COMPASS Therapeutic Notes on the Management of Dementia

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Glossary of terms	
RCT	Randomised Controlled Trial
Visuoperceptual difficulties	Vision difficulties that can result in a variety of 'visual mistakes' (including illusions, misperceptions, misidentifications and sometimes even hallucinations)
Cognitive Behavioural Therapy	A specific form of psychotherapy. It aims to help people to change how they think ('cognitive') and what they do ('behaviour')
Lewy bodies	Spherical protein deposits found in nerve cells
CSM	Committee on Safety of Medicines (the predecessor to the Commission on Human Medicines)
Akathisia	Unpleasant feeling of restlessness with involuntary body movements
Dystonia	Abnormal muscle tone resulting in muscular spasm and abnormal posture
Neuroleptic Malignant Syndrome	A potentially life-threatening condition characterised by hyperthermia, muscle rigidity, autonomic instability, altered consciousness and elevated serum creatine phosphokinase levels

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Introduction: Background, Symptoms & Diagnosis

What is dementia?

Dementia is a progressive degenerative neurological syndrome, used to describe a collection of symptoms.[15] 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.[9,15]
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.[15]
Other functions are also affected, including changes to mood, personality and social behaviour.[9] 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.

Incidence of dementia?

Approximately 1.3% of the UK population suffer from dementia.[6] Incidence rises with increasing age: about 1 in 20 over 65 year olds have dementia but by the age of 80 from about 1 in 5 will have some degree of dementia.[9,11] With an ageing population (and improved rate of diagnosis) the number of people with dementia is expected to rise.[6]
Early onset dementia (under the age of 65 years) is comparatively rare, accounting for 2.2% of all people with dementia in the UK.[15]
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 81 years, compared to 76 years for a man.[2,16]

Costs of dementia care in Northern Ireland

With life expectancy increasing and an increasingly ageing population, rates of dementia are expected to increase. In Northern Ireland it is estimated that as many as 18-19,000 of the population suffer from dementia. This figure may rise to approximately 60,000 by 2051.[2] This represents a major public health and societal issue, with further pressure on care and support services and on those who provide informal care.[2] This is recognised in the **Improving Dementia Services In Northern Ireland, a Regional Strategy, 2011**. The strategy addresses a wide range of issues in the management of dementia and includes an action plan to improve and redesign services.[2]

TABLE ONE: MAPPING THE DEMENTIA GAP IN NORTHERN IRELAND
Numbers of people with dementia in 2012 in local health areas and Strategic Health Authority areas[12]

Area name	Estimated number of people with dementia (diagnosed and undiagnosed)	Percentage of people with dementia with a diagnosis	Number of people without a diagnosis	Best-worst overall ranking (1=highest UK ranking, 178=lowest)
Northern Ireland	18862	63%	6980	
Belfast	3846	75.5%	941	1
South Eastern	3929	61.9%	1498	14
Northern	5027	51.4%	2445	52
Southern	3343	63.8%	1209	11
Western	2717	67.4%	887	5

Types of dementia?

Dementia is classified into various subtypes according to the different disease processes involved.[9] The most common are:

- Alzheimer's disease (present in over 50% of dementia cases)
- Vascular and Mixed dementia* (approx. 27% of dementia cases)
- Dementia with Lewy Bodies (approx. 15% of dementia cases)

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.[2]

*Mixed dementia (both Alzheimer's disease and vascular factors) is commonly seen and is difficult to differentiate clinically.[2,9,15]

What is the prognosis?

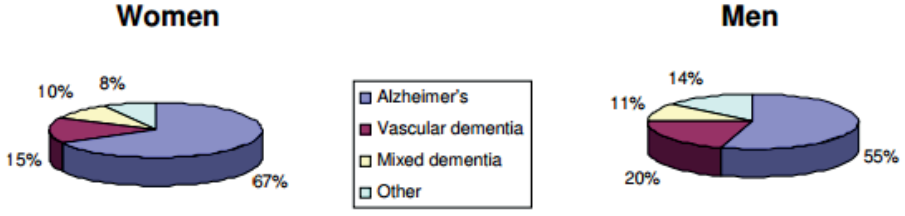
Much individual variability is seen in people with dementia. Median survival with Alzheimer's disease has been estimated at 7.1 years (6.7-7.5 years) while vascular dementia has been estimated at 3.9 years (3.5-4.2 years).[22] Increased age and male gender are associated with higher rates of mortality in dementia.[98]

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.[15] Dementia is however a progressive, terminal disease, which is reflected in the management of the disease.[2]

TABLE TWO: Dementia Subtypes

Dementia subtype	Explanation
Alzheimer's disease	First diagnosed by German neurologist Alois Alzheimer in 1906.[15] 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.[15]
Vascular dementia	Arteries supplying blood to the brain become blocked, leading to small strokes and ischaemic damage in the brain.[9] 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. The level of confusion can fluctuate, and visual hallucinations are more common. People may also have a tremor, muscle stiffness, experience falls or difficulty with walking.[11,15]

CHART ONE: Prevalence of types of dementia in women and men (all ages) in the UK [2] (taken from the Improving Dementia Services in Northern Ireland Regional Strategy, 2011. Based on the Dementia UK report[15])



Should screening be carried out?

