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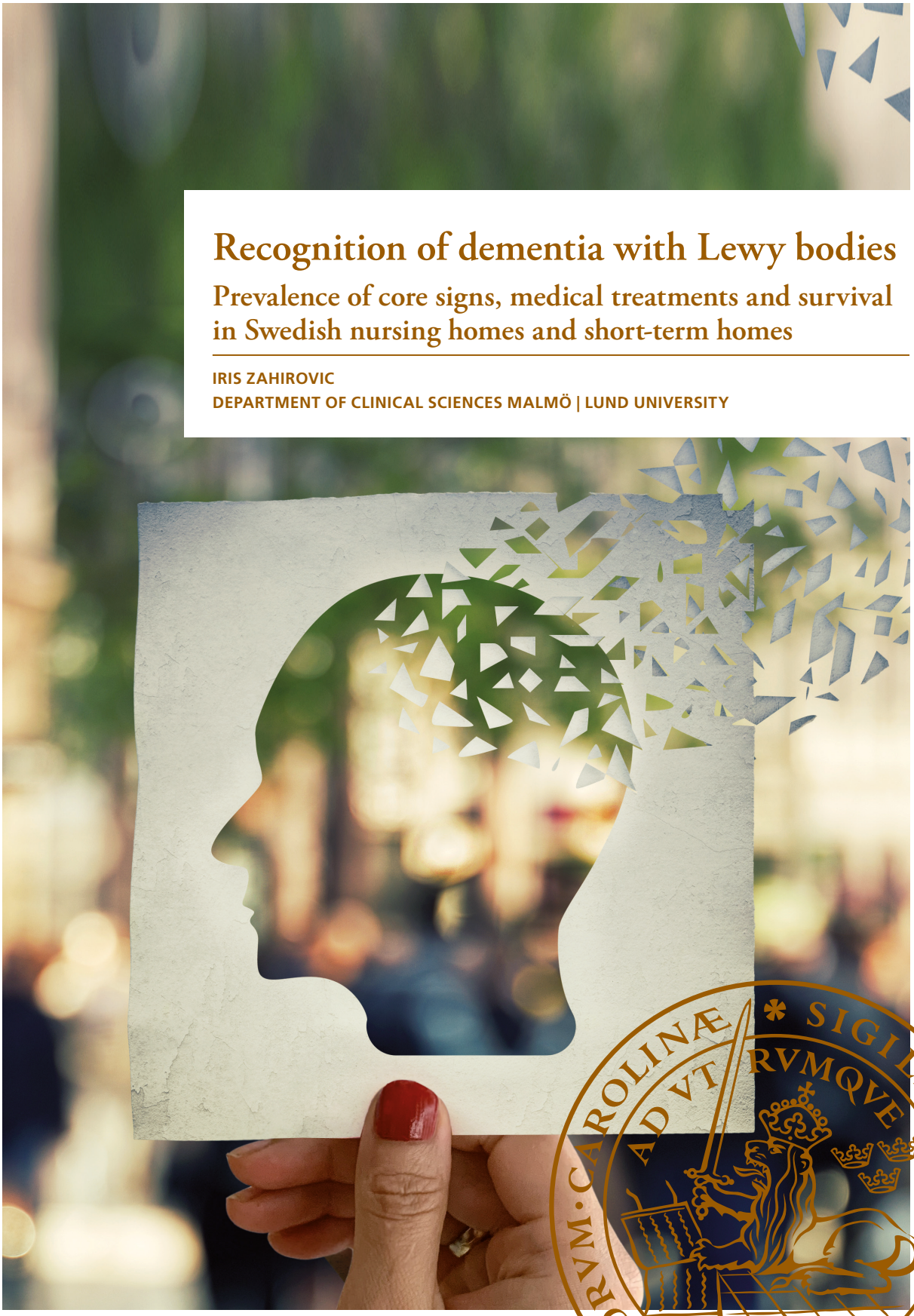

Recognition of dementia with Lewy bodies

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Iris Zahirovic

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Title and subtitle : Recognition of dementia with Lewy bodies: Prevalence of core signs, medical treatments and survival in Swedish nursing homes and short-term homes

Abstract

Background: Dementia with Lewy bodies (DLB) is an underdiagnosed neurocognitive disorder that includes several complex neurological and psychological signs, which are challenging to clinical diagnostics. Improved recognition of this neurocognitive disorder is needed because people with DLB exhibit a good treatment response to anti-dementia medications but may experience severe adverse events if treated with anti-psychotic medicine.

Aim: The main aim of this thesis was to investigate the prevalence of DLB core signs and medical treatments among older adults living at nursing homes (NHs) and short-term NHs in an entire Swedish city. A second aim was to compare the survival between residents of NHs with 0–1 and 2–4 DLB core signs.

Study population: In all papers, a specially designed form was used. This form was administered to residents of 40 NHs (N=650, mean age 86 years, 75% women) in 2012–2013 and to residents of three short-term NHs (N=141, mean age 83 years, 63% women) in 2018. The registered nurse at each NH/short-term NH completed the form and collected the study data, including medication lists. For Paper IV, data were obtained from short-term NHs and the participating residents (N=112) were given a medical examination by physicians.

Results:

In Paper I there was a 16–20% prevalence of residents with 2–4 DLB core signs in the 610 NH residents.

In Paper II, analysis of the rates of treatment with psychotropics showed use of anti-psychotics by 23% of all residents, hypnotics/sedatives by 41% and anti-dementia medications by 33% of the entire study population. Use of anti-psychotics increased from 25% to 43% in residents with an increasing number of DLB core signs.

