3.3, 95% CI 2.5 to 4.5) compared with age-matched participants with no MCI after 2 - 5 years of follow-up.[Petersen RC et al., 2018]

a. Diagnostic Criteria

DSM-5 recognises the predementia stage of cognitive impairment. The condition, which has many features of MCI, is termed mild neurocognitive disorder. Mild neurocognitive disorder recognises subtle features of cognitive impairment that are distinct from ageing but do not represent dementia.[DSM-5]

b. Assessment Tools

It is important to have a baseline cognitive measurement on MMSE or any cognitive assessment tools for patients with MCI. Majority of the tools available have cultural, religion and education bias. Thus, the interpretation of the result is individually tailored to each patient. When initial assessment is normal, clinicians can proceed to neuropsychological test to confirm the diagnosis of MCI. If both assessments are normal, the subject is recognised as having subjective memory complaint.

c. Investigation

In MCI, the investigations required are similar as in dementia in order to rule out other conditions. Refer to **Chapter 3** on **Diagnosis and Assessment**.

d. Non-pharmacological Interventions

MCI is a subjective complaint of deteriorating memory. After managing the modifiable risk factors and deprescribing cognitive suppression medication, it is advisable for patients to undergo non-pharmacological therapy.

- **Cognitive enhancing therapy**

Multimodal Enhancing Cognitive Therapy involved multiple non-pharmacological intervention that support the ability to maintain cognitive function. It is an intervention to improve cognitive function in cognitively normal person. These interventions improve and maintain cognitive function, thus reduce the progression of cognitive deterioration.[Han JW et al., 2017, level I]

Although cognitive enhancing therapy have been accepted in the management of MCI, a systematic review failed to show significant objective improvement with it.[Huckans M et al., 2013, level I]

- **Exercise**

Aerobic exercise is known to have cognition-enhancing effects. A small RCT on adults with amnestic MCI showed that high-intensity aerobic exercise improved performance of multiple test of executive function in women, while favourable effects were seen only on Trails B performance in men.[Baker LD et al., 2010, level I]

- **Diet and supplement**

In a systematic review of heterogenous evidence, there was some improvements in performance, particularly in memory, with the most consistent results shown by B vitamins in MCI. However, there was no significant effect on progression from MCI to dementia and/or AD with supplementation of vitamin E, ginkgo biloba or Fortasyn Connect.[McGrattan AM et al., 2018, level I]

e. Pharmacological Interventions

There is no recent evidence supporting the use of pharmacological treatment in managing MCI.[Petersen RC et al., 2018]

- Follow-up of patients with MCI is done with serial assessment to monitor their cognitive status.
- There is insufficient evidence to recommend the use pharmacological intervention in MCI.

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7.   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).

7.1   Acquired Brain Injury
In a Cochrane systematic review on chronic cognitive impairment (≥12 months post-injury) in traumatic brain injury (TBI), rivastigmine significantly improved only one primary measure i.e. verbal memory functioning compared with placebo. There was no significant difference in safety profile.[Dougall D et al., 2015, level]

Two Cochrane systematic reviews on non-pharmacological interventions in acquired brain injury showed:
- 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.[Kumar KS et al., 2017, level I]
- 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.[Magee WL et al., 2017, level I]

7.2   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 more scarce data in late-onset dementia.[Cheng C et al., 2017, level II-2]

Heavy alcohol use could cause ARD from:[Rehm J et al., 2019, level II-2]
- 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

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)[Day E et al., 2013, level I]
- with the use of extra processing time, explicit encouragement to generate associations and extra retrieval time, persons with Korsakoff's syndrome performed similarly to healthy population on associative verbal learning procedure[Svanberg J et al., 2013, level II-1]

However, the primary papers used in the two reviews had some methodological limitations.

7.3   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 HANDs[Wang Y et al., 2020, level II-2] and it consists of three categories:[Antinori A et al., 2007, level III]
- 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

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.[Wang Y et al., 2020, level II-2]

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.[Zipursky AR et al., 2013, level III] Apart from that, the primary papers were of moderate quality and the heterogeneity was significant.

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).[Smurzynski M et al., 2011, level I]

> - In the above 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.

8. CAREGIVER SUPPORT

Caring for PWD can be emotionally and physically challenging. The role of caregiver is a central and integral part of dementia management. Caregivers should be involved in the management of PWD from the beginning.[MoH, 2009] NICE recognises the important role of caregivers and discusses their involvement in the management of PWD in detail.[NICE, 2018]

> - The ZBI has good reliability and validity to assess burden of caregivers for PWD.[Whalen KJ & Buchholz SW, 2009, level III]

A few interventions to reduce the burden/strain of caregivers have been studied and are discussed below.

a. Respite care
Respite care is any intervention designed to give rest or relief to caregivers. A Cochrane review showed no significant difference in caregiver burden between respite care and control. However, polarity therapy reduced caregivers perceived stress compared with respite care (MD=5.80, 95% CI 1.43 to 10.17).[Maayan N et al., 2014, level I]

An Australian guidelines on dementia recommends that PWD, their carers and family should be offered respite appropriate to their needs which include in-home respite, day respite, planned activity groups and residential respite.[Australian Guidelines, 2016]

b. Carer training
A meta-analysis showed that multicomponent interventions for caregivers significantly delayed institutionalisation after 6 - 12 months post-intervention compared with minimal support or usual care in mild to moderately severe AD. The intervention among others comprised of education and support for caregivers.[Olazaran J et al., 2010, level I]

NICE also recommends ~~to offer~~ psychoeducation and skills training to carers of PWD. These include:[NICE, 2018]
- education about dementia on its symptomatology and natural progression
- development of personalised strategies and carer skills
- training on care of PWD, including understanding and responding to changes in behaviour
- training in communication skills
- advice on carers' own physical, mental health and spiritual wellbeing
- information on relevant services and their access
- advice on planning for the future

c. Spirituality and religious support
Spiritual and religious support may be useful for caregivers to improve their coping strategy and reduce emotional distress. However, some caregivers might experience negative effect with this intervention.[Giannouli V et al., 2020, level II-2] Therefore, it should be individualised according to the caregivers preference and acceptance.

Recommendation 12
- Caregivers should be actively involved and supported in the management of dementia.
  - This includes assessment of the burden of caregivers.

There are various community health and support services that are available in the country to assist PWD and their caregivers. Social and Welfare Department are involved in some of these services. Relevant information can be obtained from the Ministry of Women, Family and Community Development of Malaysia and related non-governmental organisations (NGOs).

Stigmatisation, lack of awareness and perceived lack of credibility of healthcare workers are among factors that discourage caregivers from reaching out to available services and supports.[Nikmat AW et al., 2011, level III]

Hence, collaborative efforts should be made by the government and respective stakeholders, including the MoH, Social and Welfare Department and NGOs to provide better support and service for the PWDs in Malaysia.

Refer to **Appendix 11** on **Important Points for Caregiver of People with Dementia** and **Appendix 12** on **Useful Resources**.

9. LEGAL AND ETHICAL ISSUES

The key to a person's right of autonomy is adequate decision-making capacity. In Malaysia, when a person is deemed to be mentally disordered and is incapable of managing oneself and

one's affairs, the provisions of the Mental Health Act 2001 (Part X: Section 51-Section 75) can be applied. The Act aims to protect the person from his or her own harmful decisions or actions.

a. Decision-making capacity

The key to a person's right of autonomy is possessing adequate decision-making capacity. If a PWD's decision-making capacity is intact, doctors need to respect the autonomy of the PWD to decide on treatment options. If a PWD lacks decision-making capacity, then a surrogate decision-maker will need to make decisions for the PWD based on his/her best interest. The following points need to be taken into account:

- Decision-making capacity is determined with regard to specific tasks and decisions that need to be made. PWD's can be judged to have capacity to make certain decisions, and not having capacity for other decisions at the same time.[Lo B, 2015, level III]
- If there is any doubt regarding a PWD's decision-making capacity, a formal assessment of decision-making capacity should be carried out. The assessment should be properly documented in the patient's notes.
- Where appropriate, efforts should be taken to restore the patient's decision-making capacity or encourage the PWD's involvement in the decision-making process.
- If the Mental Health Act 2001 is used, Section 77 is applicable when obtaining consent.

b. Advance directives

Although there is no law in Malaysia to govern advance directives in respect of healthcare matters, the common law right to refuse treatment is applicable.[Chan HY, 2019, level III] Making advance decisions can be immensely valuable as it can help healthcare providers in Malaysia to understand better the preferences and wishes of their patients.[Tan MKM, 2018, level III] PWD may decide to make advance decisions regarding treatment while they still possess the mental capacity to do so by way of an advance directive or an advance care plan (Section 10d). Advance directives serve to guarantee the right of mentally competent individuals to continue exercising their autonomy in the event of future incapacity. These include the following:

- A doctor should comply with a patient's unequivocal written directive to refuse a particular treatment.[MMC, 2017]
- Doctors are advised to consult the next of kin or seek legal advice if there is doubt on the validity of an advance directive, and these discussions need to be documented.[MMC, 2017]

c. Fitness to drive

Driving ability involves multiple cognitive domains and requires visuospatial, executive function, memory, attention and motor skills. Other factors important in determining driving safety are vision, mobility, head-turning and day-time somnolence. In mild dementia, some patients may retain the skills needed for driving. Patients with moderate-severe dementia are unlikely to be fit to drive. Driving risk may be greater in certain subtypes of dementia e.g. FTD (due to lack of cortical insight) and DLB (due to fluctuating consciousness and visual hallucinations).[Allan CL et al., 2016, level III]

For patients who decide to stop driving or who are forced to stop, clinicians must discuss practical alternatives, the impact on psychosocial benefits and the loss of autonomy with patients and their caregivers.[Allan CL et al., 2016, level III]

- Assessment of fitness to drive involves composite cognitive test batteries in combination with other types of assessments e.g. driving simulator test[Allan CL et al., 2016, level III] or on-road test.[Martin AJ et al., 2013, level III]
- Locally, an assessment of fitness to drive can be done by referring the patient to an occupational therapist with the prescribed form (Borang Pemeriksaan Kesihatan

Permohonan Lesen Memandu Orang Kurang Upaya) as provided in the Medical Examination Standards for Disabled Driver's Licensing.[MoH, 2011]

It is the responsibility of a PWD to report his/her disability to the authorities for licensing purposes.[Laws of Malaysia Act 333] However, medical practitioners may voluntarily report new cases of disability to the Road Transport Department.[MoH, 2011] It is good medical practice to seek the PWD's consent for such reporting. However, if the PWD does not consent to the disclosure, medical practitioners may still permissibly breach the confidentiality of the PWD utilising reasons for disclosure in the patient's medical interests and/or disclosure in the public interest if they judge that doing so will provide important benefits to the patient or prevent serious harm to third parties.[MMC, 2011] Such disclosures should be limited only to essential information for the intended purpose and only to those persons who need to be notified.[Lo B, 2015, level III]

> **Recommendation 13**
> - If there is any doubt regarding people with dementia (PWD)'s decision-making capacity, a formal assessment of decision-making capacity should be carried out.
> - A doctor should comply with a patient's unequivocal written directive to refuse a particular treatment if that decision was made while the patient had mental capacity.
> - PWD (particularly moderate to severe) should be assessed for their driving ability if they still wish to drive.