NICE do not recommend routine screening for dementia in the general population.[3]
However, opportunistic screening should be carried out in patients at increased risk of dementia, e.g. patients with Down's syndrome, post stroke and Parkinson's disease, or with a large number of vascular risk factors.[1]

Signs and Symptoms

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.[1] It is therefore essential to get an account of the person's problems from a close relative or friend.[15]

Signs and symptoms are often not specific to dementia.[1] 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:[1]

Cognitive symptoms

- Memory problems such as forgetfulness, repetitive questioning, difficulty finding names and other words, not knowing common facts.
- Misunderstanding spoken and written communication.
- Disorientation.[1]

Difficulties with activities of daily living (ADL)

- Difficulty with orientation, getting lost, loss of driving skills.
- Taking prescribed drugs erratically — for example uncharacteristic variations in INR (international normalized ratio) in a person normally taking stable doses of warfarin.
- Forgetting recipes when cooking, neglecting household chores, trouble with shopping, difficulty handling money.
- Neglecting hygiene or self-care, deterioration in personal appearance, or a reduction in social roles.
- Making mistakes at work.[1]

Challenging behaviours, psychiatric symptoms, and personality changes

- Withdrawal or apathy
- Loss of motivation
- Depression, agitation, anxiety
- Blunting of emotions and loss of interest, social withdrawal
- Disinhibition, inappropriate friendliness, flirtatiousness
- Suspiciousness, fearfulness, aggression, psychosis (delusions, hallucinations)
- Insomnia
- Restlessness, wandering, agitation, noisiness[1]

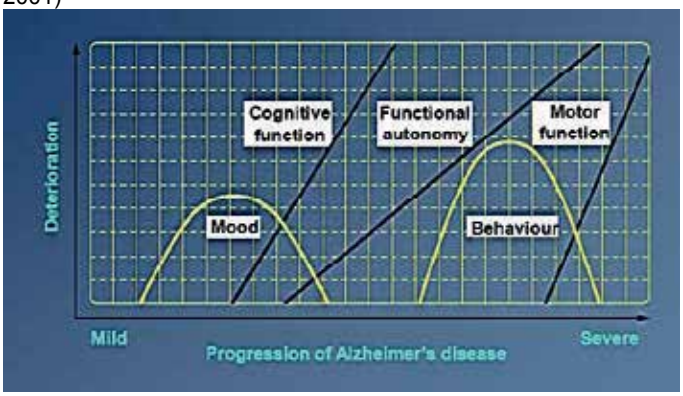
Neurological symptoms

- Gait disturbances, apraxia (loss of ability to perform learned purposeful movements).

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 self-care, 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 Behavioural and Psychological Symptoms of Dementia).[69]

GRAPH ONE: Pattern and Symptoms of Alzheimer's disease over time
(Lovestone and Gauthier, Management of Dementia, 2001)[23,86]



How is diagnosis made?

There is no simple test to make a diagnosis of dementia. Diagnosis can only be made after a comprehensive assessment, including [3]

- History taking
- Review of medication to identify any drugs that may impair cognitive functioning
- Cognitive and mental state examination
- Physical examination
- Neuroimaging

Who should make the diagnosis?

NICE clinical guidance currently recommends that the diagnosis of dementia (including subtype) should be confirmed by a specialist.[3] GPs can make an informed estimate of likelihood, and before referral start exploring and addressing the concerns of the person and their family or carer, and ensuring that people with dementia are given the opportunity to make informed decisions about their care and treatment.[1] GPs are generally the first port of call for people worried about their health and therefore it is important that GPs have a good knowledge of dementia and be aware of the importance of **early diagnosis**.[2]
The possibility of GPs taking on a more central role in the diagnosis and management of more routine and typical cases of dementia is being explored. This is in line with the concept of providing increased access to a more timely diagnosis, with better continuity of care and person-centred treatment reviews.[87]

Benefits of early diagnosis

An objective of the Dementia Strategy is to increase the numbers of people receiving a good quality early diagnosis of dementia. 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.[1] 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).
- Receive interventions which may slow the progression of the disease: start treatment early with AChE inhibitors.
- 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. [2]

What is Mild Cognitive Impairment (MCI)?

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 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.[3,90] 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.[15] See **TABLE THREE**.
Investigations should be carried out to exclude other causes:[1,3]

- A basic dementia screen at the time of presentation including:
  - Routine haematology
  - Biochemistry tests (electrolytes, calcium, glucose, and renal and liver function)
  - Thyroid function tests
  - serum vitamin B12 and folate levels
- A midstream urine test (if delirium is a possibility)
- Investigations such as chest X-ray (to rule out a chest infection) or electrocardiogram (ECG) (if a cardiovascular problem is suspected) may be considered, as determined by clinical presentation.[3]

When the onset of memory problems is **sudden**, a vascular event is often considered.[1]
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.[1]

What cognitive function tests are used?

Cognitive function tests are used alongside other investigations in determining whether a diagnosis of dementia is likely. NB – dementia is graded on overall severity, i.e. a composite of cognition, behaviour and activities of daily living (they don't always correlate).[3]

Cognitive testing is carried out using a standardised instrument, such as:[3]

- Mini Mental State Examination (MMSE)
- General Practitioner Assessment of Cognition (GPCOG)*
- Addenbrooke's Cognitive Examination
- Montreal Cognitive Assessment (MoCA)
- Alzheimer's Disease Assessment Scale (ADAS)
- 6-Item Cognitive Impairment Test (6-CIT)
- 7-Minute Screen.

* The General Practitioner Assessment of Cognition (GPCOG) tool has been designed for the primary care setting.