In Paper III, the mean survival differed between residents according to the number of DLB signs; those with 0–1 DLB sign lived 8 months longer than those with 2–4 DLB signs.

In Paper IV, when the nurses' and physicians' identification of residents with 2–4 DLB signs was combined, the prevalence was 32% of all short-term NH residents.

Conclusion: In both NHs and short-term NHs, 16–32% of residents had 2–4 DLB core signs. These "high-risk DLB residents" also received unfavourable medical treatment, as shown by the high use of anti-psychotic medicine and shorter survival compared with residents with 0–1 DLB core signs.

Key words: Lewy body dementia, Medication/anti-psychotics, Survival, Nursing homes

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To my family

Having a smart brain is not enough; we also need a warm heart.

Dalai Lama

Table of Contents

Abstract

Dementia with Lewy bodies (DLB) is an underdiagnosed neurocognitive disorder that includes several complex neurological and psychological signs, which are challenging to clinical diagnostics. The recognition of this neurocognitive disorder should be improved because people with DLB exhibit a good treatment response to anti-dementia medications but experience severe adverse events if treated with anti-psychotic medicine.

The main aim of this thesis was to investigate the prevalence of DLB core signs and medical treatments among older adults living in nursing homes (NHs) and short-term NHs in an entire Swedish city. A second aim was to compare the survival between residents of NHs with 0–1 and 2–4 DLB core signs.

Design: For all papers, I applied a specially designed form covering all four core DLB signs. This form was administered to residents of 40 NHs (N=650, mean age 86 years, 75% women) in 2012–2013 and to residents of three short-term NHs (N=141, mean age 83 years, 63% women) in 2018. The registered nurse at each NH/short-term NH completed the form and collected the study data, including medication lists. For Paper IV, data were obtained from short-term NHs, and the participating residents (N=112) were given a medical examination by physicians.

Results: In **Paper I**, we found a prevalence of 2–4 DLB core signs in 16–20% of all 610 NH residents. In **Paper II**, analysis of the rates of treatment with psychotropics showed use of anti-psychotics by 23% of residents, hypnotics/sedatives by 41% and anti-dementia medications by 33% of the entire study population. Use of anti-psychotics increased from 25% to 43% in residents with an increasing number of DLB core signs. In **Paper III,** the mean survival differed between residents according to the number of DLB signs; those with 0–1 DLB signs lived 8 months longer than those with 2–4 DLB signs. In **Paper IV**, we found a prevalence of 2–4 DLB core signs in 32% of all short-term NH residents.

Conclusion: In both NHs and short-term NHs, 16–32% of residents had 2–4 DLB core signs. These "high-risk DLB residents" also received unfavourable medical treatment, as shown by the high use of anti-psychotic medicine and shorter survival compared with residents with 0–1 DLB core signs.

List of publications

I. **Zahirovic I,** Torisson G, Wattmo C, Minthon L, Londos E. Prevalence of dementia with Lewy body symptoms: a cross-sectional study in 40 Swedish nursing homes. Journal of the American Medical Directors Association. 2016;17(8):706–11.

II. **Zahirovic I,** Torisson G, Wattmo C, Londos E. Psychotropic and anti-dementia treatment in elderly adults with signs of dementia with Lewy bodies: a cross-sectional study in 40 nursing homes in Sweden. BMC Geriatrics. 2018;18(1):50.

III. **Zahirovic I,** Torisson G, Wattmo C, Londos E. Survival among the older adults with clinical signs of Lewy body dementia in 40 Swedish nursing homes: a 6-year follow-up study. BMJ Open 2019;9:e028010.

IV. **Zahirovic I,** Torisson G, Wattmo C, Nilsson E, Gustavsson A-M, Rehn C, Stomrud E, Londos E. Recognition of Lewy body signs in Swedish short-term nursing home residents; a cross-sectional observational study. Manuscript under submission.

Abbreviations

Aβ	β-amyloid
AD	Alzheimer's disease
ADL	Activities of daily living
APOE-ε4	apolipoprotein Eε4 allele
ATC	the Anatomical Therapeutic Chemical Classification System
BPSD	behavioural and psychological symptoms of dementia
ChEI	cholinesterase inhibitors
CT	computed tomography
DAT	dopamine transporter
DLB	dementia with Lewy bodies
DSM	Diagnostic and Statistical Manual of Mental Disorders
HMRs	hospital medical records (Melior® and/or WebPASiS)
HR	hazard ratio
LBD	Lewy body dementia
MMSE	Mini-Mental State Examination
MRI	magnetic resonance imaging
NBHW	Swedish National Board of Health and Welfare
NH	nursing home
NMDA	N-methyl-D-aspartate
NMDS	National Medication Dispensing System (Pascal®)
NPI	Neuropsychiatric Inventory
NPS	neuropsychiatric symptom
OH	orthostatic hypotension
OR	odds ratio
PD	Parkinson's disease
PDD	Parkinson's disease with dementia
PET scan	positron emission tomography scan
QoL	quality of life
RBD	REM sleep behaviour disorder
RCT	randomized controlled trial
REM	rapid eye movement
SD	standard deviation
SPECT	single-photon emission computed tomography
SveDem	Swedish Dementia Registry
VaD	vascular dementia
WHO	World Health Organization
VHs	visual hallucinations

Populärvetenskaplig sammanfattning

Enligt statistiska prognoser beräknas Sveriges och världens population av äldre öka kraftigt de nästkommande åren. Kognitiva sjukdomar (demens) är åldersrelaterade och 2015 estimerades prevalensen i världen till 47 miljoner människor.