10. PALLIATIVE AND END-OF-LIFE CARE

There has been no major breakthrough in curative treatment for dementia over the past few decades. As dementia is a progressive and irreversible illness which can affect the QoL for PWD and their caregivers, palliative care should be initiated at the time of diagnosis throughout different stages of illness. As the disease progressed and the PWD become more dependent, the palliative care components should be more emphasised in their management to achieve the best quality of life.

Continuous communication with the PWD and caregivers is important to assist them to establish the advance care planning especially during early stage of disease where the PWD are still capable to make their own decision. Education, spiritual and psychological support should be offered to improve QoL and reduce burden of the caregivers.

Evidence for best practice during end-of-life care for PWD is limited and heterogenous. Nevertheless, best supportive care should be offered to them based on their preference and the principles of basic medical ethics.

a. Artificial nutrition and hydration

Dysphagia is a common problem in advance dementia. In a systematic review, dysphagia diagnostic assessment e.g. clinical swallowing examination, video fluoroscopy swallowing study and flexible endoscopic examination of swallowing can be used to determine the type of deficits in oropharyngeal dysphagia. However, there was limited evidence on the benefits of postural change, diet and liquid modification, and medication in management of this condition.[Alagiakrishnan K et al., 2012, level I]

In another systematic review, there was moderate quality of evidence on the use of high-calorie supplements to improve weight gain in person with advance dementia and not on function and survival.[Hanson LC et al., 2011, level I] There was limited evidence to show that enteral tube feeding may prolong the survival rate and reduce aspiration pneumonia in advanced dementia based on a systematic review. On the other hand, percutaneous enterogastrostomy tube was

associated with increased risk of pressure ulcer development or aggravation.[Salomon ALR et al., 2015, level I]

NICE does not recommend routine use of enteral feeding in people with severe dementia, unless indicated for a potentially reversible co-morbidity.[NICE, 2018]

> - There was insufficient evidence to recommend enteral feeding in patients with severe dementia. Thus, the choice of oral or enteral feeding in severe dementia depends on the clinician after discussion with caregivers and taking into consideration PWD's wish or advance directives.

b.   Pain management

Pain is another prevalent and distressing issue for person with advance dementia. However, the affected person is not able to express themselves accurately on the pain they experience and very often it is manifested as behavioural problems.

An RCT examining on the impact of a stepwise protocol for treating pain on PWD in nursing home showed that pain medication significantly improved pain control in the intervention group.[Sandvik RK et al., 2014, level I] However a systematic review showed that evidence on pain management for advance dementia was limited and heterogenous. Despite increased use of analgesia, pain was still prevalent in PWD.[Husebo BS et al., 2016, level I]

c.   Restraints

Restraints are used to protect people with severe dementia from harming themselves because of their behaviour. These can be physical, chemical or psychological restraints.

A multinational cohort study on PWD in nursing homes showed that physical restraint was associated with a higher risk of both functional (RR=2.30, 95% CI 1.52 to 3.49) and cognitive decline (RR=1.93, 95% CI 1.44 to 2.58) compared with AP alone. These risks were even higher among residents receiving both AP and physical restraints with RR of 2.49 (95% CI 1.89 to 3.27) and 2.31 (95% CI 1.54 to 3.48) respectively.[Foebel AD et al., 2016, level II-2]

A Belgian evidence-based guidelines on older adults in home care recommend that physical restraints should be avoided as much as possible due to the negative physical and psychosocial consequences to the patient.[Scheepmans K et al., 2020]

d.   Advance care planning

Every PWD has the right to plan ahead for their future when they still have the capability to make decision. Hence, advance care planning should be discussed with PWD and their family members as early as possible after the diagnosis is established. The discussion should include lasting power of attorney (for decisions unrelated to healthcare as permitted under the Power of Attorney Act 1949) and future medical care direction based on their own preference, value and goals of life. PWD and their family members are allowed to review and change any advance statements they have made as the disease progresses.[NICE, 2018]

A systematic review showed that intervention with advance care planning significantly reduced inappropriate hospital admissions and health care costs for PWD compared with control group.[Robinson L et al., 2012, level I] Therefore, attending clinicians should actively offer advance care planning to PWD and their family members when they are ready for it. Refer to **Appendix 13** on **Advance Care Planning** for more details.

> **Recommendation 14**
> - Physical restraints should be avoided in dementia.
> - Advance care planning should be considered in the management of dementia once the diagnosis is established.

11. REFERRAL

Patients suspected of dementia should be referred to specialist care centres (e.g. geriatrics/psychiatry/neurology) for confirmation of diagnosis and management of complexities. This is because of the need for comprehensive assessments and investigations. At the moment, medication for dementia is not available at primary care locally.

Once a diagnosis is made, stable PWD can be co-managed in both primary and secondary/tertiary care as an integrated care system. Management aspect than can be offered in primary care include management of medical co-morbidities and non-pharmacological treatment (e.g. cognitive stimulation and designing meaningful activities). However, these cases should be referred back to secondary/tertiary care when there is difficult behaviour problem, psychiatric co-morbidity, rapid deterioration in clinical condition, etc.

> **Recommendation 15**
> - All patients with suspected dementia should be referred to a geriatric psychiatrist/psychiatrist, geriatrician or neurologist for assessment, diagnosis and management

12. IMPLEMENTING THE GUIDELINES

The management of dementia should be guided by an evidence-based approach, in order to provide quality care to the PWD. Several factors may affect the implementation of recommendations in the CPG.

12.1 Facilitating and Limiting Factors

Existing facilitators for application of the recommendations in the CPG include:
- wide dissemination of the CPG (soft- and hardcopies) to healthcare providers
- training and updates in relation to dementia
- public awareness campaigns related to cognitive impairment including dementia
- inter-ministerial collaboration and involvement of non-governmental organisations to support the PWD and their caregivers

Existing barriers for application of the recommendations of the CPG are:
- limited exposure and training among healthcare providers on management of dementia
- variation in availability of expertise and access to service provision
- lack of awareness among patients, families, community and healthcare workers
- lack of local data on dementia, e.g. research, registry, etc., for planning on services

12.2 Potential Resource Implications

In local setting, dementia is very much underdiagnosed due to lack of awareness and misconception that it is normal part of ageing among the public and healthcare providers. Besides that, PWD always present late with behavioural issues.

In terms of pharmacotherapy, AChEI is strongly recommended in the treatment of dementia. However, it is not readily available in the primary/secondary/tertiary care due to financial constraints. Apart from that, many non-pharmacological interventions may not be easily available due to lack of manpower/expertise to conduct it.

The CPG recommends early detection and referral, comprehensive assessment and treatment of the disorder. This requires increased awareness among public, caregivers and healthcare providers to establish diagnosis and early intervention to PWD as well as support to the caregivers.

Thus, the implementation of this CPG requires resources to provide:
- training of healthcare providers and caregivers
- better access to referral centres
- better caregiver support network
- access to policy makers e.g. National Dementia Action Plan

Based on the key recommendations, the following are proposed as clinical audit indicators for quality management of dementia:

$$\text{Percentage of patients with suspected dementia referred to a relevant specialist* for assessment and diagnosis} = \frac{\text{Number of patients with suspected dementia referred to a relevant specialist* for assessment and diagnosis in a period}}{\text{Number of patients with suspected dementia in the same period}}$$

$$\text{Percentage of newly diagnosed Alzheimer's Disease** offered donepezil or rivastigmine} = \frac{\text{Number of newly diagnosed Alzheimer's Disease** offered donepezil or rivastigmine in a period}}{\text{Number of newly diagnosed Alzheimer's Disease** in the same period}}$$

*geriatric psychiatrist/psychiatrist, geriatrician or neurologist
**all severity

Implementation strategies will be developed following the approval of the CPG by MoH which include launching of the CPG, Quick Reference and Training Module.

REFERENCES

1. Abraha I, Rimland JM, Lozano-Montoya I, et al. Simulated presence therapy for dementia. The Cochrane database of systematic reviews. 2017;4(4):Cd011882.
2. Agli O, Bailly N, Ferrand C. Spirituality and religion in older adults with dementia: a systematic review. International psychogeriatrics. 2015;27(5):715-25.
3. Alagiakrishnan K, Bhanji RA, Kurian M. Evaluation and management of oropharyngeal dysphagia in different types of dementia: a systematic review. Archives of gerontology and geriatrics. 2013;56(1):1-9.
4. 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.
5. Allan CL, Behrman S, Baruch N, et al. Driving and dementia: a clinical update for mental health professionals. Evidence Based Mental Health. 2016;19(4):110.
6. 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.
7. Antinori A, Arendt G, Becker JT, et al. Updated research nosology for HIV-associated neurocognitive disorders. Neurology. 2007;69(18):1789-99.
8. Bahar-Fuchs A, Clare L, Woods B. Cognitive training and cognitive rehabilitation for mild to moderate Alzheimer's disease and vascular dementia. The Cochrane database of systematic reviews. 2013;2013(6):Cd003260.
9. Baillon SF, Narayana U, Luxenberg JS, et al. Valproate preparations for agitation in dementia. The Cochrane database of systematic reviews. 2018;10(10):Cd003945.
10. Baker LD, Frank LL, Foster-Schubert K, et al. Effects of aerobic exercise on mild cognitive impairment: a controlled trial. Arch Neurol. 2010 Jan;67(1):71-9.
11. Birks J, McGuinness B, Craig D. Rivastigmine for vascular cognitive impairment. The Cochrane database of systematic reviews. 2013(5):Cd004744.
12. Birks JS, Grimley Evans J. Rivastigmine for Alzheimer's disease. The Cochrane database of systematic reviews. 2015(4):Cd001191.
13. Birks JS, Harvey RJ. Donepezil for dementia due to Alzheimer's disease. The Cochrane database of systematic reviews. 2018;6(6):Cd001190.
14. Blanco-Silvente L, Capellà D, Garre-Olmo J, et al. Predictors of discontinuation, efficacy, and safety of memantine treatment for Alzheimer's disease: meta-analysis and meta-regression of 18 randomized clinical trials involving 5004 patients. BMC Geriatr. 2018;18(1):168.
15. Bond M, Rogers G, Peters J, et al. The effectiveness and cost-effectiveness of donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of Technology Appraisal No. 111): a systematic review and economic model. Health technology assessment (Winchester, England). 2012;16(21):1-470.
16. Boyle PA, Yu L, Wilson RS, et al. Person-specific contribution of neuropathologies to cognitive loss in old age. Ann Neurol. 2018 Jan;83(1):74-83.
17. Buoli M, Serati M, Caldiroli A, et al. Pharmacological Management of Psychiatric Symptoms in Frontotemporal Dementia: A Systematic Review. Journal of geriatric psychiatry and neurology. 2017;30(3):162-9.
18. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674-694
19. Canevelli M, Adali N, Voisin T, et al. Behavioral and psychological subsyndromes in Alzheimer's disease using the Neuropsychiatric Inventory. International journal of geriatric psychiatry. 2013;28(8):795-803.
20. Chan ES, Bautista DT, Zhu Y, et al. Traditional Chinese herbal medicine for vascular dementia. The Cochrane database of systematic reviews. 2018;12(12):Cd010284.
21. Chan HY. Regulating advance decision-making: potential and challenges for Malaysia. Asian Bioethics Review. 2019;11:111-22.
22. Chandra A, Dervenoulas G, Politis M. Magnetic resonance imaging in Alzheimer's disease and mild cognitive impairment. Journal of neurology. 2019;266(6):1293-302.

