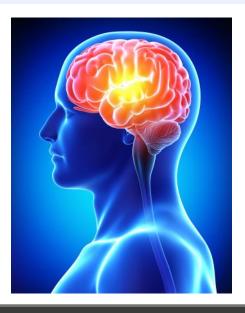
COMPASS May 2019

### Therapeutic Notes on the Management of Dementia



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\*Please note: paper copies are no longer available and MCO answers should be submitted online\*

Glossary	
ADAS score	Alzheimer's Disease Assessment Scale-Cognitive (a measure of cognition)
Akathisia	Unpleasant feeling of restlessness with involuntary body movements
Cognitive Behavioural Therapy	A specific form of psychotherapy. It aims to help people to change how they think ('cognitive') and what they do ('behaviour')
CSM	Committee on Safety of Medicines (the predecessor to the Commission on Human Medicines)
Dysphasia	Language disorder marked by deficiency in the generation of speech, and sometimes also in its comprehension, due to brain disease or damage
Dystonia	Abnormal muscle tone resulting in muscular spasm and abnormal posture
Lewy bodies	Spherical protein deposits found in nerve cells
Neuroleptic Malignant Syndrome	A potentially life-threatening condition characterised by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated serum creatine phosphokinase levels
Visuoperceptual difficulties	Vision difficulties that can result in a variety of 'visual mistakes' (including illusions, misperceptions, misidentifications and sometimes even hallucinations)

### Introduction and background

### **Updated NICE guidance (2018)**

NICE carried out a full update of their guideline *Dementia:* assessment, management and support for people living with dementia and their carers in June 2018. This COMPASS Therapeutic Note has been updated from the 2013 edition, to keep in line with the new NICE recommendations.

### What is dementia?

Dementia is a progressive degenerative neurological syndrome, used to describe a collection of symptoms. <sup>15</sup> It is characterized by cognitive decline, impaired memory, reduced reasoning and communication skills, and a gradual loss of skills needed to carry out daily activities. <sup>9,15</sup> Dementia is not part of normal ageing; it is caused by structural and chemical changes in the brain as a result of physical diseases such as Alzheimer's disease and cerebrovascular disease. <sup>15</sup>

Other functions are also affected, including changes to mood, personality and social behaviour. See later for Behavioural and Psychological Symptoms of Dementia (BPSD).

This publication will discuss mainly the management of **Alzheimer's disease**, as vascular dementia is managed by the modification of vascular risk factors.

#### What is the incidence of dementia?

In 2014, an estimated 1.3% of the UK population were living with dementia.<sup>45</sup> With an ageing population (and improved rate of diagnosis) the number of people with dementia is expected to rise.<sup>6</sup>

Incidence rises with increasing age:

- 0.9% for those aged 60-64 years.
- 1.7% for those aged 65-69 years.
- 3.0% for those aged 70-74 years.
- 6.0% for those aged 75-79 years.
- 11.1% for those aged 80-84 years.
- 18.3% for those aged 85-89 years.
- 29.9% for those aged 90-94 years.
- 41.1% for those aged 95 years and over.<sup>45</sup>

Early onset dementia (under the age of 65 years) is comparatively rare, accounting for 2.2% of all people with dementia in the UK.<sup>15</sup>

Dementia is more common in women. This is partly due to women living longer than men: the average life expectancy for a woman in Northern Ireland is currently 82 years, compared to 78 years for a man. <sup>16</sup>

### Prevalence of dementia

**CHART ONE** shows the prevalence of types of dementia in women and men (all ages) in the UK (taken from the Improving Dementia Services in Northern Ireland Regional Strategy, 2011. Based on the Dementia UK report). <sup>2,15</sup>



### Rates of dementia diagnosis

There is a gap between the number of people estimated to be living with dementia across the UK, including NI, and the number that have received a diagnosis of dementia (based on the QoF dementia register). This gap can be due to difficulty diagnosing in the early stages, the slow progression of the disease, and limited public awareness. TABLE ONE shows the NI diagnosis rates, taken from the 2014 Dementia UK report.

TABLE ONE: NORTHERN IRELAND DEMENTIA DIAGNOSIS RATES (2014)		
Area	Estimated number of people with dementia (diagnosed and undiagnosed)	Percentage of people with dementia with a diagnosis
Northern Ireland	19,765	64.8%
Belfast	4,083	72.9%
South Eastern	4,132	64.3%
Northern	5,244	55.9%
Southern	3,477	66.2%
Western	2,830	68.7%

This is encouraging as it shows improved diagnosis of dementia.

### Types of dementia

Dementia is classified into various subtypes according to the different disease processes involved. The most common are:

- Alzheimer's disease (50–75% of cases)
- Vascular and Mixed dementia\* (up to 20% of cases)
- Dementia with Lewy Bodies (10–15% of cases).

\*Mixed dementia (both Alzheimer's disease and vascular factors) is commonly seen and is difficult to differentiate clinically. <sup>2,9,15</sup>

Other types of dementia include frontotemporal lobar degeneration, alcohol-related dementia, and dementia related to diseases such as Parkinson's disease, Creutzfeldt-Jacob disease, HIV/AIDs and Huntington's disease. TABLE TWO summarises the more common dementia subtypes.

	TABLE TWO: Dementia Subtypes	
	Dementia subtype	Explanation
	Alzheimer's disease	First diagnosed by German neurologist Alois Alzheimer in 1906. <sup>15</sup> In Alzheimer's disease changes occur to the chemistry and structure of the brain, causing brain cells to die. The exact cause is unknown. Findings include reduced synthesis of the neurotransmitter acetylcholine and the development of protein plaques and 'tangles' in the brain. <sup>15</sup>
	Vascular dementia	Arteries supplying blood to the brain become blocked, leading to small strokes and ischaemic damage in the brain.  The most common form is subcortical vascular dementia. Sometimes a patient will be stable for several months or years but further deterioration can manifest as subsequent strokes occur. Vascular dementia will affect different parts of the brain and this dictates the resultant symptoms: poor executive function, memory loss, poor concentration, word finding difficulties, mood swings or depression. Some people have hallucinations. Physical problems can develop, such as difficulties with walking or incontinence. It is more common in smokers and patients with heart disease, hypertension, diabetes or high cholesterol.  11,15
	Dementia with Lewy Bodies (DLB)	DLB is caused by tiny spherical protein deposits that develop inside nerve cells in the brain, similar to Parkinson's Disease. As such, symptoms often overlap with Alzheimer's disease and Parkinson's disease.   11,15 REM sleep behaviour disorder is a core clinical feature, along with fluctuating cognition, recurrent visual hallucinations, and one or more features of Parkinsonism (e.g. tremor, muscle stiffness, experience falls or difficulty with walking).

### Symptoms and diagnosis

### What is the prognosis?

Much individual variability is seen in people with dementia. Median survival with Alzheimer's disease has been estimated at 7.1 years (6.7-7.5 years) while vascular dementia has been estimated at 3.9 years (3.5-4.2 years).<sup>22</sup> Increased age and male gender are associated with higher rates of mortality in dementia.<sup>98</sup> Co-morbid health conditions (which may or may not be related to dementia) often exist, making it difficult to determine the contribution of dementia to mortality.<sup>15</sup> Dementia is however a progressive, terminal disease, which is reflected in the management of the disease.<sup>2</sup>

### Signs and symptoms of dementia

A deterioration in memory accompanied by functional decline is the principle symptom. Often relatives are concerned about the person's memory or behaviour, but they themselves are not.<sup>1</sup> It is therefore essential to get an account of the person's problems from a close relative or friend.<sup>3,15</sup>

Signs and symptoms are often not specific to dementia.<sup>1</sup> The following are possible signs and symptoms of dementia. If any of the following are reported (by the person or by someone close to them) to be new or deteriorating then an assessment is advisable:<sup>1</sup>

### Cognitive impairment, including:

- Memory problems the person may defer to family when answering questions, have difficulty learning new information or remembering recent events or people's names, be vague with dates, and/or miss appointments.
- · Receptive or expressive dysphasia.
- Difficulty in carrying out coordinated movements such as dressing.
- Disorientation and unawareness of the time and place.
- Impairment of executive function, such as difficulties with planning and problem solving.<sup>1</sup>

### Difficulties with activities of daily living (ADLs):

- In the early stages of dementia this may lead to neglect of household tasks, nutrition (causing weight loss), personal hygiene, and grooming. People with dementia who are in employment may find that they are increasingly making mistakes at work.
- In the later stages, basic ADLs such as dressing, eating, and walking become affected.<sup>1</sup>

## Behavioural and psychological symptoms of dementia (BPSD) tend to fluctuate, may last for 6 months or more and include:

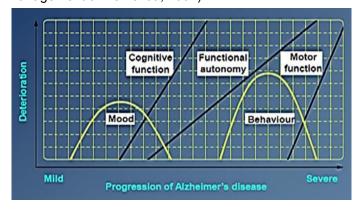
- Psychosis the person may have delusions (which may be persecutory) and/or hallucinations (visual and auditory).
- Agitation and emotional lability the person may be easily upset, argumentative, shout, have mood swings, and/or be physically and verbally aggressive.
- Depression and anxiety the person may follow their carer around due to this. The onset of depression in later life is a warning sign of dementia.
- Withdrawal or apathy.
- Disinhibition the person may exhibit social or sexually inappropriate behaviour.

