



**ADVISORY REPORT OF THE SUPERIOR HEALTH COUNCIL no. 8890**

**Dementia : Diagnosis, behaviour management, ethical issues**

In this scientific advisory report on public health policy, the Superior Health Council of Belgium provides recommendations on diagnosis, behaviour management and ethical issues for dementia

This report aims at providing professionals with specific recommendations on diagnosis, behaviour management and ethical issues for dementia.

This version was validated by the Board on  
February 2016<sup>1</sup>

Keywords and MeSH *descriptor terms*<sup>2</sup>

MeSH terms*	Keywords	Sleutelwoorden	Mots clés	Schlüsselwörter
Dementia	Dementia	Dementie	Démence	Demenz
Alzheimer disease	Alzheimer	Alzheimer	Alzheimer	Alzheimer
Neurocognitive Disorders	Neurocognitive disorder	Neurocognitieve stoornis	Trouble neurocognitif	neurokognitive Störung
Mild cognitive impairment	Mild cognitive impairment	Milde cognitieve stoornis	Trouble cognitif léger	leichte kognitive Beeinträchtigung
Diagnosis	Diagnosis	Diagnose	Diagnostic	Diagnose
	Behavioural and psychological symptoms of dementia (BPSD)	Gedrags- en psychologische symptomen van dementie	Symptômes psychologiques et comportementaux de la démence	verhaltensbezogene und psychologische Symptome der Demenz
	Practice	Praktijk	Pratique	Praxis
Ethics	Ethics	Ethiek	Ethique	Ethik

MeSH (Medical Subject Headings) is the NLM (National Library of Medicine) controlled vocabulary thesaurus used for indexing articles for PubMed <http://www.ncbi.nlm.nih.gov/mesh>.

<sup>1</sup> The Council reserves the right to make minor typographical amendments to this document at any time. On the other hand, amendments that alter its content are automatically included in an erratum. In this case, a new version of the advisory report is issued.

<sup>2</sup> The Council wishes to clarify that the MeSH terms and keywords are used for referencing purposes as well as to provide an easy definition of the scope of the advisory report. For more information, see the section entitled "methodology".

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### List of abbreviations used

AChEI	Acetylcholinesterase inhibitors
ACP	Advance care planning
AD	Alzheimer's disease
ADL	Activities of daily living
ALCOVE	Alzheimer Cooperative Valuation in Europe

Belpep	Belgian Psychotropics Expert Platform
BPSD	Behavioural and psychological symptoms of dementia
bvFTD	Behavioral variant of frontotemporal dementia
CBZ	Carbamazepine
CMAI	Cohen-Mansfield Agitation Inventory
CSF	Cerebrospinal fluid
CVD	Cerebrovascular disease
DLB	Dementia with Lewy bodies
FTD	Fronto-temporal dementia
FTLD	Frontotemporal lobar degeneration
GP	General Practitioner
IADL	Instrumental Activities of Daily Living
IQCODE	Informant Questionnaire for Cognitive Decline in the Elderly
IWG	International Working Group
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
MRI	Magnetic Resonance Imaging
NINCDS-ADRDA	National Institute of Neurological and Communicative Disorders and Stroke – Alzheimer's Disease and Related Disorders
NPI	Neuropsychiatric Inventory
PNFA	Progressive nonfluent aphasia
PPA	Primary progressive aphasia
PET	Positron Emission Tomography
RCT	Randomized Controlled Trial
SSRI	Serotonin-specific reuptake inhibitors

## I INTRODUCTION AND ISSUE

In 2012, a WHO report on the world-wide issue of dementia ("Dementia: a public health priority") estimated that the number of cases of dementia will have tripled by 2050. The report also deplored the fact that only 20 to 50% of dementia cases are diagnosed, often too late. Hence the need for early diagnosis but also of raising public awareness of dementia-related disorders and of reducing the stigmatisation of patients. Indeed, the latter often face social isolation, which is linked to a lack of information on and understanding of dementia. Early care and the differential diagnosis also stand to benefit from a better knowledge of the first clinical signs. Finally, special attention should also be paid to the providing of help to those with the illness and those taking care of them, the issue of residential care as well as healthcare staff training in long-term clinical care.

Moreover, this is obviously an issue that concerns us all. The increased life-expectancy has had as a corollary that the number of age-related diseases too is on the rise. Also, this is an issue that not only affects the individuals themselves, as the illness may also have consequences for their families, those close to them, and society as a whole. In addition, there is no cure for dementia, but an optimal offer of care and services may alleviate its impact on the individuals themselves, those close to them or society.

Given these findings, the Superior Health Council (SHC) decided to offer recommendations with the intent of providing proper information on this illness to the public, patients and their families, the professionals concerned as well as the authorities. In order to do so, the Council examined the various existing "dementia plans" and reports available on this issue in Belgium as well as the

various guidelines provided in the international literature. In addition, the SHC devoted particular attention to the 2013 ALCOVE report (*Alzheimer Cooperative Valuation in Europe – European Joint Action on Dementia - 2013*), which offers a series of recommendations on epidemiological issues, diagnosis, behaviour disorders, advance directives and exposure to neuroleptics. Among other things, the aim was to assess how these recommendations could be implemented in Belgium. The Council also cooperated with the *Belgian Psychotropics Expert Platform* (BelPEP) in order to draw up recommendations regarding the use of psychopharmaceuticals in elderly people.

Taking into account all of these documents as well as the research conducted on this issue, the working group ultimately decided that the SHC advisory report should focus on the quality of the diagnosis on the one hand, and on the appropriateness of taking an analytical approach to managing the altered behaviour that may be linked to dementia on the other. Indeed, these alterations often worsen the distress of the patients and those close to them, whilst the only treatment provided for them often merely consists of a pharmacological approach, the full limits of which have, however, been revealed in a previous advisory report of the SHC (SHC 8571, 2011). Finally, the SHC also considered it important to look at several ethical (and legal) questions raised by this issue.

## I METHODOLOGY

After analysing the request, the Board and, when appropriate, the Chair of the area mental health identified the necessary fields of expertise. An *ad hoc* working group was then set up which included experts in psychiatry, neurology, psychology, ethics, geriatrician, general practice. The experts of this working group provided a general and an *ad hoc* declaration of interests and the Committee on Deontology assessed the potential risk of conflicts of interest.

This advisory report is based on a review of the scientific literature published in both scientific journals and reports from national and international organisations competent in this field (peer-reviewed), as well as on the opinion of the experts.

Once the advisory report was endorsed by the working group, it was ultimately validated by the Board.

## II ELABORATION AND ARGUMENTATION

### 1 Dementia: illness and care diagnostics and recommendations for practice

#### 1.1 Introduction

Older individuals often find themselves facing cognitive problems. As the latter can range from age-related cognitive changes through mild cognitive problems to a full-blown dementia syndrome, it is important to recognize the deficits. This allows professional caregivers to intervene when necessary and to provide support for the patients and their caregivers.

The normal ageing brain is characterized by a loss of brain weight and volume, which is a process that starts in the frontal lobes. The frontal lobe plays a crucial role in executive functions, attention and concentration, multitasking, speed processing, ... and it is these functions that are usually compromised in the elderly. This may lead to certain difficulties in activities of daily living (ADL), but their neurocognitive functions remain “normal” as long as they are still able to live independently. Typical problems arising among healthy older individuals are difficulties concentrating in a distracting environment as well as difficulties multitasking, difficulties remembering the names of people, things or facts and a slowing reaction speed.

Being aware of the factors that can adversely affect cognition and concentration (such as e.g. fatigue and/or depressive feelings) and addressing them are the most important tools for living with age-related cognitive problems.

With the growing knowledge on cognitive functioning, it became quickly apparent that there was a wide discrepancy between normal cognitive ageing and a dementia syndrome. According to Petersen's criteria, **Mild Cognitive Impairment** (MCI) refers to a degree of cognitive impairment that is not normal for healthy individuals of the same age, but does not induce dependency in daily functional abilities, which can be normal or slightly abnormal. Mild cognitive loss refers to the first stage of cognitive impairment, when patients or their relatives become aware of the signs and symptoms of cognitive decline. MCI is a well-described risk factor for dementia and thus often referred to as a prodementia phase of impaired cognition and functioning, even if the evolution of the syndrome is quite variable.

MCI comprises a heterogeneous group of neurocognitive disorders, characterised by memory loss, and/or impaired executive functions, language or visual-spatial skills, which are severe enough to be noticed by others, but not severe enough to significantly interfere with daily living. An impairment in episodic memory (i.e., the ability to learn and to memorize new information consciously) is more commonly observed when Alzheimer's disease (AD) is the underlying cause of the MCI, which may, in these cases, progress to AD dementia.

Between 6 and 25 % of MCI patients will evolve into Alzheimer's dementia or other dementia syndromes each year (McKhann et al., 2011; AAN, 2001).

**Dementia** is a common syndrome in the elderly. It occurs in 10% of people over 65, and 1 in 2 over-85-year-olds will suffer from a dementia syndrome. As the life-expectancy of the developed world in particular goes up, the prevalence of dementia is liable to take on epidemic forms.

However, other very recent data also show that there is a decrease in incidence in the West (Matthews et al, 2013), which is probably due to the fact that about 50% of AD cases are linked to lifestyle choices (Barnes & Yaffé, 2011).

For these reasons, the early detection and diagnosis of cognitive decline or dementia are highly situated on the political healthcare agenda. In recent years, the development of diagnostic tests that allow diagnosing AD in the prodromal and even in its preclinical phase (biomarkers, presymptomatic genetic testing) have taken a leap forward.

The diagnostic process may in fact be divided into four key stages, viz. detection, diagnosis, care diagnosis and monitoring (Buntinx et al, 2011; The European Joint Action on Dementia, 2013).

## 1.2 Screening and detection

### 1) *Screening*

Screening is a process that aims at identifying people who appear to be healthy but who may be at an increased risk of developing a particular disease or condition. They can then be offered information, further tests and appropriate treatment to reduce their risk and/or any complications arising from the disease or condition. For screening programs and strategies to be carried out, they need to meet the Jungner and Wilson criteria (Wilson & Jungner, 1968).

According to the literature, systematic screening for neurodegenerative brain disorders is not advisable, given the following facts :

- The Wilson and Jungner criteria are not sufficiently met to justify screening (Wilson & Jungner, 1968).
- Tests to detect pre-clinical stage/asymptomatic AD and other forms of dementia (screening) do not display sufficient efficacy (except for genetic testing in familial cases).

- There are no reliable tests available (except for genetic testing in familial cases) to screen for early signs of cognitive decline that make it possible to predict a future diagnosis until people actually complain of memory loss (as per symptom definition).
- Dementia and cognitive impairment due to neurodegenerative brain disorders are still untreatable conditions, as there is no physical cure available, nor any means to stop its progress .
- It is not yet possible to reverse or stabilise the loss of memory through pharmacological intervention.
- There are currently no scientific data available that show whether or not identifying cognitive decline in non-at-risk elderly people is cost-effective, even though some publications do show a decrease in institutionalisations in the event of early identification (Barnett et al., 2014; Getsios et al., 2012).
- Several publications have shown that it is not always appropriate to make an early diagnosis (De Lepeleire et al., 2004; De Lepeleire, 2009; Vernooij-Dassen et al., 2005; De Lepeleire & Heyrman, 1999). The risks include: negative attitudes towards dementia, misdiagnosis, and loss of autonomy. Screening is liable to cause harm to the patients and their relatives that could be of a personal, economic, psychosocial and legal nature.