Mini Mental State Examination (MMSE)
MMSE is the most commonly used test to assess cognitive function. However, due to copyright issues with MMSE, some clinicians are looking at alternative tests in assessing cognition (see above).
MMSE is essentially a series of questions and tests, each of which scores points if answered correctly. A maximum of 30 points is possible.[15]
Severity of dementia is frequently defined by Mini Mental State Examination (MMSE) score:[24]

- Mild Alzheimer's disease: MMSE 21-26
- Moderate Alzheimer's disease: MMSE 10-20
- Moderately severe Alzheimer's disease: MMSE 10-14
- Severe Alzheimer's disease: MMSE less than 10 [24]

Factors that may affect performance in these tests, such as educational level, skills, prior level of functioning and attainment, language, sensory impairment, psychiatric illness and physical or neurological problems must be taken into account.[3]

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 activities of daily living (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)[86,95]

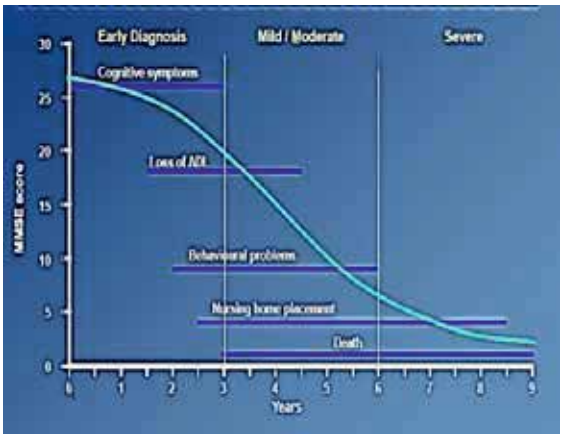


TABLE THREE: Differential Diagnosis of Dementia

Condition	Difference to dementia
Normal ageing	Normal ageing is associated with a mild decline in cognitive function. In dementia, the cognitive impairment is more severe and global, and results in clinically significant functional disability. Lapses of memory can occur due to physical illness or stress. If in doubt about the significance of memory lapses, offer to review in 3 months.[1]
Mild cognitive impairment	In mild cognitive impairment the person notices memory problems. However, the memory problems do not interfere with activities of daily life or social and occupational functioning, and general cognition is preserved. In dementia the person is not always aware of their symptoms.[1]
Depression	It is important to recognise depression because it is common, treatable, and can present with features similar to those of dementia. In comparison with dementia, the onset of depressive symptoms may be more rapid. Depression may become evident over a few weeks or months, while the symptoms of dementia may have been present for several months by the time the person presents to the healthcare professional. Depression can co-exist with dementia, and if both are new diagnoses, depression should usually be treated and controlled before managing the dementia.[1]
Delirium/ acute confusional state	It is important to recognise delirium (or acute confusional state) because it is common and treatable. In comparison with non-vascular dementia, the onset of symptoms are more rapid (over a few hours or days). Symptoms generally worsen at night, with increased confusion, disorientation, and emotional disturbance (fear, irritability, aggression). Paranoia and hallucinations (visual or auditory) are common. Common causes of delirium include chest infection, urinary tract infection, adverse effects of drugs, biochemical imbalance, and alcohol withdrawal. Delirium can co-exist with dementia, and if both are new diagnoses, delirium should usually be treated and controlled before managing the dementia.[1]
Parkinson's disease versus Lewy body dementia	Parkinson's disease dementia is diagnosed if the motor symptoms appear more than 12 months before the cognitive symptoms. Dementia with Lewy Bodies is diagnosed when someone has symptoms of dementia before or at the time of developing Parkinson's disease-like symptoms.[15]
Drugs – adverse effects and drug interactions	**Psychoactive drugs** Psychoactive drugs are the commonest causes of drug-induced cognitive impairment and delirium (e.g. benzodiazepines, antidepressants, analgesics, anticonvulsants, antipsychotics and anti-Parkinsonian drugs). **Non-psychoactive drugs** Non-psychoactive drug-induced confusion is harder to spot as they are often peculiar to the individual and the diagnosis is easily missed. Examples include proton pump inhibitors, digoxin, calcium antagonists, corticosteroids and some antibiotics.[1] **Anticholinergic burden** Drugs with anticholinergic activity can increase the risk of cognitive impairment and delirium in those aged over 65 years. A drug may be given an anticholinergic burden (ACB) score on the basis of the strength of its anticholinergic activity. Drugs with a high ACB score include tricyclic antidepressants, antipsychotics such as quetiapine and olanzapine (risperidone has a slightly lower ACB score), and antimuscarinic drugs used for urinary incontinence/frequency, e.g. oxybutynin, tolterodine, darifenacin (alpha blockers such as tamsulosin would not be included under anticholinergics). Effects are additive: individuals who take multiple medicines with individually modest anticholinergic activity may also have increased risk of adverse effects. Therefore the combined anticholinergic burden should be taken into account.[91-94] For further information on the anticholinergic burden please refer to HSCB Medicine Safety Alert: http://www.hscboard.hscni.net/medicinesmanagement/Medicines%20Safety%20Alerts/011%20No11%20Anticholinergic%20Syndrome%20-%20October%202012%20-%20PDF%20395KB.pdf

Following diagnosis

People who are assessed for possible dementia should be asked whether they wish to know the diagnosis and with whom it should be shared.[3]
At the time of diagnosis, and regularly afterwards, medical and psychiatric co-morbidities, including depression and psychosis should be assessed.[3]
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. [2]

Voluntary agencies such as **Alzheimer's Society** (www.alzheimers.org.uk/ helpline: 028 9066 4100) and **Age NI** (www.ageuk.org.uk/northern-ireland; advice line: 0808 808 7575) can be extremely useful support networks.

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.

Prevention Strategies

Is dementia preventable?

According to the Improving Dementia Services in Northern Ireland Strategy, delaying the onset of dementia in the population by five years could halve its prevalence.[2] Therefore it is important that steps are taken to reduce the risk of dementia.

What are the main risk factors?

