MINISTRY OF HEALTH
SINGAPORE

Dementia

MOH Clinical Practice Guidelines 1/2013

College of Family Physicians, Singapore

Academy of Medicine, Singapore

College of Physicians, Academy of Medicine, Singapore

Singapore Medical Association

Clinical Neuroscience Society, Singapore

Society for Geriatric Medicine Singapore

Singapore Psychiatric Association

ADA Alzheimer's Disease Association

National Neuroscience Institute
SingHealth

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Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1^{++}	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias.
1^{+}	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1^{++} and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1^{++} or 1^{+}
C	A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2^{++}
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2^{+}
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

Dementia

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Addendum

These guidelines were initially available on the MOH website on 5 April 2013. This updated version is published on 10 July 2013. The following minor changes to the text of the guidelines were made based on feedback received.

a. Page 25 – Addition of 'Liver Function Tests' to the list of tests to rule out metabolic and structural causes of dementia
b. Page 26 – Clarification on the value of neuroimaging
c. Page 29 – Clarification on use of the term 'Mild Cognitive Impairment'

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

Contents

Foreword

Dementia represents a major public health concern in Singapore and worldwide. Being the most prevalent neurodegenerative disease, dementia is expected to affect 55,000 patients in Singapore by the year 2020. The commonest cause of dementia is Alzheimer's disease with vascular dementia being the next most important cause. Right from the stage of mild dementia up to the stages of severe dementia, this condition poses a significant health and socio-economic burden to patients, caregivers and the nation as a whole. Early diagnosis will allow appropriate use of pharmacological and non-pharmacological management. Along with disease stabilization, efforts to address caregiver burden, patient safety and medico legal concerns should form the principles of management. Clear practise guidelines will allow holistic and optimal care in dementia.

I am pleased to present the revised clinical practise guidelines for dementia. In this regard the workgroup has performed a thorough review of the existing literature to recommend both pharmacological and non-pharmacological aspects of management for patients ranging from mild cognitive impairment to severe dementia. This revised guidelines also highlights issues related to the management of mild cognitive impairment, young onset dementia and ethical aspects of care for patients with dementia.

I am confident that clinicians will find these guidelines useful in their clinical practise.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES

Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

Diagnosis and screening

C Individuals who should be evaluated for dementia include those with progressive cognitive or behavioural complaints suggestive of dementia, as well as patients who arouse the physician's or caregiver's suspicion of cognitive impairment despite absence of complaints (pg 17).

Grade C, Level 2^{+}

GPP Assessment of dementia should be done via a comprehensive evaluation. This approach will aim to diagnose dementia early, assess for complications of dementia and establish the cause of the dementia (pg 18).

GPP

B In individuals with suspected cognitive impairment, diagnosis should be made using the DSM-IV criteria for dementia with history from a reliable informant. This should be supplemented by an objective approach with bedside cognitive tests and/or neuropsychological assessment (pg 18).

GradeB, Level 2^{++}

D In the evaluation for suspected dementia, the presence of depression should be considered (pg 21).

Grade D, Level 4

B The complications of dementia can be broadly divided into behavioural and psychological symptoms, functional problems and social problems. These should be evaluated in all patients with dementia as these issues are the major causes of stress on the caregiver and assessment would enable the clinician to target subsequent management effectively (pg 22).

Grade B, Level 2^{++}

GPP In the clinic setting, the physician should routinely ask about depression, anxiety, agitation, paranoia, hallucinations and sleep problems, as these are potentially amenable to treatment, by way of either psychosocial interventions or pharmacologic agents (pg 22).

GPP

D The aim of determining dementia aetiology is to rule out potentially reversible causes of dementia and selecting appropriate treatment strategies for the irreversible dementias. This should be done via clinical history and physical examination, followed by laboratory investigations and neuroimaging where appropriate (pg 24).

Grade D, Level 4

GPP Screening for neurosyphilis should be considered for patients with young onset dementia, patients with a history of sexually transmitted diseases and patients presenting with a neuropsychiatric syndrome (pg 25).

GPP

B Clinicians should make a diagnosis of a specific type of dementia based on available criteria. A number of well-validated clinical criteria may be used for the various types of dementia (Alzheimer's disease, vascular dementia, dementia with Lewy bodies, Parkinson's disease dementia and fronto-temporal dementia) (pg 26).

Grade B, Level 2^{++}

D Patients' and, where appropriate, their family's preferences for disclosure should be sought with respect to the diagnosis of dementia and acted upon accordingly. The communication of diagnoses should be done in a sensitive and empathic manner, the patient and family should be given time to come to terms with diagnosis (pg 27).

Grade D, Level 4

GPP Genetic testing should not be routinely carried out in the clinical evaluation of dementia (pg 29).

GPP

B Routine testing of APOE (Apolipoprotein E) gene is not recommended in dementia diagnosis and in tailoring dementia risk reduction (pg 30).

Grade B, Level 2^{++}

Pharmacological management of dementia

GPP Pharmacotherapy should be part of a multi-pronged strategy to dementia management that encompasses a well-established diagnosis and consideration of stage-specific challenges, such as education of patient and caregiver, non-pharmacological measures and comprehensive caregiver psychosocial intervention (pg 31).

GPP

GPP Pharmacotherapy should not be used in isolation in the management of dementia but in conjunction with non-pharmacological management including education and counselling of patient and caregiver (pg 31).

GPP

GPP Patients with dementia should be screened and treated for reversible identifiable causes (such as depression, B_{12} deficiency and hypothyroidism) and vascular risk factors (pg 32).

GPP

GPP The current evidence for the use of cognitive enhancers is generally based on clinical trials of up to 1 year duration. The use of cognitive enhancers for longer periods will need to include a detailed discussion with the patient and caregivers on the overall benefit of treatment and specific needs of the patient (pg 34).

GPP

A Acetylcholinesterase inhibitors (donepezil, galantamine or rivastigmine) should be considered for the management of patients with mild to moderate Alzheimer's disease (pg 34).

Grade A, Level 1^{++}

A Acetylcholinesterase inhibitors may be considered for the management of moderately severe to severe Alzheimer's disease (pg 35).

Grade A, Level 1^{+}

A Where tolerated, acetylcholinesterase inhibitors should be titrated to recommended doses (5-10 mg/day donepezil; 16-24 mg/day galantamine; 6-12 mg/day oral and 4.6-9.5 mg/24 hr transdermal rivastigmine), which have been shown to confer greater benefit compared with lower doses (pg 35).

Grade A, Level 1^{++}

A N-methyl D-aspartate antagonists (memantine) may be considered for the management of moderately severe to severe Alzheimer's disease, either alone or in combination with acetylcholinesterase inhibitors (pg 36).

Grade A, Level 1^{+}

A N-methyl D-aspartate antagonists (memantine) may be considered for treatment of mild to moderate Alzheimer's disease, if acetylcholinesterase inhibitor therapy is contra-indicated, not tolerated or if there is disease progression despite an adequate trial of acetylcholinesterase inhibitor (pg 36).

Grade A, Level 1^{+}

A Acetylcholinesterase inhibitors have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia (pg 37).

Grade A, Level 1^{+}

A N-methyl D-aspartate antagonists (memantine) have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia (pg 38).

Grade A, Level 1^{+}

GPP Appropriate treatment of vascular risk factors and lifestyle changes including a healthy diet and regular exercise is recommended for all patients with vascular dementia (pg 39).

GPP

B Acetylcholinesterase inhibitors may be considered for the management of cognitive and behavioural symptoms related to Parkinson's disease dementia (pg 39).

Grade B, Level 1+

B Acetylcholinesterase inhibitors or N-methyl D-aspartate antagonists (memantine) may be considered for the management of cognitive and behavioural symptoms related to dementia with Lewy bodies (pg 40).

Grade B, Level 1+

B Selective serotonin reuptake inhibitors (SSRIs) may be considered for the management of behavioural symptoms related to frontotemporal dementia (pg 40).

Grade B, Level 1+

C N-methyl D-aspartate antagonists (memantine) and acetylcholinesterase inhibitors may be considered for the management of cognitive and behavioural symptoms related to frontotemporal dementia (pg 40).

Grade C, Level 2+

GPP The choice of acetylcholinesterase inhibitors should be based upon factors such as experience of the clinician, tolerance to side effects, ease of use, and the clinical profile of the individual to be treated (pg 41).

GPP

GPP The decision to initiate cognitive enhancers, such as acetylcholinesterase inhibitors or N-methyl D-aspartate antagonists (memantine), should be made in consultation with the patient and family after careful consideration of the expected magnitude of benefit, side effects, co-morbidities and costs of treatment (pg 42).

GPP

B Patients who are started on acetylcholinesterase inhibitors should be monitored for side effects such as nausea, vomiting, diarrhoea and anorexia, and bradycardia (pg 43).

Grade B, Level 1+

GPP Patients who are started on cognitive enhancers should be assessed for cognition, mood and behaviour, and function within 3-6 months of starting therapy and thereafter, at least once yearly or as clinically indicated (pg 43).

GPP

A Anti-inflammatory agents (such as non-steroidal anti-inflammatory agents and cyclo-oxygenase 2 inhibitors) are not recommended for the prevention of cognitive decline in Alzheimer's disease (pg 44).

Grade A, Level 1^{++}

B Prednisolone is not recommended for the prevention of cognitive decline in Alzheimer's disease (pg 44).

Grade B, Level 1^{+}

A Oestrogen is not recommended for the prevention of cognitive decline in women with Alzheimer's disease (pg 44).

Grade A, Level 1^{++}

A Selegiline is not recommended for the treatment of core or associated symptoms in Alzheimer's disease (pg 44).

Grade A, Level 1^{+}

B High dose vitamin E (in excess of 400 IU per day) is not recommended for the prevention or treatment of Alzheimer's disease (pg 45).

Grade B, Level 1^{+}

B Ginkgo is not recommended for the routine treatment of dementia (pg 45).

Grade B, Level 1^{+}

A Omega 3 fatty acid is not recommended for the prevention or routine treatment of dementia (pg 46).

Grade A, Level 1^{+}

A Statin therapy is not recommended for the prevention or routine treatment of Alzheimer's disease (pg 46).

Grade A, Level 1^{++}

A Folic acid and vitamin B supplementation are not recommended for the prevention and treatment of dementia in the absence of B vitamin deficiency (pg 46).

Grade A, Level 1^{++}

A Rosiglitazone is not recommended as monotherapy or as adjunctive therapy to cholinesterase inhibitors in mild to moderate Alzheimer's disease (pg 46).

Grade A, Level 1^{+}

A A Multi-component and individualised caregiver interventions should be considered for holistic dementia care (pg 49).

Grade A, Level 1^{+}

GPP Where appropriate, respite care may be offered to relieve the burden of caregiving on caregivers of persons with dementia (pg 50).

GPP

B Therapy incorporating cognitive and behavioural strategies may be considered for persons with dementia (pg 51).

Grade B, Level 1^{+}

Management of behavioural and psychological symptoms of dementia (BPSD)

C Environmental design features may be incorporated in care facilities to reduce behavioural and psychological symptoms of dementia (BPSD) in people with dementia (pg 52).

Grade C, Level 2^{+}

D Art therapy may be considered for persons with behavioural and psychological symptoms of dementia (BPSD) (pg 52).

Grade D, Level 3

B Reminiscence therapy (RT) may be considered for persons with behavioural and psychological symptoms of dementia (BPSD) (pg 52).

Grade B, Level 1^{+}

C Persons with dementia may be encouraged to participate in structured exercise programmes to improve physical function (pg 53).

Grade C, Level 2^{+}

B Music therapy, wherever feasible, is encouraged in the care of persons with dementia and helps in ameliorating the behavioural and neuropsychiatric symptoms of dementia (pg 53).

Grade B, Level 1^{+}

B Aromatherapy is not recommended for reducing agitation in persons with Alzheimer's disease (pg 55).

Grade B, Level 1^{+}

B Massage therapy could be considered in reducing agitation in persons with Alzheimer's disease (pg 56).

Grade B, Level 1^{+}

A Multisensory stimulation is not recommended in the care of elderly patients with dementia (pg 56).

Grade A, Level 1^{+}

GPP Antidepressants may be used for the treatment of comorbid depression in dementia provided their use has been evaluated carefully for each patient (pg 57).

GPP

A Antipsychotic medications may be considered in the treatment of behavioural and psychological symptoms of dementia when clinically appropriate and non-pharmacological management has not been useful (pg 57).

Grade A, Level 1^{++}

B Potential side-effects and risk/benefit ratio of antipsychotic medication should be discussed with patients and/or caregivers (pg 58).

Grade B, Level 2^{+}

A Routine use of mood stabilizers, such as carbamazepine and sodium valproate, is not recommended for treatment of behavioural symptoms associated with dementia (pg 59).

Grade A, Level 1+

GPP An individualized approach to managing behavioural problems in dementia patients is required (pg 59).

GPP

GPP Acetylcholinesterase inhibitor therapy may be considered in treatment of patients with behavioural problems if antipsychotics are inappropriate (pg 59).

GPP

GPP The decision to start antipsychotic therapy to control behavioural problems in dementia patients should be made in consultation with the patient and family, after careful consideration of the benefit, adverse-effects and co-morbidities (pg 59).

GPP

B For patients with dementia with Lewy bodies and behavioural problems, when considering the use of pharmacotherapy, acetylcholinesterase inhibitors should be considered first for management of the behavioural problems (pg 60).

Grade B, Level 1+

GPP In all patients started on antipsychotic medication, they should be monitored carefully for side effects and response to treatment. In patients who are stable, antipsychotic withdrawal should be considered (pg 60).

GPP

Ethical and legal issues

GPP Persons with dementia deemed to have decision making capacity (after clinical evaluation) are encouraged to make a Lasting Power of Attorney (LPA) (pg 62).

GPP

B Routine testing of APOE (Apolipoprotein E) gene is not recommended in dementia diagnosis and in tailoring dementia risk reduction (pg 66).

Grade B, Level 2^{++}

D The judgement with respect to the ability to drive safely of a person with dementia should only be made after a systematic and comprehensive assessment (pg 68).

Grade D, Level 4

D In general, persons whom the physician is unsure if the diagnosis of cognitive impairment might affect driving safety should be referred for further clinical and driving assessment (pg 69).

Grade D, Level 4

GPP In general, the diagnosis of dementia should be disclosed to the patient, unless explicitly stated otherwise (pg 71).

GPP

GPP In disclosure, the doctor should also be mindful of the impact the diagnosis can have on the patient's life and family relationships (pg 71).

GPP

Palliative care

B Patients with advanced dementia should be assessed for pain and treated accordingly (pg 75).

Grade B, Level 1^{+}

D A stepped protocol is recommended for pharmacological management of pain in dementia, and the WHO analgesic ladder or the American Geriatric Society's pain guidelines may be used (pg 75).

Grade D, Level 4

C Decisions on the use of antibiotics in advanced dementia should be individualized to the patient by weighing the risk and benefits of antibiotic treatment (pg 76).

Grade C, Level 2^{+}

GPP Decisions on tube feeding should be individualised given the lack of evidence for its efficacy in advanced dementia (pg 77).

GPP

D Advance care planning with regard to cardiopulmonary resuscitation (CPR) should be encouraged given the poor outcomes of CPR in advanced dementia (pg 78).

Grade D, Level 2+

Young onset dementia

GPP Patients with young onset dementia should receive specialist multidisciplinary care for the diagnosis and management of their condition (pg 79).

GPP

GPP In the diagnostic work up of patients with young onset dementia, neuroimaging and cerebrospinal fluid examination should be considered (pg 79).

GPP

GPP Caregivers of patients with young onset dementia should receive adequate counselling on the disease process, community resources and financial assistance (pg 79).

GPP

Community resources

B Caregivers of persons with advanced dementia should be provided with adequate information on available community and medical resources (pg 80).

Grade B, Level 2

B Referral to day care services and respite services should be considered as part of a comprehensive management plan (pg 81).

Grade B, Level 2

1 Introduction

1.1 Objectives and scope of guideline

The aim of the guidelines is to provide guidance to healthcare professionals in Singapore to assess, evaluate and manage dementia in their patients. This booklet includes chapters on epidemiology, diagnosis, screening and management of dementia. There is discussion on ethical and legal issues related to dementia, palliative care and young-onset dementia. Useful information on community resources are also provided in this booklet.

1.2 Target group

The target group of the guidelines include primary care and specialist doctors, nurses and all allied health staff involved in the care of patients with dementia.

1.3 Guideline development

These guidelines have been produced by a committee comprising general practitioners, neurologists, geriatricians, psychiatrists, psychologists, dementia nurses, social workers and patient representatives appointed by the Ministry of Health. They were developed using the best available current evidence and expert opinion.

1.4 What's new in the revised guidelines

The following is a list of major revisions or additions to the guidelines:

(1) Updated recommendations on the pharmacological treatment of the different types of dementia
(2) Discussion on the approach to informing patients and carers on the diagnosis of dementia
(3) Diagnostic considerations for Mild Cognitive Impairment (MCI)
(4) Ethical and Legal Issues with discussion of the Mental Capacity Code of Practice 2008

(5) Section on the management aspects of Young Onset Dementia

1.5 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review 5 years after publication, or if new evidence appears that requires substantive changes to the recommendations.

2 Introduction and epidemiology

2.1 Introduction and epidemiology

Improved healthcare over the last century, coupled with rising standards of living, have brought with it increasing life expectancies and a growing tide of older populations that will sweep across both developed and developing countries across the world.[1] Such demographic changes are anticipated to bring along numerous challenges to healthcare systems, not least in terms of the growing number of patients with dementia that we will be faced with.