- Motor disturbance wandering, restlessness, pacing, and repetitive activity may be reported.
- Sleep cycle disturbance or insomnia.
- Tendency to repeat phrases or questions.<sup>1</sup>

### **Progression of symptoms**

Symptoms of **Alzheimer's disease** tend to change over time as the disease progresses. **GRAPH ONE** illustrates how Alzheimer's disease usually begins with mild memory impairment, gradually progressing through stages of increasing cognitive decline, diminishing functioning, compromised judgment, deterioration in selfcare, and eventually inability to manage life independently. In many cases, the course of Alzheimer's disease is complicated further by disturbances in mood and behaviour (see later for BPSD).<sup>69</sup>

# **GRAPH ONE: Pattern and Symptoms of Alzheimer's disease over time** (Lovestone and Gauthier, Management of Dementia, 2001)<sup>23,86</sup>



### Should case findings be carried out?

Case finding is not recommended by NICE. Case finding is intermediate between screening and people who present with symptoms. The reason that this is not recommended is that there is a problem with false positives, i.e. diagnosis of dementia in people who do not have the condition.<sup>3</sup>

### How is diagnosis made?

There is no simple test to make a diagnosis of dementia. Diagnosis can only be made after a comprehensive assessment.

### There should be an initial assessment in the nonspecialist setting:

- Take a full history from the person with suspected dementia and if possible, from someone who knows the person well.
- If dementia is still suspected after initial assessment, conduct a more comprehensive assessment including a physical examination, appropriate tests, and a validated brief structured cognitive instrument (see page 5).
- Do not rule out dementia solely because the person has a normal score on a cognitive instrument.
- Refer the person to a specialist dementia diagnostic service if reversible causes of cognitive decline or impairment have been investigated and dementia is still suspected.

### What is meant by referral to a specialist?

Specialists are those with the appropriate knowledge and skills and include secondary care medical specialists (for example psychiatrists, geriatricians and neurologists) and other healthcare professionals (for example GPs, nurse consultants and advanced nurse practitioners) with specialist expertise in assessing and diagnosing dementia.<sup>3</sup>

Referral may just be a discussion with a specialist - not all patients have to go to memory clinic.<sup>3</sup>

### Benefits of early diagnosis

Diagnosis of dementia is often delayed for many reasons, including a reluctance to seek help for a condition that the person or their family perceive as stigmatising and untreatable. Early diagnosis is however very important as it allows the person with dementia to:

- Exclude any other potential causes of the symptoms (e.g. depression, stress, delirium, adverse effects of medicines).
- Start treatment early with acetylcholinesterase (AChE) inhibitors (note: AChE inhibitors are symptomatic treatments rather than disease modifying treatment, but early initiation shows the greatest benefits).
- Receive care and support which may improve their quality of life and make choices and plans for the future, with their family, while the condition still permits this
- Ensure appropriate intervention and support which is tailored to individual needs of the person.<sup>2</sup>

### What is mild cognitive impairment?

Mild cognitive impairment (MCI) is a term used to describe a slight but noticeable and measurable decline in cognitive abilities, including memory and thinking skills. The changes are not severe enough to interfere with daily life or independent function. Therefore, a person with MCI does not meet diagnostic criteria for dementia. Those with MCI have an increased risk of eventually developing Alzheimer's disease or another type of dementia. The conversion rate from MCI to Alzheimer's is 10 to 20% each year; over 50% of people with MCI later develop dementia. Therefore not all people with MCI get worse

and some eventually get better. 1.89 Consider referring people who show signs of MCI for assessment by Memory Assessment Services to aid early identification of dementia.

### **Differential diagnosis**

It is important to exclude other conditions or illnesses that can cause memory loss, including depression, alcohol problems and some physical illnesses with organic brain effects — see **TABLE THREE**.

Appropriate blood and urine tests should be undertaken to exclude reversible causes of cognitive decline.<sup>3</sup>

When the onset of memory problems is **sudden**, a vascular event is often considered.<sup>1</sup>

When the onset is **sub-acute**, an infection (or other cause of acute confusion/delirium) is likely, especially if there is alteration in level of consciousness.<sup>1</sup>

TABLE THREE: Differential Diagnosis of Dementia <sup>1</sup>		
Condition	Difference to dementia	
Normal ageing	Normal ageing is associated with a mild decline in cognitive function, and memory lapses are common, especially during times of physical illness or stress.	
Mild cognitive impairment	MCI differs from dementia in that symptoms do not fulfil the diagnostic criteria for dementia, for example only one cognitive domain may be affected or activities of daily life may not be significantly affected. In dementia the person is not always aware of their symptoms.	
Depression	Symptoms of depression include low mood, loss of interest, anhedonia, and self-neglect which can be similar to those of dementia.  In older people, features of depression may be less obvious, with somatic symptoms (such as reduced appetite, fatigue, and insomnia) more common.	
Delirium (acute confusional state)	Delirium is an acute, fluctuating syndrome of disturbed consciousness, attention, cognition, and perception. It is a common condition in the differential diagnosis for dementia.  People with cognitive impairment are at increased risk of delirium, and the two conditions often coexist.	
Drugs – adverse effects and drug interactions	Many medicines, including benzodiazepines, analgesics (such as opioids, naproxen, and ibuprofen), anticholinergics, anti-depressants, antipsychotics, anti-convulsants (especially older preparations, such as phenytoin and phenobarbital), and corticosteroids can affect cognition.  Concomitant use of medication increases the risk of drug interactions and druginduced confusion.  In older people, drugs may be metabolized and excreted more slowly therefore, toxicity can occur with normal doses and present as dementia or delirium. See page seven on Anticholinergic Burden.	
Vitamin deficiency	Thiamine deficiency and vitamin B12 deficiency can produce symptoms such as memory loss.	
Hypothyroidism	Symptoms of hypothyroidism can include low mood, and impaired concentration and memory.	
Sensory deficits	Problems with vision and hearing can contribute significantly to an apparent decline in cognitive ability.	
Normal pressure hydrocephalus	Normal pressure hydrocephalus can present with symptoms of early cognitive impairment, urinary incontinence, and gait disorder.	
Sleep apnoea	Sleep apnoea is increasingly recognised as a cause of cognitive impairment. It is more common in people with Alzheimer's disease than age/gender matched controls. Screening tools such as <a href="STOP-BANG">STOP-BANG</a> may be used in primary care for people with sleep disordered breathing.	

### What cognitive function tests are used?

Cognitive function tests are used <u>alongside</u> other investigations in determining whether a diagnosis of dementia is likely.

When using cognitive testing, NICE recommend using a validated brief structured cognitive instrument such as:

- the 10-point cognitive screener (10-CS)
- the 6-item cognitive impairment test (6CIT)
- the 6-item screener
- the Memory Impairment Screen (MIS)
- the Mini-Cog
- Test Your Memory (TYM).<sup>3</sup>

NB: Do not rule out dementia solely because the person has a normal score on a cognitive instrument:

factors such as educational level, skills, prior level of functioning and attainment, language, sensory impairment, psychiatric illness and physical or neurological problems may affect performance in these tests, and must be taken into account.