23. Cheng C, Huang CL, Tsai CJ, et al. Alcohol-Related Dementia: A Systemic Review of Epidemiological Studies. Psychosomatics. 2017;58(4):331-42.
24. 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.
25. Cohen-Mansfield J, Golander H. The measurement of psychosis in dementia: a comparison of assessment tools. Alzheimer disease and associated disorders. 2011;25(2):101-8.
26. Cummings-Vaughn LA, Chavakula NN, Malmstrom TK, et al. Veterans Affairs Saint Louis University Mental Status examination compared with the Montreal Cognitive Assessment and the Short Test of Mental Status. J Am Geriatr Soc. 2014 Jul;62(7):1341-6.
27. Davis DH, Creavin ST, Yip JL et al. Montreal Cognitive Assessment for the diagnosis of Alzheimer's disease and other dementias. Cochrane Database Syst Rev. 2015 Oct 29;(10):CD010775
28. 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.
29. Dou KX, Tan MS, Tan CC, et al. Comparative safety and effectiveness of cholinesterase inhibitors and memantine for Alzheimer's disease: a network meta-analysis of 41 randomized controlled trials. Alzheimers Res Ther. 2018;10(1):126.
30. Dougall D, Poole N, Agrawal N. Pharmacotherapy for chronic cognitive impairment in traumatic brain injury. The Cochrane database of systematic reviews. 2015(12):Cd009221.
31. Dyer SM, Harrison SL, Laver K, et al. An overview of systematic reviews of pharmacological and non-pharmacological interventions for the treatment of behavioral and psychological symptoms of dementia. International psychogeriatrics. 2018;30(3):295-309.
32. Farina N, Llewellyn D, Isaac MGEKN, et al. Vitamin E for Alzheimer's dementia and mild cognitive impairment. Cochrane Database Syst Rev. 2017 Apr 18;4(4):CD002854.
33. Farlow MR, Grossberg GT, Sadowsky CH, et al. A 24-week, randomized, controlled trial of rivastigmine patch 13.3 mg/24 h versus 4.6 mg/24 h in severe Alzheimer's dementia. CNS neuroscience & therapeutics. 2013;19(10):745-52.
34. Foebel AD, Onder G, Finne-Soveri H, et al. Physical Restraint and Antipsychotic Medication Use Among Nursing Home Residents With Dementia. Journal of the American Medical Directors Association. 2016;17(2):184.e9-14.
35. Forbes D, Blake CM, Thiessen EJ, et al. Light therapy for improving cognition, activities of daily living, sleep, challenging behaviour, and psychiatric disturbances in dementia. The Cochrane database of systematic reviews. 2014(2):Cd003946.
36. Forrester LT, Maayan N, Orrell M, et al. Aromatherapy for dementia. The Cochrane database of systematic reviews. 2014(2):Cd003150.
37. Giannouli V, Giannoulis K. Gazing at Medusa: Alzheimer's dementia through the lenses of spirituality and religion. Health Psychol Res. 2020 May 27;8(1):8833.
38. Groot C, Hooghiemstra AM, Raijmakers PG, et al. The effect of physical activity on cognitive function in patients with dementia: A meta-analysis of randomized control trials. Ageing research reviews. 2016;25:13-23.
39. Grossberg GT, Kohegyi E, Mergel V, et al. Efficacy and Safety of Brexpiprazole for the Treatment of Agitation in Alzheimer's Dementia: Two 12-Week, Randomized, Double-Blind, Placebo-Controlled Trials. Am J Geriatr Psychiatry. 2020 Apr;28(4):383-400.
40. Grossberg G, Cummings J, Frölich L, et al. Efficacy of higher dose 13.3 mg/24 h rivastigmine patch on instrumental activities of daily living in patients with mild-to-moderate Alzheimer's disease. Am J Alzheimers Dis Other Demen. 2013;28(6):583-91.
41. 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.
42. Guideline Adaptation Committee. Clinical Practice Guidelines and Principles of Care for People with Dementia. Sydney: Guideline Adaptation Committee; 2016.
43. Han JW, Lee H, Hong JW, et al. Multimodal Cognitive Enhancement Therapy for Patients with Mild Cognitive Impairment and Mild Dementia: A Multi- Center, Randomized, Controlled, Double-Blind, Crossover Trial. J Alzheimers Dis. 2017;55(2):787-796.
44. 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.

45. Hanson LC, Ersek M, Gilliam R, et al. Oral feeding options for people with dementia: a systematic review. Journal of the American Geriatrics Society. 2011;59(3):463-72.

46. Harper L, Barkhof F, Fox NC, et al. Using visual rating to diagnose dementia: a critical evaluation of MRI atrophy scales. J Neurol Neurosurg Psychiatry. 2015;86(11):1225-33.

47. Harrison JK, Stott DJ, McShane R, Noel-Storr AH et al. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the early diagnosis of dementia across a variety of healthcare settings. Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD011333

48. Hendry K, Green C, McShane R, Noel-Storr AH et al. AD-8 for detection of dementia across a variety of healthcare settings. Cochrane Database of Systematic Reviews 2019, Issue 3. Art. No.: CD011121.

49. Huckans M, Hutson L, Twamley E, et al. Efficacy of cognitive rehabilitation therapies for mild cognitive impairment (MCI) in older adults: working toward a theoretical model and evidence-based interventions. Neuropsychol Rev. 2013 Mar;23(1):63-80.

50. Husain M, Schott JM. Oxford Textbook of Cognitive Neurology and Dementia: Oxford University Press; 2016.

51. Husebo BS, Achterberg W, Flo E. Identifying and Managing Pain in People with Alzheimer's Disease and Other Types of Dementia: A Systematic Review. CNS drugs. 2016;30(6):481-97.

52. Jackson TA, Naqvi SH, Sheehan B. Screening for dementia in general hospital inpatients: a systematic review and meta-analysis of available instruments. Age Ageing. 2013 Nov;42(6):689-95.

53. Jellinger KA. Dementia with Lewy bodies and Parkinson's disease-dementia: current concepts and controversies. J Neural Transm (Vienna). 2018 Apr;125(4):615-650.

54. Jeon YH, Sansoni J, Low LF, et al. Recommended measures for the assessment of behavioral disturbances associated with dementia. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry. 2011;19(5):403-15.

55. Jin BR, Liu HY. Comparative efficacy and safety of cognitive enhancers for treating vascular cognitive impairment: systematic review and Bayesian network meta-analysis. Neural regeneration research. 2019;14(5):805-16.

56. Jordan F, Quinn TJ, McGuinness B, et al. Aspirin and other non-steroidal anti-inflammatory drugs for the prevention of dementia. Cochrane Database Syst Rev. 2020 Apr 30;4(4):CD011459.

57. Karantzoulis S, Galvin JE. Distinguishing Alzheimer's disease from other major forms of dementia. Expert Rev Neurother. 2011 Nov;11(11):1579-91.

58. Kellermann AJ, Kloft C. Is there a risk of bleeding associated with standardized Ginkgo biloba extract therapy? A systematic review and meta-analysis. Pharmacotherapy. 2011;31(5):490-502.

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

60. Kishi T, Matsunaga S, Iwata N. Memantine for the treatment of frontotemporal dementia: a meta-analysis. Neuropsychiatric disease and treatment. 2015;11:2883-5.

61. 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.

62. Kongpakwattana K, Sawangjit R, Tawankanjanachot I, et al. Pharmacological treatments for alleviating agitation in dementia: a systematic review and network meta-analysis. British journal of clinical pharmacology. 2018;84(7):1445-56.

63. 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.

64. 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.

65. Law ZK, Todd C, Mehraram R, et al. The Role of EEG in the Diagnosis, Prognosis and Clinical Correlations of Dementia with Lewy Bodies-A Systematic Review. Diagnostics (Basel, Switzerland). 2020;10(9).

66. Laws of Malaysia Act 333 Road Transport Act 1987. (Available at: http://www.agc.gov.my/agcportal/uploads/files/Publications/LOM/EN/Act%20333%20-%20Road%20Transport%20Act%201987.pdf)

67. Leontjevas R, Gerritsen DL, Vernooij-Dassen MJ, et al. Comparative validation of proxy-based Montgomery-Åsberg depression rating scale and cornell scale for depression in dementia in nursing home residents with dementia. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry. 2012;20(11):985-93.

68. Lim L, Ng TP, Ong AP, et al. A novel language-neutral Visual Cognitive Assessment Test (VCAT): validation in four Southeast Asian countries. Alzheimers Res Ther. 2018 Jan 22;10(1):6.

69. 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.

70. Lo B. Resolving Ethical Dilemmas: A Guide for Clinicians (5th Edition): Lippincott Williams & Wilkins; 2015.

71. Maayan N, Soares-Weiser K, Lee H. Respite care for people with dementia and their carers. The Cochrane database of systematic reviews. 2014(1):Cd004396.

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

73. Malaysian Medical Council (MMC). MMC Guideline: Consent for Treatment of Patients by Registered Medical Practitioners. Kuala Lumpur: MMC 2017.

74. Martin AJ, Marottoli R, O'Neill D. Driving assessment for maintaining mobility and safety in drivers with dementia. The Cochrane database of systematic reviews. 2013;2013(8):Cd006222.

75. Matías-Guiu JA, Valles-Salgado M, Rognoni T, et al. Comparative Diagnostic Accuracy of the ACE-III, MIS, MMSE, MoCA, and RUDAS for Screening of Alzheimer Disease. Dement Geriatr Cogn Disord. 2017;43(5-6):237-246.

76. McCleery J, Morgan S, Bradley KM, et al. Dopamine transporter imaging for the diagnosis of dementia with Lewy bodies. The Cochrane database of systematic reviews. 2015;1(1):Cd010633.

77. McCleery J, Abraham RP, Denton DA, et al. Vitamin and mineral supplementation for preventing dementia or delaying cognitive decline in people with mild cognitive impairment. Cochrane Database Syst Rev. 2018 Nov 1;11(11):CD011905.

78. McGrattan AM, McEvoy CT, McGuinness B, et al. Effect of dietary interventions in mild cognitive impairment: a systematic review. Br J Nutr. 2018 Dec;120(12):1388-1405.

79. McGuinness B, Craig D, Bullock R, et al. Statins for the prevention of dementia. Cochrane Database Syst Rev. 2016 Jan 4;(1):CD003160.

80. McShane R, Westby MJ, Roberts E, et al. Memantine for dementia. The Cochrane database of systematic reviews. 2019;3(3):Cd003154.

81. Meng YH, Wang PP, Song YX, et al. Cholinesterase inhibitors and memantine for Parkinson's disease dementia and Lewy body dementia: A meta-analysis. Experimental and therapeutic medicine. 2019;17(3):1611-24.

82. Ministry of Health Malaysia. Management of Dementia (Second Edition). Kuala Lumpur: MoH Malaysia; 2009.

83. Ministry of Health Malaysia. Medical Examination Standards For Disabled Driver's Licensing. Putrajaya: MoH Malaysia; 2011.

84. Ministry of Health, Singapore. Dementia MOH Clinical Practice Guidelines 1/2013. Singapore. 2018

85. Möhler R, Renom A, Renom H, et al. Personally tailored activities for improving psychosocial outcomes for people with dementia in long-term care. The Cochrane database of systematic reviews. 2018;2(2):Cd009812.

86. Nardell M, Tampi RR. Pharmacological treatments for frontotemporal dementias: a systematic review of randomized controlled trials. American journal of Alzheimer's disease and other dementias. 2014;29(2):123-32.

87. National Institute for Health and Care Excellence (NICE). Dementia: assessment, management and support for people living with dementia and their carers. London: NICE; 2018.