Since the Delphi Consensus statement[2] that was published in 2005, a more robust systematic review of the global prevalence of dementia[3] has been published which shows an estimated increase of 10% in the prevalence of dementia compared to previous publications. It is now estimated that there were 35.6 million people with dementia in 2010, with the numbers doubling every 20 years to 65.7 million in 2030 and 115.4 million in 2050. In Southeast Asia, the number of people with dementia is predicted to increase from 2.48 million in 2010 to 5.3 million in 2030.[2]

2.2 Epidemiology of dementia in Singapore

2.2.1 Age-adjusted prevalence in Singapore ranges from 2.38% to 5.2%

Singapore has one of the fastest ageing populations in the Asia-Pacific region with 21.5% of total population consisting of persons aged 65 and above by the year 2025.[3] Recent publications based on local cross-sectional surveys that were conducted in the period from 2003 to 2005 suggest that the age-adjusted prevalence of dementia locally may range from 2.38% to 5.2%.[4-5] These rates are, however, likely to be underestimates of the true prevalence because of study limitations in terms of sampling techniques and methodologies for the diagnosis of dementia. Nonetheless the estimated prevalence rates are in keeping with estimates from the World Alzheimer Report 2009.[6]

2.3 Vascular risk factors and dementia

A number of cohort studies and systematic reviews have demonstrated that vascular risk factors contribute to an increased risk of not just vascular dementia but *also* Alzheimer dementia. In particular, mid-life hypertension (R.R 1.24-2.8), mid-life hypercholesterolaemia (R.R. 1.4-3.1), diabetes mellitus (R.R. 1.39-1.47) and strokes have all been shown to be associated with an increased risk of incident dementia.[7-8]

In keeping with studies published elsewhere, our local data have similarly shown that vascular and metabolic factors contribute to the prevalence and risk of dementia. These risk factors represent possible windows of opportunity for intervention that may allow a reduction of dementia risk in the years ahead.[8-11]

Table 1 Prevalence of vascular risk factors amongst Singapore residents

	Prevalence
Diabetes Mellitus (aged 18–69)	**11.3%**
Hypertension (aged 30–69)	**23.5%**
Hypercholesterolaemia (aged 18–69)	**17.4%**

(Source: National Health Survey 2010, Ministry of Health, Singapore).

2.4 Conclusion

Our awareness of the impending tide of persons with dementia awaiting us, coupled with the ever increasing accrual of data regarding risk factors and possible intervention strategies that is made available, should form the basis for a concerted effort in formulating a rational national strategy to tackle the immense challenges in the management of dementia in the years ahead.

3 Diagnosis and screening

3. 1 Screening

C Individuals who should be evaluated for dementia include those with progressive cognitive or behavioural complaints suggestive of dementia, as well as patients who arouse the physician's or caregiver's suspicion of cognitive impairment despite absence of complaints.

Grade C, Level 2+

There is currently insufficient evidence for routine screening for dementia in older adults. Consistent with current evidence, neither the US Preventive Services Task Force (USPSTF) nor UK National Institute for Health and Clinical and Health Excellence (NICE) recommend population screening for dementia.[12-13]

The evaluation of dementia should be targeted at patients in whom there is some suspicion of cognitive impairment. They include:

- subjects with memory and other cognitive complaints, either reported by the patient himself or a significant other.
- progressive forgetfulness.[14]
- subjects who arouse the physician's suspicion of cognitive impairment during interview despite absence of memory or cognitive complaints.
- those who are at increased risk for dementia (such as those with a strong family history of dementia).
- elderly patients who need to make important decisions (such as the sale of a house or making a will) and in whom mental competency is questionable.
- review of specific aspects such as fitness to drive (in the elderly driver).

3.2 Assessment of dementia

GPP Assessment of dementia should be done via a comprehensive evaluation. This approach will aim to diagnose dementia early, assess for complications of dementia and establish the cause of the dementia.

GPP

In evaluating patients who present with forgetfulness or confusion, it is important to exclude delirium (acute confusional state) if this is of an **acute nature**. If the forgetfulness or confusion is of a **subacute nature** (weeks to few months), potentially reversible neurological conditions and depression have to be excluded.

(I) Diagnosis of dementia

B In individuals with suspected cognitive impairment, diagnosis should be made using the DSM-IV criteria for dementia with history from a reliable informant. This should be supplemented by an objective approach with bedside cognitive tests and/or neuropsychological assessment.

Grade B, Level 2^{++}

Subjective approach

a) The **Diagnostic and Statistical Manual of Mental Disorders - IV (DSM-IV) criteria**[15] are very often used as the gold standard for the clinical diagnosis of dementia.[16-18] The criteria require memory impairment to be present, as well as deficits in one other cognitive domain (aphasia, apraxia, agnosia and executive dysfunctioning). Moreover, these cognitive declines must be of sufficient severity to cause perceptible impairment in social or occupational functioning (Table 2).

Table 2 DSM-IV clinical criteria for diagnosis of dementia[16]

Cognitive domain	Questions
Amnesia	Any forgetfulness? Did it start graduallyor suddenly? Is it progressively worse? Andif so, is it smoothly declining or showing a step-wise/ fluctuating decline? Is it over short-term or long-term matters?
AND declines in one of the following domains:	
Aphasia	Any word-finding difficulty or other difficulties with communication?
Apraxia	Any problems with buttoning or dressing? Any difficulties with using utensils during mealtimes?
Agnosia	Any problems recognising familiar faces or familiar items?
Executive dysfunctioning	Any problems handling money (loose change)? Any change in general problem-solving abilities? Is one's work getting to be more disorganised?
OF sufficient severity to cause significant impairment in social or occupational functioning	AS a result of the above, is he becoming less independent in the - community? - home-care? - self-care level?

(Source: American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 1994).

b) The **Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)**[19-20] is a 26-item test that enquires about the subject's memory, cognition and language ability for the last 10 years (see Appendix 1).

There is recent evidence of the **Brief Informant Screening Test**[21] consisting of a single-item informant report of memory problem and a 4-item Instrumental Activities of Daily Living, as a useful screening instrument for patients with early cognitive impairment.

Objective approach

This is an observer-based approach using either performance-based instruments, such as mental status test (brief screening instruments), or a more detailed neuropsychological tests, which is usually administered by clinical psychologists.

a) The **Elderly Cognitive Assessment Questionnaire (ECAQ)**[22-23] is a 10-item test screening for cognitive impairment assessing memory and information-orientation (Appendix 2).

b) The 10-item **Abbreviated Mental Test (AMT)** (Appendix 3).

c) The 8-item **AD8** questionnaire.

d) 28-item **Chinese Mini Mental State Examination (CMMSE)** have also been validated locally with age and education-adjusted cut-off values available.[24] The CMMSE is more useful in those with higher educational attainment as the AMT may not be as sensitive.

e) The 30-item modified **Mini Mental State Examination (MMSE)** has also been validated locally, with specific education-specific cut-offs.

The abovementioned bedside cognitive screening instruments are mainly memory-biased.

f) The Chinese version of the **Frontal Assessment Battery** (FAB) which predominantly assesses executive function has also been validated locally.[25]

g) The Singaporean version of the **Montreal Cognitive Assessment** (MoCA) which assessed visuo-executive, naming, attention, language, abstraction, delayed recall and orientation has also been found to be more sensitive in screening for post-stroke cognitive impairment.[16] The MoCA has also been found to be useful for the diagnosis of mild cognitive impairment and mild dementia in Singapore.[26]

h) **Neuropsychological testing** is usually administered by neuropsychologists or clinical psychologists. It is useful in detecting subtle cognitive difficulties which are not picked up by the brief screening instruments. They should be performed on subjects:
   - who have memory complaints but do not yet satisfy criteria for dementia;
   - depressed subjects who present with memory complaints to help in determining whether the memory complaints are due solely to the depression or whether they have concomitant dementia;
   - Subjects in whom decision-making capacity is being assessed.

Psychometric testing can be a useful adjunct in the latter scenario. They are also useful in aetiologic differentiation of dementia.

Neuropsychological tests are also useful in individuals in whom the diagnosis of dementia is inconclusive whereby serial monitoring for decline in cognitive performance over time may be useful in establishing the diagnosis.

Neuropsychometric batteries have been validated locally in the elderly Chinese[26-28] and the Vascular Dementia Battery test has also been validated in the Singapore population.[29]

D In the evaluation for suspected dementia, the presence of depression should be considered.

Grade D, Level 4

Patients with depression may exhibit symptoms resembling dementia including forgetfulness and language difficulties. It is thus important that patients with cognitive symptoms be evaluated and treated for depression.

(II) Assessing complications of dementia

B The complications of dementia can be broadly divided into behavioural and psychological symptoms, functional problems and social problems. These should be evaluated in all patients with dementia as these issues are the major causes of stress on the caregiver and assessment would enable the clinician to target subsequent management effectively.

Grade B, Level 2^{++}

GPP In the clinic setting, the physician should **routinely ask about depression, anxiety, agitation, paranoia, hallucinations and sleep problems**, as these are potentially amenable to treatment, by way of either psychosocial interventions or pharmacologic agents.

GPP

a) Behavioural problems

Behavioural problems occur frequently in dementia patients; they affect 10% to 75% of all patients at some stage of their dementia.[30] They can present severe problems to all who interact with them,[31] leading to premature institutionalization, increased costs of care and significant loss in quality of life for the patient and family. Most of the major behavioural problems are amenable to treatment and are capable of reducing the suffering of the patients and their caregivers.

Different behavioural problems (Appendix 4) present at the different stages of the dementia process; anxiety and depression being common in early stages while aberrant motor behaviour is more common during the later stages of illness.[32]

These behavioural problems can also be rated objectively using behaviour scales which may be either self-rated, caregiver-based or observer reports. The Behavioural Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD),[33] Neuropsychiatric Inventory (NPI),[34] Cohen-Mansfield Agitation Inventory (CMAI)[35] are examples of behaviour scales, but they are often used only in research settings.

Depression in the elderly may not show the classical features indicated in the DSM-IV and, in this regard, clinicians may find the brief depression scales useful in practice. Locally, the single-question test for depression, Geriatric Depression Scale (GDS)[36-37] and Even Briefer Assessment Scale for Depression (EBAS-DEP) have been validated in cognitively intact, community-dwelling Chinese elderly.[38] The Cornell Depression Scale in Dementia specifically assesses depression in dementia[39] and has been shown to be a useful screening instrument in our local population.[40]

b) Functional difficulties

Functional difficulties can be assessed at three levels: community functioning, home functioning and self-care (see Appendix 5).[41] They are generally affected with the progression of dementia in a descending order and also allow these functional deficits to serve as markers of dementia severity. It is also important to make sure that these difficulties result from cognitive difficulties and not physical disabilities. The severity of dementia can be staged using the Diagnostic and Statistical Manual of Mental Disorders - 3rd revised edition (DSM-III-R)(Appendix 5)[15] or other formal functional assessment scales which include Clinical Dementia Rating Scale (CDR),[42-43] Functional Assessment Staging (FAST), Barthel Index and Blessed Dementia Scale (BDS).

c) Social problems

As a result of dementia, there is also loss of social role of the patient as a parent, spouse, friend and member of the larger society and these often result in caregivers' coping difficulties. Identification of caregiver's stress can allow targeted family education and counselling at tertiary dementia care centres, or even dementia day-care centres, and this has been shown to reduce institutionalisation. Elder abuse may also occur when the frustrated caregiver directs his or her stress at the vulnerable patient whose care is proving to be difficult.[44] Likewise, financial difficulties should be asked for and if problems are identified, families can be referred to a social worker.

(III) Determining the aetiology of dementia

Having determined the cognitive impairment to be chronic and having met clinical criteria for dementia, as well as assessing for the complications of dementia, the final step of the clinical evaluation involves determining the dementia aetiology. The types of dementia can be broadly divided into 2 categories – irreversible and reversible causes.

The more common causes of dementia can be classified into irreversible and potentially reversible causes.

- The irreversible causes include degenerative causes (Alzheimer's disease, fronto-temporal dementia and dementia with Lewy bodies), cerebrovascular disease (vascular dementia), prion-associated disorders (Creutzfeld-Jakob disease) and neurogenetic disorders.
- The potentially reversible causes include infectious disorders (meningitis and encephalitis), inflammatory disorders (autoimmune encephalopathy), toxic or metabolic encephalopathies (hypothyroidism, vitamin B_{12} deficiency, and alcohol-related syndromes), neoplastic causes and hydrocephalus (obstructive or normal pressure hydrocephalus).

Diagnostic differences for the common dementias are enclosed in Appendix 6.

D The aim of determining dementia aetiology is to rule out potentially reversible causes of dementia and selecting appropriate treatment strategies for the irreversible dementias. This should be done via clinical history and physical examination, followed by laboratory investigations and neuroimaging where appropriate.[45-48]

Grade D, Level 4

History

It is important to ask for the nature of the cognitive decline (sudden or gradual), progression – either gradually progressive (more suggestive of Alzheimer's disease) or stepwise/fluctuating course (suggestive of vascular dementia). A history of significant

alcohol ingestion and medication use (such as antipsychotics, antidepressants, anticholinergic agents and sedative-hypnotic agents) and history of medical, neurological and psychiatric illness is important.

Physical examination and mental state examination

The examination includes looking for evidence of depression, focal neurological deficits (such as visual field defects, hemiparesis, hemisensory loss, asymmetric deep tendon reflexes or unilateral extensor plantar responses). It is also possible to examine for extrapyramidal signs such as rigidity and bradykinesia, movement disorders and gait abnormalities as these may point to certain aetiologic diagnoses.

Diagnostic tests to rule out metabolic and structural causes of dementia

Dementias which are related to metabolic abnormalities are thought to be reversible. The haematological tests include **full blood count, urea and electrolytes, serum calcium, serum glucose, Liver Function Tests (LFT), thyroid function tests and vitamin B_{12} levels.**

Routine testing for neurosyphilis is problematic given the difficulties in interpretation of test results. It is best done when patients exhibit clinical features of neurosyphilis.

GPP Screening for neurosyphilis should be considered for patients with young onset dementia, patients with a history of sexually transmitted diseases and patients presenting with a neuropsychiatric syndrome.

GPP

Other biomarkers which can help in establishing dementia diagnosis include apolipoprotein-E ε4 allele, CSF-tau and β-amyloid for Alzheimer's disease, CSF 14-3-3, neuron-specific enolase and electroencephalogram for Creutzfeld-Jakob disease. However, these are not performed routinely but may be considered on a case by case basis.

Neuroimaging

Neuroimaging is useful in the differential diagnosis of dementia and also necessary in the diagnostic criteria in Alzheimer's disease and vascular dementia. It is also useful in detection of very early dementia as the functional and structural brain changes takes place before clinical manifestation of cognitive deficits. It consists of either

- Structural imaging techniques (computed tomography (CT) scan of head and magnetic resonance imaging (MRI)), or
- Functional neuroimaging techniques (Positron emission tomography and single-photon emission tomography).

Whether all patients with dementia require a structural imaging is an important clinical question, for which there is no consensus. The value of neuroimaging is in the identification of cerebral infarcts and potentially treatable lesions such as surgical brain lesions (SBLs), subdural haematomas, cerebral tumours and normal pressure hydrocephalus. The Canadian Consensus Conference on the Assessment of Dementia (CCCAD)[49] (Appendix 8) has outlined the criteria for undertaking a CT scan of the head, only if certain clinical conditions are met. In a patient with advanced dementia of a long duration (>2 years based on CCCAD's recommendations), we believe a brain scan is not warranted to detect potentially reversible SBLs. Conversely, if the patient's dementia is only mild to moderate (even after 2 years), it is still advisable to request for an initial CT scan of the brain.[50] If the clinician is not inclined to perform a brain scan, there is immense value in discussing the matter with the caregivers and in securing their agreement not to order a neuroimaging procedure.

Neuroimaging is also useful for aetiologic differentiation of the different dementias.

B Clinicians should make a diagnosis of a specific type of dementia based on available criteria. A number of well-validated clinical criteria may be used for the various types of dementia (Alzheimer's disease, vascular dementia, dementia with Lewy

bodies,[51] Parkinson's disease dementia and fronto-temporal dementia).[52]

Grade B, Level 2^{++}

In Alzheimer's disease, the common clinical criteria used include DSM-IV criteria for DAT, National Institute on Aging-Alzheimer's Association, National Institute of Neurologic, Communicative Disorders and Stroke-Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA).[53] In vascular dementia, the common clinical criteria used include DSM-IIIR, National Institute of Neurologic Disorder and Stroke and the Association Internationale pour la Recherche et l'Enseignment en Neurosciences (NINDS-AIREN),[54] State of California AD Diagnostic and Treatment Centers criteria (ADDTC),[55] Hachinski Ischemic Score (HIS),[56] modified Rosen scale[57] (the latter two being clinical scales).

Clinical Criteria for dementia with Lewy bodies[51] and fronto-temporal dementia[52] have been developed.

3.3 Informing the patient and carer

D Patients' and, where appropriate, their family's preferences for disclosure should be sought with respect to the diagnosis of dementia and acted upon accordingly. The communication of diagnoses should be done in a sensitive and empathic manner, the patient and family should be given time to come to terms with diagnosis.