Not all risk factors will be modifiable and others will be specific to particular types of dementia.[2]
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.[2]
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.[2]

NICE are currently developing public health guidance on delaying the onset of disability, frailty and dementia in later life. The guidance will focus on preventive approaches that may be adopted in mid-life. It is expected to be issued February 2015.[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.

TABLE FOUR: Non-modifiable Risk Factors

Risk factor	Perception of risk
Age	Advancing age is the biggest risk factor for dementia. [2]
Gender	Women are slightly more likely to develop Alzheimer's disease than men (even discounting for increased life expectancy).[12] 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] 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. These are much rarer and include examples such as 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 blood circulation all significantly affect a person's chances of developing dementia, particularly vascular dementia. Examples include: diabetes, heart problems, atrial fibrillation, and stroke.[2] 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.[2] Some factors affecting cardiovascular disease are modifiable – see Modifiable Risk Factors. **Depression** 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. Management of depression in Alzheimer's disease is discussed later.[12] **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.[2] **Other Medical Conditions** Examples include: Parkinson's disease, multiple sclerosis, chronic kidney disease and HIV.[12]

TABLE FIVE: Modifiable Risk Factors

Risk factor	Perception of risk
Smoking	Risk factor for both Alzheimer's and vascular dementia. Likely due to harmful effects on the heart, lungs and vascular system, including the blood vessels in the brain.
Alcohol	Risk is linked to excessive consumption. Drinking within the recommended limits is unlikely to increase the risk of dementia. Some research suggests that drinking light to moderate amounts of alcohol may actually protect against dementia. Alcohol-related Brain Injury (Korsakoff's syndrome) is caused by a lack of vitamin B1. It is seen in people who regularly drink excessive amounts of alcohol over a long period of time. It is not strictly a dementia, but is characterised by memory loss.[12]
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.
Hypertension	In mid-life this has been shown to be a risk factor for the development of both vascular dementia and Alzheimer's.
Raised cholesterol	Has been associated with the development of Alzheimer's. It is also a risk factor for cardiovascular disease, and therefore, vascular dementia.
Raised homocysteine levels	Raised homocysteine levels in the blood and low levels of folate may be associated with heart disease, stroke and an increased risk of dementia.[2]
Benzodiazepines	Benzodiazepines are associated with cognitive impairment. Use of benzodiazepines (or similar drugs) may also be associated with 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. [56,57]

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.

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.[12] Fresh fruit and vegetables contain many vitamins and antioxidants, which may help prevent dementia. In addition to this, low levels of vitamin D are associated with an increased risk of developing dementia. Good dietary sources of vitamin D include eggs and oily fish. Fatty acids also found in oily fish may also help reduce the risk of developing dementia.[12]

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.[12] 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.[2] 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.[12] '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'.[12]

Social activity

Research suggests that people who are more socially active have a slightly reduced risk of developing dementia.[12]

Interventions for prevention?

NICE specify that the following are <u>not</u> used for primary prevention of dementia: statins, hormone replacement therapy, vitamin E and NSAIDs.[3] For the secondary prevention of dementia, vascular and other modifiable risk factors should be reviewed in people with dementia.[3]

Any evidence for alternative therapies?

Alternative therapies that have been tried for primary prevention of dementia include ginkgo biloba[54] and omega 3 fish oils[27]. To date, there is inconclusive evidence that either is effective.

A Cochrane review in 2012 reported that direct evidence of omega 3 fish oils in reducing the incidence of dementia is lacking; the available trials showed no benefit of omega 3 fish oil supplementation on cognitive function in cognitively healthy older people.

A 2009 Cochrane review reported that there is no conclusive evidence on the efficacy of Ginkgo biloba for dementia or cognitive impairment. The review found that available evidence is inconsistent and unreliable.[54]

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.[2,15] 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.[2,15]

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 [2]

What about Medical Foods?

There are currently three medical foods that claim to offer symptomatic benefits for people with Alzheimer's

disease: Axona®, CerefolinNAC® and Souvenaid®. They contain ingredients such as omega fatty acids and phospholipids. More extensive studies are needed to provide clearer information on the benefit of each product. To date, most studies have been conducted in patients with mild Alzheimer's disease and it is not possible to generalise results to all stages of Alzheimer's disease.[72] There is no evidence that these products benefit people with moderate Alzheimer's disease or in those already taking drugs for Alzheimer's disease.
Cost of Souvenaid®: £3.49 per 125mL drink.

Drug Treatments

Vascular dementia

The major difficulty clinically is that in older people vascular disease and Alzheimer's disease commonly co-exist. Pure vascular dementia is quite rare. Treatment of vascular dementia focuses on controlling underlying risk factors for cardiovascular disease.[9] There are no medicines licensed in the UK for vascular dementia.[9] Trials to investigate the benefit of acetylcholinesterase (AChE) inhibitors or memantine in vascular dementia have been inconclusive.[58] 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.[9]

Dementia with Lewy Bodies (DLB)

The effect of AChE inhibitors in DLB remains unclear.[79] Rivastigmine is licensed for mild to moderately severe Alzheimer's dementia and mild to moderately severe dementia in patients with idiopathic Parkinson's disease dementia.[73] Due to clinical similarities between DLB and dementia in patients with Parkinson's disease, rivastigmine would seem a logical choice of AChE inhibitor for patients with DLB. There is some evidence that rivastigmine can reduce some behavioural problems in DLB – see later.

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

Who should initiate drug treatment?

Currently, NICE recommend that only specialists in the care of patients with dementia (that is, psychiatrists including those specialising in learning disability, neurologists, and physicians specialising in the care of older people) should initiate treatment. GPs may continue treatment under Shared Care arrangements. Drugs for dementia are currently amber listed. [29]

NICE Guidance [3]

Mild to Moderate Alzheimer's disease:
One of the three acetylcholinesterase (AChE) inhibitors are recommended as options:

- Donepezil
- Galantamine
- Rivastigmine.