In order to facilitate a process of adjustment and adaptation, it is proposed that early diagnosis should be replaced by **timely diagnosis**, a diagnosis made at the right moment, at the earliest stage as acceptable for patients and relative(s), and in response to an unmet need of a patient or relative occurring at a point when the person in question and their family are ready to undergo assessment. “Timely” implies a more person-centred approach that benefits the patient, one that does not tie the diagnosis to any particular stage of the disease but rather to the need 1/ for accurate information on new developments in the field of dementia, especially as regards novel biomarkers and treatments (cure & care + clinical studies) and 2/ for enhancing the empowerment of all patients and, in fact, for promoting advanced care planning, which is organised in cooperation with these patients (especially if there is NO screening).

## 2) *Detection – Timely diagnosis*

**Early detection** refers to recognizing possible warning signs of a disease and taking prompt action that leads to early diagnosis (WHO). This strategy is often applied in primary care and described as case finding. The aim is e.g. to identify specific target groups with specific risks (familial risk, patients with Down syndrome and other learning disabilities, stroke patients, patients with Parkinson's disease or with suspicious signs and symptoms (e.g. cognitive complaints)).

Targeted screening essentially begins with direct observation and communication.

It is also important to recognise the presence of an **MCI syndrome**, thus making it possible to give the patients and their caregivers all necessary information and evidence-based treatments. The cognitive impairment should always be examined in order to determine its aetiology. In many cases no therapeutic action will be undertaken, but follow-up remains mandatory in order to predict future problems (e.g. MCI in Lewy-body related syndromes, in frontotemporal lobar degeneration (FTLD), in vascular pathologies). Many disorders apart from AD are liable to induce MCI. It follows that the prognosis for MCI will differ depending on the aetiological diagnosis and that treatment is available for certain causes (such as depression, hypothyroidism, sleep disorders, side effects of medication etc.).

The NICE guideline [NICE, 2006] suggest that the assessment in patients with a cognitive problem includes

- a thorough anamnesis of the patients and their caregivers. An additional tool in this assessment can be the IQCODE (Informant Questionnaire for Cognitive Decline in the Elderly). (Harrison et al., 2014). However, there are not enough data available to date to suggest that the IQCODE should be part of the work-up of cognitive disorders (Cochrane, 2015);
- profiling of cognitive functioning and mental health. As depression can induce cognitive dysfunction that may be severe enough to be mistaken for a dementia syndrome, screening for depression should also be performed;
- a general physical and clinical neurological examination ;
- checking the medication in order to identify and minimize the use of drugs. Attention should also be paid to over-the-counter products that may have a (side) effect on cognitive functioning.

Next to the anamnesis and physical examination, the NICE guidelines suggest that further work-up should include a blood test (complete blood cell count, glucose, electrolytes, liver, kidney and thyroid functioning, VitB12 and folate levels).

As regards **MCIs that are induced by a neurodegenerative disorder**, the debate on the benefits, desirability and necessity of disclosing the diagnosis is still ongoing.

If the diagnosis is one of an incurable neurodegenerative disorder, patients may decide how far they wish to go in the diagnostic procedure. We emphasize that this thorough work-up is not mandatory nor obligatory for every patient with a cognitive disorder, as the patient has the right not to know, given the incurable nature of neurodegenerative brain disorders. The decision to initiate a diagnostic procedure or not, regardless of whether the latter is conducted by the general practitioner (GP) or hospital specialists, should always be taken with the patients and their caregivers. Whether or not a diagnostic process should be initiated depends on factors that are inherent to the patient as well as on relative characteristics. An analysis of the risks and benefits of examining the signs and symptoms should therefore be conducted before embarking on this course of action. Patients who are assessed for the possibility of dementia should be asked whether they wish to know the diagnosis and with whom this should be shared.

More specifically, if they do decide they want to know the diagnosis, the patients and their caregivers should be well aware of what the consequences are of knowing the diagnosis, of what can be and can't be done in terms of treatment, , and of how the disease will evolve, ... This information will be offered progressively and in a manner that is tailored to the patients' and caregivers' growing ability to take it all in (advance care planning).

From a patient and caregiver perspective, there are several reasons why a further diagnostic approach has an additional value:

- Acknowledging the problem can induce a sense of relief in patients and caregivers. « Our complaint is taken seriously ».
- Knowing that cognitive problems that are induced by certain conditions (e.g. sleep disorders, depression, side effects of medication, ...) will not progress into dementia will be of great relief to patients and caregivers and will allow for appropriate action to be taken.

- Having a diagnosis allows the patients and their (professional) caregivers to get a better understanding of the problem, and makes it possible to manage the patients and their cognitive problems more appropriately. Also, counselling can only start once a correct diagnosis is available.
- It offers the opportunity of addressing the right to know, increasing the quality of life, providing early access to intervention or treatment. Dementia and cognitive impairment due to neurodegenerative brain disorders can be treated symptomatically (psycho-education, cognitive rehabilitation, symptomatic pharmacological treatment options). There are currently only few clinical trials on curative or slowing therapeutic strategies that might have an effect on cognition in MCI patients (see Dominantly Inherited Alzheimer Network; Belleville, 2006; Belleville, Brain 2011; Grande, 2014). It also remains important to follow these patients, in order to, initiate a disease slowing therapy when a beginning Alzheimer's dementia is suspected.
- It offers the opportunity of allowing the patient to take decisions with regard to the end of life and advanced care planning.
- Some cognitive disorders can be caused by treatable or modifiable conditions, e.g. hypovitaminosis, hypothyroidism, or medication-related side effects.
- The prognosis depends on underlying aetiologies (i.e. vascular dementia has a worse prognosis than AD; the prognosis is different in the event of dementia with Lewy-body (DLB) than in AD).
- Treatments are disease-dependent.

The first steps towards further diagnosis are taken as a result of a thorough consideration and complex interaction between the patients and their relatives or social networks. In most cases, the latter are the requesting party and plan the first contact with the healthcare professional (i.e. the GP or hospital specialist).

Before consulting a medical doctor, the patient and the relative should ask themselves the following questions:

- do I want a diagnosis or do I want not to have it ?
- why do I want a diagnosis or want to ignore it ?
- what will I want to know and will I ask first ?

When patients and relatives suspect a cognitive decline, they are entitled to the following:

- efficient measures and instruments adapted to them ;
- competent and skilled professionals ;
- accessible professional care ;
- awareness of the problem by the community and healthcare organizations ;
- information ;
- adapted care and treatment.

Most persons with symptoms of cognitive decline first turn to their family doctor.

This professional is expected to

- detect and find cases,
- initiate the diagnostic and differential diagnostic process,
- meet and draw up a list of care needs,
- provide care,

- refer,
- follow up on the patient,
- be aware of the patient context,
- initiate advance care planning and contribute to it.

Most GPs feel reluctant to talk about cognitive decline and they enumerate many barriers to further exploring the issue. These barriers can be lowered when the following conditions are met (Schoenmakers & De Lepeleire, 2011; De Lepeleire, Gorissen, Vermandere, & Schoenmakers, 2009):

- GPs possess knowledge: through educational interventions.
- GPs have direct access to specialized care: direct and low threshold contact with specialists and short waiting-lists.
- GPs are supported by a case manager.

GPs receive the support of and have access to guidelines: access to acceptable guidelines and to decision support mechanisms (It could also be useful to set up a computerised system using "pop-up" windows to provide doctors with a clear picture of what needs to be done and when in real time during the consultation.

- GPs are skilled and trained as reference doctors.

Patients and relatives turn to other professional caregivers with a particular unmet care need. In a growing number of cases and depending on the local care provision, these services can also initiate a diagnostic assessment, provided they work in close coordination with the GP and the memory clinic team.

Most of these professional caregivers are neuropsychologists, nurses, social workers and occupational therapists who are well-versed in the particular features of dementia and the concomitant care needs. These caregivers should

- possess knowledge through educational interventions,
- be aware of the problems and unmet needs,
- be in direct contact with the treating physician (in most cases, the GP, but also members of memory clinics),
- be able to draw up inventories of the care needs (assessment), organise care and set up a multidisciplinary consultation (intervention). They should use a personalised care approach to do so.
- guarantee follow-up,
- see the patients at home.

Professional caregivers assess and intervene in an objective way that is tailored to the patient's needs. Their approach is guided and supported by

- direct and indirect observation,
- adequate instruments: OLD-questionnaire, Niet-pluis index, FRAIL, scales adapted for instrumental activities of daily living (IADL), grids for daily activities, MiniCog.

Some patients turn to a specialist straight away, viz. in descending order of frequency : a neurologist, a geriatrician or a psychiatrist.

When initiating the diagnostic process, the following issues should be addressed or discussed:

- Pre-assessment counselling should be given ('informed consent'): level of knowledge, coping, needs, ...
- Psycho-social support should be available and offered.
- There should be enough insight into the pre-existing relationship between people with symptoms and their relatives.
- There should be enough time available, as well as appropriate and sufficiently equipped facilities.
- The follow-up should be explicitly planned.

Upon ethical consideration and following the informed consent of the patient and/or caregiver a further diagnosis may be considered. The following issues should be addressed prior to proposing further diagnostic investigation as well as in order to plan the follow-up:

- Evidence of a change in cognition compared with previous functioning;
- Performance in one or more cognitive domains is worse than would be expected based on the patient's age and educational background, including memory, executive function, attention, language, visual-spatial skills or behaviour;
- Extent to which the patient's independence in functional abilities is preserved, although these abilities may be altered, and the person may be less efficient at performing normal ADL;
- Insufficient impairment for a diagnosis of dementia.

Patients and relatives should prepare their visit to the medical doctor. For this purpose they can use a checklist as proposed by the World Alzheimer-organization 'Know the 10 signs', "IQCODE", (Jorm, 1994; Law & Wolfson, 1995). Thus, such tools aimed at providing assistance in putting problems into words should be made available to patients and their families in the waiting rooms of non-specialist physicians (GP and others), in conjunction with a large-scale information campaign aimed at the general population.

Second, it is preferable that patients be accompanied by a close relative during at least one such contact to contribute to the anamnesis and to help draw up an inventory of the unmet needs of both parties.

As a later step, objective measures and instruments can be applied to confirm the suspected cognitive decline, although there is little evidence in support of the efficacy of instruments for targeted screening. Indeed, the latter lack specificity and display a variable sensitivity. These instruments include:

The Mini Mental State Examination (MMSE) ; 5 words; Clock drawing test; BREF, MOCA, ACE and ACE-R, MiniCog (<http://www.azalma.be/download/geriatrie/Mini-COG.pdf>).

Less frequently used possibilities include 6-item Cognitive Impairment Test (6-CIT), General Practitioner Assessment of Cognition (GPCOG), 7-minute screen.

In patients in whom cognitive decline is suspected, cognitive testing should include examining attention and concentration, short and long term memory, orientation, language and executive function and praxis. Neither the GP nor even the specialist should make the diagnosis on their own, as this requires a team, made of at least a specialist and a skilled neuropsychologist.