Grade D, Level 4

Although patients generally would like to know the truth about their own medical condition, the rights of those who do not want to know should also be respected. Health care professionals should therefore seek to understand their patients' preferences with respect to the diagnosis of dementia and act appropriately according to their choice.[58]

Studies have shown that the vast majority of patients with mild dementia wish to be fully informed.[59-60] Therefore, unless a patient suffering from dementia explicitly declines to be informed of the diagnosis, the default mode should be to inform truthfully as it will enable the patient to:

a) plan for optimal life experiences in remaining years of intact capacities
b) designate and appoint a surrogate decision maker to take over the making of treatment decision upon eventual incompetence
c) settle personal financial and legal matters
d) participate in treatment decision-making and advance care planning
e) consider possible enrolment in research programmes and participate in informed consent process

When informing the diagnosis, the doctor needs to take into account the patient and family's prior knowledge and their perception of the problems. The doctor should also be mindful of the impact the diagnosis can have on the patient's life and family relationships. The communication should therefore be conducted sensitively and empathically, and should include a discussion on treatment options and available support services both in the hospital and the community.

After the diagnosis has been communicated, the patient and family should be given time to process the information and to come to terms with it. They should be given ample opportunity to ask questions and seek clarification from the doctor.

The objectives of truthful disclosure of diagnosis to patients with dementia are to empower the patient with: the courage to request for information, the cognition to understand information and the strength and resources to cope with the burden of information.

3.4 Mild cognitive impairment (MCI) and biomarkers

There is evidence to show that these pathological changes begin many years prior to the onset of dementia.[61] The challenge for physicians would be to identify subtle changes in cognition when the pathological changes are only beginning to develop. These earlier stages of disease have been described using several terminologies including mild cognitive impairment (MCI) and cognitively impaired not demented (CIND).[62-63]

Of the various classification systems, the Mayo Clinic's mild cognitive impairment (MCI) has received the most attention. Its pathological validity is supported by conversion rates to dementia of approximately 12% annually and 80% at six years of follow-up. Originally, MCI diagnosis required the presence of memory complaint (preferably corroborated by an informant), objective memory impairment for age, essentially preserved general cognitive function, normal functional activities and no dementia. The heterogeneity within MCI has lead to the proposal of a new classification system, based predominantly on neuropsychological profiles and includes amnestic or single memory MCI, multiple-domain MCI and single non-memory MCI.[63] However, the existing clinical criteria for diagnosis of MCI are subjective, variable in operationalisation, and highly dependent on clinical judgment. They are also unable to reliably predict who amongst those with MCI would progress to dementia. Thus, the differentiation between normal cognitive aging and MCI (especially the early stages of MCI) would be extremely challenging using only clinical methods. This has prompted research into the use of more objective neuroimaging (structural and functional), cerebrospinal fluid (CSF), genetic and molecular biomarkers which reflect AD pathogenesis,[64] to complement clinical approaches towards an early and accurate diagnosis of AD. Initial drug trials have not shown clinical benefit, likely related to the heterogeneity of this MCI entity. These issues currently render MCI to be mainly a research entity at this moment. When used in the clinical context, the physician should explain the lack of homogeneity within the diagnosis of MCI, the variable conversion rates to dementia and the lack of current evidence for the pharmacological treatment of MCI.

This has prompted revisions in the upcoming DSM-V due in 2013[65] which include major and minor neurocognitive disorder classification. The proposed revision of NINCDS-ADRDA criteria for AD is to include prodromal AD and preclinical AD which characterises earliest stage of AD (with the aid of biomarkers) that predate crossing of the dementia threshold of functional disability.[66-67]

3.5 Role of genetic testing in dementia

GPP Genetic testing should not be routinely carried out in the clinical evaluation of dementia.

GPP

B Routine testing of APOE (Apolipoprotein E) gene is not recommended in dementia diagnosis and in tailoring dementia risk reduction.

Grade B, Level 2^{++}

There is currently no evidence for routine testing of APOE (Apolipoprotein E) in dementia diagnosis and tailoring dementia risk reduction. There is a body of evidence that APOE ε4 is strongly associated with late-onset Alzheimer's Disease (AD) and that when present may represent an important risk factor for the disease. However, at the present time, it is not recommended for use in routine clinical diagnosis nor should it be used for predictive testing.

a. APOE genotyping does not provide sufficient sensitivity or specificity to be used alone as a diagnostic test for AD.[68] It is therefore not recommended as a diagnostic tool in routine clinical evaluation of patients for sporadic early- and late-onset AD.[68-74]

b. Based on presently available data, APOE genotyping is not established as a predictive marker of AD. There is currently inconsistent or contradictory evidence for APOE testing to assist with tailoring risk reduction recommendations for dementia.

c. Also susceptibility testing in asymptomatic individuals may be associated with potential psychological harm.[75-76]

4 Pharmacological Management of Dementia

4.1 Overview

GPP Pharmacotherapy should be part of a multi-pronged strategy to dementia management that encompasses a well-established diagnosis and consideration of stage-specific challenges, such as education of patient and caregiver, non-pharmacological measures and comprehensive caregiver psychosocial intervention.

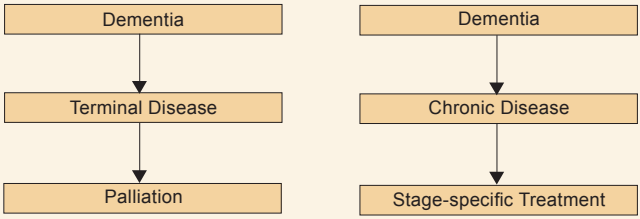
GPP

GPP Pharmacotherapy should not be used in isolation in the management of dementia but in conjunction with non-pharmacological management including education and counselling of patient and caregiver.

GPP

In the past, dementia was often perceived as a terminal illness for which the main focus of treatment is palliation. Increasingly, there is a paradigm shift towards treating dementia as a chronic disease, not unlike conditions like diabetes mellitus, where specific treatment goals can be formulated depending on the stage of the disease (Figure 1).[77] In the mild stage, the focus is on maintenance of patient independence and autonomy, whereas in the advanced stages, care and psychosocial issues predominate. Thus, a comprehensive multi-pronged strategy to dementia management involves skilful adjustment of pharmacotherapy depending on the stage of disease, done in conjunction with caregiver education, non-pharmacological measures and comprehensive caregiver psychosocial intervention.

Figure 1: Paradigm shift in dementia treatment



Pharmacological interventions can be broadly classified in the following categories:

- Reverse or stabilize the underlying disease
- Improve cognitive symptomatology (cognitive enhancers and ancillary treatment)
- Treat behavioural, mood or psychiatric symptoms associated with dementia

4.2 Pharmacological interventions to reverse or stabilize the underlying disease

GPP Patients with dementia should be screened and treated for reversible identifiable causes (such as depression, B_{12} deficiency and hypothyroidism) and vascular risk factors.

GPP

Pharmacological strategies to address the underlying disease include treating identifiable reversible causes, reduction of established risk factors, and disease modifying measures to slow the rate of disease progression (Table 3).[77]

Table 3 Possible pharmacological strategies to address underlying disease

1. Treating identifiable reversible causes
   - Treat depression (pseudodementia)
   - Replace deficiency states (e.g. B_{12} deficiency, hypothyroidism)
   - Correct metabolic abnormalities (e.g. hypocalcaemia, hypoglycaemia)
   - Treat infections (e.g. neurosyphilis)
2. Reduction of vascular risk factors
   - Hyperlipidaemia, hypertension, diabetes mellitus, smoking cessation, obesity
   - Anti-platelet agents for secondary stroke prevention
   - Anti-coagulation for atrial fibrillation and cardioembolic strokes
3. Slowing rate of disease progression (disease modifying)

It is now established that vascular risk factors are putative not only in vascular dementia, but also in Alzheimer's disease.[78] Vascular risk factors should thus be sought and appropriately managed in all dementia cases. However, it should be noted that whilst promising observational data exists, it remains to be shown in a randomised controlled clinical trial if any prevention strategy such as blood pressure reduction or antiplatelet treatment for the secondary prevention of stroke, will reduce the incidence of vascular or Alzheimer's dementia.[79-80]

While a search for reversible causes should be undertaken in all newly diagnosed dementia patients, in practice, only a small percentage of potentially reversible abnormalities are truly reversible, most notably conditions such as depression and hypothyroidism.[47] There are concomitant neurodegenerative causes such as Alzheimer's disease in many of these patients. Moreover, when significant neuronal damage has occurred, treatment of potentially reversible causes often arrests the underlying pathophysiology but does not reverse the dementia.

Over the last decade, there has been extensive research on disease modifying agents for the treatment of Alzheimer's disease. Agents targeting the amyloid pathway and the tau pathway are

currently undergoing phase 3 clinical trials. The outcomes of these clinical trials will determine the role of disease modifying agents in the management of dementia.

4.3 Cognitive enhancers

GPP The current evidence for the use of cognitive enhancers is generally based on clinical trials of up to 1 year duration. The use of cognitive enhancers for longer periods will need to include a detailed discussion with the patient and caregivers on the overall benefit of treatment and specific needs of the patient.

GPP

4.3.1 Alzheimer's disease

A Acetylcholinesterase inhibitors (donepezil, galantamine or rivastigmine) should be considered for the management of patients with mild to moderate Alzheimer's disease.

Grade A, Level 1^{++}

There are currently three acetylcholinesterase inhibitors (AChEI) regularly used for the symptomatic treatment of dementia: donepezil, galantamine and rivastigmine (Table 4). Clinical trials (the majority lasting one year or less in duration) involving the use of donepezil, galantamine or rivastigmine that are conducted in patients with mild to moderate Alzheimer's disease consistently demonstrate modest improvement in: (1) cognition and global functioning (on average, a 3-point difference on the 70-point Alzheimer's disease assessment scale over a 6-month period), (2) activities of daily living and (3) neuropsychiatric symptoms (delay in emergence of symptoms, improvement in apathy, and variable patterns of improvement for milder degrees of anxiety, depression and hallucination). [81-84]

It is unclear whether AChEI therapy confers benefit in terms of reducing time to institutionalisation.[85] Three studies that evaluated resource utilization and associated costs with donepezil use in Alzheimer's disease reported variable results.[85-87] However, economic evaluation studies are highly contextual depending on the health system, period of study, apportionment of costs (such

as costs of unpaid carer time), handling of missing data and the severity of dementia.

The duration of benefit may persist as long as three years in some patients.[88] AChEI may provide greater benefit when started as soon as dementia is diagnosed, rather than waiting until symptoms deteriorate further and become more prominent.[89] This is supported by results of open-label extensions of double-blind trials in which the placebo group showed improvement when switched to AChEI but did not "catch up" with the group that received AChEI since trial inception.[90] In addition, drug holidays can be associated with clinical deterioration that may not revert to baseline even on resumption of therapy.

A Acetylcholinesterase inhibitors may be considered for the management of moderately severe to severe Alzheimer's disease.

Grade A, Level 1^{+}

A Cochrane review showed that donepezil was effective in improving cognitive function in moderate to severe AD treated for up to 52 weeks; the benefits for patients on 10 mg/day dose of donepezil were only marginally larger than those on the 5 mg/day dose.[83] Another randomized controlled trial (RCT) reported that donepezil improves cognition and preserves function in individuals with severe Alzheimer's disease (Mini Mental State examination score 1-10) who were living in assisted care nursing homes.[91] In the SERAD (Safety and Efficacy of Reminyl in Alzheimer's Disease) study, galantamine improved cognitive function but not activities of daily living.[92]

A Where tolerated, acetylcholinesterase inhibitors should be titrated to recommended doses (5-10 mg/day donepezil; 16-24 mg/day galantamine; 6-12 mg/day oral and 4.6-9.5 mg/24 hr transdermal rivastigmine), which have been shown to confer greater benefit compared with lower doses.

Grade A, Level 1^{++}

To reduce intolerability to gastrointestinal adverse effects, AChEI are often started at lower doses (donepezil 2.5 mg/day; galantamine 8 mg/day; rivastigmine 1.5 mg twice daily) (Table 4). Studies have consistently shown that patients who received

recommended doses of AChEI exhibited better outcomes than those who received placebo or lower doses.[81-84] Thus, where tolerated, AChEI should be gradually titrated to recommended doses (5-10 mg/day donepezil; 16-24 mg/day galantamine; 6-12 mg/day oral and 4.6-9.5 mg/24 hr transdermal rivastigmine).

A N-methyl D-aspartate antagonists (memantine) may be considered for the management of moderately severe to severe Alzheimer's disease, either alone or in combination with acetylcholinesterase inhibitors.

Grade A, Level 1+

Pooled data indicate a beneficial effect of N-methyl D-aspartate (NMDA) antagonists (memantine) in mild to moderate Alzheimer's disease on cognition (2.97 points on the 100 point Severe Impairment Battery), global function, activities of daily living and behaviour at six months.[93] A study of moderate to severe Alzheimer's disease patients on stable doses of donepezil (5-10 mg a day) reported that the addition of NMDA antagonist (memantine) 20 mg a day slightly improved cognitive, functional and global scores at 6 months compared with placebo.[94] Further analysis of the same study revealed that NMDA antagonist (memantine) reduced agitation/aggression in patients who were agitated at baseline and delayed its emergence in those who were free of agitation at baseline.[95] However, the DOMINO study in patients with moderate to severe Alzheimer's disease who had progressed despite donepezil treatment found that adding NMDA antagonist (memantine) while continuing donepezil was not better than continuing donepezil alone in terms of cognition and function at 1 year.[96]

A N-methyl D-aspartate antagonists (memantine) may be considered for treatment of mild to moderate Alzheimer's disease, if acetylcholinesterase inhibitor therapy is contra-indicated, not tolerated or if there is disease progression despite an adequate trial of acetylcholinesterase inhibitor.

Grade A, Level 1+

A Cochrane review, based on three RCTs found that NMDA antagonist (memantine) (20 mg/day) showed a small beneficial effect on cognition at 24 weeks in mild to moderate Alzheimer's

disease but of a smaller magnitude (0.99 points on the ADAS-Cog) compared with AChEI.[93] There was no benefit in activities of daily living or behaviour. The DOMINO study which also included a group of patients with moderate Alzheimer's disease who had progressed despite donepezil treatment found that adding NMDA antagonist (memantine) upon discontinuation of donepezil confer benefits in cognition and function at one year compared with placebo.[96] Taken together, NMDA antagonist (memantine) may provide a treatment option if AChEI treatment is contra-indicated, not tolerated, or if there is disease progression despite an adequate trial of AChEI.

The initial dose of NMDA antagonist (memantine) is 5 mg once a day, with 5 mg increments at intervals of at least 1 week until a maximum of 20 mg daily.[97] It should be used with caution in patients with epilepsy and renal impairment, and the clinician should be aware of interactions involving commonly prescribed medications such as dextromethorphan and L-dopa.

4.3.2 Vascular dementia

A Acetylcholinesterase inhibitors have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia.

Grade A, Level 1+

Deficient cholinergic neurotransmission has been postulated to contribute to the cognitive impairment of vascular dementia. Three randomized, double-blind, parallel-group, placebo-controlled trials with a total of 2,193 people suffering from mild to moderate probable or possible vascular dementia have been published.[98-100] Donepezil, at doses of 5 or 10 mg a day was compared with placebo for 24 weeks. A meta-analysis that includes these studies showed that the donepezil treated patients had a statistically significantly improvement in cognitive outcome compared to placebo treated patients on the cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-Cog) as well as on the Mini-Mental State Examination (MMSE) at 12 and 24 weeks at both doses. However, in terms of global function and activities of daily living, patients showed a less uniform dose response.[101]

Donepezil was well tolerated; most of the side effects were transient and were resolved by stopping the medication.

Moreover, galantamine showed statistically significant improvements in cognition (ADAS-cog), global functioning (CIBIC-plus), activities of daily living (DAD) and behaviour (NPI) in patients with vascular dementia as well as patients with Alzheimer's disease and coincidental radiographic findings of cerebrovascular disease.[102] A further study on vascular dementia patients showed significant benefits for cognition and a measure of executive function but not in activities of daily living although there was trend for benefit in global function.[103]

Rivastigmine has been less extensively investigated but has also been shown to have significant cognitive benefits in vascular dementia[104] and on a measure of executive function in patients with vascular cognitive impairment no dementia.[105]

Thus, AChEI have been shown to be effective and safe for the treatment of cognitive symptoms in vascular dementia. However, no AChEI has been licensed for the treatment of vascular dementia due to concerns as to the aetiological heterogeneity of patients included in the trials as well as lack of consistent effects on domains other than cognition.

A N-methyl D-aspartate antagonists (memantine) have been shown to be of clinical benefit and may be considered for use in the management of mild to moderate vascular dementia.

Grade A, Level 1+

There have been 2 clinical trials of NMDA antagonist (memantine) in mild to moderate vascular dementia.[106-107] A Cochrane review[108] of these 6-month studies showed that whilst NMDA antagonist (memantine) improved cognition and behaviour the clinical global measures did not show a significant difference. There was no difference in drop-out or adverse event rates between treatment and placebo groups.

Thus, NMDA antagonist (memantine) has been shown to be effective and safe for the treatment of cognitive symptoms in vascular dementia. However, NMDA antagonist (memantine) has

not been licensed for the treatment of vascular dementia due to concerns as to the aetiological heterogeneity of patients included in the trials as well as lack of consistent effects on domains other than cognition.

GPP Appropriate treatment of vascular risk factors and lifestyle changes including a healthy diet and regular exercise is recommended for all patients with vascular dementia.

GPP

However, it should be noted that whilst promising observational data exists, it remains to be shown in a randomised controlled clinical trial if any prevention strategy such as blood pressure reduction, statins and antiplatelet treatment for the secondary prevention of stroke, or lifestyle modifications such as diet or physical activity, will reduce the incidence of vascular dementia.