I Sverige idag finns det 160000 människor med en demensdiagnos, med en årlig ökning med 25000 nya insjuknande. Demens, ett paraplybegrepp med flera olika sjukdomar, består av den vanligaste Alzheimers sjukdom följd av andra subtyper såsom vaskulär demens och Lewy body demens (LBD). I denna avhandling har vi fokuserat på LBD vars diagnoskriterier först sammanställdes i början av 90-talet. Lewy body demens är inte enkel att diagnostisera, med bl.a. tecken på varierande parkinsonliknande rörelsebesvär, minnesbesvär, synhallucinationer med insikt och störd drömsömn.

Dagens forskning och nationell statistik indikerar att det finns en underdiagnostik av LBD. Statistik från Sveriges nationella demensregisters årsrapport från 2017 presenterar endast en prevalens på 4-6% av LBD och under 2012 fanns det inga studier på prevalensen av LBD på äldreboende.

Målet med denna avhandling var att undersöka prevalensen av LBD på demensboende i Malmö stad. Efter datainsamling under 2012-13 (40 olika boende, 650 vårdtagare) visade resultaten från första studien att mellan 16 och 20% av vårdtagarna var högrisk individer för en odiagnostiserad LBD.

En av de kliniska utmaningarna för dagens sjukvård är att minska användningen av olämpliga läkemedel hos äldre som t ex. psykofarmaka som sömnmedicin, ångestdämpande läkemedel och neuroleptika preparat. Hos individer med LBD är det extra viktigt att anpassa olika läkemedelstrategier där neuroleptika är strikt förbjuden p.g.a. den starka biverkningsprofilen och förhöjda risken för död, samtidigt som just neuroleptika används ofta vid bl.a. synhallucinationer.

Resultat från den andra studien visade att neuroleptikaanvändning var högst hos högrisk individer för LBD. I den tredje studien, sex år efter datainsamlingen, kunde överlevnadsdata analyseras. Denna visade på signifikant förkortad överlevnad, 8 månader, hos högriskindivider för LBD. Detta i en population av äldre med redan förväntat kortare livstid.

I fjärde studien analyserades ny data, insamlad under 2018, från tre stora korttidsboenden i Malmö stad, med 141 vårdtagare där sjuksköterskor och läkare gjorde kliniska bedömningar av samtliga. Resultat visade en prevalens på 32% av högrisk individer för LBD.

Slutsatsen med denna avhandling blir att LBD sannolikt även är underdiagnostiserad på både demens- och korttidsboenden. Dessutom, att möjligheten till rätt diagnos förbättrades genom nära samarbete emellan olika yrkesgrupper. Teamwork, kring de

olika LBD kärnsymptomen, mellan sjuksköterskor och läkare kan öka chansen att hitta odiagnostiserade LBD individer.

Dagens kliniska forskare inom demens och LBD, socialstyrelsens nationella riktlinjer och läkemedelsverket, är alla överens om att individanpassad behandling bör användas i större utsträckning för att förbättra dagens omvårdnad. Genom att identifiera högriskindivider för LBD blir det lättare att anpassa behandlingen av våra äldre genom bl.a. minskning av olämpliga läkemedel såsom neuroleptika.

Thesis at a glance

Table 1)
Thesis at a glance

Paper	Setting and type of study	Primary outcome	Statistics	Main results
I	Nursing homes (N=620) Cross-sectional	Prevalence of observable DLB core signs	Student's *t* test, Mann–Whitney *U* test, chi-square, mean (95% CI)	Prevalence of ≥2 DLB signs: 16–20%
II	Nursing homes (N=610) Cross-sectional	Prevalence of psychotropic medication in at-risk DLB residents	Student's *t* test, Mann–Whitney *U* test, chi-square, mean (95% CI)	Prevalence of anti-psychotics: no DLB signs 16% one DLB sign 25% two DLB signs 28% three DLB signs 33% four DLB signs 43%
III	Nursing homes (N=610) Longitudinal	Survival in nursing home residents with ≥2 DLB signs	Kaplan–Meier, multivariate Cox regression analysis	Mean 8-month shorter survival time in residents with ≥2 DLB signs
IV	Short-term nursing homes (N=112) Cross-sectional	Prevalence of observable DLB signs Conformity between nurses' and physicians' clinical reports of DLB signs	Student's *t* test, Mann–Whitney *U* test, chi-square, mean (95% CI).	Prevalence of ≥2 DLB signs when reported by: Nurses 20% Physicians 21% Combined 32%

* DLB: dementia with Lewy bodies

Introduction

Dementia and neurocognitive disorders

The definition of dementia according to World Health Organization (WHO) describes dementia as a syndrome involving a disease of the brain that is of a chronic or progressive nature. Dementia is characterized by cognitive decline that affects a person's independency in activities of daily living (ADL) or social functioning [1]. Dementia is one of the most frequent diagnoses that contribute to major disabilities affecting older people, and there is an increasing need for nursing care and nursing home (NH) admission [2, 3].

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) by the American Psychiatric Association, dementia was renamed to major neurocognitive disorder (NCD). This renaming was intended to facilitate a faster identification of dementia, definition of the aetiology and treatment by including both neurological and cognitive symptomologies [4, 5].

The content of the NCD definition is summarized in Table 2. The NCD diagnosis includes a significant decline from the previous level of performance in one or more of the cognitive domains: complex attention, executive functions, learning and memory, language, perceptual–motor abilities and social cognition. An important difference from the earlier DSM-4 criteria is that memory impairment is not needed for the diagnosis of a major NCD/dementia, as shown in Table 2 [4, 6, 7].