Indeed, only a thorough neurological examination can uncover any dysfunction, especially given the fact that there are amnesic MCIs and other dysexecutive syndromes.

The circumstances of each individual patient (i.e. age, level of education, skills, prior level of functioning, psychiatric illnesses, sensory or other physical impairments) should be taken into account when interpreting the results of these tests.

Of course, the accuracy of the diagnosis is determined by the clinical follow-up, and the detection of the underlying pathology is dependent on further examinations such as neuropsychological profiling, biomarker analyses such as brain imaging, cerebrospinal fluid (CSF) biomarker analysis or even DNA analysis.

Moreover, even if no cognitive complaints were objectified during the neuropsychological examination, regular follow-up should then be offered and this assessment should be carried out again because the risk goes up once there has been a complaint (Steward, 2012). Normal test results do not mean that there is no need to conduct a more thorough examination, nor do low scores mean that this is a case of dementia, and especially of neurodegenerative disease. Therefore, in case of a (hetero-)anamnesis suggestive of cognitive decline, patients with a normal screening test too can be referred to a memory clinic if a diagnostic work-up is desirable.

In case an aetiological diagnosis of the dementia syndrome is desired, this will require additional diagnostic tests in order to obtain (biomarker) evidence for the causative brain disorder. **Structural brain imaging can also be used to exclude other treatable causes.**

A biomarker-based diagnosis of AD can be used in clinical practice to diagnose AD in the early stage of dementia; viz.

- in case of minimal or mild cognitive impairment, provided that the patient wants to know the result;
- in atypical forms with prominent non-memory impairment;
- to identify AD in patients with mixed pathologies and
- in case of an ambiguous (AD versus non-AD) dementia diagnosis (Engelborghs, 2013; Molinuevo et al., 2014).

Biomarkers that can be used are MR brain imaging to assess medial temporal lobe / hippocampal atrophy, FDG-PET scan of the brain and a lumbar puncture for CSF biomarker analyses.

At the time of the diagnosis of dementia, as well as at regular intervals afterwards, assessments should be made for comorbidities and psychiatric features associated with dementia (Behavioural and Psychological Signs and Symptoms of Dementia – BPSD), to ensure the optimal management of these conditions.

### 1.3 Diagnosis

#### 1.3.1 Subjective cognitive impairment

People with a subjective complaint of decline in their cognitive abilities, but in whom no impairment could be identified even after a comprehensive assessment, display a slightly elevated risk of developing an MCI and possibly dementia.

Unlike MCI, there are no clear diagnostic criteria for SCI. The fact that it is a risk factor means that such complaints should not be neglected and that a follow-up should be offered.

#### 1.3.2 Mild cognitive impairment

Diagnosing an MCI involves verifying whether the patient meets Petersen's (2004) criteria: complaints of cognitive disorders that are confirmed by their relatives, objective confirmation of a cognitive impairment taking into account the person's age, overall cognitive preservation, and whether or not the functional activities of daily living are normal or slightly abnormal. The cognitive impairment can concern either isolated memory or any other function, isolated or in association. The assessment should be performed by means of a full neurological assessment (Bedeco, 2015).

Depending on the cognitive profile, an aetiological search aimed at finding markers of the underlying disease may be conducted with the patient's consent.

### 1.3.3 Alzheimer's disease

AD has traditionally been defined as a type of dementia. The clinical diagnostic criteria such as those from the National Institute of Neurological and Communicative Disorders and Stroke – Alzheimer's Disease and Related Disorders (NINCDS-ADRDA) were based on ruling out other conditions and disorders that could lead to the same clinical symptoms. Two major limitations of these criteria were that: i) the clinical diagnosis of AD could only be considered as 'probable' during the patient's lifetime and could only be definitive if a post-mortem was done to confirm it ; ii) the clinical diagnosis of AD could only be made when the disease had progressed to the point of causing significant functional disability, and met the threshold criteria of dementia. The fact that there were no clinical criteria available at the time for the other types of dementia and the lack of biomarkers resulted in a low specificity in differentiating AD from other dementias.

In 2007, the International Working Group (IWG) (Dubois et al., 2007) for new research criteria for the diagnosis of AD provided a new conceptual framework that no longer looked upon AD as a clinico-pathological entity, but rather as a clinico-biological entity. These 2007 IWG criteria suggested that AD could be recognized in vivo and independently of dementia if two mandatory features were present. The first was a core clinical phenotypic criterion, requiring evidence of an amnesic syndrome of the hippocampal type. The second criterion was the presence of biomarker evidence consistent with AD in structural Magnetic Resonance Imaging (MRI), molecular neuroimaging with Positron Emission Tomography (PET) or CSF analysis of amyloid  $\beta$  and tau protein (total and phosphorylated) levels. These criteria were updated in 2010 and 2014 (Dubois et al., 2010; Dubois et al., 2014). The diagnosis of AD can be simplified by requiring the presence of an appropriate clinical AD phenotype (typical or atypical) and a pathophysiological biomarker consistent with the presence of Alzheimer pathology.

### 1.3.4 Vascular dementia

Next to AD, vascular dementia accounts for approximately 17% of all dementia disorders [<http://www.alzheimers.org.uk>]. Another 10% of patients with dementia suffer from mixed dementia, i.e. the combination of Alzheimer's pathology and vascular changes in the brain. The NINDS-AIREN Workshop for Vascular Dementia proposed clinical criteria to facilitate a standardized definition of Vascular dementia (Erkinjuntti, 1994) :

- Dementia defined by cognitive decline from a previously higher level of functioning and manifested by impairment of memory and of at least one other cognitive domain. Deficits should be severe enough to interfere with ADL not due to the physical effects of stroke alone.
- Cerebrovascular disease (CVD) defined by the presence of focal signs on neurologic examination consistent with stroke (with or without history of stroke) AND evidence of relevant CVD by brain imaging (CT or MRI).
- A relationship between the above two disorders manifested or inferred by the presence of one or more of the following:
  - (a) onset of dementia within 3 months following a recognized stroke;
  - (b) abrupt deterioration in cognitive functions; or
  - (c) fluctuating, stepwise progression of cognitive deficits.
- Clinical features consistent with the diagnosis of probable vascular dementia include:

- (a) early presence of gait disturbance;
- (b) history of unsteadiness and frequent, unprovoked falls;
- (c) early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease;
- (d) pseudobulbar palsy;
- (e) personality and mood changes, abulia, depression, emotional incontinence, or other subcortical deficits including psychomotor retardation and abnormal executive functions.

### 1.3.5 Frontotemporal Dementia (Sieben et al, 2014)

FTLD is an anatomopathological descriptive term referring to a disorder characterized by the relatively selective atrophy of the frontal and anterior temporal lobes of the brain. Apart from this commonality, FTLD is a clinically, genetically and pathologically heterogeneous group of disorders. Because disease onset often occurs before the age of 65 in 75–80 % of the patients, FTLD is considered a presenile dementia. In the age group 45 to 65, the prevalence of FTLD has been estimated between 10 and 30 per 100,000. In the elderly, FTLD is less common, accounting for approximately 5 to 10% of dementia syndromes.

FTLD can manifest as two clinically recognized subtypes based on the presenting and predominant features of either behavioural and personality changes, or language disturbances. The behavioural variant of frontotemporal dementia (bvFTD) is characterized by severe changes in behaviour and personality such as disinhibition, apathy, loss of empathy, or stereotypic behaviour, leading to a loss of social competence. Executive functions are impaired, while at least in the initial stages of the disease, memory and perceptual-spatial skills are well preserved. As the differential diagnosis in patients with psychiatric disturbances or AD is not always straightforward, the 'International Behavioural Variant FTD Criteria Consortium' developed international consensus criteria for bvFTD. According to these criteria, sub-classifications were made in possible bvFTD defined by clinical criteria, probable bvFTD supported by neuro-imaging data, and definite bvFTD confirmation by neuropathological evidence or a pathogenic mutation (Rascovsky et al., 2011). bvFTD accounts for more than 50 % of the FTLD patients. The onset of bvFTD is typically before the age of 65 years, with an average onset age of 58 years.

If the patient presents with language difficulties, a diagnosis of primary progressive aphasia (PPA) is made. PPA was originally further categorized into progressive non-fluent aphasia (PNFA) and semantic dementia (SD) (Josephs et al., 2011). However, the clinical picture of a number of PPA patients did not fit either diagnosis, which led to the description of the third variant, logopenic progressive aphasia (LPA). The lack of clear definitions of the three subtypes led in 2011 to new recommendations for the sub-classification of PPA into non-fluent/agrammatic variant PPA (the former PNFA), semantic variant PPA (the former SD) and the logopenic variant PPA (also known as LPA) (Gorno-Tempini et al., 2011). Non-fluent/agrammatic variant PPA or PNFA is characterized by effortful speech and grammatical error-making, with relatively preserved language comprehension. PNFA is the second most prevalent presentation of FTLD, accounting for a large 25 %. Semantic variant PPA or SD presents with impaired comprehension and conceptual knowledge with concomitant development of anomia, while speech production is spared. SD presents in 20–25 % of the FTLD patients. LPA is mostly associated with a neuropathological diagnosis of AD and is not considered part of the FTLD group of disorders. Based on the evidence supporting the diagnosis of PPA, the label "possible" (clinical features), "probable" (clinical findings in combination with neuro-imaging) and "definite" (after post-mortem examination or when a gene mutation is known) are provided.

### 1.3.6 DLB and Parkinson Dementia (McKeith et al, 2005)

Another 10% of patients with dementia suffer from a Parkinson-related dementia. It is important to look upon Lewy-body dementia and Parkinson dementia as both ends of the Lewy-body disease spectrum. In Lewy-body dementia, the cognitive syndrome manifests itself before the motor difficulties, or within a year after the onset of motor symptoms, whereas Parkinson dementia occurs in 78% of patients with Parkinson's disease (McKeith & Mosimann, 2004).

Consensus guidelines for the clinical and pathologic diagnosis of DLB were published in a report of the consortium on DLB international workshop (McKeith et al., 2005) :

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#### Consensus criteria for the clinical diagnosis of *probable* and *possible* dementia with Lewy bodies (DLB)

1. The central feature required for a diagnosis of DLB is progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention and of frontal-subcortical skills and visuospatial ability may be especially prominent.
  2. Two of the following core features are essential for a diagnosis of *probable* DLB; one is essential for *possible* DLB.
    - a. Fluctuating cognition with pronounced variations in attention and alertness
    - b. Recurrent visual hallucinations that are typically well formed and detailed
    - c. Spontaneous motor features of parkinsonism
  3. Features supportive of the diagnosis are the following:
    - a. Repeated falls
    - b. Syncope
    - c. Transient loss of consciousness
    - d. Neuroleptic sensitivity
    - e. Systematized delusions
    - f. Hallucinations in other modalities  
(Depression and REM sleep behavior disorder have been suggested as additional supportive features.)
  4. A diagnosis of DLB is less likely in the presence of
    - a. Stroke disease, evident as focal neurologic signs or on brain imaging
    - b. Evidence on physical examination and investigation of any physical illness, or other brain disorder, sufficient to account for the clinical picture
- 

### 1.4 Care diagnostics

The ideal way to meet the care needs is to provide the best possible compromise between the wishes of the patient and what is deemed necessary by professional healthcare providers. The complaints associated with dementia process often make it impossible for the individuals

themselves to define their own care needs. In order to do so, an appeal will have to be made to those close to the patient (informal and formal care).