Moderate to Severe Alzheimer's disease:
Memantine is recommended as an option for managing Alzheimer's disease for people with:

- Moderate Alzheimer's disease who are intolerant of or have a contraindication to AChE inhibitors or
- Severe Alzheimer's disease.[3]

How do AChE inhibitors work?

One theory of the cause of Alzheimer's disease is progressive loss of cholinergic neurons and decreasing levels of acetylcholine in the brain.[36] Acetylcholinesterase and butyrylcholinesterase play an important role in the degradation of acetylcholine.[37] Therefore inhibitors of these enzymes increase the concentration of acetylcholine at sites of neurotransmission.[9,24]

Which AChE inhibitor to choose?

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. Few head-to-head studies have been published and there have been differences in both populations studied and trial design.[9] However, to date, similar efficacy and tolerability between AChE inhibitors is assumed.[9] 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.[42]
All three AChE inhibitors are available generically as oral formulations.[74]

TABLE SIX: Cost of dementia drugs for 28 days [74]

Dementia drug	Strength and formulation	Brand name	Cost (28 days)
Donepezil	5mg tablets	Non-proprietary	£2.19
		Aricept®	£59.85
	10mg tablets	Non-proprietary	£2.89
		Aricept®	£83.89
	5mg orodispersible tablets	Non-proprietary	£36.49
		Aricept Evess®	£59.85
	10mg orodispersible tablets	Non-proprietary	£50.58
		Aricept Evess®	£83.89
Galantamine	8mg MR capsules	Acumor® XL	£49.26
		Galsya® XL	£51.88
		Reminyl® XL	£51.88
	16mg MR capsules	Acumor® XL	£61.65
		Galsya® XL	£64.90
		Reminyl® XL	£64.90
	24mg MR capsules	Acumor® XL	£75.81
		Galsya® XL	£79.80
		Reminyl® XL	£79.80
Rivastigmine	1.5mg capsules	Non-proprietary	£66.51
		Exelon®	£66.51
	3mg capsules	Non-proprietary	£66.51
		Exelon®	£66.51
	4.5mg capsules	Non-proprietary	£66.51
		Exelon®	£66.51
	6mg capsules	Non-proprietary	£66.51
		Exelon®	£66.51
	4.6mg/24hr patch	Exelon®	£77.97 (30 days)
	9.5mg/24hr patch	Exelon®	£77.97 (30 days)
Memantine	10mg tablets	Ebixa®	£34.50
	20mg tablets	Ebixa®	£69.01

Practices are asked to **prescribe generically** so savings can be made as soon as the generic price drops. Also, consider the need before prescribing an orodispersible donepezil formulation.

How is response to treatment determined?

It is difficult to predict how an individual will respond to treatment.[9] Clinical effects are measured in terms of cognition, function, behaviours and global assessments.[3] Patient response can be described as one of three ways:

- **Non-responders** – continue to decline at the anticipated rate (33.3% of patients over six months)
- **Non-decliners** – neither improve significantly or decline further (33.3% of patients over six months)
- **Improvers** – improve to a clinically significant extent* (33.3% of patients over six months)

* Show a > 4-point improvement on ADAS score.[9]

Benefit is assessed by repeating the cognitive assessment at **around 3 months**. Drugs for dementia should be discontinued in those thought not to be responding. Many specialists repeat the cognitive assessment 4 to 6 weeks after discontinuation to assess deterioration; if significant deterioration occurs during this short period, consideration should be given to restarting therapy.[74]

Duration of treatment?

Patients who continue on treatment should be reviewed regularly using cognitive, global, functional and behavioural assessment.[3]
Studies have reported benefits of continued donepezil 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.[29] 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.[80]

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[9] (NB – tolerability appears to be related to speed of dose titration; more adverse effects are seen during titration).[9]
Switching AChE inhibitors is not recommended in patients who show loss of benefit several years after initiation of treatment.[81]
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.[43]
Another reason for changing therapy is if the working diagnosis is changed: patients may sometimes be switched to rivastigmine if the diagnosis is changed from Alzheimer's disease to Dementia with Lewy Bodies (it can take up to 18 months for diagnosis to be confirmed).

Prescribing Points with AChE inhibitors [9,24,73-77]

► 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 below

► AChE inhibitors are hepatically cleared.[80] Therefore caution in hepatic impairment

► Excess cholinergic stimulation can lead to nausea, vomiting, dizziness, insomnia and diarrhoea. Most 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

► Urinary incontinence has been reported [9]

► 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[9]

► 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 with donepezil and rivastigmine; avoid in galantamine

► Ulcers: caution in patients susceptible to peptic or duodenal ulcers (due to increased cholinergic activity causing increased gastric acid secretion)

TABLE SEVEN: Starting and maintenance doses of acetylcholinesterase inhibitors[74]

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 SPCs specify 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.[66]

If switching, withdraw gradually or 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.[38,39] A faster titration may be adopted.[41,80,81]
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.[81]

What about combination treatment?

Currently NICE do not recommend combination treatment of memantine with an AChE inhibitor.[3] However, in practice, memantine is often added in to existing AChE inhibitor therapy. For patients with moderate to severe Alzheimer's disease, memantine is usually initiated once patients have been maintained on stable AChE inhibitor therapy. This is often for management of behavioural symptoms, particularly agitation[3] (as per NICE – see BPSD later).
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)[50] and a delay in nursing home placement.[51]
Adding memantine to an AChE inhibitor appears to be well tolerated.[9,47-49] In terms of drug interactions, no pharmacokinetic or pharmacodynamic interactions have been found between donepezil and memantine or galantamine and memantine.[52,53] Patients who are established on an AChE inhibitor should not have this treatment stopped when memantine is prescribed as a dramatic decline in functioning is seen which may not be fully regained when restarted.