4.3.3 Other dementias

4.3.3.1 Parkinson's disease dementia

B Acetylcholinesterase inhibitors may be considered for the management of cognitive and behavioural symptoms related to Parkinson's disease dementia.

Grade B, Level 1+

50-90% of patients with Parkinson's disease (PD) will develop dementia during the course of the disease. Recent evidence also suggests that PD patients with early stage disease are at risk of developing cognitive impairment and dementia. Managing dementia along with the motor symptoms will significantly improve the quality of life of patients with PD.[109] There is growing evidence that AChEIs are useful in the management of PD dementia. A RCT using rivastigmine demonstrated improvement in both cognitive scores (2.9 point difference on the 70-point ADAS-Cog, $p<0.001$, 1 point difference on the 30-point MMSE, $p=0.03$)[110] and activities of daily living (ADCS-ADL, $p=0.025$). An open label study with galantamine showed improvement in behavioural status among PD patients (NPI, $p<0.001$).[111]

4.3.3.2 Dementia with Lewy bodies

B Acetylcholinesterase inhibitors or N-methyl D-aspartate antagonists (memantine) may be considered for the management of cognitive and behavioural symptoms related to dementia with Lewy bodies.

Grade B, Level 1+

Patients having dementia with Lewy bodies commonly demonstrate extrapyramidal signs, dementia, fluctuating symptoms and vivid visual hallucinations. Both cognitive deficits and behavioural symptoms significantly contribute to a poor quality of life for patients and carers. A placebo controlled RCT of rivastigmine demonstrated improvement in behavioural scores (NPI, p=0.048).[112] In the same study, there was improvement in attention span, working memory and episodic memory.

In a RCT of 75 patients having dementia with Lewy bodies, comparing NMDA antagonist (memantine) with placebo, improvement in global cognition (ADCS-CGIC, p=0.023) and behaviour (improvement in delusions, p=0.021; hallucinations, p=0.015; appetite/eating disorder, p=0.032) were demonstrated.[113]

4.3.3.3 Frontotemporal dementia

B Selective serotonin reuptake inhibitors (SSRIs) may be considered for the management of behavioural symptoms related to frontotemporal dementia.

Grade B, Level 1+

C N-methyl D-aspartate antagonists (memantine) and acetylcholinesterase inhibitors may be considered for the management of cognitive and behavioural symptoms related to frontotemporal dementia.

Grade C, Level 2+

Frontotemporal dementia (FTD) is commonly seen in patients below 65 years of age. The predominant symptoms include behavioural changes and language difficulties.[114-116] Several SSRIs have demonstrated efficacy in improving behavioural symptoms among patients with FTD. In a RCT with Trazodone,

improvement in NPI scores (p=0.028) were evident.[117] In a randomized study with paroxetine, improvement in NPI scores and Cornell depression scores were noted.[118] In an open label study with fluvoxamine, improvement in the stereotypy inventory ($p< 0.01$) and NPI ($p<0.05$) were noted.[119] For the management of cognitive symptoms related to FTD, several open label studies have demonstrated benefit in patients who were treated with NMDA antagonist (memantine) with doses up to 20mg/day.[120] In an open label study of 16 FTD patients improvement on ADAS-Cog (p=0.02) was demonstrated. One open label study of rivastigmine demonstrated improvement in behaviour (NPI, $p<0.001$; Cornell, $p<0.001$)). In another open label study with galantamine in 39 FTD patients, improvement in global function was noted (CGI, p=0.009). When treating FTD patients with AChEIs, clinicians need to be weary of paradoxical worsening of behaviour. In one open label study of 24 FTD patients with donepezil, worsening in behaviour was observed in 4 patients on donepezil.[121] However a recent RCT of 81 patients did not demonstrate a clear benefit with NMDA antagonist (memantine).[122]

4.3.4 Treatment considerations

GPP The choice of acetylcholinesterase inhibitors should be based upon factors such as experience of the clinician, tolerance to side effects, ease of use, and the clinical profile of the individual to be treated.

GPP

There is no definite evidence to support a difference in clinical efficacy between the three available agents. A Cochrane systematic review found that all three AChEI were efficacious for mild to moderate Alzheimer's disease, with no significant differences between them.[81] The few head-to-head comparative studies are all industry sponsored, small, inconsistent in results, and offer little basis to make a clinical choice.[81, 123] The choice of AChEI therapy depends on the experience of the clinician, tolerance to side effects, ease of use, and the clinical profile of the individual to be treated (such as co-morbid diseases and drug interactions). For instance, where medication compliance is an issue, once-daily formulations would be helpful. For patients who

require medications to be crushed due to swallowing difficulties, the capsule formulations should be avoided (Table 4).

GPP The decision to initiate cognitive enhancers, such as acetylcholinesterase inhibitors or N-methyl D-aspartate antagonists (memantine), should be made in consultation with the patient and family after careful consideration of the expected magnitude of benefit, side effects, co-morbidities and costs of treatment.

GPP

Despite the evidence of efficacy from clinical studies, there is debate over whether AChEI and NMDA-antagonist therapy are cost effective, because the treatment effects are small and not always apparent in practice.[85, 93, 124] Cost-effectiveness issues become increasingly relevant in the advanced stages of dementia, since the magnitude of treatment benefit becomes less obvious and there are often competing demands on the available financial resources with regards to provision of care and placement. Until definitive findings are available, practitioners should continue to individualise treatment decisions for each patient.[77] For instance, where financial resources are limited, the opportunity cost of employing a maid to look after a patient requiring help with activities of daily living may override the modest benefits of symptomatic therapy.

For many, the diagnosis of dementia can be devastating and thus, individuals with dementia and their family may have high, sometimes unrealistic, expectations of any treatments offered. It is therefore important to communicate from the onset that:[77, 124]

- The medications are not a cure.
- The medications may not be effective for everyone.
- Although there may be a response in terms of modest improvement or stabilization of symptoms, symptomatic therapy ultimately does not prevent progression of disease and cognitive decline will continue even with treatment.
- The medication may be discontinued if the patient does not demonstrate stabilisation after an adequate trial of 3-6 months.

B Patients who are started on acetylcholinesterase inhibitors should be monitored for side effects such as nausea, vomiting, diarrhoea and anorexia, and bradycardia.

Grade B, Level 1+

The most common side effects with AChEI treatment are dose-related gastrointestinal side effects such as nausea, vomiting, diarrhea, and anorexia.[81, 83-84] These are transient and can often be alleviated by slower dose titration and taking the medication with food. Using healthcare databases from Ontario, Canada, Gill et al reported that the use of AChEI is associated with increased rates of hospital visits for syncope, bradycardia, pacemaker insertion and hip fracture in older adults with dementia.[125] Compared with AChEI, gastrointestinal-related side effects are uncommon with NMDA antagonist (memantine) use. A Cochrane review reported no significant differences in adverse events between NMDA antagonist (memantine) and placebo.[93] Adverse events of NMDA antagonist (memantine) include dizziness, headache, fatigue, hallucinations and confusion, but these tend to be transient.

GPP Patients who are started on cognitive enhancers should be assessed for cognition, mood and behaviour, and function within 3-6 months of starting therapy and thereafter, at least once yearly or as clinically indicated.

GPP

Stabilisation or modest improvement above baseline may be observed with cognitive enhancers in the first 6-9 months, followed a lesser decline thereafter.[126]

During follow-up, patients should be assessed using: (i) *clinical methods*, via assessment of cognitive, functional and behavioural domains through interview with the patient and caregiver; and/or (ii) *mental status tests*.

A trial of withdrawal of symptomatic treatment should be considered when the harm outweighs the benefit, and should be undertaken only after careful discussion with the patient and caregiver.[77, 127] Examples include intolerable or serious side effects, and progression of disease to the severe stages despite optimising treatment. The DOMINO study in patients with moderate to severe Alzheimer's disease who had progressed

despite donepezil treatment found that discontinuing donepezil was associated with slightly poorer cognition (1.2-1.9 points on the 30-item Standardized MMSE) and function at 1 year compared with continuation of donepezil or switching to NMDA antagonist (memantine).[96] Many patients, however, discontinue donepezil without obvious difficulty; and notably, only half the patients who were assigned to continue donepezil in this trial maintained their treatment for the entire 1-year study period, suggesting that many patients perceived that continuing the medication was not effective.[128]

4.4 Ancillary treatment

A Anti-inflammatory agents (such as non-steroidal anti-inflammatory agents and cyclo-oxygenase 2 inhibitors) are not recommended for the prevention of cognitive decline in Alzheimer's disease.[128-129]

Grade A, Level 1^{++}

B Prednisolone is not recommended for the prevention of cognitive decline in Alzheimer's disease.[130]

Grade B, Level 1^{+}

A Oestrogen is not recommended for the prevention of cognitive decline in women with Alzheimer's disease.

Grade A, Level 1^{++}

Contrary to evidence from epidemiological studies which suggests a protective role of oestrogens in Alzheimer's disease, evidence from randomized controlled trials supports the ineffectiveness of oestrogen for the treatment of Alzheimer's disease.[131-132] In addition, there are concerns about increased risk for heart attacks, strokes, breast cancer and thromboembolism with combination (oestrogen plus progestin) therapy.[133]

A Selegiline is not recommended for the treatment of core or associated symptoms in Alzheimer's disease.[134]

Grade A, Level 1^{+}

B High dose vitamin E (in excess of 400 IU per day) is not recommended for the prevention or treatment of Alzheimer's disease.

Grade B, Level 1+

One RCT reported a modest benefit of high dose vitamin E (2000 IU per day) in retarding progression in moderately severe Alzheimer's disease.[135] However, the result have not been replicated and more patients taking vitamin E suffered falls. A meta-analysis reported a slight but significant risk for all-cause mortality with vitamin E dosage ≥ 400 IU a day (risk ratio 1.04, 95% CI 1.01-1.07).[136] Both the NICE guidelines and Cochrane review concluded that vitamin E (2000 IU per day) had more risk of adverse events than benefit in the treatment of dementia.[137-138]

B Ginkgo is not recommended for the routine treatment of dementia.

Grade B, Level 1+

A Cochrane systematic review of 35 placebo-controlled RCTs (n=4247) of ginkgo biloba (120 mg to 240 mg/day) concluded that the evidence that Ginkgo biloba had predictable and clinically significant benefit in dementia was inconsistent and unconvincing.[139] The magnitude of benefit is smaller compared with AChEI.[140] In a recent study with a 5-year follow up, 120 mg standardised ginkgo biloba extract did not reduce the risk of progression to Alzheimer's disease compared with placebo in elderly patients with memory complaints.[141] Practitioners need to be mindful that the dose of the active ingredient may not be standardised and may differ among preparations. There are also clinically relevant drug interactions involving ginkgo, such as increased bleeding risk when combined with warfarin and antiplatelet agents, and the antagonism of thiazides and anticonvulsants (valproate and carbamazepine).[142]

A Omega 3 fatty acid is not recommended for the prevention or routine treatment of dementia.

Grade A, Level 1+

Two placebo-controlled RCTs did not demonstrate a benefit of omega-3 fatty acid in delaying the rate of cognitive decline in Alzheimer's disease.[143-144] In one study, subgroup analysis in

those with very mild cognitive dysfunction (MMSE >27) revealed a significant reduction in MMSE decline rate.[144] A Cochrane review did not show any benefit of omega-3 fatty acid in the prevention of dementia.[145]

A Statin therapy is not recommended for the prevention or routine treatment of Alzheimer's disease.

Grade A, Level 1++

A Cochrane review of 3 RCTs did not find any significant difference in cognition or global function between statin and placebo groups.[47] The LEADe study examined the effect of adding Atorvastatin 80 mg to donepezil in mild to moderate Alzheimer's disease (MMSE 13-25) but did not reveal benefit in the primary endpoints of cognition and global function at 72 weeks.[146]

A Folic acid and vitamin B supplementation are not recommended for the prevention and treatment of dementia in the absence of B vitamin deficiency.

Grade A, Level 1++

A Cochrane review concluded that there is no consistent evidence that folic acid alone or in combination with vitamin B12 had any effect on cognition and activities of daily living.[147] In the Alzheimer Disease Cooperative Study (ADCS), high dose vitamin supplements (5 mg/day folic acid, 1 mg/day vitamin B12, 25 mg/day vitamin B6) for 18 months did not confer benefit in cognition in mild to moderate AD.[148-149] There was an excess number of adverse events, especially depression, in the high-dose group (NNH=10, p=0.02).

A Rosiglitazone is not recommended as monotherapy or as adjunctive therapy to cholinesterase inhibitors in mild to moderate Alzheimer's disease.

Grade A, Level 1+

There was no evidence of efficacy of 2 mg or 8 mg Rosiglitazone extended-release monotherapy in cognition or global function after 24 weeks in a phase 3 study.[150] Similarly, Rosiglitazone did not improve cognition or global function at 48 weeks when used as adjunctive therapy to AChEI in two other phase 3 RCTs in mild-to-moderate Alzheimer's disease.[151] There was no evidence of an interaction between treatment and APOE status in all three studies. Oedema was the most common side effect with rosiglitazone treatment; anaemia and heart failure were also common in the rosiglitazone group compared with placebo.

Table 4 Dosing recommendations of cognitive enhancers in clinical use**

Medication	Forms	Starting Dose	Titration	Example of titration schedule
(1) Cholinesterase inhibitors				
Donepezil (Aricept®)	Tablet (5mg, 10mg)	2.5 – 5mg once daily	Increase to 10mg/ day after 4-8 weeks	2.5mg om → 5mg om → 10mg om
Rivastigmine (Exelon®)	Capsule (1.5mg, 3mg, 4.5mg, 6mg) Patch (4.6mg/24h, 9.5mg/24h)	1.5mg bid after meals 4.6mg/24h once daily	Increase by 1.5mg bid every 2-4 weeks up to 6mg bid Increase to 9.5mg/24h after 4 weeks	1.5mg bid → 3mg bid → 4.5mg bid → 6mg bid 4.6mg/24h → 9.5mg/24h
Galantamine (Reminyl®)	IR Tablet (4mg, 8mg, 12mg)* PR Capsule (8mg, 16mg and 24mg)* Solution (4mg/ml; 100ml bottle)†	4mg bid after meals‡	Increase by 4mg bid every 4 weeks up to 12mg bid‡	4mg bid → 8mg bid → 12mg bid‡
(2) NMDA antagonists				
Memantine (Exiba®)	Tablet (10mg)	5mg once daily	Increase by 5mg every 1-2 weekly up to 10mg bid Increase by 5mg every 1-2 weekly up to 20mg om	5mg om → 5mg bid → 10mg om 5mg on → 10mg bid 5mg om → 10mg om → 15mg om → 20mg om

* IR: immediate release; PR: prolonged release once-a-day formulation.

† Solution can be mixed with non-alcoholic beverage, but must be consumed immediately.

‡ Dose expressed in terms of immediate release formulation. To calculate the equivalent dosing for the PR formulation, simply add up the total daily dose e.g. galantamine 4mg IR tab bid = galantamine 8mg PR cap once daily; galantamine 8mg IR tab bid = galantamine 16mg PR cap once daily.

** For information, doctors should check the medication labels for updates to dosages occurring after the publication of this clinical practice guideline.

4.5 Caregiver interventions

Psychosocial interventions are targeted at both the person with dementia as well as the family caregiver. The goal is to enable appropriate care to be given according to the needs of the person with dementia and his caregiver, and these needs vary depending on the unique backgrounds of the person with dementia and his caregiver, the systems in their ecological space and the effects of the disease on the person with dementia. Interventions for family caregivers are important for the following reasons:

1) The person with dementia is, by nature of the disease, largely unable to help himself, care needs to be delivered through the caregiver
2) Caregivers need to be empowered with the necessary knowledge and skills, and psychosocial support to facilitate them in their task.
3) Caregivers who face much negative consequences as a result of long-term caregiving need to be helped and supported.

Caregiver intervention can take several forms and they include:
1) Individual and family counselling
2) Home based intervention
3) Caregiver support group
4) Technology-based interventions
5) Respite care
6) Psychoeducation and skills training for family caregivers, professional caregivers and domestic helpers.

A Multi-component and individualised caregiver interventions should be considered for holistic dementia care.

Grade A, Level 1+

In the past decade, caregiver interventions have adopted improved methodologies and yielded promising results. In particular, the NYU spouse-caregiver intervention and the REACH (Resources for Enhancing Alzheimer's Caregiver Health) initiatives are noteworthy.[152-155] These randomized controlled studies provide evidence that caregiver interventions can reduce caregiver burden and depression, ease caregiver reaction to behavioural problems and delay nursing home

placement. Home based interventions, in the form of nurse led case management and community based occupational therapy have been shown to be beneficial with respect to improving caregiver well being, and reducing caregiver burden and ratings of behavioural problems in the person with dementia.[156-159]

Several meta-analyses and systematic reviews[160-165] have also found that caregiver interventions improve caregivers' mental health and well-being, reduce caregiver burden and delay institutionalization for the person with dementia. Specifically, support groups as well as psychoeducational interventions help to alleviate depression and improve psychological well being. However, no one approach is necessarily sufficient to meet the varied needs and situations of individual caregivers. Therefore, multi-component interventions have a greater effect than narrowly focused ones. A support system that is tailored to the particular needs of different caregivers, and be able to provide on-going responsive and continuous support, is most beneficial.

In addition, technology-based interventions such as web-based learning, on-line discussions and support groups, and telecommunications systems have burgeoned in the last decade.[166-168] Improvements in caregiver outcomes like depression and strain have been demonstrated in interventions involving technology. Caregivers also report they find the on-line resources useful and appreciate the ability to communicate with each other and health care professionals. Given the rapid advancement and easy availability of technology, it should be harnessed more fully to make help available to more family caregivers in a continuous, timely and economical way.