The care diagnosis is also inextricably linked to the diagnosis of the illness (De Malsche & De Lepeleire, 2011; Vermandere, 2009; Vermandere et al., 2012). The former must be an integral part of the diagnostic process. It is concerned with making an inventory of care needs, which is of paramount importance. Thus, a care diagnosis allows for better and timely care planning as well as a greater quality of life for the patient and the informal carer. With the GP often possessing valuable information on the patients and their informal carers, there should be enough emphasis on communication between the GP and the specialist and vice versa. In addition, it is the GP who will follow up on the patients after their visit to the specialist.

The care diagnosis includes both aspects that pertain to the patient as well as aspects that relate to the informal care. As regards the patient, attention needs to be paid to the following items, which need to be checked on a regular basis :

- Information on disclosing the diagnosis and its impact on the patient;
- Information on the patient's mood and how they experience their quality of life as well as how it can be improved;
- Assessment of ADL and IADL functioning;
- Identity and individuality of the patient: profession, ideology, purpose, values and norms; spirituality;
- Falling hazard and adjustments to the home to avoid falls;
- Discuss the ability to drive and possibly refer to CARA;
- Advance care planning, provided the diagnosis was disclosed: wishes for the future, views on institutionalisation, legal aspects of patient representation and guardianship, declaration of intent regarding the care to be provided in case of legal incapacity. It is of crucial importance to initiate a dialogue on these issues.

As regards the informal carer, heed needs to be paid the following items:

- Information on balancing between burden and capacity (mental and social well-being) and personal experience of the burden of care with possible referral to single or group psycho-education;
- Assessment of physical health;
- Role in overseeing the intake of any medication;
- Need for personal supervision by the informal carer: partial or continuous.

As regards advance care planning, it is of paramount importance to initiate the dialogue on this issue. The GP is a key point of contact in this regard.

### 1.5 Monitoring the illness- and care process

More time will be required for supervision as the illness progresses. In moderate to severe dementia, informal carers often take it upon themselves to provide full-time support (in terms of ADL, incontinence, help with taking a bath, and help with taking meals and with mobility). Most informal carers experience a heavy burden of care. They report that the responsibility they have taken upon themselves has resulted in twice more physical stress as well as a high level of emotional stress (Waldemar et al., 2007; Schoenmakers & Maturitas, 2010). Vacations, leisure time and personal activities fade into the background. The timely involvement of home care and respite care services can be helpful.

Psychosocial interventions need to be available in a flexible manner (i.e. based on and tailored to the patient's needs, upon request) to the families of people with dementia (Brodaty et al., 2003). The autonomy of the informal carer should always be a key priority. Yet providing efficient training to informal carers or offering them psychosocial support is an intervention that covers a wide range of activities. Their aim, however, is always the same: to strengthen the informal carer's load-bearing capacity (offer strategies to manage stress, to be able to cope with behavioural problems, to reduce the workload, to get more satisfaction from providing informal care). Interventions with multiple components are usually effective, whilst studies involving a single component yield contradictory results. Such components include advisory sessions, taking part in support groups, telephone counselling, assessment of the patient's individual situation, referral to a psychiatrist, and joining a network of families (KCE, 2011). Furthermore, every person with dementia or those close to them should have access to a personal care attendant with expert knowledge on dementia during the dementia process.

It is advisable to use the BelRAI tool for the further monitoring of the care process. Furthermore, the guidance for care diagnosis is also useful during a multidisciplinary consultation that aims at drawing up an inventory of the care needs of a person with dementia living at home. This document is divided into 4 chapters: the patient, the informal carer, the safety of the patient and decisions concerning the end of life (Vermandere et al., 2012).

Performing illness and care diagnostics, interpreting the data, providing treatment for symptoms such as BPSD, meeting the needs of the patients and alleviating the stress faced by their informal carers require specific professional skills and, ideally, a multidisciplinary approach at various levels.

## 1.6 Recommendations

It is not easy to make an aetiological diagnosis of dementia (aside from certain genetic forms and possibly some biomarkers). This would require binding quality criteria that would need to be complied with for e.g. the reimbursement of diagnostic procedures and any subsequent treatment. The reimbursement of neuropsychological testing depends on the impairments that characterise neurocognitive deterioration. The reliability of the diagnostic procedure is a current requirement for admitting patients into cognitive rehabilitation, without it being specified what such a procedure should involve. Reimbursement for AChE-inhibitor medication is subject to a diagnostic procedure that goes back to the 1980s: an update is required. Note that these quality criteria should apply to all types of dementia, not just AD.

There are currently no guidelines available in Belgium on the diagnosis of dementia. The NIHDI and the CEBAM have adapted international guidelines to fit the situation in Belgium. They have done this for various diseases, including dementia (Project Duodecim Guidelines), but these guidelines have yet to be implemented and their use needs to be promoted.

The procedure which allows GPs to correctly convey all the necessary information to medical specialists should also be promoted to physicians as a means to boost its use.

The funding provided for the diagnosis should also enhance the quality of the procedure, especially as regards its multidisciplinary nature. Currently there is no funding for consultations between GPs and specialists. One possibility would be to use and adapt the example of the "COM" (multidisciplinary oncology consultation) funding, which has been set up for cases of cancer, in order to promote such consultations. The KCE's assessment of this project (KCE Reports 239B) has revealed that in 2011, the cases of over 80% of patients were presented at a COM and that this improved the quality of care. The use of modern means of communication for these COMs should be encouraged with a view to dealing with organisational issues and promoting the involvement of GPs.

As the quality criteria for clinical work-ups and reimbursement for the diagnosis are enhanced, each patient could be authorised to receive more than one opinion, as this often turns out to be useful (Cruys et al., 2012).

Thus, the following quality criteria should apply:

- The patients and their caregivers have been given access to a preliminary consultation where they could express their needs and expectations and the potential risks and benefits of a diagnostic work-up have been reviewed and the patients have consented to this procedure.
- The diagnostic procedure included
  - a mental status examination ;
  - a thorough neuropsychological examination including precisely defined tests ;
  - structural brain imaging using appropriate (defined) incidences and sequences ;
  - other biomarkers if structural imaging was insufficient to provide the diagnosis.
- The patients and their caregivers have been informed of the results of these procedures and of their implications in term of prognosis and have been offered different therapeutic interventions and kinds of support (psychological, social).
- The patients' GPs have received a detailed report of each of the diagnostic steps.

## 2 BPSD and psychopharmacology

### 2.1 Introduction

Changes in behaviour are highly prevalent in patients suffering from cognitive impairment, as early as in the MCI stage. Addressing them is not tantamount to choosing the proper medication.

The history of the Behavioural and Psychological Symptoms in Dementia (BPSD) concept is recalled in the IPA BPSD Specialists Guidelines released by the International Psychogeriatric Association

*"In 1996, the International Psychogeriatric Association (IPA) convened the Consensus Conference on the Behavioural Disturbances of Dementia. The 1999 Update Consensus group, produced a statement on the definition of the BPSD: "The term behavioural disturbances should be replaced by the term behavioural and psychological symptoms of dementia (BPSD), defined as: symptoms of disturbed perception, thought content, mood, or behaviour that frequently occur in patients with dementia." (Finkel & Burns, 1999)*

*The European Alzheimer's Disease Consortium also noted that the term BPSD is not a unitary concept and recommended that it should be divided into several or more groups of symptoms (e.g., apathy, mood/agitation, psychosis), each possibly reflecting a different prevalence, course over time, biological correlate, and psychosocial determinants (Robert et al, 2005)."*

Different groups, subgroups and clusters have been proposed over time. The aim here is not to discuss which of them is the most valuable but to use this approach to provide a practical guide on how to manage patients who have dementia and who experience behavioural and/ or psychological changes.

In its 2011 advisory report on "The impact of psychopharmaceuticals on health, with a particular focus on the elderly" (SHC 8571, 2011), the SHC had already pointed out several items of concern regarding the use medication in elderly patients, especially elderly people with dementia. Thus, the following observations were made in this advisory report:

"- The adverse effects of benzodiazepines are more frequent and more severe in the elderly and may worsen any existing dementia or interfere with its diagnosis.

- A rise in mortality has recently been observed for all antipsychotic medication in elderly people with dementia, in all likelihood as a result of strokes (Schneider & al., 2006).

- Antipsychotic medication can be discontinued without too much difficulty. Most studies have been conducted with patients with Alzheimer-type dementia or other forms of dementia who were receiving antipsychotic medication as a means to treat behavioural problems. In these studies, antipsychotic medication was discontinued abruptly in patients with Alzheimer's disease, without gradual tapering. (Ballard & al., 2008 ; Ballard & al. 2009 ; Cohen-Mansfield & al., 1999 ; Ballard & al., 2004 ; Bridges-Parlet & al., 1997 ; van Reekum & al., 2002 ; Ruths & al., 2004 ; Ruths & al., 2008).

- The high prescription rate is not consistent with the latest scientific evidence and guidelines regarding the indications for initiating psychotropic medication, the effectiveness of alternatives to medication, and the limited time during which these drugs should be prescribed as a rule (in case of insomnia, anxiety, stress, acute depression and aggressiveness).

- These data reveal a public health problem, especially as regards the health of the elderly. It is paradoxical to see that these products are mainly prescribed to elderly people, who are in fact more sensitive to side effects that are liable to enhance the symptoms of dementia, thus complicating the diagnosis even more. There is not only a rise in morbidity but also in mortality among elderly people with dementia taking antipsychotic medication. "

There is no denying that the issue of using medication has already been well documented. However, those working in the field are not always aware that there are alternatives to medication. That is why the SHC offers to describe a different type of approach to managing the behavioural symptoms of dementia. Clearly, there is no single strategy (pharmacological or other) that has unequivocally been shown to be effective. This report must be looked upon as a set of recommendations that are based on both the experience of the experts who drew them up as well as on existing guidelines (e.g., Voyer, 2009).

## 2.2 BPSD: Towards a more effective therapeutic approach

### 2.2.1 *General principles.*

Keep in mind the goal of a given intervention.

The first issue is actually the attitude of caregivers (both professionals and non-professionals) when faced with unexpected behaviours: is their main objective to protect themselves or to improve their patients' quality of life, considering that altered behaviour, including agitation, reflects some degree of distress (Cummings et al., 2015).

If the first is true, which is a highly common, if not the most prevalent, kind of response, the aim is to suppress the disturbing behaviour quickly by using neuroleptics or physical restraints, in a stereotyped way, regardless of what has caused this type of behaviour. Clinical studies have repeatedly demonstrated the poor efficacy and the low benefit / harm ratio of this approach (Azermi, 2015, for a review).

The alternative response, i.e. taking into account the subject's feelings and attempting to suppress the cause of the disturbing behaviour, requires an analytical approach. Besides having an effect on the administration of medication, it gives the caregiver a sense of control, which can in turn have beneficial effects for the patient (Gitlin et al., 2001, Sink et al., 2006).