Today, the term dementia is still most commonly used in the general population and among clinicians and patients. The terms "dementia" and "major NCD" are used interchangeably throughout this thesis.

Table 2)
Diagnostic criteria for major neurocognitive disorder according to DSM-5

Diagnostic criteria for major neurocognitive disorder according to DSM-5	
A.	Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains based on:
	1) Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and
	2) A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.
B.	The cognitive deficits interfere with independence in everyday activities (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).
C.	The cognitive deficits do not occur exclusively in the context of a delirium.
D.	The cognitive deficits are not better explained by another mental disorder (e.g., major depressive disorder, schizophrenia).

*

Prevalence and cost of dementia

According to the Delphi consensus study on the global prevalence of dementia in 2005, there were 24 million people with dementia [8]. In addition, there is a predicted doubling of dementia every 20 years, and 131 million people are expected to be living with this neurocognitive disorder by 2050 (Figure 1) [9].

In 2017, Wimo et al presented a summary of the 2015 World Alzheimer Report on both the estimated prevalence of people with dementia (47 million) and the economic impact of the disease (818 billion US dollars) [10, 11].

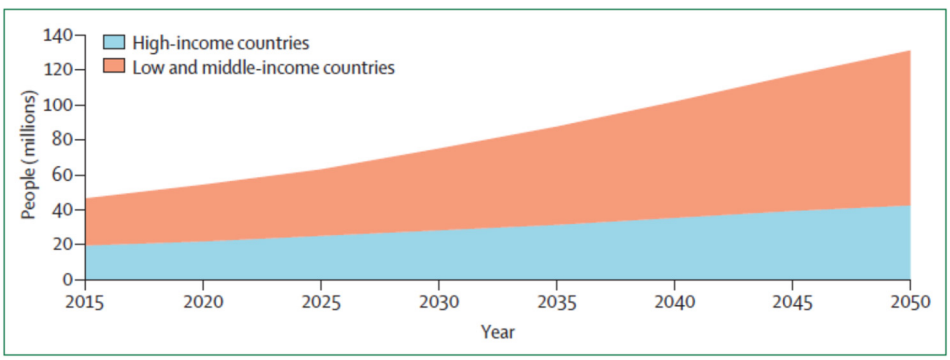

Figure 1) The number of people with dementia
Prevalence of dementia (millions).in high income (HIC) and low and middle income countries (LMIC) by permission obtained from Elsevier and Alzheimer's Disease International [11, 12]

Dementia: a global health problem

Dementia is one of the greatest global challenges for health and social care in the 21st century. This challenge has led to the production of several important guidelines and reports [11-13].

In 2017, WHO published a global action plan for the public health response to dementia, which presented seven action areas for the better care of older people with dementia and their families, as summarized in Table 3 [14]. The WHO action plan focuses on providing better health and well-being for both the present and future generations of those affected by dementia and their families. This is to be achieved by promoting the diagnosis of dementia, treatment, care and support of those with dementia, awareness and friendliness of dementia, and steps for risk reduction (Tables 3 and 4).

Table 3)
WHO: Global action plan for the public health response to dementia 2017–2025

Seven action areas identified by WHO	
1	Dementia as a public health priority
2	Dementia awareness and friendliness
3	Dementia risk reduction
4	Dementia diagnosis, treatment, care and support
5	Support for dementia carers
6	Information systems for dementia
7	Dementia research and innovation

Jwe0gujew0hg0ewherj

Livingstone et al published a similar approach that focuses on the clinical possibilities for better dementia prevention, intervention and care in the form of 10 key messages [12], as shown in Table 4.

Table 4)
Key messages about dementia prevention, intervention and care, Lancet Commissions 2017

Ten key messages by the Lancet Commissions from 2017	
1	The number of people with dementia is increasing globally
2	Be ambitious about prevention
3	Treat cognitive symptoms
4	Individualize dementia care
5	Care for family carers
6	Plan for the future
7	Protect people with dementia
8	Manage neuropsychiatric symptoms
9	Consider end of life
10	Technology

Risk factors

Even though there is no cure for dementia, there are several strategies to try to prevent or ameliorate dementia at the individual level; these involve diagnostic procedures, suitable pharmacological and non-pharmacological treatment strategies and possibilities of NH care. These are discussed throughout this thesis.

Starting with risk factors, Livingstone et al presented 35-percentage reduction in risk for dementia, during different life courses, as summarized in figure 2 as potentially modifiable risk factors. Positive lifestyle factors such as regular physical activity, effective social contact, healthy living without obesity, and smoking cessation or avoidance may improve cognition and lower the risk for dementia.

However, somatic diseases such as diabetes and hypertension are risk factors that should be prioritized by the health-care services and by increasing understanding among the population. In addition, psychiatric diseases such as depression are also potential risk factors and should be identified and treated earlier. Supporting research has shown that prompt treatment for depression, and differentiation from dementia, "late in life" has a beneficial effect on cognition.