Longer tests such as the Mini–Mental State Examination (MMSE) test are used in specialist memory clinics. However the above shorter tests are useful in primary care as preliminary testing.

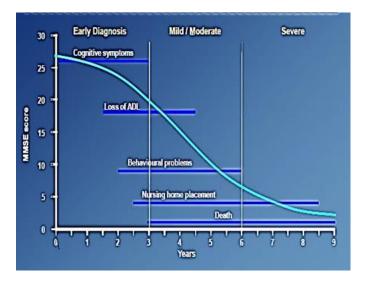
It is important to emphasise that dementia is suspected when a change in cognition <u>and</u> changes in activities of daily living (ADL) are seen.

### Stages of dementia

The progression of **Alzheimer's disease** may be divided into three stages: early, mild to moderate and severe. This is illustrated in **GRAPH TWO**. This is based on MMSE scores. The symptoms change over time, starting with cognitive symptoms, progressing to loss of ADL and behavioural symptoms.

The progression of **vascular dementia** tends to follow a step-wise course with periods of stability (although the actual course is difficult to predict).

**GRAPH TWO: The Progress of Alzheimer's disease** (Feldman H, Gracon S. Clinical Diagnosis and Management of Alzheimer's disease. 1996:239-253)<sup>86,95</sup>



#### Following a diagnosis

Getting a diagnosis of dementia is often distressing and the way in which information, advice and support are offered can make a huge difference in helping people cope with the diagnosis.<sup>2</sup>

From the start of the diagnostic process, and for the rest of the person's life, give people (and their carers and family members) accessible information about their condition and what to expect in the future. 3,107

Written information should be provided to the person with dementia and their family about:

- Signs and symptoms
- · Course and prognosis
- Treatments
- · Local care and support services
- Support groups
- Sources of financial and legal advice and advocacy
- Medico-legal issues, including driving
- Local information sources, including libraries and voluntary organisations.

Voluntary agencies can be extremely useful support networks — see Patient Resources box.



### **Patient Resources**

**Alzheimer's Society** (<u>www.alzheimers.org.uk/</u>; advice line: 028 9066 4100)

**Age NI** (<u>www.ageuk.org.uk/northern-ireland</u>; advice line: 0808 808 7575)

**Dementia NI** (<a href="https://www.dementiani.org/">https://www.dementiani.org/</a>; advice line: 028 9068 6768)

**Dementia Navigators** are available in each Health and Social Care Trust in NI. Contact your local dementia navigator through your local Memory Services team.

NICE patient decision aids (PDAs) (https://www.nice.org.uk/guidance/ng97/resources)

- two PDAs have been produced by NICE for people with dementia:
- (i) Antipsychotic medicines for treating agitation, aggression and distress in people living with dementia.
- (ii) Enteral (tube) feeding for people living with severe dementia.

### **Prevention Strategies**

### Is dementia preventable?

Lifestyle factors might reduce or increase an individual's risk of developing dementia. <sup>111</sup> Indeed, modification of risk factors has been shown to contribute to prevention or delay of dementia in some populations. It is therefore important to consider prevention strategies.

#### What are the main risk factors?

Not all risk factors will be modifiable and others will be specific to particular types of dementia.<sup>2</sup>

More research is needed to determine which risk factors play the greatest role in the development of dementia, and whether intervening to modify these risk factors will impact significantly on the development of dementia. Until the evidence in relation to risk factors is determined, large scale promotion of prevention strategies to the general public cannot be adopted. However, promotion of healthy lifestyle choices and avoidance of potential risk factors to the general population will obviously have general health benefits and may reduce or delay the onset of dementia.

The NICE guideline *Dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset* (NG16) makes recommendations in order to increase the amount of time that people can be independent, healthy and active in later life (successful ageing). 88

Essentially what is good for general health and cardiovascular health is also likely to be good for dementia: staying healthy both mentally and physically.

### Risk factors for dementia

Risk factors for dementia can be divided into non-modifiable and modifiable, and are summarised in **TABLE FOUR** and **TABLE FIVE**.

TABLE FOUR: Non-modifiable Risk Factors	
Risk factor	Perception of risk
Age	Advancing age is the biggest risk factor for dementia. <sup>2</sup>
Gender	Women are slightly more likely to develop Alzheimer's disease than men (even discounting for increased life expectancy). The reasons for this are unclear. Rates of vascular dementia are higher among men. 2
Genetics	The role of genetics is not fully understood. A number of genes have been identified that do not directly cause dementia but are thought to affect a person's risk of developing the disease, e.g. the gene apolipoprotein E has been shown to be a susceptibility gene, i.e. it does not predict that dementia will develop but if there is a dementia onset, then it will come on earlier. 12 Although much rarer, it is also possible to inherit genes that can directly cause dementia, i.e. there is a clear inheritance of dementia from one generation to the next. Examples include Huntington's disease and familial Alzheimer's. 12
Medical history	A Medical or Family History of Cardiovascular Disease Conditions that affect the heart, arteries or

Medical history (cont.)	blood circulation all significantly affect a person's chances of developing dementia, particularly vascular dementia.  Stroke is a major risk factor for dementia – it is thought that a history of stroke doubles the risk of dementia in the older population. Note: some factors affecting cardiovascular disease are modifiable – see Modifiable Risk Factors.
	<b>Depression</b> Patients with either a history of depression or who experience depression later in life are at a likely increased risk of dementia. Sometimes depression can be an early symptom of dementia. <sup>12</sup>
	Repeated Head Injuries It has been suggested that deposits that form in the brain as a result of the injury may be linked to the onset of dementia. Professional boxers can develop a form of dementia known as dementia pugilistica. 12
	Learning Disability The ageing process for people with learning disability begins much earlier. People with Down's syndrome have high rates of Alzheimer's type dementia. <sup>2</sup>
	Other Medical Conditions Examples include: Parkinson's disease, multiple sclerosis, chronic kidney disease and HIV. <sup>12</sup>

TABLE FIVE: Modifiable Risk Factors		
Risk factor	Perception of risk	
Social isolation	Social isolation increases the risk of hypertension, coronary heart disease, and depression. It may also result in cognitive inactivity, which is linked to faster cognitive decline and low mood. <sup>111</sup>	
Hearing loss	Peripheral hearing loss is a significant risk factor for dementia. <sup>111</sup>	
Smoking	Smoking is a risk factor for both Alzheimer's and vascular dementia. This is most likely due to harmful effects on the heart, lungs and vascular system, including the blood vessels in the brain. <sup>2</sup>	
Alcohol	Risk is linked to excessive consumption. Drinking within the recommended limits is unlikely to increase the risk of dementia. <sup>2</sup>	
Obesity	Obesity in mid-life may be associated with an increased risk of Alzheimer's in later life. Obesity is also a risk factor for diabetes, heart disease and stroke and, therefore, vascular dementia. <sup>2</sup>	
Hypertension	In mid-life this has been shown to be a risk factor for the development of both vascular dementia and Alzheimer's disease. Active treatment of hypertension in middle aged (45–65 years) and older people (aged older than 65 years) without dementia may reduce dementia incidence. 111	
Raised cholesterol	This has been associated with the development of Alzheimer's disease. It is also a risk factor for cardiovascular disease, and therefore, vascular dementia. <sup>2</sup>	

### How significant is lifestyle in the development of dementia?

In addition to addressing possible risk factors for dementia, consideration should be given to adopting lifestyle choices that may actively protect against the development of dementia.