88. Neal M, Barton Wright P. Validation therapy for dementia. The Cochrane database of systematic reviews. 2003(3):Cd001394.

89. Nikmat AW, Hawthorne G, Al-Mashoor SHA. Dementia in malaysia: Issues and challenges. Asian Journal of Psychiatry. 2011. 12. 1-7.

90. Olazarán J, Reisberg B, Clare L, et al. Nonpharmacological therapies in Alzheimer's disease: a systematic review of efficacy. Dementia and geriatric cognitive disorders. 2010;30(2):161-78.

91. Orgeta V, Qazi A, Spector A, et al. Psychological treatments for depression and anxiety in dementia and mild cognitive impairment: systematic review and meta-analysis. The British journal of psychiatry : the journal of mental science. 2015;207(4):293-8.

92. 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.

93. Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018 Jan 16;90(3):126-135.

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

95. Ribeiro Salomon AL, Carvalho Garbi Novaes MR. Outcomes of enteral nutrition for patients with advanced dementia: a systematic review. The journal of nutrition, health & aging. 2015;19(2):169-77.

96. Ritchie C, Smailagic N, Noel-Storr AH et al. CSF tau and the CSF tau/ABeta ratio for the diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). Cochrane Database Syst Rev. 2017 Mar 22;3(3):CD010803.

97. Robinson L, Dickinson C, Rousseau N, et al. A systematic review of the effectiveness of advance care planning interventions for people with cognitive impairment and dementia. Age Ageing. 2012 Mar;41(2):263-9.

98. Rolinski M, Fox C, Maidment I, et al. Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. The Cochrane database of systematic reviews. 2012(3):Cd006504.

99. Román GC, Salloway S, Black SE, et al. Randomized, placebo-controlled, clinical trial of donepezil in vascular dementia: differential effects by hippocampal size. Stroke. 2010;41(6):1213-21.

100. Rosli R, Tan MP, Gray WK, et al. Cognitive assessment tools in Asia: a systematic review. International psychogeriatrics. 2016;28(2):189-210.

101. Rubino A, Sanon M, Ganz ML, et al. Association of the US Food and Drug Administration Antipsychotic Drug Boxed Warning With Medication Use and Health Outcomes in Elderly Patients With Dementia. JAMA Netw Open. 2020 Apr 1;3(4):e203630.

102. Rutjes AW, Denton DA, Di Nisio M, et al. Vitamin and mineral supplementation for maintaining cognitive function in cognitively healthy people in mid and late life. The Cochrane database of systematic reviews. 2018;12(12):Cd011906.

103. Ryan NS, Rossor MN. Correlating familial Alzheimer's disease gene mutations with clinical phenotype. Biomark Med. 2010 Feb;4(1):99-112.

104. Sáiz-Vazquez O, Puente-Martínez A, Ubillos-Landa S, et al. Cholesterol and Alzheimer's Disease Risk: A Meta-Meta-Analysis. Brain Sci. 2020;10(6):386.

105. Sandvik RK, Selbaek G, Seifert R, et al. Impact of a stepwise protocol for treating pain on pain intensity in nursing home patients with dementia: a cluster randomized trial. European journal of pain (London, England). 2014;18(10):1490-500.

106. Scheepmans K, Dierckx de Casterlé B, Paquay L, et al. Reducing physical restraints by older adults in home care: development of an evidence-based guideline. BMC geriatrics. 2020;20(1):169.

107. Seddon N, D'Cunha N, Mellor D, et al. Effects of Curcumin on Cognitive Function—A Systematic Review of Randomized Controlled Trials. 2019;4:1-11.

108. Schroeck JL, Ford J, Conway EL, et al. Review of Safety and Efficacy of Sleep Medicines in Older Adults. Clin Ther. 2016 Nov;38(11):2340-2372.

109. Sikkes SA, de Lange-de Klerk ES, Pijnenburg YA, et al. A systematic review of Instrumental Activities of Daily Living scales in dementia: room for improvement. Journal of neurology, neurosurgery, and psychiatry. 2009;80(1):7-12.

110. Smailagic N, Vacante M, Hyde C, et al. ^{18}F-FDG PET for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). The Cochrane database of systematic reviews. 2015;1(1):Cd010632.

111. 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.

112. Sooryanarayana R, Sazlina SG. The Malaysian National Health and Morbidity Survey (NHMS) 2018: Older Persons' Health in Malaysia. Geriatrics & gerontology international. 2020;20 Suppl 2:5-6.

113. 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.

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

115. Tan Kiak Min M. Considerations for Introducing Legislation on Advance Decisions in Malaysia. Asian Bioeth Rev. 2018;10(1):87-92.

116. Tan MS, Yu JT, Tan CC, et al. Efficacy and adverse effects of ginkgo biloba for cognitive impairment and dementia: a systematic review and meta-analysis. Journal of Alzheimer's disease : JAD. 2015;43(2):589-603.

117. Terum TM, Andersen JR, Rongve A, et al. The relationship of specific items on the Neuropsychiatric Inventory to caregiver burden in dementia: a systematic review. International journal of geriatric psychiatry. 2017;32(7):703-17.

118. Tsoi KK, Chan JY, Hirai HW, et al. Cognitive Tests to Detect Dementia: A Systematic Review and Meta-analysis. JAMA Intern Med. 2015 Sep;175(9):1450-8.

119. US Preventive Services Task Force, Owens DK, Davidson KW, et al. Screening for Cognitive Impairment in Older Adults: US Preventive Services Task Force Recommendation Statement. JAMA. 2020 Feb 25;323(8):757-763.

120. 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.

121. van der Steen JT, Smaling HJ, van der Wouden JC, et al. Music-based therapeutic interventions for people with dementia. The Cochrane database of systematic reviews. 2018;7(7):Cd003477.

122. Vilela VC, Pacheco RL, Latorraca COC, et al. What do Cochrane systematic reviews say about non-pharmacological interventions for treating cognitive decline and dementia? Sao Paulo medical journal = Revista paulista de medicina. 2017;135(3):309-20.

123. Wang YY, Zheng W, Ng CH, et al. Meta-analysis of randomized, double-blind, placebo-controlled trials of melatonin in Alzheimer's disease. International journal of geriatric psychiatry. 2017;32(1):50-7.

124. Wang Y, Liu M, Lu Q, et al. Global prevalence and burden of HIV-associated neurocognitive disorder: A meta-analysis. Neurology. 2020 Nov 10;95(19):e2610-e2621.

125. Warren JD, Rohrer JD, Rossor MN. Clinical review. Frontotemporal dementia. BMJ. 2013 Aug 6;347:f4827.

126. Whalen KJ, Buchholz SW. The reliability, validity and feasibility of tools used to screen for caregiver burden: a systematic review. JBI library of systematic reviews. 2009;7(32):1373-430.

127. Woods B, Aguirre E, Spector AE, et al. Cognitive stimulation to improve cognitive functioning in people with dementia. The Cochrane database of systematic reviews. 2012(2):Cd005562.

128. Woods B, O'Philbin L, Farrell EM, et al. Reminiscence therapy for dementia. The Cochrane database of systematic reviews. 2018;3(3):Cd001120.

129. World Health Organization. Risk Reduction of Cognitive Decline and Dementia: Geneva: World Health Organization; 2019.

130. World Health Organization. Dementia Fact Sheet. 2020.

131. World Health Organization. Tobacco Fact Sheet 2020

132. Wu J, Wang Y, Wang Z. The effectiveness of massage and touch on behavioural and psychological symptoms of dementia: A quantitative systematic review and meta-analysis. Journal of advanced nursing. 2017;73(10):2283-95.

133. Xiao H, Su Y, Cao X, et al. A meta-analysis of mood stabilizers for Alzheimer's disease. Journal of Huazhong University of Science and Technology Medical sciences = Hua zhong ke ji da xue xue bao Yi xue Ying De wen ban = Huazhong keji daxue xuebao Yixue Yingdewen ban. 2010;30(5):652-8.

134. Yunusa I, Alsumali A, Garba AE, et al. Assessment of Reported Comparative Effectiveness and Safety of Atypical Antipsychotics in the Treatment of Behavioral and Psychological Symptoms of Dementia: A Network Meta-analysis. JAMA network open. 2019;2(3):e190828.

135. Zhang S, Smailagic N, Hyde C, et al. (11)C-PIB-PET for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). The Cochrane database of systematic reviews. 2014;2014(7):Cd010386.

136. 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.

EXAMPLE OF SEARCH STRATEGY

Clinical Question: What are the safe and effective pharmacological treatments for dementia?
- Acetylcholinesterase inhibitors (rivastigmine, donepezil, galantamine) & NMDA antagonists (memantine)

1. DEMENTIA/
2. dementia*.tw.
3. (familial adj1 dementia*).tw.
4. (senile adj2 paranoid dementia*).tw.
5. DEMENTIA, VASCULAR/
6. (acute onset adj3 vascular dementia*).tw.
7. ((arteriosclerotic or vascular) adj1 dementia*).tw.
8. (subcortical adj2 arteriosclerotic encephalopathy*).tw.
9. (binswanger* adj2 (encephalopath* or disease*)).tw.
10. chronic progressive subcortical encephalopathy.tw.
11. (subcortical adj2 vascular dementia*).tw.
12. (subcortical arteriosclerotic adj2 encephalopath*).tw.
13. (chronic progressive adj3 subcortical encephalopath*).tw.
14. (subcortical adj1 leukoencephalopath*).tw.
15. FRONTOTEMPORAL DEMENTIA/
16. ((frontotemporal or frontotemporal lobe) adj2 dementia*).tw.
17. (frontotemporal dementia adj4 (parkinsonism or parkinsonism 17 or parkinsonism-17)).tw.
18. ((grn-related or grn related) adj3 frontotemporal dementia*).tw.
19. ((ubiquitin positive or ubiquitin-positive) adj3 frontotemporal dementia*).tw.
20. (frontotemporal lobar degeneration adj6 (ubiquitin positive inclusion or ubiquitin-positive inclusion)).tw.
21. (semantic adj1 dementia*).tw.
22. familial pick* disease*.tw.
23. ftd-grn.tw.
24. ftd-pgrn.tw.
25. ftdp-17.tw.
26. ftld-17 grn.tw.
27. ftld with tdp 43 pathology.tw.
28. ftld with tdp-43 pathology.tw.
29. ftld-tdp.tw.
30. DEMENTIA, MULTI-INFARCT/
31. (lacunar adj1 dementia*).tw.
32. ((multiinfarct or multi infarct or multi-infarct) adj2 dementia*).tw.
33. ALZHEIMER DISEASE/
34. alzheimer* dementia*.tw.
35. (alzheimer* disease adj2 (early onset or late onset or focal onset)).tw.
36. (familial adj2 alzheimer* disease).tw.
37. ((Alzheimer* type or Alzheimer-type) adj3 (dementia* or senile dementia*)).tw.
38. ((senile or presenile) adj1 dementia*).tw.
39. (primary senile degenerative adj3 dementia*).tw.
40. presenile alzheimer dementia.tw.
41. Mixed dementia*.tw.
42. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41
43. CHOLINESTERASE INHIBITORS/