GPP Where appropriate, respite care may be offered to relieve the burden of caregiving on caregivers of persons with dementia.

GPP

Respite care can take place in the home of the person with dementia or a daycare centre. It may also vary in terms of who provides care; trained staff, relatives of the patient or volunteers. The care provided can also differ in duration, ranging from a couple of hours to weeks. Caregivers often express the need for respite to allow them sometime to rest, rejuvenate and have some time

to themselves. The few studies published on respite care did not show improvements in caregiver burden, although improved caregiver satisfaction was reported.[169-170] A systematic review[20] failed to show any benefit in caregiver outcomes but as the review was only based on 3 studies that met inclusion criteria, it reflects the lack of high quality research rather than an actual lack of benefit. Nevertheless, it is noteworthy that a US study on a day care plus programme that provided care management and support to family caregivers in addition to day respite for elders resulted in reduced caregiver depression and fewer nursing placements.[171] It is hoped that more of such studies will be conducted to provide a stronger evidentiary base on the usefulness of caregiver respite and support services.

4.6 Cognitive training

Individualized and group-based programmes in cognitive training[172-173] and cognitive stimulation[174] have positive effects on improving and maintaining specific cognitive skills in people with dementia.[161] These specific cognitive gains do not usually generalize over the long term to other cognitive functions or practical life applications.[175]

Multicomponent cognitive interventions, enriched with physical exercise and training in activities of daily living, are beneficial in enhancing general cognition and quality of life for people with dementia and may delay their decline in cognitive function and skills in activities of daily living.[176]

There is emerging evidence that community-based occupational therapy, incorporating cognitive and behavioural strategies to train persons with dementia to compensate for cognitive decline, improves their daily functioning, increase their sense of competence, and decrease in their need for assistance in performing daily activities.[159]

B Therapy incorporating cognitive and behavioural strategies may be considered for persons with dementia.

Grade B, Level 1+

5 Management of behavioural and psychological symptoms of dementia (BPSD)

5.1 Non-pharmacological - BPSD

C Environmental design features may be incorporated in care facilities to reduce behavioural and psychological symptoms of dementia (BPSD) in people with dementia.[177]

Grade C, Level 2+

There is evidence that environmental features in special care units such as privacy and personalization in bedrooms, residential character, and an ambient environment that residents can understand are associated with both reduced aggressive and agitated behaviour and fewer psychological problems.

D Art therapy may be considered for persons with behavioural and psychological symptoms of dementia (BPSD).[178]

Grade D, Level 3

Art therapy groups effect significant positive changes in mood both immediately within sessions and later outside the sessions to impact behaviour such as mental acuity, physical involvement, calmness, and sociability in the day care/ residential care setting

B Reminiscence therapy (RT) may be considered for persons with behavioural and psychological symptoms of dementia (BPSD).[179]

Grade B, Level 1+

Reminiscence therapy (RT) involves the discussion of past activities, events and experiences, with another person or group of people. This is often assisted by aids such as videos, pictures, archives and life story books. Taking studies together, some significant results were identified: cognition and mood improved 4 to 6 weeks after the treatment, care-givers participating with their relative with dementia in a reminiscence group reported lower strain, and people with dementia were reported to show some indications of improved functional ability. But there is more quality research in the field.

C Persons with dementia may be encouraged to participate in structured exercise programmes to improve physical function.

Grade C, Level 2+

It is generally accepted that physical activities can be beneficial for the physical, emotional and cognitive domains of people of all ages. Structured exercises usually involve training in the domains of strength, balance, flexibility and endurance. Recent meta-analyses[180-181] suggest that structured physical exercises can be helpful in improving physical parameters such as functional mobility, endurance, balance and strength in persons with dementia. These benefits can go beyond physical parameters and include better outcomes in activities of daily living as well. However, the studies performed suffer from much heterogeneity in design and quality. Therefore, while exercise should be encouraged for persons with dementia, we need more studies to be clearer about the optimal frequency and intensity, the best combination of exercise components as well as the need for adaptation to the cognitive and functional level of the patient.

B Music therapy, wherever feasible, is encouraged in the care of persons with dementia and helps in ameliorating the behavioural and neuropsychiatric symptoms of dementia.

Grade B, Level 1+

Music therapy (MT) was defined by Munro and Mount (1978)[182] as the controlled use of music and its influences on the human to aid in the physiological, psychological and emotional integration of the individual during the treatment of illness or disability. While a Cochrane Review in 2004 stated the methodological quality of studies on the impact of MT on dementia was generally poor and no useful conclusions could be drawn, recent studies since then have revealed more encouraging data on the use of music MT. A review of nursing literature (involving 13 studies)[183] on the effect of MT for older people with dementia revealed the impact of MT in 3 ways:

1. Effects of music on agitated behaviours. MT reduced agitation, irritability, aggressive behaviour and anxiety.
2. MT and the role of carers. Although music therapists provide MT, other professional and family caregivers can

also provide MT to induce therapeutic effect. While background music could reduce aggression and agitation, the effect was intensified when caregivers sang.[184] Communication is enhanced as music and dance are interventions that convey gestures and emotions that go beyond simple words. Caregivers' distress is also reduced. Other positive findings included an increase in meaningful interactions among the patients, staff and family members.

3. The positive effects of music therapy on mood and socialization. Active music interventions may enhance life force through bio-physiological responses and through self-discovery, awareness, increased self-esteem and pleasure[185] Success in singing, playing instruments, moving to music, or sharing memories related to music may help to meet a person's unmet needs for self-expression, achievement and meaning in life (Clair and Bernstein, 1990; Tomaino, 2000).[186-187]

The review also concluded that the studies had numerous limitations, including the selection of the most effective number of participants to generalize findings, the length and quantity of the music therapy sessions, and the most appropriate timing and implementation of music therapy sessions for greatest effect on behaviour.

Other studies have demonstrated the effectiveness of MT, albeit with small sample sizes. A randomized control blinded study[188], showed that MT helped in anxiety and depression in mild to moderate Alzheimer's disease patients. While a randomized controlled study (unblinded)[189] showed that delusions, agitation, anxiety, apathy, irritability, aberrant motor activity, and night-time disturbances) significantly improved with MT. A nursing home study in Japan[190] which followed up the residents for two years showed that persons with moderate or severe dementia were able to participate in the group music therapy and also demonstrated that systolic blood pressure was lower in MT participants. Locally, a controlled naturalistic study[191] showed that a weekly structured music therapy and activity programme (over 8 weeks) helped to ameliorate behavioural and depressive symptoms in persons with dementia.

Overall, while there are limitations in the modality and implementation, MT forms a valuable therapeutic arm in positively influencing the behaviour of persons with dementia. Where possible, MT, as part of the holistic person centred approach, is encouraged in the care of persons with dementia.

B Aromatherapy is not recommended for reducing agitation in persons with Alzheimer's disease.

Grade B, Level 1+

A review of the evidence supporting the use of aromatherapy involved a search Medline, Cochrane, EMBASE and the reference lists of all relevant papers in English up to March 2007.[192] Eleven prospective randomised studies of aromatherapy in BPSD were identified. The aromatherapy oils tested, method of administration and outcome measures used varied widely across the studies. Most of the studies included very small numbers of patients and were designed in such a way that made interpretation of the findings difficult. The conclusion was that evidence supporting the efficacy of aromatherapy is scarce; the available studies reported positive and negative consequences for both people with dementia and their caregivers.

More recent noteworthy studies include:

1. A study done on 70 patients in Hong Kong[193] using Lavender (through aroma diffusers at night) in a cross-over randomized trial, This showed a decrease in agitation after 3 weeks of treatment with Lavender. The authors concluded that lavender was effective as an adjunctive therapy in alleviating agitated behaviours in Chinese patients with dementia.

2. A observational cohort study on 28 patients done in Japan[194] using a combination of rosemary and lemon essential oils in the morning and lavender and orange in the evening. These were diffused into the room using fans. All patients showed significant improvement in personal orientation related to cognitive function. There were no side effects and no change in the burden scores in the caregivers.

3. A study done in England enrolled the largest cohort included in a study on aromatherapy in dementia (114 patients). The

study was a double-blind parallel-group placebo-controlled randomized trial across 3 specialist old age psychiatry centres in England. The efficacy of Melissa oil[195] (Melissa Officinalis) in reducing agitation was compared with donepezil in care home residents with Alzheimer's disease. Raters wore nose clips to ensure full blinding. Aromatherapy was administered by massaging the oil into the hands and upper arms. At the end of 12 weeks, there were substantial improvements in all three group; however, there was no evidence that melissa aromatherapy was superior to placebo or donepezil, in the treatment of agitation in people with Alzheimer's disease. The authors also commented that the sizeable improvement in the placebo group emphasized the potential non-specific benefits of touch and interaction in the treatment of agitation in people with Alzheimer's disease.

B Massage therapy could be considered in reducing agitation in persons with Alzheimer's disease.

Grade B, Level 1+

The effect of massage therapy in reducing agitation has been demonstrated by several studies albeit with small cohort sizes.[196-197] This was also highlighted in a recent large RCT[195] on aromatherapy whereby the improvement demonstrated in the placebo group was attributed to the importance of touch and interaction in reducing agitation. A previous paper[198] also showed the synergistic effect of aromatherapy and massage in reducing agitation. Larger studies over a longer period will help further consolidate the efficacy of massage therapy.

A Multisensory stimulation is not recommended in the care of elderly patients with dementia.

Grade A, Level 1+

A recent review did not demonstrate any efficacy of multisensory stimulation (MSS) on behaviour and mood in dementia.[199] Two earlier RCTs (2003, 2001) by Baker[200-201] also showed MSS was found to be no more effective than an activity in changing the behaviour, mood or cognition of patients with dementia in the short- or long-term. A recent study by Milev[202] (2008) however, did show that patients had overall global improvement as well as

direct observations in a 24 week study on the effect of MSS. Overall, a recent review of evidence showed no efficacy of multisensory stimulation (MSS) on behaviour and mood in dementia.[199]

5.2 Pharmacological interventions to manage behavioural and psychological symptoms of dementia (BPSD)

5.2.1 Antidepressants

GPP Antidepressants may be used for the treatment of comorbid depression in dementia provided their use has been evaluated carefully for each patient.

GPP

The use of antidepressants for patients with dementia and depressive symptoms is common, however, their efficacy on depression and cognitive function is weak.[203-204]

Evidence for use of older tricyclic antidepressants (clomipramine and imipramine) is weak.[203] Selective serotonin reuptake inhibitor's (SSRIs) which are commonly used to treat depression in the elderly does not appear effective in the treatment of neuropsychiatric symptoms of dementia other than depression.[203-204]

5.2.2 Antipsychotics

A Antipsychotic medications may be considered in the treatment of behavioural and psychological symptoms of dementia when clinically appropriate and non-pharmacological management has not been useful.

Grade A, Level 1^{++}

Conventional antipsychotics have been used to treat behavioural problems associated with dementia. There is evidence for slight benefit of haloperidol over placebo for treatment of aggression. However, adverse events of extrapyramidal side effects and somnolence may limit its routine use.[204]

Since their introduction, the use of the atypical antipsychotics has become much more common than the typicals due to their generally favourable side effect profile The atypical antipsychotics, olanzapine and risperidone have been shown to have some benefits (although with small effect size) in the management of behavioural problems in patients with moderate to severe dementia at doses of olanzapine at 5-10 mg/day and risperidone 1.0 mg/day.[204-206] There is some evidence of quetiapine at doses of 25-100 mg/day showing improvement in agitation scores.[206-207]

B Potential side-effects and risk/benefit ratio of antipsychotic medication should be discussed with patients and/or caregivers.

Grade B, Level 2+

Adverse effects of somnolence (5-8 times greater) and gait disturbance is 7.5-11 times more common in olanzapine-treated group compared to placebo.[208] Serious adverse events occurred in 16.8% of risperidone versus 8.8% of placebo group, including 5 strokes and 1 transient ischaemic attacks, all in risperidone group.[209] Meta-analysis of adverse events performed showed 3-fold statistically increased risk of cerebrovascular adverse events with risperidone and olanzepine.[210] Similarly, in 2005 the FDA issued warnings for aripiprazole regarding the risk of CVAEs (cerebrovascular adverse events), including stroke, in elderly patients with dementia.[211-212]

Another meta-analysis comparing risk of death with atypical antipsychotics (aripiprazole, olanzapine, risperidone and quetiapine) with placebo showed increased risk of death (OR 1.54, 95% CI 1.06-2.23) with number need to harm = 100 (95% CI 50-250).[213] Other serious adverse events reported included somnolence and metabolic complications of hyperglycaemia and weight gain.

A recent retrospective cohort study had shown increased mortality among subjects using conventional antipsychotics compared to atypical antipsychotics.[214]

5.2.3 Mood stabilisers

A Routine use of mood stabilizers, such as carbamazepine and sodium valproate, is not recommended for treatment of behavioural symptoms associated with dementia.

Grade A, Level 1+

There is no improvement in behavioural symptoms with mood stabilizers (carbamazepine and sodium valproate).[204]

5.2.4 Benzodiazepines

There is no evidence of the efficacy of benzodiazepines in the treatment of behavioural problems associated with dementia.

There are no systematic reviews or randomised controlled trials of the use of benzodiazepines in the management of behavioural symptoms of dementia.

5.2.5 Treatment considerations

GPP An individualized approach to managing behavioural problems in dementia patients is required.

GPP

GPP Acetylcholinesterase inhibitor therapy may be considered in treatment of patients with behavioural problems if antipsychotics are inappropriate.

GPP

GPP The decision to start antipsychotic therapy to control behavioural problems in dementia patients should be made in consultation with the patient and family, after careful consideration of the benefit, adverse-effects and co-morbidities.

GPP

In view of the potential adverse effects associated with antipsychotic therapy, non-pharmacological interventions and identification of pain and other environmental factors should be assessed and managed accordingly.

If the above fails and the behavioural problems are assessed to be significant causing difficulty in caring process (medically and functionally) with significant amount of caregiver distress, there has to be a discussion with the family members with regards to antipsychotic therapy, with the attendant risks of adverse effects (extrapyramidal side effects, somnolence, stroke, metabolic complications), especially in those patients with risk factors for cerebrovascular disease.

A recommended algorithm for management of neuropsychiatric symptoms of dementia is available (see Figure 2).

B For patients with dementia with Lewy bodies and behavioural problems, when considering the use of pharmacotherapy, acetylcholinesterase inhibitors should be considered first for management of the behavioural problems.

Grade B, Level 1+

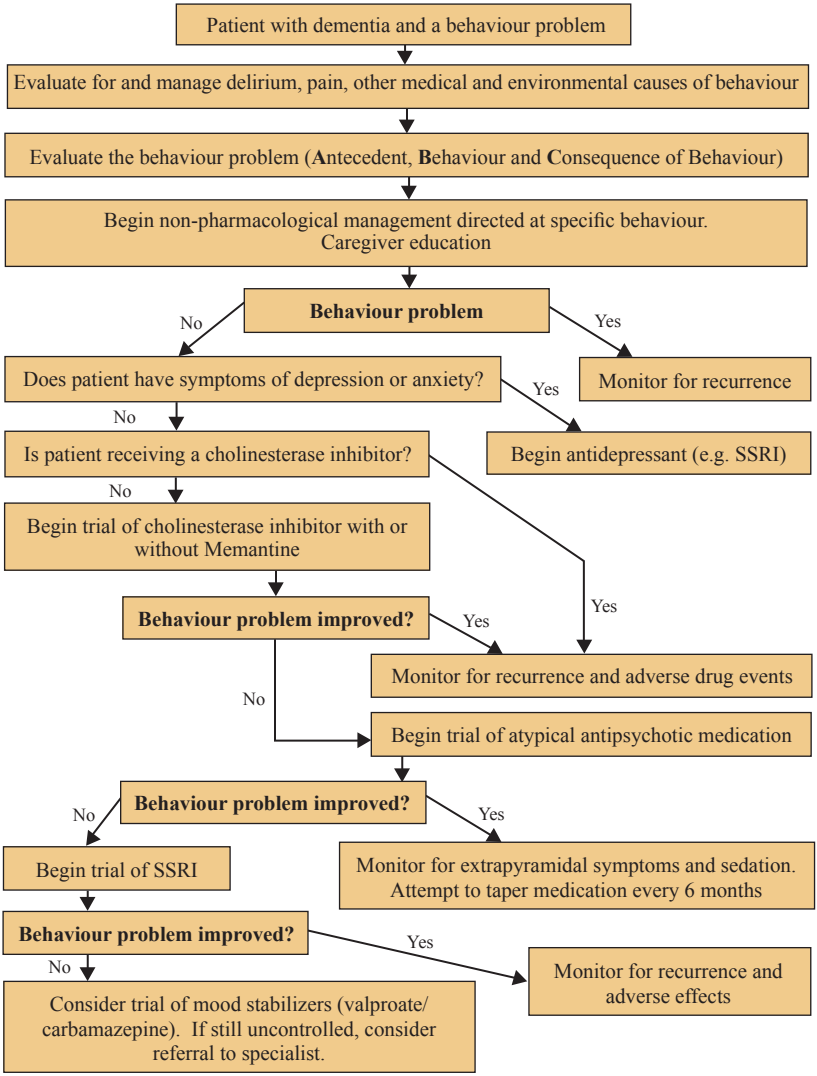
Antipsychotic medication should be used cautiously in patients suspected to have dementia with Lewy bodies as these patients have marked sensitivity to neuroleptic agents, including life-threatening neuroleptic malignant syndrome.[215]

There is evidence of improvement of neuropsychiatric symptoms with rivastigmine therapy in dementia with Lewy bodies patients (see earlier section on acetylcholinesterase inhibitors treatment on dementia with Lewy bodies).