TABLE SIX: LIFESTYLE FACTORS	
Diet	A healthy and balanced diet that enables a person to maintain a normal body weight is recommended. A Mediterranean diet with a high proportion of fish, fruit, vegetables and unsaturated fat, and a low proportion of dairy products, meat and saturated fat will help to manage cholesterol and blood pressure. <sup>12</sup> Fresh fruit and vegetables contain many vitamins and antioxidants, which may help prevent dementia.
Exercise	Exercise helps to protect against many conditions, including dementia. Regular physical exercise helps to keep the cardiovascular system healthy. At least 30 minutes of moderate intensity exercise, five times a week is recommended. Participation in physical activity for 20 to 30 minutes twice a week in mid-life has been shown to be associated with a lower risk of dementia in later life. 12
Mentally challenging activities	E.g. reading, learning, puzzles, playing a musical instrument, board games, dancing. Research suggests that people who take part in mental activities are less likely to develop dementia, but this requires further research. <sup>2</sup> It is thought that mental activity increases the brain's ability to cope with (and compensate for) damage to the brain and hence symptoms of dementia are delayed. <sup>12</sup> 'Brain training' games may be more important over the age of 60 in preventing or delaying dementia than when used in younger people to 'improve mental fitness'. <sup>12</sup>
Social activity	Research suggests that people who are more socially active have a slightly reduced risk of developing dementia. <sup>12</sup>

### Are food supplements protective in preventing or treating dementia?

NICE advise that we do not offer ginseng, vitamin E supplements, or herbal formulations to treat dementia.<sup>3</sup>

Souvenaid<sup>®</sup> is a supplement that contain ingredients such as omega fatty acids and phospholipids. It is marketed as a means to increase levels of certain nutrients that are often low in people with early Alzheimer's disease. However, research published in the Lancet Neurology (2017) showed that a trial into the use of Souvenaid ultimately failed to meet its primary goal, which was to slow memory and thinking decline in people with mild cognitive impairment due to Alzheimer's disease. There has been some evidence that Souvenaid<sup>®</sup> may improve memory function in people in the early stages of Alzheimer's disease (treatment naïve people). However, trials were not able to show any effect on the ability to slow or prevent cognitive decline. 112

The Alzheimer's Society advise that patients would be better spending their money on regular exercise, as this is a far more effective way of reducing cognitive decline, and that NHS money would be better spent on other treatments for Alzheimer's disease. <sup>12</sup>

Souvenaid<sup>®</sup> is not on the ACBS list and therefore should not be prescribed on HS21 prescription.

Cost of Souvenaid<sup>®</sup>: £3.49 per 125ml drink (daily dose).

### Can benzodiazepines increase the risk of developing dementia?

Benzodiazepines have been associated with cognitive impairment. Use of benzodiazepines (or similar drugs) may also be associated with a subsequent risk of development of dementia. Clinicians should ensure that any new prescriptions are in line with NICE and MHRA advice and reserved for the short-term relief of anxiety or insomnia that is severe, disabling and causing unacceptable distress to patients. Other interventions such as cognitive behavioural therapy should be considered as first line for anxiety and insomnia. <sup>56,57</sup>



### Anticholinergic burden: Medicines that can cause cognitive impairment <sup>3</sup>

Some commonly prescribed medicines are associated with increased anticholinergic burden, and therefore cognitive impairment. This is an important area for primary care to review. Deprescribing agents with high anticholinergic activity and looking for alternative agents is important both when assessing whether to refer a person with suspected dementia for diagnosis and during medication reviews with people living with dementia.

There are validated tools for assessing anticholinergic burden (for example, the Anticholinergic Cognitive Burden Scale). There is insufficient evidence to recommend one over the others. A simple online checker might be useful: <a href="http://www.medichec.com/">http://www.medichec.com/</a>.

## Management of Cognitive Symptoms of Dementia

#### Aim of treatment

For the majority of dementias, it is not possible to alter the progressive course of the disorder. The aims of treatment are therefore to promote independence, maintain function and treat symptoms including cognitive, non-cognitive, behavioural and psychological symptoms. Treatment should be person centred, respecting the individual patient's circumstances. Offering appropriate support services can make a significant difference to the lives of people with dementia and their caregivers. For the support services can make a significant difference to the lives of people with dementia and their caregivers.

### Non-drug treatment

Giving people with dementia the opportunity to take part in activities that are **suited to their capabilities** has been shown to improve quality of life. Attention must be focused on the whole person and may include:

- Modifying environments
- Simplifying tasks
- Establishing structure and routine
- · Practising tasks through repetition
- Using effective cueing and communication strategies
- Assistive technology
- Skills training
- Education of family and caregivers.<sup>2</sup>

### What is occupational therapy (OT) memory rehabilitation?

OT memory rehabilitation training may be useful for mild stage dementia of any aetiology. It helps people who are experiencing memory difficulties that are impacting on their day to day life, by teaching them techniques to compensate for these everyday memory difficulties. The service is available through some of the local Trusts.

### Drug treatments

Drug treatment will depend on the type of dementia.

#### Vascular dementia

The major difficulty clinically is that, in older people, vascular disease and Alzheimer's disease commonly coexist. Pure vascular dementia is quite rare. Treatment of vascular dementia focuses on controlling underlying risk factors for cardiovascular disease. There are no medicines licensed in the UK for vascular dementia. Trials to investigate the benefit of acetylcholinesterase (AChE) inhibitors or memantine in vascular dementia have been inconclusive. As it is often difficult to diagnose dementia subtypes, it might explain why AChE inhibitors do not always produce consistent results – in probable vascular dementia cases.

NICE advise an AChE inhibitor or memantine in vascular dementia only if the person has suspected comorbid Alzheimer's disease, Dementia with Lewy bodies or Parkinson's disease dementia [off label].<sup>3</sup>

### **Dementia with Lewy Bodies (DLB)**

DLB is managed similarly to Parkinson's disease dementia (PDD): please refer also to <u>COMPASS</u>
<u>Therapeutic Notes on Parkinson's disease</u>. There are no licensed medicines for DLB, but use is well established. NICE advise donepezil or rivastigmine for people with mild to moderate DLB. Galantamine doesn't appear to be as effective as donepezil or rivastigmine for DLB,

therefore only consider galantamine for people with mild to moderate DLB if donepezil and rivastigmine are not tolerated. Donepezil or rivastigmine may also be considered for people with severe DLB. Memantine is an option for people with DLB if AChE inhibitors are not tolerated or are contraindicated.<sup>3</sup>

From this point on this section will focus on the management of Alzheimer's disease.

### Who should initiate drug treatment?

Prescribers should only start treatment with AChE inhibitor or memantine on the advice of a clinician who has the necessary knowledge and skills. This could include:

- secondary care medical specialists such as psychiatrists, geriatricians and neurologists
- other healthcare professionals (such as GPs, nurse consultants and advanced nurse practitioners), if they have specialist expertise in diagnosing and treating Alzheimer's disease.

Once a decision has been made to start an AChE inhibitor or memantine, the first prescription may be made in primary care.<sup>3</sup> This is a change to the previous NICE quidance.

### What is the mode of action of AChE inhibitors?

One theory of the cause of Alzheimer's disease is progressive loss of cholinergic neurons and decreasing levels of acetylcholine in the brain.<sup>36</sup> Acetylcholinesterase and butyrylcholinesterase play an important role in the degradation of acetylcholine.<sup>37</sup>

AChE inhibitors differ in pharmacological action: donepezil selectively inhibits AChE, rivastigmine affects both AChE and BuChE and galantamine selectively inhibits AChE and also has nicotinic receptor agonist properties. To date, these differences have not been shown to result in differences in efficacy or tolerability.

### What is the AChE inhibitor of choice?

Initial choice is normally the AChE inhibitor with the lowest acquisition cost. However, an alternative AChE inhibitor could be prescribed if considered appropriate when taking into account side effect profile, expectations about adherence, medical co-morbidity, possibility of drug interactions and dosing profiles.<sup>3</sup>

Few head-to-head studies have been published and there have been differences in both populations studied and trial design. However, to date, similar efficacy and tolerability between AChE inhibitors is assumed. Donepezil has been reported more likely to be prescribed at an effective dose compared to rivastigmine or galantamine, perhaps due to a shorter titration schedule and better tolerability (see page 10).

### NI Formulary choices

First choice for mild to moderate dementia in Alzheimer's disease:

### Donepezil

Second choice for mild to moderate dementia in Alzheimer's disease:

Galantamine M/R

Or

Rivastigmine

http://niformulary.hscni.net

### **NI Formulary choices**

First choice for severe dementia in Alzheimer's disease or for moderate dementia in Alzheimer's disease for people who cannot take AchE inhibitors:



Memantine

http://niformulary.hscni.net

### How is response to treatment determined?

Response to treatment can be measured using cognitive function tests such as the Alzheimer's Disease Assessment Scale — cognitive subscale (ADAS-cog). Improvement of > 4 points on ADAS-cog score is seen as clinically significant. Estimates of the number needed to treat (NNT) range from 4 to 12.9

It is difficult to predict how an individual will respond to treatment. Patient response can be described as one of three ways:

- Non-responders continue to decline at the anticipated rate over six months
- Non-decliners neither improve significantly or decline further over six months
- Improvers improve to a clinically significant extent over six months (i.e. show a > 4-point improvement on ADAS-cog score).