44. (anticholinesterase* or anti cholinesterase* or anti-cholinesterase*).tw.
45. ((acetylcholinesterase or cholinesterase) adj1 inhibitor*).tw.
46. (irreversible adj2 cholinesterase inhibitor*).tw.
47. ((reversible or irreversible) adj2 cholinesterase inhibitor*).tw.
48. RIVASTIGMINE/
49. Exelon.tw.
50. (rivastigmine adj2 hydrogen tartrate).tw.
51. rivastigmine tartrate.tw.
52. Rivastigmine.tw.
53. GALANTAMINE/
54. galanthamine hydrobromide.tw.
55. donepezil.tw.
56. aricept.tw.
57. MEMANTINE/
58. ebixa.tw.
59. memantin*.tw.
60. or/43-59
61. 42 and 60
62. limit 61 to (yr="2009 -Current" and "all adult (19 plus years)" and English and humans)
63. limit 62 to systematic reviews

CLINICAL QUESTIONS

1. What are the risk factors for dementia?
2. What are the risk reduction interventions/strategies for dementia?
3. What are the diagnostic criteria for dementia?
4. What are the accurate assessment tools for dementia?
5. What are the accurate assessment tools for non-cognitive domains in dementia?
6. What are the safe and effective pharmacological treatments for dementia?
   - Acetylcholinesterase inhibitors (rivastigmine, donepezil, galantamine) & NMDA antagonists (memantine)
   - Antipsychotics/antidepressants/mood stabilisers for BPSD
   - Drugs to use with caution (anticholinergic burden)
7. What are the safe and effective non-pharmacological treatments for dementia?
8. What are the safe and effective TCM for dementia?
9. What are the safe and effective treatment in mild cognitive impairment?
10. What are the safe and effective palliative care for dementia?
11. What are the basic social, legal and ethical issues in dementia?
12. What are the safe and effective interventions for caregivers of dementia?
13. What are the safe and effective management in the following special groups of dementia?
    - Acquired brain injury
    - Alcohol-related dementia
    - HIV-associated neurocognitive disorder
14. When should patients with dementia be referred to a tertiary specialist service?

10 WARNING SIGNS OF DEMENTIA

Source: Alzheimer's Disease Foundation Malaysia (Available at: http://adfm.org.my/10-warning-signs/)

INITIAL ASSESSMENT TOOLS

a.   Abbreviated Mental Test Score (AMTS)

The following questions are put to the patient. Each question correctly answered scores one point:

Question	Score
What is your age? (1 point)	
What is the time to the nearest hour? (1 point)	
Give the patient an address, and ask him or her to repeat it at the end of the test. (1 point) e.g. 42 West Street	
What is the year? (1 point)	
What is the name of the hospital or number of the residence where the patient is situated? (1 point)	
Can the patient recognize two persons (the doctor, nurse, home help, etc.)? (1 point)	
What is your date of birth? (day and month sufficient) (1 point)	
In what year did World War 1 begin? (1 point) (other dates can be used, with preference for dates some times in the past)	
Name the present monarch/prime minister/president. (1 point)	
Count backwards from 20 down to 1. (1 point)	

A score of 6 or less suggests delirium or dementia, although further tests are necessary to confirm the diagnosis.

b.   Mini-Cog

The Mini-Cog

1. Instruct the patient to listen carefully and repeat the following:

APPLE   WATCH   PENNY

2. Administer the Clock Drawing Test (CDT)

3. Ask the patient to repeat the three words given previously.

_____   _____   _____

Scoring:
Number of correct items recalled _____ [if 3 then negative screen. STOP]

If answer is 1-2
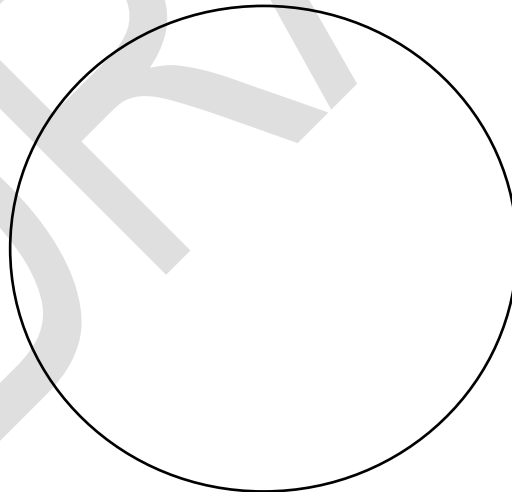   Is CDT Abnormal?   No   Yes

If No, then negative screen
        If Yes, then screen positive for cognitive impairment.

Instructions for CDT:
Inside the circle draw the hours of a clock as if a child would draw them. Place the hands of the clock to represent the time "forty-five minutes past ten o'clock"

**DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDER FIFTH EDITION
(DSM-5)**

Diagnostic criteria for major neurocognitive disorder (or dementia)

A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor or social cognition) based on:
   1. Concern of the individual, a knowledgeable informant or the clinician that there has been a significant decline in cognitive function; and
   2. A substantial impairment in cognitive performance, preferably documented by standardised neuropsychological testing or in its absence, another quantified clinical assessment.
B. The cognitive deficits interfere with independence in everyday activities (that is, at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).
C. The cognitive deficits do not occur exclusively in the context of a delirium.
D. The cognitive deficits are not better explained by another mental disorder. Specify:
   - Without behavioural disturbance: if the cognitive disturbance is not accompanied by any clinically significant behavioural disturbance.
   - With behavioural disturbance (specify disturbance): if the cognitive disturbance is accompanied by a clinically significant behavioural disturbance (for example, psychotic symptoms, mood disturbance, agitation, apathy or other behavioural symptoms). For example, major depressive disorder or schizophrenia.

Diagnostic criteria for mild neurocognitive disorder

A. Evidence of modest cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor or social cognition) based on:
   1. Concern of the individual, a knowledgeable informant or the clinician that there has been a mild decline in cognitive function; and
   2. A modest impairment in cognitive performance, preferably documented by standardised neuropsychological testing or in its absence, another quantified clinical assessment.
B. The cognitive deficits do not interfere with capacity for independence in everyday activities (that is complex instrumental activities of daily living such as paying bills or managing medications are preserved, but greater effort, compensatory strategies or accommodation may be required).
C. The cognitive deficits do not occur exclusively in the context of a delirium.
D. The cognitive deficits are not better explained by another mental disorder (for example, major Depressive Disorder or Schizophrenia).

Source: American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. Arlington, VA: American Psychiatric Association, 2013

INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS, 10TH REVISION (ICD-10)

Dementia

F00 Dementia in Alzheimer's disease
  F00.0 Dementia in Alzheimer's disease with early onset
  F00.1 Dementia in Alzheimer's disease with late onset
  F00.2 Dementia in Alzheimer's disease, atypical or mixed type
  F00.9 Dementia in Alzheimer's disease, unspecified

F01 Vascular dementia
  F01.0 Vascular dementia of acute onset
  F01.1 Multi-infarct dementia
  F01.2 Subcortical vascular dementia
  F01.3 Mixed cortical and subcortical vascular dementia
  F01.8 Other vascular dementia
  F01.9 Vascular dementia, unspecified

F02 Dementia in other diseases classified elsewhere
  F02.0 Dementia in Pick's disease
  F02.1 Dementia in Creutzfeldt-Jakob disease
  F02.2 Dementia in Huntington's disease
  F02.3 Dementia in Parkinson's disease
  F02.4 Dementia in human immunodeficiency virus [HIV] disease
  F02.8 Dementia in other specified diseases classified elsewhere

F03 Unspecified dementia

A fifth character may be added to specify dementia in F00-F03, as follows:
  .x0 Without additional symptoms
  .x1 Other symptoms, predominantly delusional
  .x2 Other symptoms, predominantly hallucinatory
  .x3 Other symptoms, predominantly depressive
  .x4 Other mixed symptoms

Dementia
A general description of dementia is given here, to indicate the minimum requirement for the diagnosis of dementia of any type, and is followed by the criteria that govern the diagnosis of more specific types.

Dementia is a syndrome due to disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language and judgement. Consciousness is not clouded. Impairments of cognitive function are commonly accompanied and occasionally preceded, by deterioration in emotional control, social behaviour or motivation. This syndrome occurs in Alzheimer's disease, in cerebrovascular disease and in other conditions primarily or secondarily affecting the brain.

In assessing the presence or absence of a dementia, special care should be taken to avoid false-positive identification: motivational or emotional factors, particularly depression, in addition to motor slowness and general physical frailty, rather than loss of intellectual capacity, may account for failure to perform.

Dementia produces an appreciable decline in intellectual functioning and usually some interference with personal activities of daily living, such as washing, dressing, eating, personal hygiene, excretory and toilet activities. How such a decline manifests itself will depend largely on the social and cultural setting in which the patient lives. Changes in role performance, such as lowered ability to keep or find a job, should not be used as criteria of dementia because of the large cross-cultural differences that exist in what is appropriate and because there may be frequent, externally imposed changes in the availability of work within a particular culture.

If depressive symptoms are present but the criteria for depressive episode (F32.0-F32.3) are not fulfilled, they can be recorded by means of a fifth character. The presence of hallucinations or delusions may be treated similarly.

.*x*0 Without additional symptoms
.*x*1 Other symptoms, predominantly delusional
.*x*2 Other symptoms, predominantly hallucinatory
.*x*3 Other symptoms, predominantly depressive
.*x*4 Other mixed symptoms

Source: World Health Organisation. ICD-10 Classifications of Mental and Behavioural Disorder: Clinical Descriptions and Diagnostic Guidelines. Geneva. 2016. (Available at: https://icd.who.int/browse10/2016/en#/F90.0)

THE GLOBAL DETERIORATION SCALE FOR ASSESSMENT OF
PRIMARY DEGENERATIVE DEMENTIA

The Global Deterioration Scale (GDS), developed by Dr. Barry Reisberg, provides caregivers an overview of the stages of cognitive function for those suffering from a primary degenerative dementia e.g. AD. It is broken down into seven different stages. Stages 1 - 3 are the pre-dementia stages while Stages 4 - 7 are the dementia stages. Beginning in stage 5, an individual can no longer survive without assistance. Within the GDS, each stage is numbered (1 - 7), given a short title (i.e., forgetfulness, early confusional, etc. followed by a brief listing of the characteristics for that stage. Caregivers can get a rough idea of where an individual is at in the disease process by observing that individual's behavioural characteristics and comparing them to the GDS. For more specific assessments, use the accompanying Brief Cognitive Rating Scale (BCRS) and the FAST measures.

Level	Clinical Characteristics
1 **No cognitive decline**	No subjective complaints of memory deficit. No memory deficit evident on clinical interview.
2 **Very mild cognitive decline** **(Age Associated Memory Impairment)**	Subjective complaints of memory deficit, most frequently in the following areas: (a) forgetting where one has placed familiar objects; (b) forgetting names one formerly knew well. No objective evidence of memory deficit on clinical interview. No objective deficits in employment or social situations. Appropriate concern with respect to symptomatology.
3 **Mild cognitive decline** **(Mild Cognitive Impairment)**	Earliest clear-cut deficits. Manifestations in more than one of the following areas: (a) patient may have gotten lost when traveling to an unfamiliar location; (b) co-workers become aware of patient's relatively poor performance; (c) word and name finding deficit becomes evident to intimates; (d) patient may read a passage or a book and retain relatively little material; (e) patient may demonstrate decreased facility in remembering names upon introduction to new people; (f) patient may have lost or misplaced an object of value; (g) concentration deficit may be evident on clinical testing. Objective evidence of memory deficit obtained only with an intensive interview. Decreased performance in demanding employment and social settings. Denial begins to become manifest in patient. Mild to moderate anxiety accompanies symptoms.