GPP In all patients started on antipsychotic medication, they should be monitored carefully for side effects and response to treatment. In patients who are stable, antipsychotic withdrawal should be considered.

GPP

Figure 2 Algorithm for management of neuropsychiatric symptoms of dementia



SSRI = selective serotonin reuptake inhibitor
Adapted with permission from Sink KM et al. JAMA 2005;293; 596-608. Recommended algorithm for management of neuropsychiatric symptoms of dementia.

6 Ethical and legal issues

6.1 Preamble

Dementia is a clinical syndrome characterized by global cognitive decline and impairments, which can result in a loss of a patient's individuality and autonomy. At different stages, the disease causes different extents of functional decline, and different severities in behavioural and psychiatric symptoms. The disease also results in varying extents of impairments in decision-making capacity, and at some point, a patient becomes mentally incompetent and ceases to be an autonomous agent.

Nevertheless, person-centred care that emphasises the dignity and autonomy of the patient, should be upheld at all stages irrespective of the patient's functional status. Therapeutic goals and treatment options that are coherent and appropriate to patient's functional status should be individually tailored and adjusted at different stages of dementia, with an emphasis on quality for life of the patient, as well as the caregiver. The important question to ask for each individual patient is therefore what value of life holds for the patient, and directed at how life is experienced by the patient under the contextual circumstances specific to the patient. It is important to distinguish such evaluations from morally inappropriate social-worth evaluations, which base treatment decisions on an individual's ability to contribute to society.[216] The general ethical imperative must be to delay, prevent, stabilise dementia, but not to protract life and morbidity artificially in the severe stages of the disease.[217]

6.2 Decision-making

GPP Persons with dementia deemed to have decision making capacity (after clinical evaluation) are encouraged to make a Lasting Power of Attorney (LPA).

GPP

Information on how to make a Lasting Power of Attorney (LPA) can be found on the Office of Public Guardian website (http://www.publicguardian.gov.sg/).

1. Respect for autonomous decision making is a fundamental ethical and legal right of a mentally competent individual. This right of self-determination should be respected to the fullest possible extent, even in dementia or conditions associated with cognitive impairment.
2. When affected by dementia, the key to a patient's right of autonomy is the presence of adequate decision-making capacity. As a patient's cognition and hence functional abilities for decision making is impaired in dementia, a patient may or may not possess adequate decision making capacity to make an informed choice.
3. A diagnosis of dementia per se, however, does not automatically imply a loss of decision making capacity, which is specific to each patient and to each medical decision. Therefore, those who cannot comprehend complex situations may still possess the capacity to make simple decisions, or to convey their opinions regarding the burdens and benefits of ongoing treatments.
4. In deciding if a patient with dementia possesses adequate capacity with respect to making a particular decision, a clinical evaluation of the following functional abilities should be made:[218]
    a. Ability to express a choice
    b. Ability to understand information provided
    c. Ability to appreciate significance of information and relevance to self
    d. Ability to manipulate information rationally before arriving at a decision

    This is aligned with the principles set out by the Mental Capacity Code of Practice 2008. The Act seeks to balance a person's right to make his own decisions and the need to protect him where he lacks mental capacity to make those decisions (Code of Practice, Mental Capacity Act 2008, Chap 3 Para 3.1.1).

    It sets out 5 statutory principles that anyone making any decision or taking any action for a person who appears to lack capacity must apply (Code of Practice, Mental Capacity Act 2008, Chap 3 Para 3.1.2).

Principle 1: A person must be assumed to have capacity unless it is established that he lacks capacity.

Principle 2: A person is not to be treated as unable to make a decision unless all practicable steps to help him to do so have been taken without success.

Principle 3: A person is not to be treated as unable to make a decision merely because he makes an unwise decision.

Principle 4: An act done, or a decision made, under this Act for or on behalf of a person who lacks capacity must be done, or made, in his best interests.

Principle 5: Before an act is done or decision is made, regard must be had to whether the purpose for which it is needed can be as effectively achieved in a way that is less restrictive of the person's rights and freedom of action.

The statutory principles help the individual to take part as far as possible, in making decisions that affect him and protects him when he lacks capacity to do so. The idea is to assist and support people to make particular decisions, not restrict and control them.

Everyone should apply the statutory principles when dealing with or caring for (paid or unpaid) persons with capacity issues. When acting or taking decisions on behalf of a person who lacks mental capacity, these principles should be read alongside the provisions in the Act to ensure that the appropriate action or decision is taken in each case (Code of Practice, Mental Capacity Act 2008, Chap 3 Para 3.2).

5. If the patient lacks adequate decision making capacity, the ethical imperative switches to one that aims to protect the patient from his or her own harmful decisions or actions. Patients must not be under-treated nor forced to receive inappropriate treatment just because they lack decision making capacity or legally appointed guardian(s).

Consideration of the patient's functional status and quality of life is vital in making treatment decisions for the patient.

6. In Singapore, treatment decisions for a patient who is incapable of giving a valid consent will be made:
   a. in immediate, life threatening emergencies by doctors, based on the principle of medical necessity
   b. in less emergent situations, by:
      i. a donee of a Lasting Power of Attorney with power to make health care decisions if the patient lacks capacity to make those decisions for himself.[219]
      ii. a deputy appointed by the court to make such decisions for the patient who has lost capacity and has no donee to do so.

         These powers are, however, subject to restrictions (section 13 for donees[220] and section 25 for deputies[221]) and excluded decisions (section 26[222]) mentioned in the Mental Capacity Act (MCA).
      iii. the doctor, in accordance to principle of best interests (section 6 of the Mental Capacity Act). Nevertheless, this does not exempt the doctor from communicating with patient's family members and caregivers, so as to incorporate patient's known values and established preferences in the determination of patient's best interests.[223] The opinions and sentiments of the patient's family ought to be sought, but they are not legally binding.[139]
7. For patients adjudged clinically to have permanent and global decisional incapacity as a result of dementia, decisions about health care will be recurrent over their remaining lifetime. Therefore, when such issues arise, the attending physician should find out if there is any donee with the relevant powers appointed by the patient under the Lasting Power of Attorney. And if not, whether or not an application should be made for a deputy to be appointed by the court to make such decisions for the patient who has lost capacity.

6.3 Genetic testing

B Routine testing of APOE (Apolipoprotein E) gene is not recommended in dementia diagnosis and in tailoring dementia risk reduction.

Grade B, Level 2^{++}

1. As with any medical test, the decision regarding the utility of a genetic test should take into consideration the benefits to the individual patient and the ways that a test result would modify the care that the patient would receive.
2. As in any genetic testing, especially in pre-symptomatic susceptibility testing, individuals must be clearly informed regarding:[224]
   a. potential for severe psychological complications of testing positive for an incurable, devastating illness
   b. potential ramifications in the area of employment and medical insurance
   c. probabilistic implications of a positive test on genetically related family members, who may not have participated in any counselling or consented to testing

APOE ε4

3. There is a body of evidence that APOE ε4 is strongly associated with late-onset Alzheimer's disease (AD) and that when present may represent an important risk factor for the disease. APOE genotyping has its uses in research settings e.g., (a) stratifying patients with MCI at risk for progression (b) evaluating therapeutic efficacy in clinical research on the basis of pharmacogenomic studies. However, at the present time, it is not recommended for use in routine clinical diagnosis nor should it be used for predictive testing.

   Clinical diagnosis

   APOE genotyping does not provide sufficient sensitivity or specificity to be used alone as a diagnostic test for AD.[68] It is therefore not recommended as a diagnostic tool in routine clinical evaluation of patients for sporadic early- and late-onset AD.[68-72, 74, 217, 225]

Predictive testing

Currently, while widespread APOE genotyping is not advocated for susceptibility testing of AD, this paradigm may change in future. This is due to the following reasons:
(1) Potentially modifiable AD risk factors in asymptomatic middle-aged persons. Recent epidemiological and meta-analyses sampling diverse geographical, racial and socioeconomic groups have brought to light various AD risk factors that appear to be relatively robust and amenable to modification.[226] These include (i) cardiovascular risk factors of hypertension, diabetes/pre-diabetes, hyperlipidemia, metabolic syndrome, sedentary lifestyle which may promote both AD and cerebrovascular pathology (ii) suboptimal early education and cognitive stimulation in adulthood (iii) dystrophic patterns of circulating sex hormones and other endocrine factors (iv) inadequate nutrition (v) traumatic brain injury, and (vi) psychological distress (chronic anxiety, late life depression). Current medical literature provide examples wherein presence or absence of the APOE ε4 affect the strength of associations of putative modifiable risk factors with development of AD.[227]

(2) To date, disclosure of ε4-positive status does not appear to confer psychological or social harm to cognitively intact, middle-aged individuals seeking personal AD risk estimation. While there had been previous concerns that awareness of positive ε4 allele status might precipitate anxiety, depression or suicidal ideation in asymptomatic individuals, a recent study has not borne out these fears. REVEAL[76] was a randomised control trial designed to evaluate the effect of APOE genotype disclosure for AD risk assessment in well educated adult children of individuals with clinical diagnosed or autopsy confirmed AD. In this study, genetic counselling was provided prior to testing followed by random assignment to receive or not to receive the results. Subjects in the disclosure group who were ε4 positive did not have significantly more depression, anxiety or test related distress than those who were ε4 negative at 6 weeks and 12 months. In addition, feedback of ε4 positive status did not appreciably enhance perception of vulnerability compared with the control arm matched for life-risk estimate. It was noted that larger studies with longer

follow-up are needed to detect effects such as delayed emotional repercussions and injudicious life decisions. It was also noted the results of the trial could not be applied to younger or less educated subjects.

In addition, this study also revealed that subjects testing positive for ε4 were more apt to make at least one behaviour change to reduce AD risk when compared with ε4-negative and control participants.[228] In a related study, Fanshawe et al.[229] observed similar behavioural changes that correlated with estimated AD risk and the status of APOE 34 in 162 asymptomatic first-degree relatives of patients with AD. These seminal observations suggest that awareness of AD risk in general, and APOE status in particular, may motivate healthy midlife adults to initiate activities that might protect against the disease.

To summarise, in future, while there may arise indications for APOE testing for presymptomatic mid-lifers who (i) are actively inquiring about personal dementia risk and strategies for mitigations and (ii) have one or more modifiable AD risk factors which are potentiated or muted by the influence of APOE;[227] the current recommendation is to await the results of large scale epidemiological and clinical trials linking modifiable AD susceptibility factors and therapeutic responsiveness to the genetics of APOE and other risk alleles as well as societal impact. Perhaps only then, a clinical decision can be made on the role and use of susceptibility testing of APOE genotype for AD.

Therefore, susceptibility testing in asymptomatic individuals is currently not recommended.

6.4 Driving

D The judgement with respect to the ability to drive safely of a person with dementia should only be made after a systematic and comprehensive assessment.

Grade D, Level 4

D In general, persons whom the physician is unsure if the diagnosis of cognitive impairment might affect driving safety should be referred for further clinical and driving assessment.

Grade D, Level 4

1. Driving a motor vehicle is a complex task that requires the simultaneous and coordinated application of different cognitive abilities including ability to recall and apply traffic rules, sound judgement, attention span, and quick responses. A person's ability to drive safely can therefore be affected in dementia,[230-231] with consequently higher risk of accidents.[232-233]
2. Driving also represents independence, freedom and mobility. The issue of driving in dementia requires therefore the balancing of individual freedom and patient confidentiality on one side versus public and patient safety on the other.[234]
3. Dementia adversely affects driving performance even in its mild stages, although some persons with late-onset Alzheimer's disease appear capable of driving safely for some time after disease onset.[231] A diagnosis of dementia therefore does not automatically mean that a person is incapable of driving.[231, 235-236] The decision should be based on dementia severity or a demonstration of impaired driving competence.[231]
4. Longitudinal data suggests that driving performance deteriorates as the severity of dementia progresses over time,[237] primarily in early dementia. In one study, drivers with AD at a severity of CDR 1 were found to pose a significant traffic safety problem both from crashes and from driving performance measurements.[231] A more recent longitudinal study reported that persons with mild AD remained safe for an average of 11 months while those with very mild AD remained safe drivers for an average of 1.7 years.[238]
5. In patients with mild to moderate dementia, physicians find it difficult to identify which individuals should not drive. Performance-based measures of driving skills, such as on-road driving tests, are recommended as a means of assessing driving competency.[239-240] A traffic-interactive, performance-based road test that examines cognitive behaviours provides an accurate and reliable functional assessment of driving ability.[231]

6. Even if a driver with early dementia passes a road test, progression of the disease is expected to lead to deterioration in driving skills.[237] Therefore, repeat road testing at regular intervals, usually 6 to 12 months, or earlier if suggested by significant cognitive decline, is important.
7. For patients who are assessed to be unsafe for driving, doctors should initially enlist the help of family members to persuade patient to stop driving. To encourage such patients to surrender their driving licences, alternative forms of transport should be arranged, where possible.[241] If the patient is absolutely inflexible and insists on driving, thereby creating a reasonable risk to public safety, it is then ethically and professionally permissible for the doctor to breach doctor-patient confidentiality and file a report to the relevant licensing authorities (see point 8).[217] Other measures deemed to be ethical include hiding the patient's car keys or immobilising the car if necessary.[242]

8. The following are the recommendations from Medical Guidelines on Fitness to Drive[243] (Singapore Medical Association, 2nd Edition 2011) based on severity of dementia:

Group 1 Licence

Persons with moderated to advanced dementia should not be allowed to drive.

Persons with mild dementia should be referred for a formal driving assessment.

(a) If deemed safe, they should be allowed to drive; in some instances, restrictions such as driving only when accompanied, driving only during daytime hours and not driving on expressways, may be recommended.
(b) They should be reassessed at least every 6-12 months depending on the recommendations of the driving assessment. Families and caregivers need to observe for any warning signs that may indicate unsafe driving. Whenever there is a change in status noted, considerations should be given for earlier formal driving assessment or in certain cases, cessation of driving.

Group 2 Licence

Persons with dementia who exhibit behavioural disturbances that may pose a danger to driving (such as aggression, inadequate impulse control, psychosis e.g. hallucinations, fluctuating consciousness) should be considered unsafe for driving. These persons should not drive vocationally or operate any heavy goods vehicles.

9. Driving assessment centre for the cognitively impaired / dementia in Singapore is shown below:

1	Driving Assessment Rehabilitation Programme, Department of occupational therapy, Tan Tock Seng Hospital	11 Jalan Tan Tock Seng, Singapore 308 433	Tel. 63578338 / 63578339

6.5 Truth-telling of diagnosis to patient

GPP In general, the diagnosis of dementia should be disclosed to the patient, unless explicitly stated otherwise.

GPP

GPP In disclosure, the doctor should also be mindful of the impact the diagnosis can have on the patient's life and family relationships.

GPP

1. Although patients generally would like to know the truth about their own medical condition, the rights of those who do not want to know should also be respected. Health care professionals should therefore seek to understand their patients' preferences with respect to the diagnosis of dementia and act appropriately according to their choice.[58]
2. Studies have shown that the vast majority of patients with mild dementia wish to be fully informed.[59-60] Therefore, unless

a patient suffering from dementia explicitly declines to be informed of the diagnosis, the default mode should be to inform truthfully as it will enable the patient to:

   a. plan for optimal life experiences in remaining years of intact capacities
   b. designate and appoint a surrogate decision maker (donee of Lasting Power of Attorney as in the Mental Capacity Act) to take over the making of treatment decision upon eventual incompetence
   c. settle personal financial and legal matters
   d. participate in treatment decisions
   e. consider possible enrolment in research programmes and participate in informed consent process

3. When informing the diagnosis, the doctor needs to take into account the patient and family's prior knowledge and their perception of the problems. The doctor should also be mindful of the impact the diagnosis can have on the patient's life and family relationships. The communication should therefore be conducted sensitively and empathically, and should include a discussion on treatment options and available support services both in the hospital and the community. Disclosure should not be a one-off event and must be seen as an ongoing, dynamic process and a fundamental part of the care of a patient with dementia.[244]
4. After the diagnosis has been communicated, the patient and family should be given time to process the information and to come to terms with it. They should be given ample opportunity to ask questions and seek clarification from the doctor.
5. The objectives of truthful disclosure of diagnosis to patients with dementia are to empower the patient with: the courage to request for information, the cognition to understand information and the strength and resources to cope with the burden of information.

6.6 Restraints

1. Restraints, whether environmental, physical or pharmacological, are used in the management of patients

with dementia to restrict or control the patient's movement or behaviour that may compromise the safety of the patient and/or others.

2. However, the use of restraints is not without potential problems:
   a. Risk of harm and injury
   b. Decrease in ability to perform cognitive and physical activities, thereby resulting in cognitive and functional decline, and ultimately loss of independence.
   c. Loss of freedom, leading to loss of confidence and self-esteem.
3. The preferred choice should therefore be to avoid the use of restraints. Restraints should not be a substitute for a proactive search for reversible precipitating factors for patient's behavioural problems, or for good communication with the patient.
4. Staff education can increase knowledge, change attitudes, and reduce the use of physical restraints in persons with dementia; without any change in the incidence of falls or use of psychoactive drugs.[245]
5. If restraints have to be used on a patient, it should be seen as a temporary means and should be stopped as soon as the indication is no longer present. Excessive use of restraints should be avoided - any restraint should therefore be instituted for the minimal period of time and at the minimal strength or degree needed to achieve the intended outcome for the patient. The patient should also be carefully monitored while on restraints.