Achieving any improvement or temporary stability on the ADAS-cog score (or other assessments) may represent a significant therapeutic benefit, given that without treatment a continuous decline may be seen.

### **Duration of treatment?**

Studies have reported benefits of continued AChE inhibitor therapy as disease progresses (with respect to cognitive and functional outcomes). 103,104

Stopping medicines in late stages for a patient who is at home could result in hospitalisation of the patient. In the later stages of Alzheimer's disease, AChE inhibitors and memantine are no longer used as a means of reducing decline in memory and cognitive functions (as these functions are no longer viable). Instead their role is to support basic psychomotor processes required to help caregivers deliver basic care involving feeding, dressing, and bathing, including the processes of movement, swallowing, and functional communication. The benefits may also extend to reducing antipsychotic usage. 80

In patients progressing to very advanced dementia, the overall benefit of these agents should be assessed and consideration given to discontinuation.<sup>29</sup> It may be easier to discontinue medicines in later stages if patient is in a care home and will therefore be supervised and monitored. At this stage the goal of treatment is palliation and comfort.<sup>80</sup>

### Is it worthwhile switching between AChE inhibitors?

Usually, no, as AChE inhibitors have similar efficacy. It *may* be worthwhile switching to another AChE inhibitor if the patient fails to respond to the initial AChE inhibitor, as failure to respond to one AChE inhibitor does not necessarily mean that a patient will not respond to another. The same applies for tolerability: it may be worthwhile switching to another AChE inhibitor if the first

option is not tolerated<sup>9</sup> (NB – tolerability appears to be related to speed of dose titration; more adverse effects are seen during titration).<sup>9</sup>

Switching AChE inhibitors is not recommended in patients who show loss of benefit several years after initiation of treatment.<sup>81</sup>

Rivastigmine patches are associated with a lower incidence of GI adverse effects than oral rivastigmine preparations and so may be a more appropriate choice in some patients.<sup>43</sup>

### Prescribing Points - AChE inhibitors 9,24,73-77,80

- Dose titration regimens are used to minimise side effects. Starting doses of galantamine and rivastigmine are not therapeutic doses and should be increased as per titration schedule. See table on page ten.
- ► Caution: ensure patient is not receiving a cholinesterase inhibitor and anticholinergic medication.
- ► AChE inhibitors are hepatically cleared. Therefore caution is required in hepatic impairment.
- ► Excess cholinergic stimulation can lead to adverse effects such as nausea, vomiting, dizziness, insomnia and diarrhoea. Most of these adverse effects are likely to occur at the start of therapy or when dose is increased, i.e. dose related and transient.
- ► Weight loss has been reported, as a consequence of AChE inhibitor-induced nausea. Monitor body weight.
- ► Agitation is a common side effect of donepezil. It is resolved on dose-reduction or discontinuation of treatment.<sup>75</sup>
- ▶ Vagotonic effects on heart rate, e.g. bradycardia. Therefore caution in patients with sick sinus syndrome or other supraventricular cardiac conduction disturbances, such as sinoatrial or atroventricular block.
- ▶ Pulmonary conditions: because of their cholinomimetic actions, cholinesterase inhibitors should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease.
- ► Seizures: AChE inhibitors have the potential to cause seizures. Therefore caution is recommended with donepezil and rivastigmine in people predisposed to seizures; avoid galantamine in these cases.
- ▶ Ulcers: caution in patients susceptible to peptic or duodenal ulcers (due to increased cholinergic activity causing increased gastric acid secretion).

### Caution: AChE inhibitors and urinary frequency

AChE inhibitors may cause urinary frequency or incontinence as a common side effect.

AChE inhibitors should not be given in combination with bladder antimuscarinics as the actions of bladder antimuscarinics will antagonise those of the AChE inhibitors.

### What are the recommended doses of AChE inhibitors?

Dose titration regimens are used to minimise side effects. Starting doses of galantamine and rivastigmine are not therapeutic doses and should be increased as per titration schedule, shown in **TABLE SEVEN** over the page.

### **TABLE SEVEN:** Starting and maintenance doses of acetylcholinesterase inhibitors<sup>74</sup>

-		
AChE inhibitor	Starting dose	Maintenance dose
Donepezil	5mg daily	5 to 10mg daily
Galantamine	8mg daily	16 to 24mg daily
Rivastigmine	1.5mg twice daily	3 to 6mg twice daily

### Does donepezil have to be given in the evening?

The product literature specifies that donepezil should be given in the evening just prior to retiring. This is to reduce the risk of gastrointestinal side effects: the maximal possible rise in acidity and motility occurs 2 to 3 hours after the tablet is ingested – a time when the majority would be asleep.

However if sleep disturbances are noted, particularly vivid nightmares, then a shift to morning dosing often resolves those problems. The time of dosing may therefore be chosen based on individual tolerability. <sup>66</sup>

## If switching between AChE inhibitors, is it recommended to withdraw gradually or carry out a direct switch?

This will be on specialist advice only. A direct switch is usually recommended rather than a gradual withdrawal. This is because the benefits of treatment with AChE inhibitors are rapidly lost when drug administration is interrupted and may not be fully regained when drug treatment is initiated. A faster titration may be adopted. A faster titration may be

In the event of marked adverse events, switching AChE inhibitors can be suggested, but (depending on the side effect) there should be resolution of symptoms before initiating the second agent.<sup>81</sup>

### How does memantine differ?

Glutamate is released in excess in cells damaged by Alzheimer's disease. Memantine acts as an antagonist at N-methyl-D-asparate (NMDA) glutamate receptors. Therefore memantine blocks the effects of pathologically elevated tonic levels of glutamate, preventing further neuronal dysfunction. 24,62,74,76,80

### Prescribing Points – Memantine <sup>24,62,74,76,80</sup>

- ▶ Memantine is generally well tolerated and the incidence of adverse effects is low. Common adverse effects include: dizziness, headache, constipation, somnolence and hypertension.
- ► A dose titration over 4 weeks is required.
- ► Caution is required in patients with epilepsy or a history of seizures.
- ► Hepatic impairment avoid in severe impairment.
- ▶ Memantine is renally excreted. Caution is needed when used in combination with other drugs that are renally excreted. Ensure renal function tests are up-to-date and reduce dose in renal impairment as follows:<sup>74</sup>

eGFR (ml/min)	Dose
30 to 49	10mg daily. If well tolerated after at least 7 days dose can be increased in steps to 20mg daily
5 to 29	10 mg daily
< 5	Avoid

### Is combination treatment with an AchE inhibitor and memantine recommended?

For people with an established diagnosis of Alzheimer's disease who are already taking an AChE inhibitor, the addition of memantine to the AChE inhibitor is an option in people with moderate or severe disease.<sup>3</sup> For people with an established diagnosis of Alzheimer's disease, primary care prescribers may start treatment with memantine without taking advice from a specialist clinician.<sup>3</sup> This is a change from previous NICE guidance.

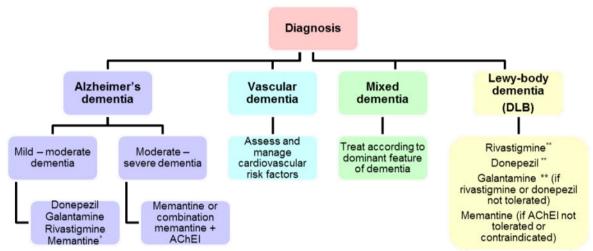
Studies on the long term effects of combination AChE inhibitor plus memantine therapy have demonstrated a slowing of both cognitive decline and functional decline (compared with monotherapy or no therapy) <sup>50</sup> and a delay in nursing home placement. <sup>51</sup>



### Don't stop established AChE inhibitor therapy

A dramatic decline in functioning is seen when drug administration is interrupted and may not be fully regained when drug treatment is initiated. <sup>9,104</sup>

### **CHART TWO:** Summary of treatment options for dementia



- \* Memantine: moderate Alzheimer's dementia in those intolerant of or in whom AChE inhibitors are contraindicated.
- \*\* Rivastigmine, donepezil and galantamine are unlicensed in DLB.