4 **Moderate cognitive decline** **(Mild Dementia)**	Clear-cut deficit on careful clinical interview. Deficit manifest in the following areas: (a) decreased knowledge of current and recent events; (b) may exhibit some deficit in memory of one's personal history; (c) concentration deficit elicited on serial subtractions; (d) decreased ability to travel, handle finances, etc. Frequently no deficit in the following areas: (a) orientation to time and place; (b) recognition of familiar persons and faces; (c) ability to travel to familiar locations. Inability to perform complex tasks. Denial is dominant defense mechanism. Flattening of affect and withdrawal from challenging situations frequently occur.
5 **Moderately severe cognitive decline** **(Moderate Dementia)**	Patient can no longer survive without some assistance. Patient is unable during interview to recall a major relevant aspect of their current lives, e.g. an address or telephone number of many years, the names of close family members (e.g. grandchildren), the name of the high school or college from which they graduated. Frequently some disorientation to time (date, day of week, season, etc.) or to place. An educated person may have difficulty counting back from 40 by 4s or from 20 by 2s. Persons at this stage retain knowledge of many major facts regarding themselves and others. They invariably know their own names and generally know their spouses' and children's names. They require no assistance with toileting and eating, but may have some difficulty choosing the proper clothing to wear.
6 **Severe cognitive decline** **(Moderately Severe Dementia)**	May occasionally forget the name of the spouse upon whom they are entirely dependent for survival. Will be largely unaware of all recent events and experiences in their lives. Retain some knowledge of their past lives but this is very sketchy. Generally unaware of their surroundings, the year, the season, etc. May have difficulty counting from 10, both backward and sometimes forward. Will require some assistance with activities of daily living, e.g. may become incontinent, will require travel assistance but occasionally will be able to travel to familiar locations. Diurnal rhythm frequently disturbed. Almost always recall their own name. Frequently continue to be able to distinguish familiar from unfamiliar persons in their environment. Personality and emotional changes occur. These are quite variable and include: (a) delusional behaviour, e.g. patients may accuse their spouse of being an impostor, may talk to imaginary figures in the environment or to their own reflection in the mirror; (b) obsessive symptoms, e.g. person may continually repeat simple cleaning activities; (c) anxiety symptoms, agitation and even previously non-existent violent behaviour may occur; (d) cognitive abulla, i.e. loss of willpower because an individual cannot carry a thought long enough to determine a purposeful course of action.

7 **Very severe cognitive decline** **(Severe Dementia)**	All verbal abilities are lost over the course of this stage. Frequently there is no speech at all, only unintelligible utterances and rare emergence of seemingly forgotten words and phrases. Incontinent of urine, requires assistance toileting and feeding. Basic psychomotor skills, e.g., ability to walk, are lost with the progression of this stage. The brain appears to no longer be able to tell the body what to do. Generalised rigidity and developmental neurologic reflexes are frequently present.

Source: Reisberg B, Ferris SH, de Leon MJ, et al. The Global Deterioration Scale for assessment of primary degenerative dementia. Am J Psychiatry. 1982;139(9):1136-9

FUNCTIONAL ASSESSMENT STAGING (FAST)

Stage	Level of Functioning
1	**No difficulty**, either subjectively or objectively
2	Complains of forgetting location of objects. **Subjective work difficulties**.
3	Decreased job functioning evident to co-workers. Difficulty in traveling to new locations. **Decreased organisational capacity**
4	**Decreased ability to perform complex tasks**, e.g. planning dinner for guests, handling personal finances (e.g. forgetting to pay bills), difficulty in marketing, etc.*
5	**Requires assistance in choosing proper clothing** to wear for the day, season or occasion, e.g. patient may wear the same clothing repeatedly unless supervised.*
6a	**Improperly putting on clothes without assistance or cuing** (e.g. may put street clothes on over night-clothes or shoes on wrong feet or have difficulty buttoning clothing) occasionally or more frequently over the past weeks.*
6b	Unable to bathe (shower) properly (e.g. **difficulty adjusting bath-water (shower) temperature**) occasionally or more frequently over the past weeks.*
6c	**Inability to handle mechanics of toileting** (e.g. forgets to flush the toilet, does not wipe properly or properly dispose of toilet tissue) occasionally or more frequently over the past weeks.*
6d	**Urinary incontinence** (occasionally or more frequently over the past weeks).*
6e	**Faecal incontinence** (occasionally or more frequently over the past weeks).*
7a	Ability to speak limited to approximately **a half a dozen intelligible different words or fewer**, in the course of an average day or **in the course of an intensive interview.**
7b	Speech ability limited to the use of **a single intelligible word** in an average day or **in the course of an interview** (the person may repeat the word over and over).
7c	Ambulatory ability lost (**cannot walk without personal assistance**).
7d	**Cannot sit up without assistance** (e.g., the individual **will fall over if there are no lateral rests [arms] on the chair**).
7e	**Loss of ability to smile**.
7f	**Loss of ability to hold up head independently**.

*Scored primarily on the basis of information obtained from a knowledgeable informant and/or caregiver.

FAST scoring instructions:
The **FAST Stage** is the highest consecutive level of disability. For clinical purposes, in addition to staging the level of disability, additional non-ordinal (non-consecutive) deficits should be noted since these additional deficits are of clear clinical relevance.

Source: Reisberg B. Functional assessment staging (FAST). Psychopharmacol Bull. 1988;24(4):653-9

MEDICATIONS USED FOR THE TREATMENT OF DEMENTIA

Name	Dosing (mg/day)	Liver impairment	Renal impairment	Common adverse effects	Precautions
Acetylcholinesterase Inhibitors (AChEI)					
Donepezil	Initial: 5 mg once daily, may increase to 10 mg once daily after 4 - 6 weeks	No dosage adjustment necessary	No dosage adjustment necessary	Gastrointestinal (GI): diarrhoea, nausea, vomiting Central nervous system (CNS): insomnia, fatigue, drowsiness Cardiovascular: chest pain, hypertension, syncope Miscellaneous: Accidental injury	Use with caution in patients: 1. at risk of prolonged cardiac repolarisation. 2. sick-sinus syndrome, bradycardia or conduction abnormalities. 3. with risk factors for rhabdomyolysis 4. at risk of peptic ulcer disease 5. with chronic obstructive pulmonary disease (COPD) and/or asthma 6. with history of seizure disorder 7. with bladder outlet obstruction/prostatic hyperplasia
Rivastigmine	Oral Initial: 1.5 mg twice daily; may increase by 3 mg daily every 2 weeks (based on tolerability) Maximum dose: 6 mg twice daily Transdermal patch Initial: Apply 4.6 mg/24 hours patch once daily. If well tolerated, may titrate (no sooner than every	Oral: No dosage adjustment necessary Transdermal: Child-Pugh class A and B: Initial and maximum dose of 4.6 mg/24 hours Child-Pugh class C: No dosage adjustment	Oral: No dosage adjustment necessary Transdermal: No dosage adjustment necessary	GI: Nausea, vomiting, diarrhoea CNS: dizziness, headache, falls Endocrine and metabolic: weight loss Local: Application site erythema (transdermal) Neuromuscular and skeletal: tremor Cardiovascular: Hypertension, syncope	Use with caution in patients with: 1. CNS depression 2. allergic dermatitis 3. extrapyramidal effects 4. sick-sinus syndrome, bradycardia or other supraventricular conduction abnormalities (Vagotonic effects) 5. at risk of peptic ulcer disease 6. COPD 7. history of seizure disorder 8. bladder outlet obstruction/ prostatic hyperplasia

	4 weeks) to 9.5 mg/24 hours and then to 13.3 mg/24 hours (maximum dose)				
Galantamine	Initial: 4 mg twice daily for 4 weeks If tolerated, increased to 8 mg twice daily for more than 4 weeks If tolerated, increase to 12 mg twice daily *If treatment interrupted >3 days, to restart at lowest dose	Moderate: Max dose 16 mg/day Severe: Use not recommended	Creatinine clearance (CrClr) 9 - 59 ml/min: Max dose 16 mg/day CrClr <9 ml/min: Max dose 8mg/day	GI: diarrhoea, nausea, vomiting, decreased appetite, abdominal pain/distress, dyspepsia CNS: dizziness, fatigue, drowsiness, depression, falling Cardiovascular: bradycardia, syncope Neuromuscular: tremors Others: weight loss	Use with caution in patients with: 1. sick-sinus syndrome, bradycardia or conduction abnormalities 2. risk of peptic ulcer disease 3. chronic obstructive pulmonary disease (COPD) and/or asthma 4. history of seizure disorder 5. bladder outlet obstruction/ prostatic hyperplasia
N-methyl-D-aspartate (NMDA) receptor antagonist					
Memantine	Initial: 5 mg once daily; increase dose by 5 mg every week as tolerated to a target maximum dose of 20 mg/day Dose may be administered once daily or two divided doses	Mild to moderate impairment: No dosage adjustment necessary Severe impairment: Use with caution	Mild impairment: No dosage adjustment necessary CrCL 30 - 49 ml/min: Initial 5 mg once daily; after at least 1 week of therapy and if tolerated, titrate up to 5 mg twice daily; may further titrate to 20 mg daily based on tolerability and clinical response (Canadian labelling) CrCL 5 - 29 ml/min Initially 5 mg once daily, after 1 week of therapy and if	Cardiovascular: hypertension CNS: dizziness, confusion, headache, fatigue GI: diarrhoea, constipation, vomiting Genitourinary: urinary incontinence Infection: influenza Neuromuscular and skeletal: back pain Respiratory: cough, dyspnoea	Hypersensitivity have been reported. Advise patients to report skin reactions immediately. Use with caution in patients with: 1. cardiovascular disease 2. hepatic impairment 3. ophthalmic disease 4. renal impairment 5. seizure disorder

| | | | | | tolerated, may titrate up to a target dose of 5 mg twice daily | | |

NOTE: All these medications are currently OFF-LABEL based on MoH National Formulary and National Pharmaceutical Regulatory Agency (NPRA)