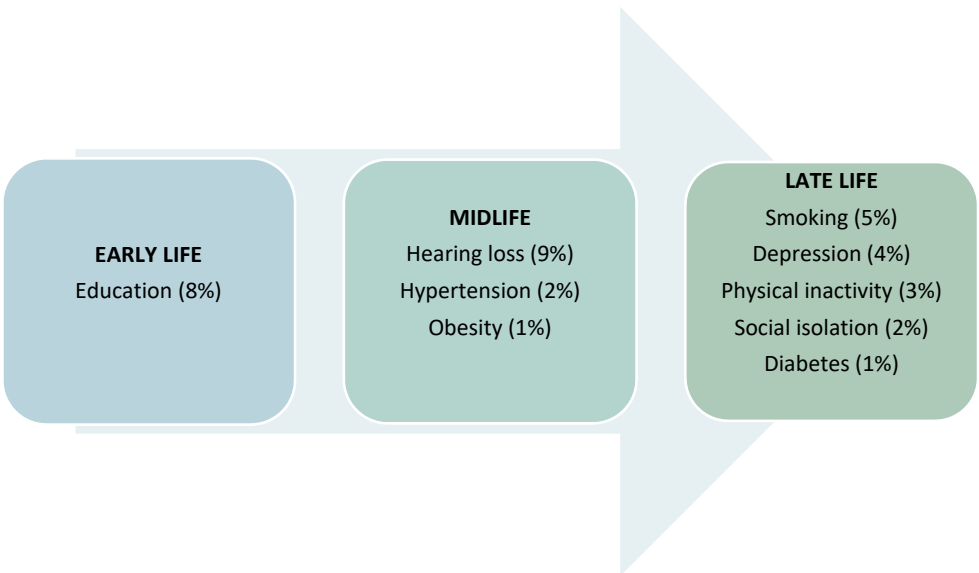

Figure 2) Potentially modifiable risk factors for preventing the development of dementia.
Presented percentages show the beneficial effects of respective activity/disease prevention or treatment according to the Lancet commission 2017, by permission obtained from Elsevier [12]

Procedures for the investigation of dementia

According to the DSM-5, procedures for the investigation of dementia should be divided into two steps: firstly, to decide whether the clinical symptomatology of dementia is present and, secondly, to investigate the dementia subtype [4].

Basal (Primary) dementia investigation

According to the Swedish National Board of Health and Welfare (NBHW), the basal dementia investigation should comprise a structured anamnesis of the patient and the family as initiated by a physician, cognitive testing (Mini-Mental State Examination (MMSE), cube and clock drawing tests) together with results from computed tomography (CT) as evaluated by a radiologist and laboratory tests [15, 16]. Basal dementia investigations are most often performed in primary care.

Specialized dementia investigation

If there is a need for a more specialized dementia investigation, further testing can follow and may include biomarker analysis of the cerebrospinal fluid, magnetic resonance imaging (MRI) or positron emission tomography (PET) scan. Specialized units, such as memory clinics, most often perform specialized dementia investigations.

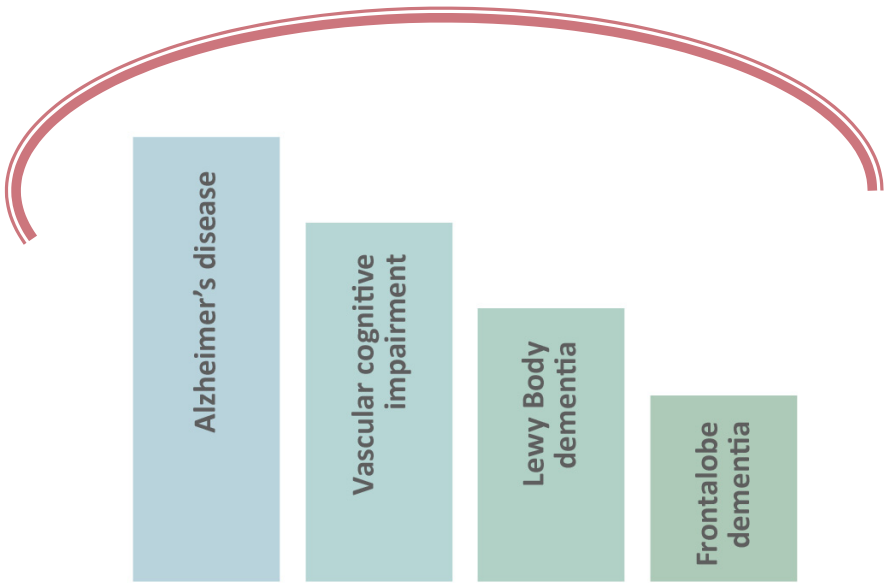

Figure 3) Illustration of an "umbrella term" of different dementia subtypes
There is a clinical and pathological overlap of different dementia diagnosis, so called mixed dementias.

Different types of dementia

There are several different dementia types: Alzheimer's disease (AD), vascular dementia (VaD), dementia with Lewy bodies (DLB), Parkinson disease dementia (PDD) and frontotemporal dementia (Figure 3). However, the boundaries between different dementia types are indistinct and mixed dementia types often coexist, which make it challenging to diagnose dementia definitively [12, 17].

AD dementia

AD is the most common type of dementia and accounts for 50–70% of all cases [18]. The progression and development of AD can be divided into a preclinical and clinical state, and the onset of clinical symptoms may occur many years after the first appearance of AD pathology [19]. According to the DSM-5, the clinical symptoms of AD focus on the decline in different cognitive domains (Table 5).

Table 5)
Diagnostic criteria for a major neurocognitive disorder caused by Alzheimer's disease according to the DSM-5

Diagnostic criteria for a major neurocognitive disorder caused by Alzheimer's disease according to the DSM-5	
A.	The criteria are met for a major neurocognitive disorder.
B.	There is insidious onset and gradual progression of impairment in at least two cognitive domains.
C.	Criteria are met for either probable or possible Alzheimer's disease as follows: probable Alzheimer's disease is diagnosed if either of the following is present; otherwise, possible Alzheimer's disease should be diagnosed.
	1.) Evidence of a causative Alzheimer's disease genetic mutation from family history or genetic testing
	2.) All three of the following are present:
	a) Clear evidence of decline in memory and learning and at least one other cognitive domain.
	b) Steadily progressive, gradual decline in cognition, without extended plateaus.
	c) No evidence of mixed aetiology.
D.	The disturbance is not better explained by cerebrovascular diseases, another neurodegenerative disease, the effects of a substance, or another mental, neurologic or systemic disorder.