Rivastigmine is licensed only for mild – moderately severe Alzheimer's dementia and mild – moderately severe dementia in those with idiopathic Parkinson's disease.

Management of Behavioural and Psychological Symptoms of Dementia (BPSD)

### What do we mean by Behavioural and Psychological Symptoms of dementia (BPSD)?

These are non-cognitive symptoms that are generally recognised as being beyond the former "in-character" nature of the person with Alzheimer's disease. BPSD are common and can be very distressing. BPSD vary in both their presentation and underlying cause. These symptoms are often associated with chemical changes in the brain or by social and environmental triggers. Behavioural problems typically begin with subtle personality changes and progress to increasing lapses of social propriety. They are the largest risk factor for people with dementia entering institutional care. 31,100

### What are the symptoms of BPSD?

Prevalence of each type of BPSD varies considerably. 96 BPSD may be divided into three main syndromes: 15,31

- 1. Psychotic symptoms (visual and auditory hallucinations and persecutory delusions)
- 2. Mood disorders (depression, anxiety, apathy)
- 3. Behavioural (including agitation, aggression, irritability, restlessness, pacing, sleep disturbance (day night reversal), calling out repeatedly / disruptive vocal activity such as shouting or screaming, wandering, hoarding, cursing, sexual disinhibition, shadowing). They are usually associated with distress or anxiety.<sup>3,15,85</sup>

### What is the incidence of BPSD?

Over 90% of people with dementia develop behavioural problems or psychiatric symptoms at some point during their illness. <sup>31</sup> BPSD occur most commonly in the middle stage of dementia. <sup>15</sup>

Depressive and apathetic symptoms are usually the earliest to appear. <sup>100</sup> Hallucinations, elation/euphoria, and aberrant motor behaviour (inability to sit still) are usually the last symptoms to emerge. <sup>100</sup>

Apathy is the most common and persistent symptom (reported in 75% of cases); delusional symptoms are least persistent. 100

### The problem with low dose antipsychotics

Low dose antipsychotics have been used historically to manage BPSD. Originally first generation antipsychotics (e.g. haloperidol) were used. Practice later changed to second generation atypical antipsychotics (e.g. risperidone, quetiapine) with a lower incidence of extrapyramidal side effects. However, antipsychotics (whether typical or atypical) have been shown to have only a limited benefit in managing BPSD. There is also the very real risk of increased mortality and an unfavourable side effect profile. Hermore, antipsychotics are often continued for long periods of time without review.



### Risk of stroke with Antipsychotics

In 2004 the CSM reported on an approximately **three-fold increased risk** of stroke compared with placebo with the use of the antipsychotics risperidone or olanzapine in elderly people with dementia. The magnitude of risk outweighs any likely benefit of treating dementia-related behavioural problems. <sup>44</sup> Product literature for <u>all</u> antipsychotics (atypical and conventional) now carry a warning about possible cerebrovascular risk. <sup>9</sup>

### **Prescribing Patterns**

Often patients are prescribed antipsychotics as a blanket first line approach to manage BPSD, before considering other non-pharmacological approaches, and without adequate monitoring. 18,34

The government commissioned Banerjee Report (2009) concluded that antipsychotic use was too high in patients with dementia, and that the associated risks outweighed the benefits in most of these patients.

According to the Report, approximately 180,000 people with dementia are treated with antipsychotic medication in England alone per year. Of these people:

- Up to 36,000 may derive some benefit from treatment
- 1,800 may die
- 1,620 may suffer a cerebrovascular adverse event (around half of which may be severe).

As a result, the government pledged to reduce prescribing of antipsychotics for patients with dementia by two thirds by 2011. Recent prescribing data has shown a positive decrease in the number of elderly patients being prescribed antipsychotics. However, targets have still not been fully met.

Many local Trusts have developed behavioural service teams which can be a valuable source of advice.



### **Adverse effects of Antipsychotics**

The most common side effects include:

- Extrapyramidal side effects (movement disorders) such as akathisia or dystonia
- Anticholinergic effects such as dry mouth, blurred vision and constipation
- Excessive sedation
- Feelings of dizziness or light headedness, unsteadiness and falls (potentially leading to fractures)
- Weight gain
- Accelerated rate of decline and disease progression in people with dementia, hence there are particular concerns over the long term use of these drugs.<sup>33</sup>

More rare, but serious, side effects include:

- Changes to blood sugar levels
- Changes to blood lipid levels
- · Increased risk of stroke
- Neuroleptic malignant syndrome (fever, faster breathing, sweating, muscle stiffness and reduced consciousness)
- Severe sensitivity in people with dementia with Lewy bodies, possibly causing death in these individuals
- Changes in ECG which can lead to cardiac arrhythmias.

### First line Management Options

Before starting non-pharmacological or pharmacological treatment for distress in people living with dementia, conduct a structured assessment to:

- · explore possible reasons for their distress and
- check for and address clinical or environmental causes (for example pain, delirium or inappropriate care).<sup>3</sup>

As initial and ongoing management, offer psychosocial and environmental interventions to reduce distress in people living with dementia.<sup>3</sup>

### **Identify trigger factors**

An early and comprehensive assessment to establish the likely factors that may generate, aggravate or improve such behaviour.<sup>3</sup> By making simple changes, a significant impact on behavioural symptoms can be seen.

### Physical health problems

Underlying physical health problems are often a cause of BPSD. Treatment of concurrent health problems can therefore lead to resolution of BPSD without the need for other treatment. The time period for emergence of BPSD can sometimes be an indication of cause: sudden emergence of BPSD often has a physical trigger. Longer onset emergence can be linked to depression. Physical health problems include infection, pain and dehydration.

'	, 1
TABLE EIGHT: PHYSICAL HEALTH PROBLEMS	
Infection	Urinary tract infections and chest infections are frequent trigger factors for BPSD. Dental infections are also common but often not recognised. <sup>84</sup>
Undetected pain	Pain is one of the most common causes of BPSD. <sup>7</sup> Many people with dementia have difficulty in communicating about their pain which can manifest as agitation. Pain is difficult to detect in dementia and hence underdiagnosed. A prescription of regular simple analgesia such as paracetamol 1g four times a day can be beneficial (note: a lower dose may be appropriate in some patients with very low body weight). <sup>5,7</sup>
Constipation or urinary retention	Faecal impaction or urinary retention can cause discomfort. Again, many people with dementia have difficulty in communicating this, which can manifest as agitation. <sup>97</sup>
Other potential discomforts	Also consider the following: is the patient too hot? Too cold? Thirsty? Hungry? Do they have pressure sores?
Visual and auditory impairment	This should be treated if possible – change glasses or hearing aid; encourage them to be worn regularly. <sup>84</sup>

#### **Environmental factors**

The characteristics of the environment are an important contributory factor to BPSD.<sup>33</sup>

A lack of meaningful stimulation can be linked to a high prevalence of BPSD. <sup>33</sup> BPSD are particularly common in care homes. There is a clear need to improve the level of social interaction and stimulation available to care home residents. People need to engage in <u>constructive</u> activities and interaction. Organised activities need to be tailored to individual needs.

On the other hand, over-stimulation can sometimes cause confusion to the person. Therefore, keeping the environment constant and in line with what the patient has been used to is advised.

Consider is the patient experiencing any of the following:

- Overstimulation
- Under-stimulation
- Unfamiliar people or surroundings (e.g. hospital admission)
- Does the person recognise the environment as home?
   Does it contain things to help them feel at home?
- Change in daily schedule or routine<sup>69</sup>
- Is the TV or radio playing something that the person can relate to and enjoy?
- If the person is mobile, can they move around freely and have access to outside space? Could assistive technology be used to improve freedom or safety?

### Watchful waiting (or 'Active Monitoring')

Watchful waiting is actually an <u>active</u> process. It involves on-going assessment over a four week period of observing possible contributing factors and reviewing simple non-drug treatments. It does not mean 'doing nothing'. A high proportion of people with dementia who have behavioural and psychological symptoms experience significant improvements over four weeks with no specific treatment. Watchful waiting is the safest and most effective therapeutic approach unless there is severe risk or extreme distress.