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.

How does memantine differ?

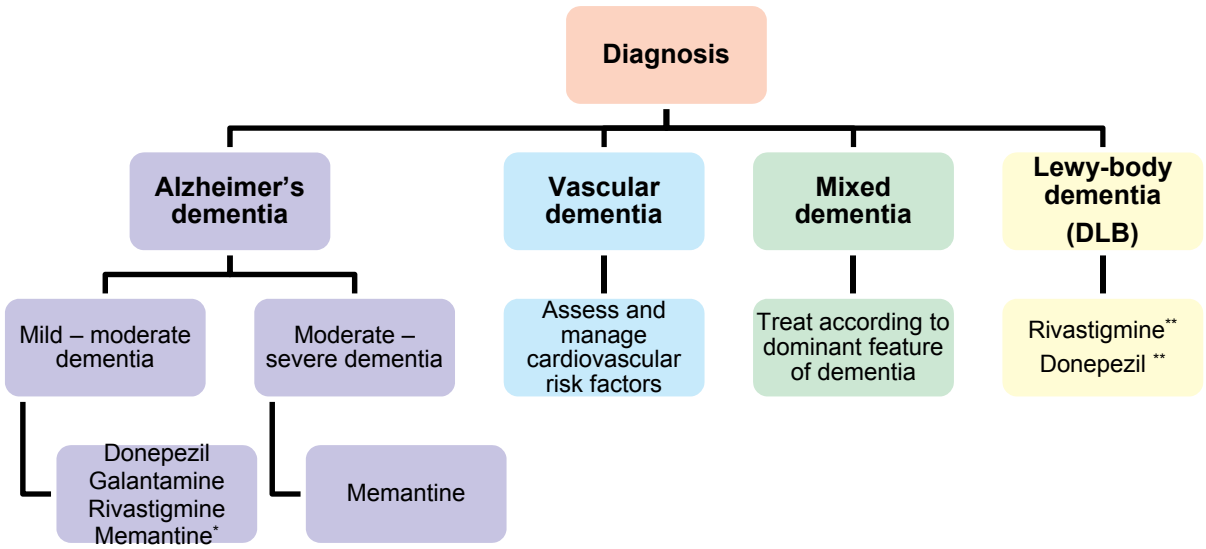
Glutamate is released in excess in cells damaged by Alzheimer's disease. Memantine is a voltage-dependent, moderate-affinity, uncompetitive N-methyl-D-asparate (NMDA) receptor antagonist. Memantine blocks the effects of pathologically elevated tonic levels of glutamate, preventing further neuronal dysfunction.[24,62,74,76,80]

Prescribing Points with memantine [24,62,74,76,80]

► 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 in patients with epilepsy or a history of seizures.
► Hepatic impairment – avoid in severe impairment.
► Memantine is renally excreted. Caution therefore 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:[74]

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

CHART TWO: Summary of treatment options for dementia
(Taken from Northern Health and Social Care Trust algorithm)



* Memantine: moderate Alzheimer's dementia in those intolerant of or in whom AChE inhibitors are contraindicated.
** Rivastigmine and donepezil 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. Donepezil is licensed for the symptomatic treatment of mild to moderately severe Alzheimer's dementia.

TABLE EIGHT: Drug Interactions with dementia drugs [9,73-77]

Drugs for dementia	Interacting drugs	Nature of Interaction
Donepezil	Ketoconazole, itraconazole, erythromycin, quinidine, fluoxetine	Increased plasma level of donepezil through CYP 3A4/2D6 inhibition
	Rifampicin, phenytoin, carbamazepine, alcohol	Decreased plasma level of donepezil through CYP 3A4/2D6 induction
	Anticholinergics	Antagonistic effect
	Anaesthesia	Additive effect on succinylcholine-type muscle relaxation
	Cholinergic agonists (e.g. bethanecol)	Additive effect
	Bradycardic drugs (e.g. beta blockers, digoxin, amiodarone, calcium channel antagonists)	Additive vagotonic effects on heart rate, e.g. bradycardia
	Antipsychotics	Increased risk of neuroleptic malignant syndrome
Rivastigmine	Non-hepatic metabolism. Therefore metabolic interactions unlikely	
	Cocaine	Rivastigmine may inhibit the butyl cholinesterase mediated metabolism of other substances
	Anticholinergics	Antagonistic effect
	Anaesthesia	Additive effect on succinylcholine-type muscle relaxation
	Cholinergic agonists (e.g. bethanecol)	Additive effect
Galantamine	Ketoconazole, erythromycin, ritonavir, quinidine, paroxetine, fluoxetine, fluvoxamine, amitriptyline	Increased plasma level of galantamine through CYP 3A4/2D6 inhibition
	Anticholinergics	Antagonistic effect. Avoid concomitant use
	Cholinomimetics	Additive effect. Avoid concomitant use
	Bradycardic drugs	Additive vagotonic effects on heart rate
	Drugs that cause torsades de point	Additive effect. ECG recommended
Memantine	Cimetidine, ranitidine, procainamide, quinidine, quinine, nicotine	
	Warfarin	Isolated cases of increased INR. Monitor closely
	Drugs that alkalinise urine (e.g. carbonic anhydrase inhibitors, sodium bicarbonate)	Reduce renal elimination of memantine
	Hydrochlorothiazide	Possible reduced level of hydrochlorothiazide
	Levodopa, dopaminergic agonists, anticholinergics	Effects enhanced
	Barbiturates and neuroleptics	Effects of these may be reduced
	Amantadine, ketamine and dextromethorphan	Risk of pharmacotoxic psychosis
	Phenytoin	One published case report on risk
	Dantrolene and baclofen	Dosage adjustment may be necessary
NB – This list is not exhaustive. Caution will be required with other drugs metabolised via CYP 3A4 and 2D6		