Vascular cognitive impairment

Vascular cognitive impairment causes around 15% of all dementia cases and can be broadly divided into subtypes such as cortical VaD (multi-infarct dementia), subcortical VaD (small vessel dementia) and VaD because of strategic infarcts, hypoperfusion and hereditary VaD (CADASIL).

The main treatment approach for VaD focuses on controlling hypertension, ischaemic heart disease, increased cholesterol level, diabetes and obesity [20]. Imaging by MRI or CT may show a wide range of pathologies such as multiple cortical and subcortical infarcts, lacunes and white matter changes [21, 22].

Mixed dementia pathologies

Among today's researchers, there is a growing acceptance of mixed pathologies [23-25]. Several studies have identified a strong association of AD pathology with other dementia groups, which makes it more difficult to diagnose the specific type of dementia. AD with plaques and tangles alongside vascular pathologies and Lewy bodies (LBs) are all likely to contribute to similar cognitive decline, which also challenges the diagnostics and choice of appropriate treatment strategies [18, 22].

Although the pathogenic pathways in VaD and AD are unclear, it is clear that there is some interaction because vascular risk factors increase the risk of developing AD. According to some studies, lacunar strokes may be an important risk contributor to the development of mixed dementia comprising VaD and AD [22, 26-28].

Overlap between the neuropathology of AD and DLB has been reported, and the co-occurrence of both is associated with a faster cognitive decline compared with that for either form [29-31].

Today, preventive strategies and new specific biomarkers together with improvement of clinical diagnosis should be prioritized when investigating dementia, especially in older adults with multiple chronic diseases and cerebral multimorbidity [28, 32].

Lewy body dementia

The pathology

From 1908 to 1923, Frederic Lewy was one of the main researchers studying the neurocognitive disorder known today as Lewy body dementia (LBD). Lewy was first to describe the pathological findings associated with PD, and he also described the neuronal eosinophilic inclusion bodies in the brainstem known as LBs [32].

In late 1980, researchers such as Kosaka, Byrne and McKeith tried to define LBD precisely by comparing the pathological and clinical findings of their patients [33-35]. Hansen, Perry and Spillantini were other important researchers who described LBD neuropathology.

The hallmarks of LBD pathology include neuronal loss and deposition of α-synuclein, a synaptic protein that aggregates in a neurotoxic fibrillary form. Neuronal inclusions, the so-called LBs and Lewy neurites, are also observed in the central and peripheral nervous systems [25, 36].

The suitable pathological staining methodology that could visualise -synuclein immunoreactivity was not found until 1997. By -synuclein immunohistochemistry

before underdiagnosed, Lewy bodies/neurites could be visualised better in LBD individuals [37].

In 2008, the role of LBs and Lewy neurites as neuroprotective or neurotoxic was discussed in the context of different clinical signs. In addition after it was recognized that different people may have different clinical signs, for example, severe α-synuclein pathology at autopsy but no clinical LBD symptoms [38]. There are issues relating to the boundaries between DLB and PDD pathologies [33]. However, today's researchers accept that, during their progression, both DLB and PDD show similar pathological changes such as abnormal neuronal α-synuclein inclusions [36, 39, 40].

Definitions and criteria

Today, expert researchers use the term LBD as an umbrella term that comprises clinically diagnosed DLB and PDD. DLB is defined as dementia with onset within 1 year before or concurrently with the first symptoms of parkinsonism and the PDD diagnosis when there is a well-established Parkinson disease that began ≥1 year before the onset of dementia (Figure 4) [25].

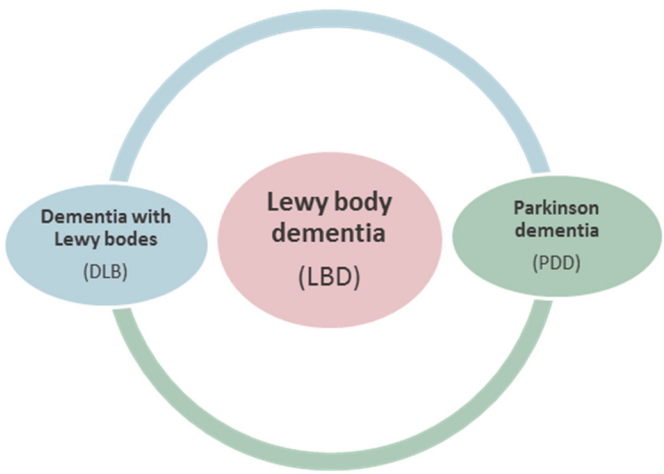

Figure 4)
Lewy body dementia

Definitions of and criteria for diagnosing DLB

In 1996, the consortium on DLB established the first consensus guidelines for the clinical diagnosis of DLB and summarized the pathological characteristics known at that time [41]. This led to the first unified disease definition in contrast to earlier different definitions used in various parts of the world. The previously used terms such as diffuse

LBD, LB variant of AD, dementia associated with cortical LBs, AD with PD changes, and senile dementia of the LB type were now unified under the umbrella terms DLB and PDD [30, 42, 43].