6.7 Living alone

1. Many patients diagnosed to have dementia continue to insist on living alone. In some of these patients, cognitive decline arising from dementia leads to poor compliance with medical treatment, lack of safety awareness and poor judgement. All these can pose a risk to the safety and well-being of the patient. The patient may also be exposed, as a result, to mistreatment, fraud and exploitation by others.
2. A diagnosis of dementia does not automatically mean that the patient is incapable of living alone. This decision should be based on an assessment of the patient's decision making

capacity with respect to placement, and ability to continue living alone in the community without posing too much risk to self and to neighbours. Considerations should also be given to the potential negative social and physical impact of moving from a familiar environment to institutional care.

3. If the patient is assessed to have adequate decision making capacity and insists on living alone, the health care professionals should then support the decision by simplifying the daily tasks at home and using available community resources. The patient should also be reassessed as the dementia progresses and erodes both his decisional capacity and ability for self-care.
4. If the patient has doubtful decisional capacity, then there should be an assessment, preferably with the occupational therapist, on the following: safety to self and to neighbours when carrying out activities of daily living and tasks such as food preparation, handling of monies, laundry and compliance to medication.
5. The final objective is to provide the patient with dementia with a safe, familiar and comfortable living environment, and to avoid premature institutionalisation.

7 Palliative care

7.1 Introduction

Palliative care, which emphasises holistic comfort care to patients with progressive and incurable diseases, is germane to dementia care. It encompasses compassionate person-centred care for patients throughout the dementia continuum whereby the dignity, individuality and autonomy of the patient are always upheld, valued and respected, and terminal care for patients at the end stage of dementia when death is imminent.

However, defining end stage dementia is a challenge as is predicting death in dementia. The survival of patients with advanced dementia varies considerably and to date no predictors have shown sufficient reliability. Patients with advanced dementia, nevertheless, have needs and symptoms that are amenable to palliative care.

The markers of dementia severity can serve as triggers whereby considerations about a palliative approach can be initiated. These severity indicators include: stage 7C of the Functional Assessment Staging (FAST) when the patient is non-ambulatory, unable to hold conversations and is dependent in all activities of daily living, recurrent infections like pneumonias, urinary tract infections and pressure ulcers, and difficulties with nutrition and hydration necessitating the consideration of artificial feeding. The issues of particular relevance to palliative care are further discussed herein.

7.2 Pain

B Patients with advanced dementia should be assessed for pain and treated accordingly.

Grade B, Level 1+

D A stepped protocol is recommended for pharmacological management of pain in dementia, and the WHO analgesic ladder[246] or the American Geriatric Society's pain guidelines[247] may be used.

Grade D, Level 4

Pain is common in older persons and significantly compromises their quality of life. Given the cognitive and language deficits in advanced dementia, pain may not be clearly communicated and thus can go undetected and untreated. Indeed, there is evidence that clinicians may not recognize pain in patients with dementia and tend to under-treat it.[248-249]

It is important, therefore, to be able to detect pain in advanced dementia and there have been several observational scales (e.g. PAINAD, DOLOPLUS2, PACSLAC) developed for this purpose. These scales have been the subject of a systematic review[250] which concluded that the scales possessed only moderate psychometric properties, mainly because they may not only detect physical pain per se but also distress due to other causes. Both pain and agitation can manifest as distress in the patient, and pain also precipitates agitation. While the relationship between pain, agitation and other behavioural and psychological symptoms of dementia (BPSD) need further clarification, it is still important to treat for suspected pain in a patient with advanced dementia. A systematic review, exploring if pain medication reduced agitation in people with dementia, was inconclusive given the dearth of rigorous studies on the subject.[251] However, a recent randomised controlled study showed that analgesics alone significantly reduced agitated behavior.[246]

Pharmacological management of pain in dementia follows the guidelines suggested for chronic pain in general. A stepped protocol is recommended and the WHO analgesic ladder[246] or the American Geriatric Society's pain guidelines[247] may be used.

7.3 Use of antibiotics in infections

C Decisions on the use of antibiotics in advanced dementia should be individualized to the patient by weighing the risk and benefits of antibiotic treatment.

Grade C, Level 2+

Patients with advanced dementia are vulnerable to infections, in particular pneumonia. While antibiotics are often prescribed, their efficacy with respect to survival and comfort has not been well established. Randomized controlled trials are lacking

because ethical reasons render it difficult to conduct such studies. Recent observational cohort studies suggest that antibiotics may prolong survival in advanced dementia but do not necessarily improve comfort and can also lengthen the dying process.[73, 252] Hence, the decision on antibiotic use needs to be tailored to the particular circumstances, considering factors such as dementia severity, co-morbidities, severity of the infection and the likelihood of treatment response. It must be emphasized that even if antibiotics are not prescribed, much can still be done to relieve the symptoms of the infection with anti-pyretics, opioids and oxygen.

7.4 Nutrition (tube feeding)

GPP Decisions on tube feeding should be individualised given the lack of evidence for its efficacy in advanced dementia.

GPP

Feeding problems are very common in advanced dementia and can be associated with significant mortality.[253] As such, the practice of tube feeding via the nasogastric route or the Percutaeneous endoscopic gastrostomy (PEG) is a commonly practiced to circumvent the problems of inadequate nutrition and hydration. However, clinical evidence supporting the use of tube feedings in patients with advanced dementia is lacking. A review by Finucane et al.[254] found no evidence that feeding tubes are effective in preventing malnutrition, aspiration pneumonia or pressure ulcers, and tube feeding was neither beneficial in reducing suffering or extending life. An updated Cochrane review in 2009 reached the same conclusions.[255] On the other hand, a recent review of oral feeding showed that high-calorie supplements with other feeding interventions such as modified diets and assisted feeding can help patients gain weight.[256] A UK initiative using rapid cycle quality improvement methodology helped to reduce use of tube feeding in acute hospitals.[257]

The decision-making process involving feeding options is often complex and involves taking in to account several issues such as advance directives, legal and financial concerns, religious and socio-cultural issues as well as emotive issues that revolve around the family caregiver's preferences. A careful consideration of

these factors with involvement of the patient's family in discussions to reach shared decisions is necessary.

7.5 Resuscitation

D Advance care planning with regard to cardiopulmonary resuscitation (CPR) should be encouraged given the poor outcomes of CPR in advanced dementia.

Grade D, Level 2+

Cardiopulmonary Resuscitation (CPR) is likely to be futile in advanced dementia. Dementia increases the odds of non-survival after CPR by up to 3 times, similar to that for persons with metastatic cancer.[258] Nursing homes residents, with a sizable representation of patients with dementia, have very poor rates of survival after CPR in general.[259-260] CPR can be burdensome, undignified and carries the risk of harm. For these reasons, it should not be routinely performed for persons with advanced dementia. In the absence of an advanced care plan or a durable power of attorney, the decision on CPR should be made following the principle of best interest. This decision is best made by considering the views of the patient's family caregivers, as well as the healthcare professionals involved in the patient's care.

8 Young onset dementia

GPP Patients with young onset dementia should receive specialist multidisciplinary care for the diagnosis and management of their condition.

GPP

GPP In the diagnostic work up of patients with young onset dementia, neuroimaging and cerebrospinal fluid examination should be considered.

GPP

GPP Caregivers of patients with young onset dementia should receive adequate counselling on the disease process, community resources and financial assistance.

GPP

Young onset dementia (YOD) refers to the onset of dementia before the age of 65 years. YOD is an important component of dementia in view of the potential reversibility with early diagnosis and treatment. YOD includes several etiological conditions including degenerative and non-degenerative diseases.[115, 261-262] The degenerative causes of YOD includes Alzheimer's disease, frontotemporal dementia and less common causes such as prion diseases. Among the non-degenerative aetiologies, vascular cognitive impairment, normal pressure hydrocephalus and immune mediated diseases are common.[263]

Patients with YOD have special requirements and will benefit from specialist multidisciplinary care. A multidisciplinary approach to YOD will allow early diagnosis and treatment of reversible syndromes while for non-reversible neurodegenerative diseases, early counselling and provision of support services would improve the quality of life of patients and their caregivers.

9 Community resources

Integral to a comprehensive management plan is the referral of persons with dementia to appropriate community resources. This assists in providing care and improving quality of life of both the person with dementia and their caregivers. (Refer to Annex 1)

Generic eldercare services such as meal services, home help, befriender services, case management, home medical, home nursing and social day care services have already been established and some agencies are able to accommodate people with dementia on an ad hoc basis. However, referrals to specialised dementia services may be more suitable for more complex cases. Such facilities have staff who were trained in dementia care as well as programmes specifically tailored to the needs of persons with dementia. At present, dementia day care centres, caregiver support and nursing homes form the core of dementia services locally. However, new services such as the eldersit programme, respite and home-based interventions are being developed to further alleviate the burden on caregivers.

Specialised dementia programmes which include activity programmes, psychosocial approaches, case management, informative meetings, discussions groups and consultation for carers have been shown to reduce behavioural problems and caregiver burden.[264]

Finally, organisations providing dementia care can also act as a resource centre that provides information, support, training and education for caregivers including the training of foreign domestic workers.

9.1 Needs of caregivers

B Caregivers of persons with advanced dementia should be provided with adequate information on available community and medical resources.[164-165, 265-269]

Grade B, Level 2+

End-of-life care for patients with dementia has been found to be extremely demanding of family caregivers. The burden experienced can be personal, emotional and economic and can result in significant levels of depression in the caregivers. Therefore, care for patients with advanced dementia needs to address caregiver issues and provide adequate support to help them cope with difficulties experienced. Access to the relevant support services should also be facilitated.[270-271]

B Referral to day care services and respite services should be considered as part of a comprehensive management plan.[264, 272-274]

Grade B, Level 2^{+}

10 Cost-effectiveness issues

The cost of caring for dementia is significant and poses a heavy burden for governments worldwide.

In the UK, it is estimated that the annual cost of caring for a patient with dementia ranges from 16,000 pounds for mild dementia to 37,000 pounds for severe dementia.[275] The cost components involved in dementia include cost of medications, cost of community services, costs of residential care and cost from lost of employment for the patient and caregiver.

Dementia being a major chronic disease is expected to pose a burden on long term costs. Data from England, suggests that the expenditure on long term care services for older people with cognitive impairment is projected to rise from 0.60% of Gross Domestic Product (GDP) in 2002 to 0.96% of GDP in 2031, an estimated increase from 5.4 billion pounds/year to 16.7 billion pounds/year under base case assumptions. These figures do not include the opportunity costs of informal care.[276]

In Singapore, there is no official data on costs involved in dementia care at the current time. A recent paper suggested that cost of care and amount of care hours required for patients with dementia in Singapore was closely linked to the stage of dementia and the presence of behavioural disturbances.[277]

Despite not currently having a cure for dementia, it is important to note that pharmacological and non-pharmacological management that can delay the onset and slow the progression of dementia would lead to significant healthcare cost savings.

Among the various interventions, there is more cost-effectiveness evidence on pharmacological therapies than other interventions. Acetyl cholinesterase inhibitors for mild-to-moderate disease and NMDA receptor antagonists (memantine) for moderate-to-severe disease have been found to be cost-effective.[278] Among the non-pharmacological interventions, cognitive stimulation therapy, tailored activity programmes and occupational therapy were found to be more cost-effective than usual care. There is also

some evidence to suggest that respite care in day settings and psychosocial interventions for carers could be cost-effective.[278]

Projections of long term care needs for patients with dementia and associated expenditure have shown that relatively small changes in the prevalence rates of functional disability can have a substantial impact on future expenditure.[279] Based on epidemiological models, there is indication that investing in cost effective public health and management of chronic conditions measures that reduce disability or slow down the progression of dementia may produce good returns in terms of reducing the future costs of long term care.[280]

11 Clinical quality improvement

The following clinical audit parameters, based on recommendations in these guidelines are proposed:

1. Proportion of patients with dementia who receive multidisciplinary care including clinical, nursing support and allied health support.
2. Proportion of patients with dementia and/or their caregivers who receive education and counselling on the dementia diagnosis, prognosis and advanced care planning.
3. Proportion of patients who were initiated on cognitive enhancers who received education on potential benefits of treatment, potential adverse events and costs of treatment.
4. Proportion of patients/carers with behavioural disturbances on anti-psychotics who received education on potential adverse events and are undergoing recommended investigations to monitor for potential adverse events.
5. Proportion of patients newly diagnosed with dementia who had a referral to community resources to meet the care needs of the person with dementia and his caregivers.

Appendix 1 Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)[21,22]

Rated on 5-point scale from 1.
Much improved, A bit improved, Not much change, A bit worse,
Much worse [1→5]

1. Recognising the faces of family and friends
2. Remembering the names of family and friends
3. Remembering things about family and friends e.g. occupations, birthdays, addresses
4. Remembering things that have happened recently
5. Recalling conversations a few days later
6. Forgetting what he/she wanted to say in the middle of a conversation
7. Remembering his/her address and telephone number
8. Remembering what day and month it is
9. Remembering where things are usually kept
10. Remembering where to find things which have been put in a different place from usual
11. Adjusting to any change in his/her day-to-day routine
12. Knowing how to work familiar machines around the house
13. Learning to use a new gadget or machine around the house
14. Learning new things in general
15. Remembering things that happened to him/her when he/she was young
16. Remembering things he/she learned when he/she was young
17. Understanding the meaning of unusual words
18. Understanding magazine or newspaper article
19. Following a story in a book or on TV
20. Composing a letter to friends or for business purposes
21. Knowing about important historical events of the past
22. Making decisions on everyday matters
23. Handling money for shopping
24. Handling financial matters, e.g. pension, dealing with bank
25. Handling other everyday arithmetic problems e.g. knowing how much food to buy, knowing how long between visits form family or friends
26. Using his/her intelligence to understand what's going on and to reason things through

(Source: Jorm AF et al, 1991; Lim HJ et al, 2003)

Appendix 2 Elderly Cognitive Assessment Questionnaire (ECAQ)[11,12]

Items		Score	
Memory			
1.	I want you to remember this number. Can you repeat after me (4517). I shall test you again in 15 min.	1	
2.	How old are you?	1	
3.	When is your birthday? OR in what year were you born?		
Orientation and information			
4.	What is the year?	1	
5.	date?	1	
6.	day?	1	
7.	month?	1	
8.	What is this place called? Hospital/Clinic	1	
9.	What is his/her job? (e.g. nurse/doctor)	1	
Memory Recall			
10.	Can you recall the number again?	1	
	Total		

(Source: Kua EH & Ko SM, 1992)

Appendix 3 Abbreviated Mental Test (AMT)[13]

Items	Score	
What is the year?	1	
What is the time? (within 1 hour)	1	
What is your age?	1	
What is your date of birth?	1	
What is your home address?	1	
Where are we now?	1	
Who is our country's Prime Minister?	1	
What is his/her job? (show picture)	1	
Memory phrase "37 Bukit Timah Road"	-	
Count backwards from 20 to 1	1	
Recall memory phase	1	
Total score		

(Source: Sahadevan S et al, 2000)

Appendix 4 Neuropsychiatric symptoms of dementia

Delusions

The types of delusions include:

Theft

The probable explanation for this is that patients cannot remember the precise location of common household objects and hence form the fertile soil for development of the compensatory delusional ideas of theft.

Spouse (or other caregiver) is an impostor – can also be classified as misidentification or as Capgras phenomenon or delusion

Infidelity

Occasionally, persons with dementia will become convinced that their spouse is unfaithful – sexually or otherwise and can lead to aggressive behaviour.

House is not one's home

Generally, the presence of delusions is a significant predictor of physical aggression

Hallucinations

The frequency of hallucinations in people with dementia ranges from 12% to 49%. Visual hallucinations are the most common (occurring in up to 30%a), and these symptoms are more common in moderate than in mild or severe dementia. In people with Lewy bodies, reports of frequency have been as high as 80%. Patients with dementia may also have auditory hallucinations (up to 10%).

One common visual hallucination involves seeing people in the home who are not really there—for example, phantom boarders, also classed as misidentification syndromes.

Depression

Studies show depressed mood to occur most frequently in 40–50% of patients with AD, with a major depressive disorder being less common than subsyndromal depression.

A premorbid history of depression increases the chance of depression developing with AD.

Depressive disorder should be considered when one or more of the following conditions are noted.

- acute, unexplained behaviour changes.
- the patient exhibits a pervasive depressed mood and loss of pleasure.
- the family suspects depression.
- family or personal history of depression prior to the onset of dementia.
- rapid decline in cognition.

Apathy

Although lack of motivation occurs in apathy and depression, the syndrome of apathy denotes lack of motivation without the dysphoria or vegetative symptoms of depression.

Anxiety

Patients with anxiety and dementia may express previously non-manifest concerns about their finances, future and health (including their memory), and worries about previously non-stressful events and activities like being away from home or being left alone.

Patients with AD sometimes develop other phobias, such as fear of crowds, travel, the dark, or activities such as bathing

Wandering

Wandering often results in persons having dementia being admitted to a long-term care facility. It is a frequent cause of referral to psychiatric services. Wandering behaviours include aimless walking and exit seeking / repeatedly attempting to leave the house.

Faulty orientation ability, changed environment, memory problem, boredom, excess energy, discomfort/pain, searching for people or past, and anxiety may underlie some wandering behaviours.