Step1.

What term can be used to describe the observed behaviour ? As mentioned above, quite a number of classifications have been offered for the disturbing behaviour observed in people with

dementia. The most widely used in daily clinical practice is that of the Neuropsychiatric Inventory (NPI, Cummings et al., 1994):

- Delusions
- Hallucinations (visual, auditory, gustatory, somesthetic)
- Agitation/Aggression
- Depression/Dysphoria
- Anxiety
- Elation/Euphoria
- Apathy/Indifference
- Disinhibition
- Irritability/Lability
- Aberrant motor behaviour (e.g. pacing, rummaging, repetitive movements)
- Sleep (night insomnia/ day hypersomnia) and Night-time Behaviour Disorders (wandering, pacing, inappropriate activities)
- Appetite (hypo / hyperphagia, weight loss or gain) and Eating Disorders

A basic way of grouping together BPSD is to distinguish behavioural signs, i.e. those identified through the observation of the patient (Agitation/Aggression, Elation/Euphoria, Apathy/Indifference, Disinhibition, Aberrant motor behaviour, Sleep and Night-time Behaviour Disorders) from psychological signs, which are identified after an interview with the patients or their families (depression, anxiety, hallucinations, delusions).

#### Step 2.

What lies behind the observed behaviour ?

Factor analysis studies (e.g. Aalten et al., 2007, Petrovic et al., 2007) have made it possible to assign individual symptoms/signs to a small number of factors (e.g. a *psychosis factor*, the components of which are irritability, agitation, hallucinations and anxiety, a *psychomotor factor*, with aberrant motor behaviour and delusions, a *mood liability factor*, with disinhibition, elation and depression, and an *instinctual factor*, with appetite disturbance, sleep disturbance, and apathy). Relationships were found to exist between these factors as well as between the latter and non-behavioural variables (Proisti et al., 2011): “psychosis” can partially explain some of the variability of “agitation”, “mood”, and “behavioural dyscontrol”; “moods” can partially account for some of the variability of “agitation”, and “behavioural dyscontrol and “agitation” can partially explain some of the variability of “behavioural dyscontrol”.

In the same study, greater cognitive impairment was a significant predictor of the “psychosis”, “moods” and “behavioural dyscontrol” factors; younger age/age at onset was a significant predictor of the “agitation” and “moods” factors, whereas older age/age at onset was a marginally significant predictor of the “psychosis” factor; female gender was a significant predictor of the “psychosis” factor, whereas male gender was a significant predictor of the “agitation” factor; long disease duration was a marginally significant predictor of the “agitation” factor only.

Many years earlier, Cohen-Mansfield et al. (1989) had shown links between environmental, psychological and general health factors and agitation (Table I), which is in line with the view of Lawton (1975), according to which the ability to receive, process and sense environmental cues is compromised in people with cognitive impairment, making it increasingly difficult for them to cope with everyday environmental stimuli.

In addition, it must be stressed that conditions such as poor eyesight or deafness can induce behavioural changes, which range from apathy to paranoid delusion and subsequent agitation. Poor eyesight as well as cerebral lesions (peduncular or other) can result in visual hallucinations that trigger paranoid delusion.

### 2.2.2 Prevention and non-pharmacological interventions.

BPSD are highly challenging for the patients themselves, their caregivers (both professionals and non-professionals), and the other residents in hospital or long-term care facilities.

A key aspect in managing the BPSD is therefore prevention, which involves avoiding both all generally acknowledged triggers or contributors, as well as those that are specific to a given patient and which are a corollary of their history and clinical characteristics.

#### Physical environment

Basically, a long-term care facility is a surrogate home. As such, it must offer the residents the feeling of being at home, of being free to move about but also to retire into the intimacy of their own bedroom. Everything should be done not only to allow them to express their needs and wishes and use their remaining capacities, but also, when needed, to assist them in the ADL. In short, a facility that adapts itself not only to the needs of its residents as a group, but also to those of each of them as an individual, is expected to find itself facing less BPSD.

#### Human environment.

Admitting someone into specialist residential accommodation means providing them with services. Each professional involved should be aware of their primary commitment, which is to preserve or even improve their residents' quality of life.

In nursing home, continued education is a key aspect of the organisation of care. It has been shown that "one-shot" training courses are useless, because their effects on daily practice fade away quickly (Kuske et al., 2009). In addition, there can be a high turnover rate in the teams; each newcomer should be trained before taking up their duties, as a means to ensure consistency in the manner in which the whole team works.

An inherent feature of institutional accommodation is multidisciplinary. This term usually refers to doctors, nurses and paramedical contributors, which is rather restrictive. Indeed, everybody, from the administrative director to the cooks and maids, should receive the same training and adapt their behaviour accordingly when interacting with each other as well as with the residents. In order to minimise the severity of the BPSD, the latter should be detected early. The systematic use of rating scales should be encouraged.

Familial caregivers should be provided with training as well, not only when the patients are still living at home, but also after they have been institutionalised. Once again, the aim is to ensure that their attitude is in line with that of the professional team.

There are many non-pharmacological interventions available, which are focused on the patients (cognition, emotion, sensory stimulation, ADL, physical activity, communication, environment modification, nutrition), the caregivers (continued education for professionals, respite care) or on both the patients and the familial caregivers (psychoeducation). The clinical trials that studied those approaches are of rather poor quality and heterogeneous, making it difficult to use them as support for guidelines. After reviewing the available evidence, the Belgian Health Care Knowledge Centre (Kroes et al., 2011) made the following recommendations:

Among all the non-pharmacological treatments for people with dementia, there are sufficient scientific data available to recommend the following categories:

- Support to and training for informal caregivers, including multiple interventions at home: a positive effect was observed on institutionalisation
- Training for professional caregivers
- Physical activity program at home or in the institution
- Cognitive training/stimulation

No precise description can be made of the modalities for administering these treatments on the basis of the studies that have been published. Nevertheless, it has been demonstrated that these interventions are more efficient if they

- are adapted to the patients and their close circle in order to better address their needs,
- are followed by well-trained professionals,
- are provided for a sufficient period of time, with regular contacts in order to produce meaningful effects.

As far as other non-pharmacological interventions are concerned, no formal recommendations can be made on the basis of the current data.

### 2.2.3 *Pharmacological intervention*

Psychotropic drugs are extensively administered to patients with dementia and BPSD. As is the case in other guidelines, we argue that these drugs should not be the first-line response or that, if given as an emergency solution, this approach should be very quickly discussed and challenged, in light of the analysis of the target behaviour, which includes ruling out any intercurrent medical condition and any side effects of existing medication. When drugs are used, this should be for precise indications for which they have been found to be efficient.

Antipsychotics in AD (Sultzer et al, 2008) have been shown to be superior to placebo against hostile suspiciousness (olanzapine and risperidone) and psychosis (risperidone).

Citalopram is an alternative (Nyth and Gottfries, 1990; Pollock et al. 2002, 2007; Porsteinsson et al. 2014): in moderate to severe AD, it has an effect on agitation and psychosis that is similar or superior to that of risperidone. Whilst citalopram does cause less extrapyramidal symptoms, it induces lengthening of the QT interval as well as a risk of hyponatremia, which require monitoring. In a retrospective analysis of the CATIE-AD data, adding citalopram to antipsychotic medication in a 44-patient sub-group had no effect on delusions and a questionable effect on hallucinations. The effect on irritability and apathy was not significant, although both were down by 60% in the group undergoing treatment (Siddique et al., 2009).

Patients with DLB did not tolerate citalopram or risperidone, and did not benefit from either (Culo et al, 2010).

Sertraline was compared to low-dose haloperidol in patients with AD, vascular dementia (VaD) or mixed dementia and agitation, with similar efficacy (Gaber et al., 2001).

When added to donepezil, sertraline had no significant effect on NPI, CGI-I or CGI-S scores (Finkel et al., 2004).

Studies were conducted on administering sertraline in cases of depression associated with AD, with variable results (reviewed in Henry et al., 2011). In advanced stages, no difference was found to exist with placebo. Patients at a moderate level (MMSE = 17) with major depression responded better to the active compound than to placebo with, in addition, a decrease in behavioural disturbance and improved ADL. In mild to moderate cases (MMSE = 21), a 24-week sertraline treatment was not associated with any improvement in mood or non-mood symptoms, function or quality of life.

In a small (n=15) open study on frontotemporal dementia (FTD) citalopram significantly reduced the total NPI score, disinhibition, irritability and depression (Herrmann et al. 2012).

In FTD, other antidepressants were reported to have a significant positive effect on the overall NPI score: trazodone, paroxetine, fluvoxamine. However, randomised, controlled trials are scarce; in such studies, trazodone was shown to significantly decrease the total NPI score, while paroxetine had a non-significant worsening effect (Huey et al., 2006).

Trazodone was compared to haloperidol in patients with AD and agitation, with a modest effect on both medication and a better tolerance to trazodone, the efficacy of which was associated with the extent of concurrent mood symptoms (Sultzer 1997, 2001)

Trazodone is widely used in patients with dementia and sleep disorder; this practice is based on data obtained from depression studies which were not always focused on older patients, but data in dementia are scarce. Trazodone was found to be the most frequently used treatment for sleep disorders in community-dwelling AD patients, with the highest proportion of subjective improvement (Camargos et al., 2011). In a short-term randomized controlled trial (RCT), trazodone administered at the dose of 50 mg increased the duration of sleep (Camargos et al., 2014).

Trazodone is also used as a means to treat anxiety. Again, this use is based on data obtained in anxiety disorders, but none of these studies were conducted with dementia patients or even elderly patients (reviewed in Bossini et al., 2012).

Doxepin at doses up to 6 mg is a selective histamine-1 receptor antagonist, therefore free of the side effects due to muscarinic and alpha-1 adrenergic receptor blockade. Studies in elderly patients showed a significant effect on sleep continuity and duration but not on sleep latency, efficacy beyond 12 weeks and no rebound after withdrawal (reviewed in Rojas-Fernandez, 2014).

Memantine has been shown to prevent agitation/ aggressiveness, irritability / liability, night-time behaviour and to reduce delusions, agitation/ aggressiveness and disinhibition in patients with moderate to severe AD (Gauthier et al., 2008). This observation was based on pooled data from several RCT where behaviour was a secondary outcome. They were not confirmed by an RCT focused on agitation in moderate-to-severe AD (Fox et al, 2012)

There is no evidence that acetylcholinesterase inhibitors (AChEI) have an effect on BPSD (Seitz et al., 2013).

In Parkinson's disease dementia and Lewy-body disease, rivastigmine had a significant effect on the NPI-10 score; hallucinations were less frequent with AChEI, though this effect was not significant (Rolinski et al., 2012).

In one small (n=12) open study on FTD, donepezil increased disinhibition and compulsive behaviour.

There is no recognized indication for administering benzodiazepines to patients with dementia. However, they are widely prescribed to patients with BPSD, in combination with antipsychotics in 40% of cases. While two studies found that lorazepam and alprazolam can reduce agitation in AD, no improvement of sleep quality was shown to occur with benzodiazepines. Benzodiazepines induce a 2.8 times higher deterioration rate over a 12 month-period and hasten death. Benzodiazepine users are 5.8 times more likely to experience falls (reviewed in Defrancesco et al., 2015).