### Non-pharmacological measures

Non-pharmacological interventions are recommended before initiating drug therapy. Simple adjustments to social interactions and environment can make a difference.<sup>7</sup>

Consider interventions tailored to the person's preferences, skills and abilities. Monitor response and adapt the care plan as needed. Depending on availability, consider options including:

- Aromatherapy
- Reflexology
- Multisensory stimulation
- Therapeutic use of music and/or dancing
- Animal-assisted therapy
- Massage.<sup>1</sup>

### Treat the target symptoms

There are no adequate drug treatments available for non-cognitive behavioural symptoms at present.<sup>12</sup> BPSDs are potentially treatable however through targeting specific symptoms when considering medication.

- 1) **Identify** the specific target symptom(s) for the patient: agitation, aggression, irritability, restlessness, pacing, visual/auditory hallucinations, delusions, depression, anxiety, apathy, insomnia?
- 2) Quantify the symptoms. How severe?
- 3) **Document** the target symptom(s).

Customise a treatment plan for the individual patient, based on target symptoms. This plan should be time limited: agree a time frame for review of symptoms with carers and document in the notes.

Individually tailored care plans can then be developed that help carers and staff address the behaviour that challenges. Care plans should focus on round the clock care, i.e. not just in the daytime, as dementia is clearly a 24-hour illness and one in which normal patterns, such as sleeping at night, can become disrupted. 33

4) **Monitor** response to treatment: changes in target symptoms should be assessed and recorded at regular intervals.

### Can Alzheimer's treatments be used for BPSD?

Dementia drugs should be optimised before considering low dose antipsychotics. Indeed, adherence to therapy should be emphasised as a means to reducing risk of BPSD.<sup>80</sup>

People at this stage of dementia are likely to already be receiving an AChE inhibitor for cognition.

There is some evidence that AChE inhibitors and memantine may be useful in the management of BPSD. However, if symptoms are severe and distressing or dangerous then antipsychotics may be needed.

AChE inhibitors and memantine appear to produce complementary benefits on different types of BPSD:

- AChE inhibitors appear to have some efficacy on negative BPSD symptoms, e.g. depression and apathy-related BPSDs
- Memantine may be more effective on positive symptoms, e.g. agitation, aggression, irritability/lability, and psychosis.<sup>80,108</sup>

AChE inhibitors and memantine can take several weeks of treatment for effects to become apparent. 51,61

### When to consider an Alzheimer's treatment for BPSD?

(If not already receiving treatment) an AChE inhibitor or memantine may be considered if a non-pharmacological approach is inappropriate or has been ineffective and symptoms are causing significant distress or potential harm to the individual.

### An AChE inhibitor may be considered for BPSD in:

- 1) People with mild to moderate Alzheimer's disease.
- 2) People with Dementia with Lewy Bodies (DLB).

Rivastigmine has shown reduced core psychiatric symptoms in patients with DLB in some studies.<sup>78</sup>
Memantine may be considered for BPSD in:

- 1) People with moderate Alzheimer's disease who are intolerant of or have a contraindication to AChE inhibitors.
- 2) People with severe Alzheimer's disease. 9,45

### When not to offer an Alzheimer's treatment for BPSD? 9,45

Do not offer to people who have purely vascular dementia. An AChE inhibitor or memantine may be *trialled* in people with mixed dementia.

### How to manage depression in dementia?

Evidence shows psychological intervention, such as positive events and exercise, are effective for mild to moderate depression and should be considered first line.<sup>3,7,84</sup> However, for more severe depression, antidepressants may be considered.<sup>7,84</sup>

If an antidepressant is to be used, drugs with anticholinergic effects (such as tricyclic antidepressants) should be avoided because they may adversely affect cognition.

Pharmacologic treatment for depression should last between 6 and 12 months, with re-evaluation (at least) monthly.<sup>70</sup> Recent studies suggest that antidepressants may have lower efficacy for depression in Alzheimer's disease.<sup>12,35</sup>

### How to manage sleep disorders in dementia?

Behavioural interventions are generally more effective than pharmacologic ones in cases of insomnia in patients with Alzheimer disease.<sup>69</sup>

Sleep hygiene measures should be adopted. It may help to consider:

- Reducing daytime napping
- Exposure to daylight
- Reduce intake of caffeine
- Increasing activities during the day (rather than napping)
- · Personalised activities
- Agreeing realistic expectations for sleep duration.<sup>3,7</sup>



### Caution: Benzodiazepines

Benzodiazepines should not <u>routinely</u> be used to manage BPSD or be considered as an alternative to antipsychotics due to:

- · Limited evidence of benefit
- · Association with cognitive decline
- · Increased risk of falls/fractures in the elderly.

When to use low dose antipsychotics in the management of BPSD

### When to consider an antipsychotic?

NICE advise that we only offer antipsychotics for people living with dementia who are either:

- at risk of harming themselves or others or
- experiencing agitation, hallucinations or delusions that are causing them severe distress.<sup>3</sup>

Before starting antipsychotics, discuss the benefits and harms with the person and their family members or carers (as appropriate). Consider using a decision aid to support this discussion. NICE has produced a <u>patient</u>

<u>decision aid</u> on antipsychotic medicines for treating agitation, aggression and distress in people living with dementia.<sup>3</sup>

### Do antipsychotics help some symptoms of BPSD more than others?

Antipsychotics are most helpful in the control of symptoms such as **hallucinations** and **delusional thinking** rather than for agitation or attenuating aggression. Hallucinations and delusions indicate psychosis and must be distinguished from disorientation, fearfulness and misunderstanding, which are common in people with dementia. Type Symptoms such as restlessness and repetitive vocalisation/shouting out can be the expression of unmet needs. There is no evidence that antipsychotics show benefit for repetitive vocalisation/shouting out.

### Which antipsychotic should be used?

Risperidone is the only antipsychotic that is licensed for the management of non-cognitive symptoms of dementia and is therefore the agent of choice: risperidone is indicated for short term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's disease unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others. <sup>30</sup>

Alternative antipsychotics may be used [off-label] if risperidone is contraindicated or not tolerated. <u>Patients and carers should be informed that use is unlicensed</u>. There is some evidence that olanzapine has reduced aggression in dementia. However, olanzapine has anticholinergic properties and is associated with rapid and significant weight gain. Be

Quetiapine has not been shown to be as effective as risperidone or olanzapine but may be effective in patients with Parkinson's disease or DLB (at very low doses) because of its lower risk of causing movement disorders.<sup>9</sup>

### Caution: Antipsychotics in people with DLB and vascular dementia

Antipsychotics should not be used in DLB without specialist advice. This is due to the increased risk of neuroleptic malignant syndrome and sensitivity to extrapyramidal side effects of atypical antipsychotics in people with DLB.

Antipsychotics should ideally be avoided in patients with vascular dementia due to risk of stroke.

### Conditions for prescribing an antipsychotic

People with Alzheimer's disease, mixed dementias or DLB with **severe** non-cognitive symptoms: (psychosis and/or agitated behaviour causing significant distress) may be *trialled* with an antipsychotic drug after the following conditions have been met:

- There should be a full discussion with the person with dementia and/or carers about the possible benefits and risks of treatment. In particular, cerebrovascular risk factors should be assessed and the possible increased risk of stroke/transient ischaemic attack and possible adverse effects on cognition discussed.<sup>3</sup>
- Changes in cognition should be assessed and recorded at regular intervals. Alternative medication should be considered if necessary.
- Target symptoms should be identified, quantified and documented.