Antipsychotics

Name	Dosing (mg/day)	Liver impairment	Renal impairment	Common adverse effects	Precautions
Aripiprazole	**Agitation/aggression and psychosis associated with dementia, severe or refractory:** Initial: 2 - 5 mg once daily; may increase dose based on response and tolerability in 5 mg increments at intervals ≥1 week up to 15 mg once daily In severe agitation associated with dementia with Lewy bodies, antipsychotics are generally avoided; if use is required, titrating above 2 - 5 mg/day is not recommended	No dosage adjustment necessary	No dosage adjustment necessary	Increased serum glucose, weight gain, constipation, nausea, vomiting, agitation, akathisia, anxiety, drowsiness, extrapyramidal reaction, fatigue, headache, sedation, insomnia, tremor	1. Suicidal thinking/behaviour 2. Cardiovascular disease 3. Dementia 4. Parkinson's Disease 5. Seizures
Olanzapine	**Agitation/aggression and psychosis associated with dementia, severe or refractory:** Initial: 2.5 mg once daily, may increase dose based on response and tolerability in increments of 2.5 - 5 mg/day at intervals ≥1 week up to 10 mg/day	Use with caution (cases of hepatitis and liver injury have been reported with olanzapine use). No dosage adjustment except when used in combination with fluoxetine (as separate components) when initial olanzapine dose should be	No dosage adjustment necessary	Orthostatic hypotension, Increased LDL, triglyceride & serum cholesterol, increased serum glucose, increased serum prolactin, weight gain, constipation, dyspepsia, increased appetite, xerostomia, decreased serum bilirubin, increased serum alanine aminotransferase, increased serum aspartate aminotransferase, akathisia, dizziness, drowsiness, extrapyramidal	1. Cardiovascular disease 2. Hepatic impairment 3. Dementia 4. Parkinson's Disease 5. Seizures 6. Renal Impairment

		limited to 2.5 - 5 mg daily.		reaction, fatigue, headache, insomnia, parkinsonism, asthenia	
Quetiapine	**Agitation/aggression and psychosis associated with dementia, severe or refractory:** Initial: 25 mg at bedtime; may increase dose gradually (e.g. weekly) based on response and tolerability up to 75 mg twice daily	IR tablet: Initial: 25 mg once daily; increase dose by 25 to 50 mg/day to effective dose, based on individual clinical response and tolerability ER tablet: Initial: 50 mg once daily; increase dose by 50 mg once daily to effective dose, based on individual clinical response and tolerability	No dosage adjustment necessary Removal by dialysis unlikely.	Increased diastolic blood pressure, increased systolic blood pressure, orthostatic hypotension, tachycardia, decreased HDL cholesterol, increased serum cholesterol, increased serum triglycerides, weight gain, increased appetite, xerostomia, decreased haemoglobin, agitation, dizziness, drowsiness, extrapyramidal reaction, fatigue, headache, withdrawal syndrome	1. Cancer 2. Impaired gastrointestinal motility 3. Hepatic impairment 4. Seizures 5. Urinary retention
Risperidone	**Agitation/aggression and psychosis associated with dementia, severe or refractory:** Initial: 0.5 mg/day in two divided doses; may increase dose based on response and tolerability in increments of 0.5 mg/day at intervals ≥2 days up to 1 mg/day	Severe impairment (Child-Pugh class C): Initial: 0.5 mg twice daily; titration should progress slowly in increments of no more than 0.5 mg twice daily; increases to dosages >1.5 mg twice daily should occur at intervals of ≥1 week	Severe impairment (CrCl <30 ml/minute): initial: 0.5 mg twice daily; titrate slowly in increments of no more than 0.5 mg twice daily; increases to dosages >1.5 mg twice daily should occur at intervals of ≥1 week	Hyperprolactinaemia, weight gain, increased appetite, nausea, upper abdominal pain, urinary incontinence, akathisia, anxiety, dizziness, drooling, drowsiness, drug-induced extrapyramidal reaction, fatigue, headache, insomnia, parkinsonism, sedation, tremor, cough, nasopharyngitis, rhinorrhea, fever	1. Cardiovascular disease 2. Hepatic impairment 3. Dementia 4. Seizures 5. Renal Impairment

mg=milligramme, GI=gastrointestinal, CNS=central nervous system, IR=immediate release, ER=extended release, CrCl=creatinine clearance, LDL=low density lipoprotein, HDL=high density lipoprotein

Source:

1. Ministry of Health Medicines Formulary (Updated April 2019) (Available https://www.pharmacy.gov.my/v2/en/apps/fukkm)

2. Lexicomp. Memantine: Drug information. UpToDate. Retrieved March 18, 2021 from https://www.uptodate.com/contents/memantine-drug-information?search=memantine&source=panel_search_result&selectedTitle=1~44&usage_type=panel&kp_tab=drug_general&display_rank=1

3. Lexicomp. Donepezil: Drug information. UpToDate. Retrieved Maech 18, 2021 from https://www.uptodate.com/contents/donepezil-drug-information?search=donepezil&source=panel_search_result&selectedTitle=1~46&usage_type=panel&kp_tab=drug_general&display_rank=1

4. Lexicomp. Rivastigmine: Drug information. UpToDate. Retrieved March 18, 2021 from https://www.uptodate.com/contents/rivastigmine-drug-information?search=rivastigmine&source=panel_search_result&selectedTitle=1~26&usage_type=panel&kp_tab=drug_general&display_rank=1

5. Lexicomp. Aripiprazole (oral and long-acting injectable [Abilify Maintena]): Drug information. UpToDate. Retrieved March 18, 2021 from https://www.uptodate.com/contents/aripiprazole-oral-and-long-acting-injectable-abilify-maintena-drug-information?search=aripiprazole&selectedTitle=1~76&usage_type=panel&display_rank=1&kp_tab=drug_general&source=panel_search_result

6. Lexicomp. Olanzapine: Drug information. UpToDate. Retrieved March 18, 2021 from https://www.uptodate.com/contents/olanzapine-drug-information?search=olanzapine&source=panel_search_result&selectedTitle=1~148&usage_type=panel&kp_tab=drug_general&display_rank=1

7. Lexicomp. Risperidone: Drug information. UpToDate. Retrieved March 18, 2021 from https://www.uptodate.com/contents/risperidone-drug-information?search=risperidone&source=panel_search_result&selectedTitle=1~122&usage_type=panel&kp_tab=drug_general&display_rank=1

8. Lexicomp. Quetiapine: Drug information. UpToDate. Retrieved March 18, 2021 from https://www.uptodate.com/contents/quetiapine-drug-information?search=quetiapine&source=panel_search_result&selectedTitle=1~132&usage_type=panel&kp_tab=drug_general&display_rank=1

ANTICHOLINERGIC BURDEN SCORE

Drugs with ACB Score of 1			
Alimemazine	Clidinium	Fluvoxamine	Nifedipine
Alverine	Clorazepate	Haloperidol	Paliperidone
Alprazolam	Codeine	Hydralazine	Prednisone
Aripiprazole	Colchicine	Hydrocortisone	Quinidine
Asenapine	Desloratadine	Iloperidone	Ranitidine
Atenolol	Diazepam	Isosorbide	Risperidone
Bupropion	Digoxin	Levocetirizine	Theophylline
Captopril	Dipyridamole	Loperamide	Trazodone
Cetirizine	Disopyramide	Loratadine	Triamterene
Chlorthalidone	Fentanyl	Metoprolol	Venlafaxine
Cimetidine	Furosemide	Morphine	Warfarin
Drugs with ACB Score of 2			
Amantadine	Cyclobenzaprine	Meperidine	Nefopam
Belladonna	Cyproheptadine	Methotrimeprazine	Oxcarbazepine
Carbamazepine	Loxapine	Molindone	Pimozide
Drugs with ACB Score of 3			
Amitriptyline	Darifenacin	Imipramine	Propiverine
Amoxapine	Desipramine	Meclizine	Quetiapine
Atropine	Dicyclomine	Methocarbamol	Scopolamine
Benztropine	Dimenhydrinate	Nortriptyline	Solifenacin
Brompheniramine	Diphenhydramine	Olanzapine	Thioridazine
Carbinoxamine	Doxepin	Orphenadrine	Tolterodine
Chlorpheniramine	Doxylamine	Oxybutynin	Trifluoperazine
Chlorpromazine	Fesoterodine	Paroxetine	Trihexyphenidyl
Clemastine	Flavoxate	Perphenazine	Trimipramine
Clomipramine	Hydroxyzine	Promethazine	Trospium
Clozapine	Hyoscyamine	Propantheline	

Categorical Scoring
• Possible anticholinergics include those listed with a score of 1
• Definite anticholinergics include those listed with a score of 2 or 3
Numerical Scoring
• Add the score contributed to each selected medication in each scoring category.
• Add the number of possible or definite anticholinergic medications.
Notes
• Each definite anticholinergic may increase the risk of cognitive impairment by 46% over six years.
• For each on point increase in the ACB total score, a decline in MMSE score of 0.33 points over two years has been suggested.
• Additionally, each one-point increase in the ACB total score has been correlated with a 26% increase in the risk of death.
Criteria for Categorisation
Score of 1: Evidence from in vitro data that chemical entity has antagonist activity at muscarinic receptor
Score of 2: Evidence from literature, prescriber's information or expert opinion of clinical anticholinergic effect
Score of 3: Evidence from literature, expert opinion, or prescriber's information that medication may cause delirium

Source: Aging Brain Care. Anticholinergic Cognitive Burden Scale 2012 Update. (Available at: http://www.idhca.org/wp-content/uploads/2018/02/DESAI_ACB_scale_-_Legal_size_paper.pdf)

SUGGESTED GUIDE TO REVIEW AND DEPRESCRIBE (POTENTIALLY INAPPROPRIATE PRESCRIPTION/PSYCHOTROPIC) IN DEMENTIA

Step 1: Evaluation

Does the patient have more than one (PIP/psychotropic)?	☐ No ☐ Yes
Has the patient been on (PIP/psychotropic) >3 months?	☐ No ☐ Yes

- If **YES** for at least one of the above, kindly proceed to **Step 2**.

Step 2: PIP/Pyschotropic Review

Parameter	Description	Review
Indication	Is there a justified reason?	☐ No ☐ Yes
Effectiveness	Has it been effective for the indication?	☐ No ☐ Yes
	Is it the recommended choice for the indication?	☐ No ☐ Yes
Safety	Is there therapeutic duplication?	☐ No ☐ Yes
	Is there any contraindication(s) to the patient?	☐ No ☐ Yes
	Is there a potential or actual and significant drug interaction?	☐ No ☐ Yes
	Is this regime a result of prescribing cascade?	☐ No ☐ Yes
Pharmacotherapy	Is the dose appropriate?	☐ No ☐ Yes
	Is the frequency appropriate?	☐ No ☐ Yes

- If **YES** for any one of the above, kindly proceed to **Step 3**.

Step 3: PIP/psychotropic Reconciliation
Kindly consider the following actions for this patient:
1. Deprescribing PIP/psychotropic
2. Substituting to a better alternative
3. Modify the regime (dose, frequency and duration, etc.)
4. Consider potential for managing all symptoms with a single PIP/psychotropic

IMPORTANT POINTS FOR THE CAREGIVER OF PEOPLE WITH DEMENTIA

1.	UNDERSTANDING DEMENTIA

- The caregivers need to understand about dementia and the importance of early detection and early diagnosis.

2.	SUPPORT FOR CAREGIVERS/CARERS

- Caring the PWD may cause stress to family and caregivers. Build-up of stress may lead to emotional problems and poor health of the caregivers. One of the ways to relieve the stress is to have someone to listen to them, e.g. using telephone counselling service or participating in support group events which are tailored to their needs. The support group should also involve other family members as well.
- Caregiver should be aware of their own physical and mental health issues e.g. increased risk of depression and over tiredness. Therefore, respite care should be offered for adequate support to help caregivers in coping with caring for PWD.