Although no study has demonstrated the validity of this approach, lorazepam is often used in case of acute agitation in patients with Lewy-body dementia or Parkinson's disease dementia.

Among mood stabilizers, carbamazepine (CBZ) has the most robust evidence in support of its efficacy on BPSD global scores, aggression, hostility, and possibly agitation; there has been no face-to-face study comparing CBZ to antipsychotics. RCTs and meta-analyses did not provide any evidence in support of the efficacy of valproate. In one RCT with topiramate, this compound reduced overall BPSD scores and agitation, without there being any significant difference with risperidone; it must be pointed out that topiramate has been reported to cause cognitive impairment in young patients with epilepsy. One RTC was carried out with oxcarbazepine and it showed negative results. There is no RCT or meta-analysis on gabapentine, lamotrigine or lithium carbonate use in BPSD (reviewed in Yeh and Ouyang, 2013).

Despite the lack of RCTs on clonazepam in rapid eye movement sleep behaviour disorder (RBD: Howell and Schenck for a review), there is a consensus on the efficacy of clonazepam, with up to 90% of patients responding to doses of 0.5 to 1 mg.

#### 2.2.4 Specific behaviours and symptoms

**Strolling** is frequently observed in institutionalised patients. Most often, it is caused by an environment that is perceived as stressful. In the early hours or days of a patient's stay, this can be compared to the behaviour we all display when arriving at a holiday destination: we drop our suitcases, go out and walk around to familiarize ourselves with our new environment. The patient is just trying to find landmarks. This can be disturbing for other patients or residents, because it implies that all the doors will be opened and that, in many cases, the rooms will be explored. This behaviour cannot be treated by means of medication. Moreover, preventing patients from behaving like this is not only liable to result in agitation that can become aggressive, but, most importantly, will prolong this type of behaviour, because it is a necessary step in their integration process. Escorting them, explaining what the different rooms are for and introducing the other patients / residents to them is both preferable and energy-saving: nobody will be distressed. When this behaviour continues after the first days of their stay, it usually reflects anxiety about the environment, either human (other residents, unusual behaviour of the team, loss of contact with their family, real or due to memory impairment, family conflicts expressed during visits...) or material (changes in furniture, in ward décor, less or more light ...). Drugs such as serotonin-specific reuptake inhibitors (SSRI) antidepressants and antipsychotics induce akathisia, i.e. the inability of staying without moving, which can be mistaken as strolling.

**Exit-seeking** is seen in middle-stage dementia, since it requires the ability to plan an action and to carry it out. The motivation is either to leave the facility for a specific purpose ("elopers" want to go to work, to be at home when the children return from school, to prepare the meal...) or to escape from an unfriendly environment ("runaways"). When residents have decided to leave, it is useless to try to convince them that they may not do so: this attitude usually upsets them and sometimes triggers aggressive behaviour from them. In elopers, exit-seeking behaviour can be avoided by engaging them in the kind of activities they think they have to carry out, by validating their wish to leave, letting them speak about their goal and then trying to engage them in a close activity after having explained that, unfortunately, there is currently no transportation available. The reason why runaways feel uncomfortable should be understood and corrected. Here too, validation is the first step: it will help understand the reason why they feel uncomfortable and provide an opportunity to make a suggestion (meeting other people, listening to a song, seeing a video of loved ones, eating, drinking...) that can correct this feeling. In the Canadian resting home "carpe diem", when caregivers see a resident crossing the portal, they offer to walk with them, which gives them time for validation.

**Wandering** is particularly distressing for familial caregivers. The questions to address are the same as in institutions. In addition, many patients want to "go back home", which, again can reflect a feeling of discomfort but also a wish to be in the home where they lived when they were young, with their parents and siblings. Basically the attitude is the same as above and consists of validation, with the difference that, at home, there is no architectural limit to wandering. The "Carpe Diem" approach is probably the best one.

**Apathy** (reviewed in Dujardin, 2007 and Cipriani et al., 2014) has been defined as "an observable behavioural syndrome consisting of a quantitative reduction of voluntary (or goal-directed) behaviours". It is the most prevalent behavioural change in patients with AD (19%-92%), where it appears early and increases as the disease progresses, as well as in the behavioural variant of frontotemporal lobe dementia (62%-89%). It is very frequently found in Parkinson's disease (24%) but is much more common in Parkinson's disease dementia (54%), progressive supranuclear palsy, Huntington's disease (21%-60%) and vascular dementia, with a higher prevalence in small-vessel dementia (64%) than in large-vessel (54%) dementia.

A differential diagnosis must be made with depression and with delirium.

The main difference with depression is the lack of dysphoria. However, these two illnesses share common symptoms that can account for the overdiagnosis of depression in patients who are unable to express their feelings (Table 1).

Table 1 : Signs and symptoms in apathy and depression

<b>Apathy-characteristic</b>	<b>Shared</b>	<b>Depression-characteristic</b>
Lack of motivation	Loss of interest	Sadness
Lack of initiative	Psychomotor slowness	Suicidal ideation
Blunted emotional responses	Fatigue, loss of energy	Worthlessness
Indifference	Hypersomnia	Feeling of guilt
Social withdrawal	Lack of insight	Pessimism, gloominess
Lack of perseverance	Hopelessness	Anorexia

Although the hypoactive form of delirium can look like apathy, its acute onset, fluctuating course and other features make it rather easy to differentiate both conditions.

Finally, apathy has to be distinguished from the effect of sedative drugs, particularly neuroleptics. Despite its high prevalence, there have been few studies on the treatment of apathy.

Non-pharmacological intervention focused on educating caregivers about the meaning, nature and pathophysiology of apathy is certainly a valuable, necessary first step. The aim is to avoid it being misinterpreted as laziness or opposition.. The caregiver can then be trained to stimulate and structure the patient's daily activities. Therapeutic activities have been found to be the only type of intervention on which enough high-quality studies have been conducted.

The problem with pharmacological interventions is that apathy was a secondary outcome measure in most studies. Some improvement has been obtained with psychostimulants (methylphenidate, dextroamphetamine), dopaminergic agonists (pergolide and bromocriptine) and there has been a case report describing a response to bupropion. There are non-randomised controlled trials (15 revealing a positive effect, 3 showing no benefit) and observational studies with controls (11 positive, 7 negative) that demonstrate that acetylcholinesterase inhibitors are beneficial in apathy. Memantine in severe dementia of various types had an effect on apathy in two RCTs; an open-label study in FTD showed no effect. Antidepressants do not improve apathy; on the contrary, serotonin specific reuptake inhibitors have been associated with indifference.

### **Depression**

Along with apathy, depression is one of the most frequent BPSDs.

The diagnosis of depression is difficult to make in elderly patients, because the meaning of complaints and signs (pain, anorexia, sleep impairment) can be blurred by concomitant diseases. In addition, patients with dementia are less able to express their feelings and display signs such as apathy or tears that erroneously suggest depression.

Diagnostic criteria that reduce the importance of verbally-expressed symptoms and include irritability and social withdrawal have been proposed for depression in AD (Table 2, Olin et al., 2002).

The Cornell Scale for depression in Dementia (Table 3 Alexopoulos et al., 1988) is widely used to quantify depression and even to diagnose it, since cut-off scores have been proposed for the diagnosis of depression.

Even with these tools the task remains difficult. It is safe to consider that any rapid (not abrupt, which rather suggests delirium) behavioural change can be caused by depression.

Table 2 : Provisional diagnostic criteria for depression in AD

<p>Three or more of the following criteria over the same 2-week period. They must represent a change from previous functioning:</p> <p>Depressed mood (sad, hopeless, discouraged, tearful)</p> <p>Decreased positive affect or pleasure in response to social contacts and activities</p> <p>Social isolation or withdrawal</p> <p>Disruption in appetite</p> <p>Disruption in sleep</p> <p>Psychomotor agitation or retardation</p> <p>Irritability</p> <p>Fatigue or loss of energy</p> <p>Worthlessness, hopelessness or excessive guilt</p> <p>Recurrent thoughts of death or suicidal ideation</p> <p>All criteria are met for dementia of the Alzheimer type</p> <p>Symptoms cause distress or disruption in functioning</p> <p>Symptoms do not occur exclusively during delirium</p> <p>Symptoms are not due to substances (medications or drug abuse)</p>
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Table 3: Cornell Scale for Depression in dementia

<p><b>Mood-related signs</b></p> <p>Anxiety: anxious expression, ruminations, worrying</p> <p>Sadness: sad expression, sad voice, tearfulness</p> <p>Lack of reactivity to present events</p> <p>Irritability: annoyed, short tempered</p> <p><b>Behavioural disturbance</b></p> <p>Agitation: restlessness, handwringing, hair pulling</p> <p>Retardation: slow movements, slow speech, slow reactions</p> <p>Multiple physical complaints (rate 0 if gastrointestinal symptoms only)</p> <p>Loss of interest: less involved in usual activities (score only if change occurred acutely, or in less than one month)</p> <p><b>Physical signs</b></p> <p>Appetite loss: eating less than usual</p> <p>Weight loss: (rate 2 if greater than 5 pounds in past month)</p> <p>Lack of energy: fatigues easily, unable to sustain activities</p> <p><b>Cyclic function</b></p> <p>Diurnal variation of mood: symptoms worse in the morning</p> <p>Difficulty falling asleep: later than usual for this individual</p> <p>Multiple awakenings during sleep</p> <p>Early morning awakening: earlier than usual for this individual</p> <p><b>Ideational disturbance</b></p> <p>Suicidal: feels life is not worth living</p> <p>Poor self-esteem: self-blame, self-depreciation, feelings of failure</p> <p>Pessimism: anticipation of the worst</p> <p>Mood congruent delusions: delusions of poverty, illness or loss</p>
<p>Scoring system</p> <p>A= Unable to evaluate; 0 = Absent; 1 = Mild to intermittent; 2 = Severe score greater than; 12 = Probable depression</p>

Despite its high prevalence in dementia, depression treatments have not been extensively studied. The studies included in meta analyses have identified various outcomes for SSRIs and mirtazapine, probably because they used different diagnostic criteria and outcome measures (reviewed in Kales et al., 2015). It follows that we have no firm recommendation to make regarding the choice of antidepressant. Given this uncertainty about their efficacy, regardless of the antidepressant used, the adverse effects and the risk/benefit ratio must be monitored carefully.

According to Cohen-Mansfield et al (1989), a distinction may be drawn between different types of **agitation**, viz. verbal non-aggressive, physical non-aggressive, and aggressive, each of which has distinct causes and requires specific approaches (Table 4).

Rating scales such as the Cohen-Mansfield Agitation Inventory or CMAI (Cohen-Mansfield et al., 1989), the NPI (Cummings et al., 1994), or the Behavioural Pathology in Alzheimer's Disease (BEHAVE-AD; Reisberg et al., 1987) rating scale are used to quantify agitation. However, until recently, no definition or diagnostic criteria were available for agitation in syndromes with cognitive impairment. The International Psychogeriatric Association set up an Agitation Definition Working Group, which provided a provisional consensus definition (i.e. one that is accepted by a majority of stakeholders, viz. 68 to 88%, depending on the definition component under consideration.) (Cummings et al., 2015):

- (1) the behaviour occurs in patients with a cognitive impairment or dementia syndrome;
- (2) patients exhibit behaviour consistent with emotional distress;
- (3) patients display excessive motor activity, verbal aggression, or physical aggression;
- (4) evidencing the patients' behaviour causes excess disability and is not solely attributable to another disorder (psychiatric, medical, or substance-related).