- Changes in target symptoms should be assessed and recorded at regular intervals.
- The effect of co-morbid conditions, such as depression, should be considered.
- The choice of antipsychotic should be made after an individual risk-benefit analysis.
- Document details of treatment, including medicine name, dose and frequency.
- The dose should be low initially and then titrated upwards.
- Treatment should be time limited and regularly reviewed – at 6 and/or at 12 weeks (according to clinical need).<sup>3,7</sup>

### What is meant by "low dose"?

Antipsychotics have routinely been advised at relatively low doses to manage BPSD. With the exception of risperidone, antipsychotics are not licensed for this indication. In the absence of licensed doses for BPSD, the following doses have been selected from the literature and clinical practice as starting doses:

TABLE NINE: Low doses of antipsychotics <sup>7,55</sup>		
Antipsychotic Low dose for BPSD		
Risperidone	250 micrograms twice daily	
Olanzapine	2.5mg once daily	
Aripiprazole	5mg once daily	
Quetiapine	12.5mg twice daily	

### Prescribing Points – Low dose antipsychotics

- ► They are for short term use only. Patients must be evaluated frequently and regularly, and the need for continuing treatment reassessed.<sup>30</sup>
- ► A cardiac risk assessment is recommended prior to starting a prescription.<sup>7</sup>
- ► Verbal and written information should be given to the patient and carer explaining the reasons for the antipsychotic and the side effects / risks involved.
- ► Reason(s) for prescribing low dose antipsychotic should be documented, e.g. severe distress.
- ▶ Monitor the patient for the emergence of severe untoward reactions, particularly neuroleptic sensitivity reactions (which manifest as the development or worsening of severe extrapyramidal features after treatment in the accepted dose range or acute and severe physical deterioration following prescription of antipsychotic drugs for which there is no other apparent cause).
- ▶ The risk of stroke appears to be highest in the first four weeks of treatment with an antipsychotic. This is thought to be due to dehydration and lack of mobility. Therefore it is important to ensure adequate hydration and movement in the first month. <sup>106</sup>

Reviewing and stopping antipsychotics

Many older people with Alzheimer's disease and BPSD can be withdrawn from chronic antipsychotic medication without detrimental effects on their behaviour. <sup>96</sup> Discontinuation programmes could be incorporated into routine practice. <sup>96</sup>

All antipsychotic prescriptions should be reviewed at 6 and/or at 12 weeks. The limited evidence for antipsychotics for BPSD indicates that on-going treatment offers no benefit over longer periods of therapy. <sup>85</sup>

Therefore treatment should only be continued beyond 12 weeks in exceptional circumstances; discontinuation should be default except in extreme circumstances. <sup>7,85</sup>

Most behavioural complications of dementia are intermittent and do not persist for longer than three months. 96 70% of people have no worsening of symptoms when antipsychotics are discontinued. 7

### Patients with a current prescription

Withdrawal from antipsychotics can be safe in people with dementia who have taken antipsychotics for prolonged periods, especially when symptoms have largely resolved.<sup>99</sup>

### Primary care audit opportunity

Identify and review patients who have dementia and are on antipsychotics, with the purpose of understanding why antipsychotics have been prescribed. In consultation with the patient, their family and carers, and clinical specialist colleagues such as those in psychiatry, establish: whether the continued use of antipsychotics is appropriate, whether it is safe to begin the process of discontinuing their use, and what access to alternative interventions is available. <sup>67</sup>

### Are withdrawal symptoms a problem?

Possible withdrawal symptoms from antipsychotics include autonomic and behavioural symptoms such as nausea, vomiting, anorexia, rhinorrhoea, diarrhoea, diaphoresis, myalgia, paraesthesia, anxiety, as well as movement disorders such as withdrawal emergent parkinsonism, withdrawal dyskinesia and covert dyskinesia. <sup>96</sup> Consult the best-practice guide from Alzheimer's Society for further details. <sup>7</sup>

### How to stop an antipsychotic?

This will depend on the current dose of the antipsychotic:

TABLE TEN: How to stop an antipsychotic?				
Dose of antipsychotic	How to discontinue			
If the person is receiving a <b>low</b> dose	Proceed directly with discontinuation. Monitor patient and review at two weeks. <sup>7</sup>			
If the person is receiving a higher dose	Taper the dose over one month – reduce to half dose for 2 weeks, review at 2 weeks, discontinue after a further 2 weeks.			

### For those with worsening of symptoms after discontinuation

The first four weeks are the most challenging but are often effectively managed with **watchful waiting**, preventing the need to restart antipsychotics. The risk of recurrence of behavioural and psychiatric symptoms after discontinuation may be more likely if:

- Previous discontinuation has caused symptoms to return
- The person currently has severe symptoms.

If symptoms remain severe (with associated severe risk and/or distress): and further treatment with antipsychotics is considered clinically necessary, a referral to specialist services is advised.<sup>7</sup>

Caution is required in residents with more severe symptoms and in people with psychosis or agitation who responded well to antipsychotic medication before. In these people, withdrawal might not be recommended until further evidence becomes available. <sup>96</sup>

### **Summary: Good practice points in managing BPSD**

- Consider specialist referral in cases of extreme risk or distress.<sup>7</sup>
- Begin management with 'watchful waiting' for 4 weeks (including assessment of medical conditions and pain) and simple non-drug assessment.<sup>7</sup>
- Use specific interventions if symptoms are severe or persist after watchful waiting and simple non-drug treatments:
  - Psychosocial treatments and behavioural interventions.
  - Orug treatment of underlying health disorders (e.g. pain relief, infections) as appropriate.
- Consider a time-limited trial of antipsychotics if specific interventions have been unsuccessful and symptoms are causing extreme distress or risk of harm.<sup>7</sup>
- All people with dementia who are receiving antipsychotic drugs should receive a clinical review from their doctor to ensure that their care is compliant with current best practice and guidelines, and that alternatives to medication have been considered.<sup>68</sup>

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Please note that every effort has been made to ensure that the content of the COMPASS Therapeutic Notes is accurate at the time of publication. Readers are reminded that it is their responsibility to keep up-to-date with any changes in practice.

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#### COMPASS THERAPEUTIC NOTES ASSESSMENT

### Therapeutic Notes on the Management of Dementia

COMPASS Therapeutic Notes are circulated to GPs, nurses, pharmacists and others in Northern Ireland. Each issue is compiled following the review of approximately 200 papers, journal articles, guidelines and standards documents. They are written in question and answer format, with summary points and recommendations on each topic. They reflect local, national and international guidelines and standards on current best clinical practice. Each issue is reviewed and updated every three years.

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- Doctors and nurses should submit their answers at: www.medicinesni.com
- Pharmacists should submit their answers at: www.nicpld.org

1	In relation to	background and	diagnosis of dementia:
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•	III I GIALIC	on to background and diagnosis of demenda.			
	а	Dementia is part of normal ageing	Т	F	
	b	Vascular dementia is more common in smokers and patients with heart disease, hypertension, diabetes or high cholesterol	Т	F	
	С	Case finding is recommended for people who are at high risk of dementia	Т	F	
	d	If the person has a normal score on a cognitive instrument then dementia can be ruled out.	Т	F	
2	In relation to risk factors for dementia:				
	а	Women are slightly more likely to develop Alzheimer's disease than men.	Т	F	
	b	Smoking is thought to be a risk factor for vascular dementia but not Alzheimer's disease	Т	F	
	С	Advancing age is the biggest risk factor for dementia	Т	F	
	d	Benzodiazepines have been associated with cognitive impairment.	Т	F	
3	In relatio	n to drug treatment for cognitive symptoms:			
	а	Starting doses of galantamine and rivastigmine are not therapeutic doses and should be increased as per the recommended titration schedule.	Т	F	
	b	People who have neither improved significantly or declined further within 6 months treatment with an acetylcholinesterase inhibitor are described as non-responders.	Т	F	
	С	Donepezil should be stopped if memantine is started.	Т	F	
	d	Acetylcholinesterase inhibitors should be switched in patients who show loss of benefit several years after initiation of treatment	Т	F	
4	In relation to management of Behavioural and Psychological Symptoms of Dementia (BPSD):				
	а	Drug treatment should be targeted to the symptoms.	Т	F	
	b	Psychosocial and environmental interventions to reduce distress in people living with dementia is very important.	Т	F	
	С	A high proportion of people with dementia who have behavioural and psychological symptoms experience significant improvements over four weeks with no specific treatment.	Т	F	
	d	Benzodiazepines should be considered a routine treatment option.	Т	F	
5	In relatio	n to low dose antipsychotics for the management of BPSD:			
	а	Low dose antipsychotics are first line treatment option	Т	F	
	b	Treatment should be time limited and regularly reviewed – at 6 and/or at 12 weeks (according to clinical need).	Т	F	
	С	There is an increased risk of stroke with the use of the antipsychotics in elderly people with dementia.	Т	F	
	d	Quetiapine is licensed for short term management	Т	F	