3.	RECOGNISE FUNDAMENTAL NEEDS OF CARE FOR PWD
a.	**Recognise the stress and challenges faced by PWD and suggested carer responses**

- PWD feel stressed when they are unable to recall what has just happened. They may also be disorientated to time, place and person. Though their memory, understanding and judgement are declining, their emotion may still be intact.

b.	Learn to engage with PWD

i.	**Forgetfulness:** PWD do not recall what they talked about and with whom they talked.	**Helpful tips:** Courteously answer the questions because PWD have difficulty to recall and may be repeatedly asking question for confirmation as a result of being anxious.
ii.	**Disorientated to time, place and person:** PWD may repeatedly ask the day, date, where they are and who the persons around them.	**Helpful tips:** PWD may have problems organising and making plans and, executing things correctly. Confirm with them the actions that they are doing and ask what they want to do next step by step.
iii.	**Impaired understanding and judgement:** For instance, PWD may become unable to cook, use remote control for television or operate the washing machine.	**Helpful Tips:** Engage in the activity together with PWD. For example, instead of allowing person with dementia to cook, let them do simple things like washing vegetables or peeling onions and, at the same time ensuring their safety.
iv.	**Delusion:** A false belief that is beyond challenge. For instance, PWD may have delusion of theft, that is the false belief that their valuable thing, e.g. money or purse, has been stolen by someone despite being reassured that this does not occur.	**Helpful tips:** Caregiver should show interest in looking for the item together with the PWD. Once search is done, distract the activity by saying for e.g. 'We have tried searching for the item, but can't find it, let's have a cup of tea and look again later'.
v.	**Wandering:** PWD may also try to leave the house to go somewhere but loses his or her way before reaching the destination.	**Helpful tips:** Person with dementia may have their own reason to go out. The carer can try to engage by asking "where are you going" and "why are you going?" Carer may then help them to achieve their purpose. It is also useful to put a name tag with their name, address and

		contact details on their clothes so that others can assist them in finding their way home
vi.	**Anger:** PWD may suddenly get upset and become verbally or physically agitated. They can be sensitive to certain conversations and may become angry and restless as they are unable to express their feelings and difficulties.	**Helpful tips:** Carers will need to be more accommodating and avoid triggers or situations that hurt their feelings.
c.	**Understand important daily life activities of PWD**	
i.	**Eating:** PWD often forget they have eaten and may also not recognise edible/food items from nonedible items	**Helpful tips:** Explain regarding timing of meals by mentioning actual time. Avoid having nonedible items within reach for those who cannot tell the difference.
ii.	**Bathing:** PWD may not be co-operative to take bath; They may refuse to undress, wash themselves or dress after their bath	**Helpful tips:** When a PWD who usually takes bath refuses to do so, it may be due to being unwell. Hence, caregiver need to ask about their physical condition. During the bathing process: • talk to them gently and be careful not to hurt their pride. During the dressing process: • replace their clothes fasteners or buttons with Velcro tape • put signs on their clothes to distinguish the front and back • prepare their clothes in the correct order of putting on
iii.	**Excretion:** PWD may urinate in inappropriate places, repeatedly go to the bathroom or do not understand the need to urinate or defecate.	**Helpful tips:** Caregiver may put a large sign on the bathroom door, keep the doorways bright and switch on the lights in the bathroom at night. Another tip is to bring the PWD to the toilet at frequent interval.

Source:

1. Division for Dementia and Community Care Promotion. Living together with people with dementia; Key points for the care of people with dementia at home. Kumamoto Prefecture; Department of Health and Social Services; 2013.
2. National Institute for Health and Care Excellence (NICE). Dementia: assessment, management and support for people living with dementia and their carers. London: NICE; 2018.

USEFUL RESOURCES

State	Organisation Information
National	ADFM National Dementia Caregivers Support Network Tel: ADFM HELPLINE at 03-79315850 Facebook: Alzheimer's Disease Foundation Malaysia - ADFM
Penang	Penang Dementia Association Tel: 016-6745429 Facebook: Penang Dementia Association
Perak	Dementia Society Perak Ipoh AD Support Group Tel: 05-2411691 / 019-5712738 Email: tdsperak@gmail.com Facebook: The Dementia Society Perak
Selangor, Wilayah Persekutuan Kuala Lumpur & Putrajaya	ADFM AD Support Group Tel: 03-79315850/016-6082513 Email: jenny@adfm.org.my / jennyho8@gmail.com Facebook: Alzheimer's Disease Foundation Malaysia - ADFM
Negeri Sembilan	Kumpulan Sokongan Dementia Negeri Sembilan (KUSDeNS) Email: wecaredementian9@gmail.com Tel: 06-7684804
Johor	Johor Bahru Alzheimer's Disease Support Association (JOBADA) Tel: 07-2222016 (JOBADA office)/012-7091277 Email: jobadajohor@gmail.com Facebook: Jobada Johor
Sabah	Sabah Alzheimer' Disease Association (Sabah AZ) Tel: 088-231030 / 088-270730 Email: kjchau88@hotmail.com Facebook: Sabah Alzheimer's Disease Support Association
Sarawak	Trinity ElderCare Centre (TEC) Tel/Fax: 082-255758 Email: tmceldercare@gmail.com Facebook: Trinity ElderCare Centre

ADVANCE CARE PLANNING

Advance care planning (ACP) is a process of discussing and recording PWD's wishes, values and preferences of future care together with their family members and healthcare providers (HCP) which will take effect once the PWD lose their capacity to make decision.

The discussion of ACP should include:
- benefits of planning ahead
- PWD's proxy or substitute decision-maker when the PWD lacks capacity to make decisions
- advance statement about their wishes, values, preferences and beliefs regarding their future care
- advance decisions to refuse certain treatments e.g. intubation, cardiopulmonary resuscitation, enteral feeding, etc.
- their preferences for place of care and place of death

Recommendations for HCP during ACP discussion.
- Start ACP as early as possible when the PWD and family members are ready.
- ACP conversations are not one-off occurrence and it should be revised from time to time especially when changes of clinical condition occur.
- Try to understand the PWD from their perspectives before initiation of discussion on ACP - explore their life stories, important values, norms, beliefs and preferences,
- Use the language which is familiar to the PWD,
- Adjust conversation style and content to the PWD's level and rhythm.
- Obtain the PWD's permit to invite family members to join the conversation.
- Evaluate their disease awareness and inform them about the expected disease trajectory and possible end-of-life decisions.
- Explore the PWD's current experiences, their fears and concerns for the future and end-of-life.
- Lead the conversation but do not force it or dominate the discussion.
- Keep connected with the PWD to ensure their maximum participation, respond to their emotions, attend to non-verbal communication and observe their behaviour.

Source:
1. National Institute for Health and Care Excellence (NICE). Dementia: assessment, management and support for people living with dementia and their carers. London: NICE; 2018.
2. Harrison Dening K, Sampson EL, De Vries K. Advance care planning in dementia: recommendations for healthcare professionals. Palliat Care. 2019;12:1178224219826579

LIST OF ABBREVIATIONS

11C-PIB-PET	11C-labeled Pittsburgh compound B-positron emission tomography
123I-FP-CIT	Iodine 123-radiolabeled 2β-carbomethoxy-3β-(4-iodophenyl)-N-(3-fluoropropyl) nortropane
123I-MIBG	123I-metaiodobenzylguanidine
ACB	anticholinergic burden
ACE-III	Addenbrooke's Cognitive Examination-III
AChEI	acetylcholinesterase inhibitors
ACP	advance care planning
AD	Alzheimer's disease
AD-8	Eight-item Interview to Differentiate Aging and Dementia
ADAS-Cog	Alzheimer's Disease Assessment Scale-Cognitive Subscale
ADCS-CGIC	Alzheimer's Disease Cooperative Study – Clinical Global Impression of Change
ADDTC	Alzheimer's Disease Diagnostic and Treatment Centres
ADL	activity of daily living
AE	adverse event
AGREE II	Appraisal of Guidelines, Research and Evaluation II
aHR	adjusted hazard ratio
AMTS	Abbreviated Mental Test Score
ANI	Asymptomatic Neurocognitive Impairment
AP	antipsychotic
APOE4	apolipoprotein E4
ARB	angiotensin II receptor blockers
ARD	alcohol-related dementia
ART	antiretroviral therapy
BEHAVE-AD	Behavioural Pathology in Alzheimer's Disease Rating Scale
BMI	body mass index
BPRS	Brief Psychiatric Rating Scale
BPSD	behavioural and psychological symptoms of dementia
bvFTD	behavioural variant of frontotemporal dementia
CBT	cognitive behavioural therapy
CGI	Clinical Global Impression
CGI-C	CGI-Corrections
CGI-I	CGI-Improvement
CGI-S	CGI-Severity
CI	confidence interval
CIBIC+	Clinician's Interview-Based Impression of Change
CIND	cognitive impairment no dementia
CIND-PD	cognitive impairment in Parkinson's Disease
cm^2	centimetre square
CMAI	Cohen-Mansfield Agitation Inventory
CNS	central nervous system
CPE	CNS penetration effectiveness
CPG	clinical practice guidelines
CQ	clinical question
CrCl	creatinine clearance
CSDD	Cornell Scale for Depression in Dementia
CSF	cerebrospinal fluid
CT	computed tomography

DAD	Disability Assessment for Dementia
DAT	dopamine transporter
DG	development group
DLB	dementia with Lewy Body
DM	diabetes mellitus
DSM-5	Diagnostic and Statistical Manual of Mental Disorders 5th Edition
EEG	electroencephalogram
ER	extended release
EGb761	ginkgo biloba extract 761
FAST	Functional Assessment Staging
FBI	Frontal Behavioural Inventory
FDG-PET	fluorodeoxyglucose-positron emission tomography
FTD	frontotemporal dementia
GDS	Global Deterioration Scale
GI	gastrointestinal
GRADE	Grading of Recommendations, Assessment, Development and Evaluations
h	hour
HAD	HIV-associated Dementia
HANDs	HIV-associated Neurocognitive Disorders
HCP	healthcare providers
HDS	HIV Dementia Scale
HIV	human immunodeficiency virus
HR	hazard ratio
HTA	health technology assessment
IADL	Instrumental Activity of Daily Living
ICD-10	International Classification of Diseases, Tenth Revision
IHDS	International HIV Dementia Scale
IM	intramuscular
IQCODE	Informant Questionnaire on Cognitive Decline in the Elderly
IR	immediate release
MADRS	Montgomery-Asberg Depression Rating Scale
MCI	mild cognitive impairment
MD	mean difference
MDS	Movement Disorder Society
mg	milligramme
MMSE	Mini Mental State Examination
MND	Mild Neurocognitive Disorder
MoCA	Montreal Cognitive Assessment
MoH	Ministry of Health
MRI	magnetic resonance imaging
NBRS-A	Neurobehavioral Rating Scale-Agitation
NCDs	non-communicable diseases
NGOs	non-governmental organisations
NIA-AA	National Institute on Aging and Alzheimer's Association
NICE	National Institute for Health and Care Excellence
NINDS-AIREN	National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences
NMDA	N-methyl-D-aspartate
NOSGER	Nurses' Observation Scale for Geriatric Patients
NPI	Neuropsychiatric Inventory
NPI-A	Neuropsychiatric Inventory-agitation

NPZ3	neuropsychological z-score 3
NRT	nicotine replacement therapy
OR	odds ratio
p	P value
PIP	potentially inappropriate prescription
PDD	Parkinson's Disease Dementia
PWD	people with dementia
QoL	quality of life
RC	review committee
RCT	randomised controlled trial
RR	relative risk
RT	reminiscence therapy
SIB	Severe Impairment Battery
SLUMS	Saint Louis University Mental Status
SMD	standardised mean difference
SPECT	single-photon emission CT
SUCRA	surface under cumulative ranking
TBI	traumatic brain injury
TC	total serum cholesterol
TCM	traditional and complementary medicine
TEAEs	treatment-emergent adverse events/effects
US FDA	United States Food and Drug Administration
VaD	vascular dementia
V-ADAS-cog	Vascular Dementia Assessment Scale Cognitive Subscale
VCAT	Visual Cognitive Assessment Test
VDRL	Venereal Disease Research Laboratory test
vs	versus
WAB	Western Aphasia Battery
WHO	World Health Organization
WMD	weighted mean difference
ZBI	Zarit Burden Interview

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DISCLOSURE STATEMENT

SOURCE OF FUNDING