In line with Cohen-Mansfield's approach, an important aspect of this definition is that agitation is looked upon as the expression of the patient's upset or distress. This definition also recognises that agitation can take different forms, which suggests that different approaches are needed. Finally, this behaviour induces excess disability, which again focuses on the patients as the primary sufferers from their state.

A recent review of RCTs using non-pharmacological approaches (Livingston et al., 2014) found evidence in support of the efficacy of:

- activities and music therapy in care homes, though no information is provided on long-term effects or nor is there any evidence concerning people with severe agitation ;
- person-centred care and dementia care mapping training of care home paid staff with supervision in severe agitation with mid- and long-term persistence of efficacy.

There was no evidence in support of the efficacy of these approaches in other settings.

No evidence was found in support of the efficacy of light therapy (which was found to be liable to worsen agitation in one study), aromatherapy, and training family caregivers in behavioural management therapy.

For some interventions, there was insufficient evidence to allow a definitive recommendation: physical exercise, training caregivers without supervision, simulated presence.

As discussed in detail above, several classes of drugs display a limited effect on different aspects of agitation: antipsychotics, the antidepressants citalopram, sertraline and trazodone, CBZ . Drug interventions should only be initiated after non-pharmacological measures have failed.

Table 4.: Possible determinants of agitation

Behaviour	Strongly linked with	Treatment
Verbal, non-aggressive	Quality of interpersonal relationships Depression Anxiety  Poor sleep quality	Improve staff behaviour Antidepressants 1. identify and correct environmental causes 2. SSRI or trazodone in small doses  causal
Physical, non-aggressive	Poor sleep quality Physical discomfort (fecaloma, pain...) Anxiety	Causal Causal 1. identify and correct environmental causes 2. SSRI or trazodone in small doses
Aggressive	Quality of interpersonal relationships Verbal / non-verbal communication Depression Poor sleep quality Delirium	Improve staff behaviour Improve staff behaviour Antidepressants Causal Causal; prn haloperidol if dangerous

**Delusions** may be part of depression. In this case, they are congruent with mood (worthlessness, guiltiness, ruin...). They respond to antipsychotics given in association with antidepressants and are still an indication for electroconvulsive therapy even in patients with dementia. If they are the consequence of hallucinations, this behaviour should be analysed first (see below). They can also be the consequence of vision or, more commonly, of hearing impairment leading to the (erroneous) interpretation of other peoples' attitudes or conversations; proper correction of the deficit must be carried out first.

**Hallucinations** are often the consequence of impaired perception (Charles Bonnet syndrome for visual impairment, or its equivalent for hearing). Unfortunately, it is not always possible to correct the deficiency; moreover, antipsychotics are rather seldom efficient. The latter should therefore be initiated only if these hallucinations cause suffering to the patient or if they induce delusional behaviours that put them or others in danger/ If they are given to the patient, the benefit / harm balance should be carefully and repeatedly estimated. Peduncular hallucinosis is a condition that was described in 1922 (Lhermitte, 1922) and is caused by lesions located in a region that stretches roughly from thalamus to the emergence of the fifth cranial nerve. Some effect has been obtained with olanzapine (Spiegel et al., 2011), but also with fluoxetine (Gilles et al., 1996). Hallucinations are one of the main symptoms of Lewy-body and of Parkinson's disease dementia, in which antipsychotics are prohibited (except for clozapine). Rivastigmine has been claimed to be an alternative (Rolinski et al., 2012) and pimavanserin, a 5HT<sub>2A</sub> inverse agonist, is promising (Schrag et al, 2015).

**Sleep disorders** are common in dementias. They are exhausting for familial caregivers and are therefore a major cause of institutionalisation. They are also difficult to manage in hospitals or nursing homes, where they induce inappropriate, toxic, ineffective drugs administration. Again, an analytical approach is the key to appropriate treatment (Table 5).

Table 5 : Sleep disorders subtype: possible causes and treatments

<b>Subtypes</b>	<b>Possible causes</b>	<b>Treatment</b>
Long sleep latency	Bedtimes don't line up with the patient's rhythm Noisy environment Low diurnal physical activity Anxiety	Inquire about patient's rhythm and respect it Correct Increase Bedtime ritual, milk, herbal tea, massage...
Awakenings	Environment (blood drawing at 4 am) Low daylight exposure Low diurnal physical activity Gastro-oesophageal reflux Dyspnea (CHF, COPD) Pain Cramps: idiopathic, arteriopathic, iatrogenic (e.g. AChEI) Incontinence  Periodic leg movements SAS Drug-induced nausea / pruritus	Correct Correct Increase Treat Bed in armchair position / treat Treat Treat / modify Rx  Modify Rx if iatrogenic (e.g. AChEI) Avoid anticholinergics Treat Treat (CPAP, diet, position in bed) Change
Awakenings activation (1) +	Environment (diurnal atmosphere outside rooms) No identified reason for awakenings	Correct (1)  1. Allow free walking, drinking, eating 2. Gentle contention (2) 3. Hypnotic (doxepin 3-6 mg)
Agitation	Delirium  REM sleep behaviour disorder	Causal. Prn haloperidol if dangerous Clonazepam
Early awakening	Early bedtime Environment (noise, light, blood withdrawal...) Depression	Correct Correct  Antidepressant
<p>(1): Awakenings in patients with dementia are almost systematically followed by activation, simply because they are not aware that it is still night-time and that they should sleep. Bright lights in the lobby, noise, people working reinforce this unawareness. In the Canadian nursing home "Carpe diem", lights are dimmed and night caregivers wear nightwear, which makes it easy to convince patients that it's still time to sleep</p> <p>(2) Just to help the patient remember that it is not time to get up. Stop if not accepted</p>		

## 2.2.5 Conclusions

The current approach for behavioural and psychological symptoms in patients suffering from dementia is highly ineffective and has a high harm / benefit ratio. The reasons are that it is driven by fear, is more targeted towards caregiver protection than it is towards patient comfort, aims at making patients adapt to an environment that is primarily organised for caregivers, and inappropriately responds to various symptoms by administering sedative drugs without understanding the causes behind those symptoms.

The alternative is to adopt an analytical view. Dissecting these common behaviours and symptoms allows to define treatment attitudes that provide a specific response to precise indications. Educating caregivers to this approach will enhance their confidence, reduce fear reactions and allow them to pay attention to patients' feelings and often suffering. The enhanced efficacy and lower toxicity of the treatments will reinforce their satisfaction.

## 3 Ethical issues

The ALCOVE project has formulated recommendations about the rights, autonomy and dignity of people with dementia, which mainly concern two areas:

- competence assessment
- advance directives

The SHC endorses the various recommendations made by the ALCOVE project regarding competence assessment<sup>3</sup>, but insists on the fact that these competences cannot be assessed in a dichotomous manner, but as a subtle continuum. In addition, it is important to respect people's gradual ability for self-determination. This can range from the full ability to decide and consent in the early stage of dementia to a very tenuous ability to communicate their wishes regarding daily-life experiences at a very advanced stage.

In addition, the SHC advises that it should be possible to conduct a neuropsychological competence assessment at certain "turning points" of the disease.

Regarding the recommendations for advance directives, it should be pointed out that Belgium is one of the countries in which they already have a strong legal status (they are binding as regards negative wishes) (Andorno, 2008), which means that they have a significantly more extensive impact than in other countries, such as France.

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<sup>3</sup> [1] A person diagnosed with Alzheimer's disease or dementia should not automatically be considered unfit to exercise their right to self-determination.

[2] When the person living with Alzheimer's disease is not able to make decisions on their own, the proxy or representative appointed by them (for future protection) should be involved.

[3] The competences must be assessed on a case-by-case basis, this assessment must be repeated for all major decisions regarding the treatment or care provided. [WP7.3]

[4] When assessing an individual's competences, contextual factors must be considered, including medical, psychological and social factors. [WP7.4]

[5] Assessing a person's ability to make decisions about the care and treatment provided to them must be performed by a trained and qualified healthcare professional.

[6] Further research is necessary on the development and validation of effective and practical assessment tools, especially for people with a progressive cognitive disease such as Alzheimer's disease. [WP7.6]

In Belgium, the main concerns are therefore the following: (1) that of transmitting the information collected in order to ensure that it is available at the right time as well as (2) the way in which the conversation is conducted (when, how, what is taboo, with whom, updating ....). How is the information collected and what is done with it ?

Thus, the SHC wishes to put the main focus on the first recommendation made by the ALCOVE project, viz. that "**Advance directives should be part of the broader context of advance care planning.**"

Indeed, the SHC insists on the fact that advance directives must be placed within a broader context and that their importance must be relativized. Thus, they reflect a certain image we have of human beings, but this image is not an absolute one.

Today, the fact that advance directives are being considered is strongly influenced by an autonomous and cognitivist image of human beings. This means that we look upon human beings as individual (independent) and rational entities with the ability to fully determine their own wishes. Based on such an individualistic image of the human being, it is possible to draw the following conclusions regarding advance directives:

- Respecting the individual's autonomy is, in this context, considered the overriding principle. Considerable attention is given to what the individual considers to be their will.
- These wishes can be determined rationally. In other words, expressing one's own wishes constitutes a rational and solitary activity.
- The wishes expressed by an individual are not subject to change and may be considered as absolutely certain.
- The wishes expressed in an advance directive are quite clear to the physician and achievable (cf. an order form)
- The wishes expressed by someone who is able to communicate their desires ('then self') always have priority over the 'wishes' expressed by someone who is unable to do so ('now self') in the face of their current experiences and perceptions.

An increasing amount of criticism is being issued on this cognitivist and individualistic approach to advance directives. This criticism is based on an integral image of human beings that takes seriously the relational solidarity between human beings and their actual experiences and perceptions. Based on such an integral image of human beings, it is possible to draw the following conclusions regarding advance directives:

- Writing down one's wishes is a difficult task that requires an effort that is cognitive, emotional as well as relational. It is best that human beings establish a dialogue with others from the start (family members, general practitioner, ...) in order to determine their own wishes gradually and write them down. It is also preferable to appoint someone who will be able to provide an oral explanation of the wishes that have been thus written down.
- Interpreting "wishes on paper" is a difficult task and requires a cognitive, emotional and relational effort from the caregiver.
- It is usually not that easy to deduce the wishes of the patient from an advance directive. On the contrary: determining these wishes usually requires interpreting what is written in the advance directive. The content of the advance directive must therefore be interpreted through dialogue between all those concerned with the patient.

- It should be borne in mind that people's wishes can evolve constantly, even when they have become unable to express them.
- People can also adapt to new situations that they initially experienced as highly negative.
- The variability of people's wishes as well as their ability to adapt to negative situations and their right to express contradictory and ambiguous views about end-of-life care, have meant that we must fully take into account the wishes of the 'now self' who is unable to express their own wishes and not only with those written down in the advance directive by the 'then self'. Indeed, these two identities should always be taken into account: the person who wrote down the advance directive, and the person with dementia, to whom they apply (whilst being careful to abide by the conditions of validity set by law, which, among other things, differ depending on whether the advance directive concerns euthanasia or treatment). The current perceptions/experiences of those unable to express their own desires must be taken seriously.