Management of Behavioural and Psychological Symptoms of Dementia (BPSD)

What are 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.[69]
BPSD are common and can be very distressing. BPSD vary in both their presentation and underlying cause.[32]
These symptoms are often associated with chemical changes in the brain or by social and environmental triggers.[7] Behavioural problems typically begin with subtle personality changes and progress to increasing lapses of social propriety.[32,69] They are the largest risk factor for people with dementia entering institutional care.[31,100]

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) Agitation (aggression, irritability, restlessness, pacing. Usually associated with distress or anxiety).[85]

These can manifest as:

- Aggression
- Restlessness
- Agitation
- Sleep disturbance (day night reversal)
- Calling out repeatedly/ disruptive vocal activity such as shouting or screaming

- Wandering
- Apathy
- Hoarding
- Cursing
- Sexual disinhibition
- Shadowing.[3,15]

Incidence of BPSD?

Over 90% of people with dementia develop behavioural problems or psychiatric symptoms at some point during their illness.[31] BPSD occur most commonly in the middle stage of dementia.[15] Depressive and apathetic symptoms are usually the earliest to appear. [100] Hallucinations, elation/euphoria, and aberrant motor behaviour (inability to sit still) are usually the last symptoms to emerge.[100]
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.[9] 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.[18,7] Furthermore, antipsychotics are often continued for long periods of time without review.[96]

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.[44]
SPCs for all antipsychotics (atypical and conventional) now carry a warning about possible cerebrovascular risk.[9]

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)[18]

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.

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.[33]

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.

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

First Line Management Options

1) Identify possible trigger factors of BPSD
2) Is there an underlying medical problem?
3) Can simple non-drug options improve symptoms?
4) Watchful waiting

Identify trigger factors

An early and comprehensive assessment to establish the likely factors that may generate, aggravate or improve such behaviour.[3] 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.[7] Physical health problems include infection, pain and dehydration.[84]

Infection
Urinary tract infections and chest infections are frequent trigger factors for BPSD. Dental infections are also common but often not recognised.[84]

Undetected pain
Pain is one of the most common causes of BPSD.[7]
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.[5,7]

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.[97]

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.[84]

Environmental factors
The characteristics of the environment are an important contributory factor to BPSD.[33]
A lack of meaningful stimulation can be linked to a high prevalence of BPSD.[33] 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 constructive 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[69]
- 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 active 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.[7]
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.[3]

Treat the Target Symptoms

There are no adequate drug treatments available for non-cognitive behavioural symptoms at present.[12]
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.[3] Care plans should focus on round the clock care, i.e. not just on the daytime, when 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.[3]

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.[80]
People at this stage of dementia are likely to already be receiving an AChE inhibitor for cognition.
Dementia drugs would only be tried where behaviours are relatively mild; if the symptoms are severe and

distressing or dangerous then antipsychotics may be needed.

AChE inhibitors
Donepezil, rivastigmine and galantamine were developed as symptomatic treatments for dementia and are licensed for the treatment of people with mild-moderate Alzheimer's disease. Evidence suggests that they may also have beneficial effects on behavioural symptoms.[33] It can take several weeks of treatment for effects to become apparent.[51]

Memantine
Ongoing RCTs in Canada and in the UK will hopefully clarify the role of memantine in the treatment of agitation/aggression in Alzheimer's disease and vascular dementia.[85] There is growing evidence to support the use of memantine for treating and preventing the behavioural symptoms of moderate to severe Alzheimer's disease.[9,59-62] Significant effects were seen as early as week 12.[61] Optimising the management of patients with Alzheimer's disease involves reducing the emergence of new symptoms as well as controlling existing behavioural changes.[61]

AChE inhibitors and memantine appear to produce complementary benefits on different types of BPSD – **AChE inhibitors:** appear to reduce depression, anxiety and apathy-related BPSDs while **Memantine:** may reduce symptoms such as agitation, aggression, irritability/lability, and psychosis.[80]

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.[78]

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.[3,9,45]

When not to offer an Alzheimer's treatment for BPSD?[3,9,45]
Do not offer to people who have purely vascular dementia. An AChE inhibitor or memantine may be *trialled* in people with mixed dementia.
Antipsychotics should ideally be avoided in patients with vascular dementia due to risk of stroke.

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.[7,84] However, for more severe depression, antidepressants are considered.[7,84]
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.[70] Recent studies suggest that antidepressants may have lower efficacy for depression in Alzheimer's disease.[12,35]

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

- Reducing daytime napping
- Increasing activities during the day (rather than napping)
- Agreeing realistic expectations for sleep duration.[7]

When sleep hygiene measures have failed, short term treatment (4 weeks) with a hypnotic such as zopiclone (3.75 mg/day) or zolpidem (5 mg/day) can be considered. However, this is only supported by anecdotal evidence.[7]

Caution: Benzodiazepines
Benzodiazepines should not routinely be used to manage BPSD or be considered 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 recommend that "medication for non-cognitive symptoms or behaviour that challenges should be considered in the first instance **only if there is severe distress or an immediate risk of harm to the person with dementia or others**. For less severe distress and/or agitation, a non-drug option should be used initially."[3] The drug should be administered orally, at the lowest effective dose, for the shortest possible time (ideally no longer than 12 weeks).