Consensus Report of the DLB Consortium (1996 &2005)

Since the first diagnostic criteria in 1996, several research groups have reported the risks of misdiagnosis and under-recognition of DLB, which led to the updating of the criteria during an international workshop in 2005 [44, 45].

The main focus of the revised criteria of 2005 was to improve DLB sensitivity while retaining a satisfactory level of specificity. This was done by adding rapid eye movement (REM) sleep behaviour disorder (RBD), severe neuroleptic sensitivity and low dopamine transporter uptake in the basal ganglia as suggestive signs together with the new at the time α-synuclein immunohistochemistry scheme for assessment of the pathology [46, 47].

Soon after, Fujimi et al reported the community-based Hishayama study, in which they found a high likelihood of finding DLB in 16% of the study sample after applying the revised clinicopathological DLB criteria [48]. Including the suggestive signs of DLB increased the sensitivity to 24% [49].

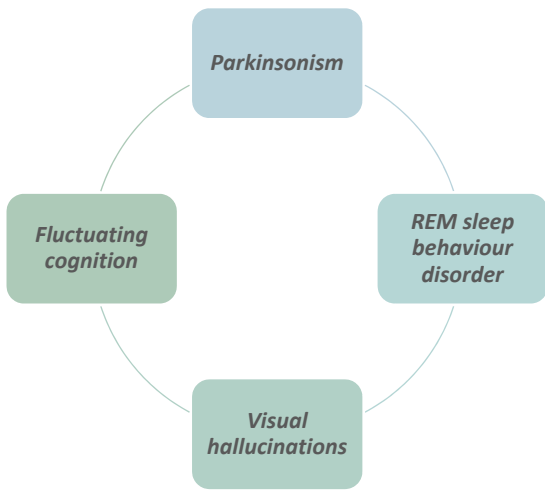

Figure 5) Four core clinical features
According to the revised criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

The Fourth Consensus Report of the DLB Consortium in 2017

More recently, the focus has shifted to further increases in the diagnostic sensitivity and improving the diagnostic tools, and the DLB criteria were updated in the Fourth Consensus Report of the DLB Consortium in 2017 [13, 50]. A fourth clinical core feature,

RBD, was added together with the updated supportive clinical signs (e.g., severe sensitivity to anti-psychotics and autonomic dysfunction, such as orthostatic hypotension). In addition, to provide guidance for clinicians worldwide, indicative biomarkers (e.g., reduced dopamine transporter uptake in the basal ganglia, abnormal ^{123}-iodine myocardial scintigraphy and RBD confirmed by polysomnography) were given greater importance, as shown in Table 6a-b.

Table 6a)
Revised criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

Revised criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)
Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.
Core clinical features *(The first 3 typically occur early and may persist throughout the course.)*
Fluctuating cognition with pronounced variations in attention and alertness. Recurrent visual hallucinations that are typically well formed and detailed. REM sleep behaviour disorder, which may precede cognitive decline. One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.
Supportive clinical features
Severe sensitivity to anti-psychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.
Indicative biomarkers
Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET. Abnormal (low uptake) 123 iodine-MIBG myocardial scintigraphy. Polysomnographic confirmation of REM sleep without atonia.
Supportive biomarkers
Relative preservation of medial temporal lobe structures on CT/MRI scan. Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity in the cingulate island sign on FDG-PET imaging. Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

Clinical diagnosis of DLB

Probable and possible DLB

The DLB diagnosis comprises four core and several supportive clinical features as well as indicative and supportive biomarkers, as shown in Table 6a-b. Using these features and biomarkers, the DLB diagnosis can be divided into probable or possible DLB (Table 6b).

Probable DLB can be diagnosed if ≥2 core features are present with or without the presence of indicative biomarkers or if only one core feature is present with ≥1 indicative biomarker.

Possible DLB can be diagnosed if one core feature is present without an indicative biomarker or if ≥1 indicative biomarker is present without any core features.

Table 6b)
Revised criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

The diagnostics
Probable DLB can be diagnosed if:
Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers, or Only one core clinical feature is present, but with one or more indicative biomarkers. Probable DLB should not be diagnosed on the basis of biomarkers alone.
Possible DLB can be diagnosed if:
Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or One or more indicative biomarkers are present but there are no core clinical features.
DLB is less likely:
In the presence of any other physical illness or brain disorder including cerebrovascular disease, sufficient to account in part or in total for the clinical picture, although these do not exclude a DLB diagnosis and may serve to indicate mixed or multiple pathologies contributing to the clinical presentation, or If parkinsonian features are the only core clinical feature and appear for the first time at a stage of severe dementia.
DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism. The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as Lewy body disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism continues to be recommended.

The main focus of this thesis was to find people at risk of DLB by using the definitions and clinical presentations of the core clinical features of mainly DLB. These features include fluctuating cognition, recurrent visual hallucinations (VHs), parkinsonism and RBD, which are presented in greater detail below.

Cognitive decline

Cognitive decline along with cortical and subcortical neuropsychological impairments has been a central criterion for the diagnosis of DLB from the first unified definition. The typical clinical presentation of cognitive impairment is progressive deterioration in attention, executive function and/or visuospatial dysfunction [44, 51].

In a systematic review, Breitve et al noted the differences in cognitive decline in people with DLB compared with those with AD. Compared with AD, memory and object naming may be less affected by DLB and there may be better verbal memory. A faster cognitive decline in people with DLB is followed by a worse prognosis in people with the mixed DLB–AD pathology [52-54]. Visuospatial deficit is more severe in people with DLB compared with those with AD and is a risk factor for a more malignant disease progression [55].