Agitation/Aggression

Agitation in persons having dementia is a complex phenomenon. Neurobiological changes, medical factors, psychological, social, and environmental factors interacting with premorbid personality influence the development of agitation

Resistiveness to care

Resistiveness to care may involve resisting taking medications, ADL assistance or eating. It is related to the ability of the person having dementia to understand, and thus, it increases in prevalence with worsening of cognitive impairment. Resistiveness to care is associated with verbally and physically abusive behaviour towards caregivers.

Inappropriate sexual behaviours

Inappropriate verbal and physical sexual behaviours involve persistent, uninhibited sexual behaviours directed at oneself or at others. These may take the form of making inappropriate sexual comments to taking their clothes off at inappropriate time or setting to inappropriately touching or molesting others. They are profoundly disruptive to caregivers (family and professional) and other individuals in the immediate surroundings.

Catastrophic reaction

Catastrophic reaction is an acute expression of overwhelming anxiety and frustration—often triggered in persons having dementia by adverse

experiences such as frustration with getting dressed or with other such experiences. These reactions are also sometimes referred to as rage reactions. They are typically brief and self-limited, and manifest as sudden angry outbursts, verbal aggression (e.g., shouting and cursing), threats of physical aggression, and physical aggression.

Sundowning

Sundowning is the occurrence and exacerbation of BPSD in the afternoon or evening. Agitation and sleep disturbances commonly accompany sundowning. Sundowning increases the burden of care on caregivers, as it often occurs when the staffing in institutional settings is at the lowest levels. The circadian, hormonal, physiological, and environmental factors are associated with sundowning.

Appendix 5 Functional complications of dementia

Variable	Questions
Community functioning	Can patient find his way around in unfamiliar surroundings, manage his finances, do shopping or marketing?
Home-care functioning	Can he prepare his own food, help in housework and cooking? Is he able to choose proper attire to dress himself? Is he safe to be left at home alone?
Self-care functioning	Is he able to bathe, dress himself? Is he able to go to toilet, transfer or feed himself? Is he continent of bladder and bowels?

(Source: MS Chong et al, 2003)

DSM-IIIr severity of dementia

MILD: capacity for independent living remains with adequate personal hygiene and relatively intact judgement.

MODERATE: independent living hazardous and some degree of supervision necessary

SEVERE: ADL so impaired that continuous supervision required; unable to maintain minimal personal hygiene

Appendix 6 Various diagnostic dementia types

Alzheimer's disease
Familial cases are rare and usually present as early onset dementia (less than 60 years). Sporadic cases usually present after the age of 60 with insidious, gradual deterioration of cognitive function. Short-term memory loss is the most common early symptom. However, other aspects of higher cognitive function may become affected over the course of time. Thus, patients may experience increasing difficulty with activities of daily living, changes in personality, behavioural and psychiatric problems, language dysfunction, loss of visuo-spatial and executive function. Features that make diagnosis of Alzheimer's disease uncertain or unlikely include: sudden, apoplectic onset; focal neurologic findings; seizures or gait disturbances at the onset or very early in the course of the illness.

Vascular dementia
Vascular dementia remains a controversial entity as there are disagreements over the validity of clinical criteria. Nevertheless, cognitive impairment and dementia is common in patients with cerebrovascular disease and it is often reported as the second most common cause of dementia in many studies.

Vascular dementia can be suspected in patients who have an abrupt onset of symptoms, stepwise deterioration, focal neurological signs and symptoms or a history of stroke. However, neuropathological studies have shown that many patients diagnosed with vascular dementia have Alzheimer's disease pathology in addition to cerebrovascular lesions giving rise to doubts whether "pure" vascular dementia exists. Due to the high variability of cerebrovascular pathology and its causative factors, no validated neuropathological criteria exist for vascular dementia.

Dementia with Lewy bodies (DLB)
DLB has been found in some studies to be the second most common form of degenerative dementia, accounting for up to 20% cases in the elderly. It is characterized by fluctuating cognition with pronounced variations in attention and alertness, spontaneous features of parkinsonism and recurrent visual hallucinations which are well formed and detailed. Recognition of DLB is clinically important in view of the high incidence (60%) of adverse and life-threatening reaction to antipsychotics.

Frontotemporal dementia

Fronto-temporal lobar degeneration is characterized by personality changes and disordered social conduct initially and throughout the disease course. Instrumental functions of perception, spatial skills, praxis and memory are intact or relatively well preserved.

Frontotemporal lobar degeneration can produce 3 clinical syndromes:

- The most common is fronto-temporal dementia, characterized by personality change and profound alteration in social conduct and associated with bilateral atrophy of the frontal and anterior temporal lobes.
- Progressive non-fluent aphasia characterized by difficulty in verbal expression in the presence of relative preservation of comprehension, and
- Semantic dementia where there is fluent speech with semantic errors and severely impaired comprehension and naming, together with a visual associative agnosia.

Appendix 7 Canadian Consensus Conference on the Assessment of Dementia (CCCAD) for performing Cranial CT in patients with dementia[42]

Criteria:

- < 60 years old
- Rapid (e.g., over 1- 2 months), unexplained decline in cognition or function
- Dementia of relatively short duration (<2 years)
- Recent, significant head trauma
- Unexplained neurologic symptoms (e.g., new onset of severe headache or seizures)
- History of cancer, especially of a type or at a site associated with metastasis to the brain
- Use of anticoagulants or history of bleeding disorder
- History of urinary incontinence and gait disturbance early in the disease (suggestive of normal pressure hydrocephalus)
- Presence of any new localising signs on physical examination (hemiparesis, Babinski's sign)
- Unusual or atypical cognitive symptoms or presentation (e.g., progressive aphasia)
- Gait disturbance
- CT is recommended if one or more of these criteria are present.

(Source: Patterson CJ et al, 1999)
CT: computed tomography

Annex 1 Community resources

(as of Mar 2013)

Diagnosis and treatment

1	Alexandra Hospital Geriatric Medicine Clinic	378 Alexandra Road Singapore 159964	Tel: 64768828 (Appointment) Tel: 63793420 (M Clinic) Fax: 64714508 Website: www.alexhosp.com.sg
2	Changi General Hospital Geriatric Clinic	2 Simei Street 3 Singapore 529889	Tel: 67888833 Fax: 67872141 Website: www.cgh.com.sg
3	Institute of Mental Health Psychogeriatric Clinic	10 Buangkok View Singapore 539747	Tel: 63892200 Fax: 63851075 Website: www.imh.com.sg
4	Khoo Teck Puat Hospital	90 Yishun Central Singapore 768828	Tel: 65558000 Fax: 66023700 Website: www.ktph.com.sg
5	National Neuroscience Institute, Alzheimer's Disease and Dementia Clinic	11, Jalan Tan Tock Seng, 308433	Tel: 63577095 Fax: 63577103 Website:www.nni.com.sg
6	National University Hospital Neuroscience Clinic	5 Lower Kent Ridge Road Singapore 119074	Tel: 67724850 Fax: 6778 6878 Website: www.nuh.com.sg
7	Singapore General Hospital Dept of Neurology/ Geriatric Medicine Clinic	Outram Road Singapore 169036	Tel: 63214377 (Appointment) Tel: 63214353 (Clinic) Fax: 62243655 (Appointment) Website: www.sgh.com.sg
8	Tan Tock Seng Hospital Geriatric Medicine Clinic	11 Jalan Tan Tock Seng Singapore 308433	Tel: 63578013 Fax: 63578682 Website: www.ttsh.com.sg

Helpline

1	Dementia Helpline (Alzheimer's Disease Association)	Caregiver Support Centre (Tiong Bahru), 298 Tiong Bahru Road #03-01 Central Plaza Singapore 168730	Tel: 63770700 Fax: 65936444 Website: www.alz.org.sg
2.	Referral Services Helpline (Agency For Integrated Care)	7 Maxwell Road #05-01 Annexe B MND Complex Singapore 069111	Tel: 66036800 Fax: 68200723 Website:www.aic.sg

Dementia Day Care Centres

1	Alzheimer's Disease Association (New Horizon Centre – Toa Payoh)	Blk 157, Toa Payoh Lorong 1 #01-1195 Singapore 310157	Tel: 63538734 Fax: 63538518 Website: www.alz.org.sg
2	Alzheimer's Disease Association (New Horizon Centre – Bukit Batok)	Blk 511, Bukit Batok St. 52 #01-211 Singapore 650511	Tel: 65659958 Fax: 65652257 Website: www.alz.org.sg
3	Alzheimer's Disease Association - (New Horizon Centre Tampines)	Blk 362 Tampines St 34 #01-377 Singapore 520362	Tel: 67865373 Fax: 67849587 Website: www.alz.org.sg
4	Alzheimer's Disease Association - (New Horizon Centre- Jurong Point)	1 Jurong West Central 2 #04-04 Jurong Point Shopping Centre Singapore 648886	Tel: 67901650 Fax: 67901521 Website: www.alz.org.sg
5	Apex Harmony Lodge	10 Pasir Ris Walk Singapore 518240	Tel: 65852265 Fax: 65852982 Website: www.apexharmony.org.sg
6	Peacehaven Bedok Multi-service Centre	Blk 121 Bedok North Road #01-163 Singapore 460121	Tel: 64451630 Fax: 64497438 Website: www. salvationarmy.org.sg
7	SASCO Day Activity Centre	Blk 30 Telok Blangah Rise #01-316 Singapore 090030	Tel: 62768713 Fax: 62768715 Website:www.sasco.org.sg
8	Sunlove Dementia Daycare Centre	70 Buangkok View Singapore 534190	Tel: 63869312 Fax: 63863716 Website: www.sunlovehome.org.sg
9	Sunshine Welfare Action Mission(SWAMI) Dementia Day Care Centre	5 Sembawang Walk Singapore 757717	Tel: 65103388 Fax: 67548443 Website:www.swami.org.sg
10	Thong Teck Home for Senior Citizens (Day Care Centre)	91 Geylang East Avenue 2 Singapore 389759	Tel: 68460069 Fax: 68460396 Website: www.thongteckhome.org
11	Yong-En Care Centre	Blk 335A Smith Street #03-57 Singapore 051335	Tel: 62251002 Fax: 62255218 Website: www.yong-en.org.sg

Nursing Homes with Dementia Ward

1	Apex Harmony Lodge	10, Pasir Ris Walk Singapore 518240	Tel: 65852265 Fax: 65852982 Website: www.apexharmony.org.sg
2	Lions Home for the Elders	41 Toa Payoh Rise Singapore 298101	Tel: 62529900 Fax: 63535725 Website: www.lionshome.org.sg
3	Ling Kwang Home for Senior Citizens	156 Serangoon Garden Way Singapore 556055	Tel: 62875466 Fax: 62843567 Website: www.iccc.org.sg/lkh/html
4	a) Salvation Army Peacehaven Nursing Home b) Salvation Army Peacehaven Hope Resident Living Area (Dementia Hostel)	9, Upper Changi Rd North Singapore 507706	Tel: 65465678 Fax: 65461831 Website: www.salvationarmy.org.sg
5	Sunshine Welfare Action Mission (SWAMI) Home	5 Sembawang Walk Singapore 757717	Tel: 62576117 / 65103361 Fax: 67548443 Website: www.swami.org.sg

Caregivers Support Groups (for family caregivers)

1	Alzheimer's Disease Association (Support Groups in English, Mandarin and Malay)	<u>Support Groups in English</u> New Horizon Centre (Toa Payoh) Blk 157, Toa Payoh Lorong 1, #01-1195 Singapore 310157 (New Horizon Centre Bukit Batok) Blk 511, Bukit Batok St. 52 #01-211 Singapore 650511 New Horizon Centre (Jurong Point) 1 Jurong West Central 2 #04-04, Jurong Point Shopping Centre Singapore 648886	Tel: 63770700 (to register) Fax: 65936444 Website: www.alz.org.sg

Caregivers Support Groups (for family caregivers) - continue

	Alzheimer's Disease Association (Support Groups in English, Mandarin and Malay)	<u>Support Groups in English</u> New Horizon Centre (Toa Payoh) Blk 157, Toa Payoh Lorong 1, #01-1195 Singapore 310157 (New Horizon Centre Bukit Batok) Blk 511, Bukit Batok St. 52 #01-211 Singapore 650511 New Horizon Centre (Jurong Point) 1 Jurong West Central 2 #04-04, Jurong Point Shopping Centre Singapore 648886 <u>Support Group in Mandarin</u> Caregiver Support Centre (Tiong Bahru) 298 Tiong Bahru Road #03-01 Central Plaza Singapore 168730 <u>Support Group in Malay</u> New Horizon Centre (Tampines) Blk 362 Tampines St 34 #01-377 Singapore 520362	Tel: 63770700 (to register) Fax: 65936444 Website: www.alz.org.sg

Training in Dementia

1	Alzheimer's Disease Association (For caregivers and domestic helpers)	Resource and Training Centre 70 Bendeemer Road Luzerne Building #06-02 Singapore 339940	Tel: 62939971 (to register) Fax: 62933438 Website: www.alz.org.sg
2	Hua Mei Training Academy of TSAO Foundation (For caregivers)	298 Tiong Bahru Road #15-01/06 Central Plaza Singapore 168730	Tel: 65939555 Fax: 65939556 Website: www.tsaofoundation.org
3	Aged Psychiatry Community Assessment and Treatment Service (APCATS) Department of Geriatric Psychiatry Institute of Mental Health Buangkok Green Medical Park (For the Central and Western Region)	10 Buangkok View Singapore 539747	Tel: 63892175 Fax: 64890100 Website: www.imh.com.sg
4	Community Psychogeriatric Programme (CPGP) Psychological Medicine Division Changi General Hospital (For Districts administered by the Northeast and Southeast Community Development Councils)	Changi General Hospital 2 Simei Street 3 Singapore 529889	Tel: 68501840 /41 Fax: 67873013 Website: www.cgh.com.sg Email: CPGP@cgh.com.sg
5.	Nanyang Polytechnic School of Health Sciences (Nursing) (Certificate in Dementia Care: 60hrs. For Healthcare providers with dementia workload and public interested in dementia care)	180, Ang Mo Kio Avenue 8 Singapore 569830	Tel: 65501300 Fax: 64596811 Website: www.nyp.edu.sg/pdc
6.	Social Service Training Institute The NCSS Academy (For social service and community sector staff and volunteers for professional, skills and volunteer development training programmes)	170 Ghim Moh Road #01-02 Singapore 279621	Tel: 62106688 Fax: 64631078 Website: www.ssti.org.sg

Home Based Care

1	Aged Psychiatry Community Assessment and Treatment Service (APCATS) Department of Geriatric Psychiatry Institute of Mental Health (For the Central and Western Region)	10 Buangkok View Singapore 539747	Tel: 63892175 Fax: 64890100 Website: www.imh.com.sg
2	Community Psychogeriatric Programme (CPGP) Psychological Medicine Division Changi General Hospital (For Districts administered by the Northeast and Southeast Community Development Councils)	Changi General Hospital 2 Simei Street 3 Singapore 529889	Tel: 68501840 / 41 Fax: 67873013 Website: www.cgh.com.sg Email: CPGP@cgh.com.sg

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category 3A (Self-Study) of the SMC Online CME System. Alternatively, you can claim one CME point under Category 3B (Distance Learning - Verifiable Self Assessment) if you answer at least 60% of the following MCQs correctly. You can submit your answers through the SMJ website at this link: http://sma.org.sg/publications/index.aspx?ID=26 (the link will only be available once the May 2013 issue of the SMJ becomes available). The answers will be published in the SMJ July 2013 issue and at the MOH webpage for this CPG after the period for submitting answers is over.

Instruction: Choose "True" or "False".

		True	False
1.	With regards to diagnosis of dementia		
	A) Dementia can be diagnosed clinically based on the DSM IV criteria	☐	☐
	B) Neuropsychological evaluation is a requirement for the diagnosis of dementia	☐	☐
	C) Corroborative history from a reliable caregiver/informant improves the diagnostic certainty of dementia	☐	☐
	D) Neuroimaging should always be performed prior to making a diagnosis of dementia	☐	☐
2.	In the pharmacological management of dementia with cognitive enhancers		
	A) Acetylcholinesterase inhibitors may be used for mild, moderate and severe stages of Alzheimer's dementia	☐	☐
	B) NMDA antagonists (memantine) may be used for the treatment of mild Alzheimer's dementia if the patient has contraindications to acetylcholinesterase inhibitors	☐	☐
	C) Combination of acetylcholinesterase inhibitors and NMDA antagonists (memantine) may be considered in selected patients	☐	☐
	D) Where tolerated, dosages should be titrated to recommended doses	☐	☐

		True	False
3.	When providing education to patients and caregivers		
	A) Cost-benefit ratio of treatment with cognitive enhancers should not be discussed	☐	☐
	B) It is important to discuss prognosis and potential complications of dementia	☐	☐
	C) Discussion on social and community resources should be included	☐	☐
	D) The importance of family support should be incorporated	☐	☐
4.	In the evaluation of dementia		
	A) Neuroimaging can increase the diagnostic accuracy and identify potential reversible causes	☐	☐
	B) Genetic testing is recommended for all patients with dementia	☐	☐
	C) Testing for neurosyphilis may be required for selected high risk patients	☐	☐
	D) For patients with Young Onset Dementia, evaluation for infective, inflammatory and neoplastic aetiology should be considered	☐	☐
5.	In patients with mild dementia		
	A) A person must be assumed to have capacity unless it is established that he lacks capacity	☐	☐
	B) Patients deemed to have intact judgement should be encouraged to make a Lasting Power of Attorney	☐	☐
	C) Patients who are still driving should be referred for a formal driving assessment	☐	☐
	D) Treatment with Ginkgo has been demonstrated to improve cognitive function	☐	☐

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