Antipsychotics are most helpful in the control of symptoms such as **hallucinations** and **delusional thinking** rather than for agitation or attenuating aggression.[69] Hallucinations and delusions indicate psychosis and must be distinguished from disorientation, fearfulness and misunderstanding, which are common in people with dementia.[97]
Symptoms such as restlessness and repetitive vocalisation/shouting out can be the expression of unmet needs.[12] There is no evidence that antipsychotics show benefit for repetitive vocalisation/shouting out.[105]

Which antipsychotic should be used?
NICE recommend that if antipsychotic treatment is appropriate, the specific drug should be chosen after an individual risk-benefit analysis, including an analysis of the cerebrovascular risk of the patient. There is evidence to support risperidone and olanzapine in reducing physical aggression, agitation and psychosis.[44] Quetiapine appears to be widely used in elderly people but there is no evidence to support

effectiveness in BPSD and it can cause significant postural hypotension and sedation.[82]
Olanzapine has anticholinergic properties and is associated with rapid and significant weight gain.[82]

Licensed use of antipsychotics
Risperidone is licensed for: short-term treatment (up to 6 weeks) of persistent aggression in patients with moderate to severe Alzheimer's dementia unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others.[30]
Other than risperidone, use of antipsychotics to manage BPSD is off-label. Service users/carers should be informed of this

Conditions for prescribing an antipsychotic

According to NICE, people with Alzheimer's disease, vascular dementia, 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.
- 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; there is no 'preferred choice'.
- 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).**[3,7]

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

Antipsychotic	Low dose for BPSD
Risperidone	250 micrograms twice daily[55]
Olanzapine	2.5mg once daily
Aripiprazole	5mg once daily
Quetiapine	12.5mg twice daily[7]

Prescribing Points for Low Dose Antipsychotics
► They are for short term use only. Patients must be evaluated frequently and regularly, and the need for continuing treatment reassessed[30]
► A cardiac risk assessment is recommended prior to starting a prescription[7]
► 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[106]

People with Dementia with Lewy Bodies:
Rivastigmine is the first line treatment; this should be tried for several weeks.
An antipsychotic should only be used after **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.

Review & Stopping antipsychotics

A recent Cochrane Review (2013) concluded that many older people with Alzheimer's disease and BPSD can be withdrawn from chronic antipsychotic medication without detrimental effects on their behaviour.[96] Discontinuation programmes could be incorporated into routine practice.[96]
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.[85] Therefore treatment should only be continued beyond 12 weeks in exceptional circumstances; discontinuation should be default except in extreme circumstances.[7,85] 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.[99]

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.[67]

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.[96]

Consult the best-practice guide from Alzheimer's Society:[7]
http://alzheimers.org.uk/site/scripts/download_info.php?downloadID=609

TABLE TEN: How to stop an antipsychotic?

Dose of antipsychotic	How to discontinue
If the person is receiving a **low** dose	Proceed directly with discontinuation. Monitor patient and review at two weeks.[7]
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 [7]

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.[7]

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.[96]

Summary: Good practice points in managing BPSD

- Consider specialist referral in cases of extreme risk or distress.[7]
- Begin management with 'watchful waiting' for 4 weeks (including assessment of medical conditions and pain) and simple non-drug assessment.[7]
- Use specific interventions if symptoms are severe or persist after watchful waiting and simple non-drug treatments:
  - Psychosocial treatments and behavioural interventions.
  - Drug treatment of underlying health disorders (e.g. pain relief, infections) as appropriate.[7]
- Consider a time-limited trial of antipsychotics if specific interventions have been unsuccessful and symptoms are causing extreme distress or risk of harm.[7]
- 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.[68]

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COMPASS THERAPEUTIC NOTES ASSESSMENT
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1	**In relation to background and diagnosis of dementia:**			
	a	Dementia is part of normal ageing	T	F
	b	Vascular dementia is more common in smokers and patients with heart disease, hypertension, diabetes or high cholesterol	T	F
	c	Opportunistic screening should be carried out in patients at increased risk of dementia, e.g. patients with Down's syndrome	T	F
	d	Patients with symptoms of mild cognitive impairment do not need to be assessed for dementia	T	F
2	**In relation to risk factors for dementia:**			
	a	It is thought that delaying the onset of dementia in the population by five years could halve its prevalence	T	F
	b	Smoking is thought to be a risk factor for vascular dementia but not Alzheimer's disease	T	F
	c	Advancing age is the biggest risk factor for dementia	T	F
	d	Vascular dementia is more common in women than men	T	F
3	**In relation to drug treatment for cognitive symptoms:**			
	a	Weight loss is a reported side effect and the patient's weight should be monitored	T	F
	b	People who have neither improved significantly or declined further within 3 months treatment should be discontinued	T	F
	c	Dose titration regimens are used to minimise side effects	T	F
	d	Acetylcholinesterase inhibitors should be switched in patients who show loss of benefit several years after initiation of treatment	T	F
4	**In relation to management of Behavioural and Psychological Symptoms of Dementia (BPSD):**			
	a	Drug treatment should be targeted to the symptoms	T	F
	b	Memantine is often added to existing acetylcholinesterase inhibitor therapy to manage behavioural symptoms	T	F
	c	Antidepressants are considered first line treatment option for depression	T	F
	d	Benzodiazepines should be considered a routine treatment option.	T	F
5	**In relation to low dose antipsychotics for the management of BPSD:**			
	a	Low dose antipsychotics are first line treatment option	T	F
	b	It is OK to continue for long periods of time without review	T	F
	c	Studies have shown on-going treatment offers no benefit over longer periods (more than 12 weeks)	T	F
	d	Quetiapine is the only drug licensed for short term management	T	F