Starting with an integral image of human beings that takes both the wishes of the 'then self' as well as those of the 'now self' seriously, we call for the integration of the advance directive into the advance care planning model. This model ensures that there is a continuous communication process between the patients and all those who, in a positive way, are concerned with them (family members, caregivers ...). Such a context allows for a growing awareness of the care that is best suited for end-stage patients.

It follows that advance care planning is a model that provides good support to communication between all stakeholders. It also allows taking into account the context, which is all too often obscured in advance directives, but often fluctuates. It is indeed more comprehensive than the advance directive because it conveys the wishes for the patient's future existence, and has a much greater effect on the quality of the end of life. In contrast, the advance directive only concerns the medical sphere, the care provided.

Flanders is currently working on practical guidelines on advance care planning (see [http://www.palliatief.be/template.asp?f=k\\_en\\_e\\_vroegtijdige-zorgplanning.htm](http://www.palliatief.be/template.asp?f=k_en_e_vroegtijdige-zorgplanning.htm) and <http://www.pallialine.be/template.asp?f=welkom.htm>).

Thus, advance directives should not be looked upon as an end in themselves, but rather as a means to discuss the future. The main purpose is to promote dialogue with the person concerned in order to have a shared understanding of their wishes, priorities and preferences, so as to strengthen their rights and respect their autonomy whilst protecting them and taking into account their environment. It is especially the dialogue that is important when drawing up advance directives and implementing them. Also, a distinction should be drawn between the dialogue process that aims at understanding these people's wishes and the product of this dialogue, which should not necessarily result in advance directives.

It follows that another recommendation made by the ALCOVE project is of paramount importance, viz. the fact that **"Advance directives are preferably accompanied by a personal statement of values containing information about what is important and meaningful in the life of the person who has drawn up the directive."**

Given the fact that it is virtually impossible to describe all possible future scenarios in an advance directive, the latter should record the broad framework of the patient's values. This broad framework of values should clearly reveal how the patients look upon their own lives and vulnerability.

It should therefore contain a set of information on the patients, their lives, values but also aspects of their everyday existence (intimacy, sexuality, etc....) that are important for their quality of life. This information can help healthcare providers and relatives to understand what kind of end-of-life care is best suited for the patients.

This can also justify encouraging advance care planning (ACP) independently of any context of dementia and diagnosis (especially of dementia or Alzheimer's disease).

Moreover, the ALCOVE project also issues the following recommendation: **"It is important to advise persons living with dementia of the possibilities of advance care planning and the use of advance directives whilst they still have the necessary competence and mental capacities to make use of them.** Therefore, the importance of a timely and disclosed diagnosis needs to be underlined. Nevertheless, a sensitive approach is necessary, taking into consideration that not all persons are prepared to decide about their future."

Elderly people need to be correctly advised about ACP and advance directives. In this context, it is paramount to avoid or correct erroneous assumptions or errors regarding the implementation of the advance directive. Hence, it is important that elderly people understand the relationship between advance directives and euthanasia. The elderly should be advised about the meaning of all medical decisions regarding the end of life (e.g. not initiating/ stopping medical treatments that prolong life; palliative sedation; fight against pain, euthanasia ...). They must receive correct information about the scope of advance directives in terms of euthanasia. This item could, for example, be a fixed component in the care diagnosis.

This also requires a great deal of transparency (especially as regards the diagnosis) in the relationship between doctor and patient. Thus, heed must be taken to promote it.

But it should be borne in mind that giving too much importance to these advance directives could provide a false sense of security with respect to what will happen in the future because eventually, their impact will often be but limited (if they have no legal value).

This is also in line with two other recommendations of the ALCOVE project that the SHC considers crucial, and which must be repeated systematically, viz. **"Although the use of advance directives should be promoted, nobody can be forced to make up an advance directive"** and **"The person's current attitude towards a certain treatment or a care intervention - ascertained feelings, desires and wishes - should always be taken into account,** even if there is an advance directive or a designated proxy, since there can be major changes in values and preferences between the time when persons complete their advance directive and when it comes into effect".

Indeed, no-one can be compelled to think about the end of their life and plan end-of-life care in advance. Patients may have good reasons to put complete trust into their relatives and caregivers for their end-of-life care. Thus, the aim is not to write an advance directive, but to seek to take into account the views of the patients as much as possible. Hence, the various possibilities for achieving this goal must be assessed.

In addition, there should always be the possibility of reviewing the advance directives, which should not be looked upon as static documents.

Thus, the mere existence of advance directives does not suffice, and the manner in which they are used should also be considered. Indeed, it is often difficult to interpret information prior to

taking a decision. It follows that the SHC also abides by the recommendations made by the ALCOVE project as regards the concerns in terms of the quality and professional training that are required to implement the advance directives :

- **"Proper models and good practices specifically oriented towards people living with dementia need to be implemented, further developed and disseminated".**
- **"Doctors and other healthcare professionals involved in the care of people living with dementia should be properly trained in advance care planning and the use of advance directives."**

Elderly people, their relatives and caregivers should be advised about the importance of early communication about end-of-life care.

There is also a need to raise awareness and provide training at various levels.

The training and continued training for caregivers should mainly focus on the communicative and interdisciplinary nature of advance care planning. Nursing and medical students should receive common training on this subject. Nursing and medical students should be introduced to the ethical and legal aspects of end-of-life care as well as to the use of advance directives.

In order to gain a better understanding of the factors that do or do not facilitate the initiation of advance care planning, reference can be made to the systematic review of Van der Steen et. al (in press). These authors have shown that a broad variety of factors are involved. Family-related factors seem to be the most important, followed by the healthcare professional's attitude and factors related to the patient's health. The continuity of care and the healthcare system also seem to have an effect on whether or not an advance directive is initiated.

Finally, care must be taken not to overproceduralise the drawing up of advance directives, as this practice must not be reduced to rigid theoretical models. Still, it is necessary to set up models, especially in institutions, that are tailored to the population. Specific care settings and patient groups require specific ACP models.

Nursing homes, health centres and hospitals must develop a written ethics policy and guidelines for clinical practice concerning medical decisions for the end of life (e.g. not initiating/stopping life-prolonging medical treatment, palliative sedation, fight against pain, euthanasia....) as well as advance directives and ACP.

Moreover, the Fondation Roi Baudoin supports various projects pertaining to the implementation of ACP for people suffering from dementia (see also the report *Penser plus tôt ... à plus tard. Projet de soins personnalisé et anticipé: Réflexions sur son application en Belgique avec une attention particulière pour le déclin cognitif* sur <http://www.kbs-frb.be/publication.aspx?id=295125&langtype=2060>).

Perhaps advance care planning should be encouraged before the diagnosis is made: as early as during the first consultation, or for the population in general, from a certain age? The advantage of making such planning normal would be that this would reduce the stigma. GP's should also be made aware of this issue.

The "Federatie Palliatieve Zorg Vlaanderen" has developed guidelines on advance care planning, and the Fondation Roi Baudoin is in turn looking into the adaptations that need to be made for people with dementia. These directives may also be used.

### III CONCLUSION AND RECOMMENDATIONS

Dementia is an issue that has a human, ethical and societal component. It affects not only the patients, but also their families, professionals from various disciplines, and society as a whole. It is also an issue that evolves rapidly. Whilst there is no curative treatment available to date, action can be taken as regards the quality of life of the patients and their families.

In order to do so, it is necessary improve the information provided and promote expert knowledge, multidisciplinary and interdisciplinarity as a means to ensure coordination between all of those concerned as well as the continuity of care.

Hence, the SHC advises that action be taken at three levels: (1) promote teamwork in specialized centres, (2) provide better training to all healthcare professionals, (3) provide better information to the public on this illness.

#### 1) Promote expertise, multidisciplinary and interdisciplinarity

Dementia is a complex issue that affects many areas and on which knowledge is evolving rapidly. It could therefore be useful and interesting to set up training for medical consultants on dementia, as is already the case for palliative care, as a means to ensure that the best possible primary care is offered. Thus, the GP plays a valuable role in the shared care provided in cooperation with the medical specialist.

As regards second-line care, teamwork in diagnostic centres should also be strongly encouraged, be it only in terms of the quality of the diagnoses.

#### 2) Improve the information provided to all healthcare professionals both in terms of detection as well as of daily care.

As part of their initial and continued training, physicians and other healthcare professionals (especially those providing primary care) should be made aware of the significance of this issue as well as of the solutions that may be considered, potential tools to detect the first signs and various kinds of treatment that are available and/or need to be invented on a case-by-case basis. In this regard, it seems useful to provide for training curricula on dementia. They also need to include the specificity of early-onset dementia, given the fact that the signs are not always recognised in time by healthcare professionals.

Lifelong learning for professionals in dementia care is preferable above one shot course of one day and has to be framed into a whole dementia policy of the institution

When desired and possible, the patient's staying at home should be facilitated by improving the access to home care, providing better information to carers and those close to the patients and improving the cooperation between the latter and the (medical, legal, psychosocial) services.

In addition, all these interventions with these vulnerable patients mean that one has to be aware that there is a risk of potential adverse effects. It follows that all steps taken require prior ethical review.

#### 3) Providing better information to the public

Preventive measures make it possible to act on environmental factors (e.g. inactivity). It is crucial to provide proper information on this subject to the whole of society. The latter should have a more accurate notion of what cognitive and behavioural disorders are, so as to enable people to pick up on the signs in time. Finally, providing correct and proper information to the public is also very important as means to fight against the all too frequent stigmatisation of people with dementia.

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## V COMPOSITION OF THE WORKING GROUP

The composition of the Committee and that of the Board as well as the list of experts appointed by Royal Decree are available on the following website: [composition and mode of operation](#).

All experts joined the working group **in a private capacity**. Their general declarations of interests as well as those of the members of the Committee and the Board can be viewed on the SHC website (site: [conflicts of interest](#)).

The following experts were involved in drawing up and endorsing this advisory report. The working group was chaired by DE MOL Jacques; the scientific secretary GERARD Sylvie.

BAEYENS Jean-Pierre Joseph    Geriatrics                      University of Luxembourg

.be

BIER Jean-Christophe	Neurology	ULB
BRAND Daniel	Psychiatry	CHU Saint Pierre
DE LEPELEIRE Jan	General practice	KULeuven
DE MOL Jacques	Psychology	ULB
DIERCKX Eva	Gerontology	AZ St Jan Brugge – Oostende
ENGELBORGHS Sebastiaan	Neurology	UAntwerpen
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LEMEY Lieve	Psychiatry	AZ Sint Jan
PETROVIC Mirko	Geriatrics	UGent
SALMON Eric	Neurology	ULg
SCHOENMAKERS Birgitte	General practice	KULeuven
SIEBEN Anne	Neurology	UGent
VANDENBULCKE Mathieu	Psychiatry	UZ Leuven
VERSCHRAEGEN Jurn	Social nursing	Expertisecentrum Dementie Vlaanderen