Fluctuating cognition

Fluctuations in cognitive function, occurring in 40–75% among DLB individuals, presents most often as delirium-like fluctuations with shifting degrees of alertness, attention and cognition. Fluctuations occur with a variety of time spans, from minutes to hours or days. Fluctuating cognition is often described by individuals and family as daytime drowsiness, staring into space or disorganized speech [13, 56, 57]. Fluctuations in wakefulness are evidenced as unusual tiredness, sleeping many hours at night and during the day, and falling asleep easily.

Parkinsonism

Spontaneous parkinsonism is highly prevalent (85%) among people with DLB that is not caused by anti-dopaminergic medications or stroke. The cardinal features include bradykinesia, rest tremor and rigidity, postural instability, gait difficulties and minimized facial mimicking, the so-called "masked face" [13].

The main reason for "missing" parkinsonism may be the lack of tremor or suspicion of cerebrovascular disease. In addition, the supportive clinical features and biomarkers noted in the Fourth Consensus Report may be helpful. Reduced dopamine transporter uptake in the basal ganglia as demonstrated by SPECT or PET imaging may support a DLB diagnosis and, because of the high sensitivity (78%), may help to distinguish DLB from AD. However, a normal scan does not exclude a DLB diagnosis, especially if the patient has clinical parkinsonism.

REM sleep behaviour disorder

RBD is a core feature that is defined as an "early" sign of DLB because it may appear several years before other clinical signs, which is why it is often missed. The definition of RBD is a loss of normal muscle atonia during REM sleep that presents as limb movements and/or vocalizations that may mimic dream content [13].

RBD was included in the latest criteria because of the high frequency (76%) found in autopsy of people with DLB and the knowledge that people with idiopathic RBD may have a 5–10-year increased risk of developing LBD [58]. Including questions on RBD when clinicians obtain a medical history from family and patients during a dementia investigation may therefore be beneficial for identifying DLB. Polysomnography may also be a good complement during dementia investigation [59].

Recurrent VHs

The presence of VHs is the most specific feature found in up to 80% of DLB patients and the most specific DLB feature that differentiates DLB from AD [25, 60]. Some studies of the pathologies show correlations between VHs and increased number of LBs in the

anterior and inferior parts of the temporal lobe, mainly because these areas generate complex visual images [61].

The description of recurrent VHs in people with DLB contains a wide range of well-formed, generally mute, visual illusions (vivid, colourful or three-dimensional) most often featuring people, children or animals, or "a sense of presence" (Figure 6) [44].

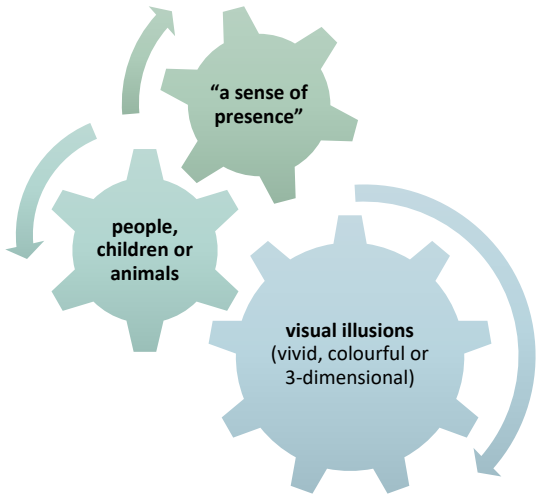

Figure 6)
Illustration of visual hallucinations in people with dementia with Lewy bodies

VHs are pathologically associated with deficits in cortical acetylcholine. Patients treated with a cholinesterase inhibitor (ChEI) show a good clinical response, which is one reason why it is important to identify patients experiencing VHs.

Prevalence of DLB

Systematic reviews show that the prevalence of DLB varies between 15–41% in autopsy series and 1.7–31% in clinical studies of elderly people with dementia [62, 63].

Prevalence of autopsy-verified DLB

Earlier studies from NHs have shown a 5% prevalence of PD. A study by Ince et al of Norwegian NHs showed that 20% of all elderly residents aged >80 years had some LB pathology and that this rate did not differ between men and women [64, 65].

The Hishayama study by Fujimi et al reported a 30% prevalence of LB pathology in people with a diagnosis of clinical dementia and in 10% of those considered to not be demented in a community-based autopsy series. They also reported a so-called

"intermediate–high" likelihood for the mixed AD+DLB pathology in 16%, including people with possibly unidentified DLB [48].

Prevalence of clinically diagnosed DLB

The first systematic review of the prevalence of clinically diagnosed DLB published by Zaccai et al in 2005 showed a wide range (0–30%) in the prevalence of DLB [63].

Even though, a growing DLB research have developed since then with unified DLB diagnostic criteria, the newest systematic review by Hogan et al presents similar prevalence differences as Zaccai with a wide range (0.3-24.4%) in DLB of all dementia cases [66]. The underestimation of the prevalence of DLB remains a major problem area [53].

In its latest report, the SveDem discussed the underestimation of the prevalence of DLB and PDD. The data from 2017 showed a 6% prevalence [67].

A summary of the studies of the clinically diagnosed prevalence and incidence of DLB is presented in Table 7. The table contains details of the population sizes, mean ages, DLB criteria used (1996 or 2005) at the time of diagnosis and living status (private home, community or secondary home care, or NH).

One of the main aims of this thesis is investigating clinically the prevalence of high-risk DLB individuals at NHs and short-term NHs, when applying the 2017 DLB criteria.

Table 7) Summary of studies assessing DLB prevalence and incidence
Summarized population and clinical prevalence studies on people with dementia with a focus on DLB. Studies are presented in alphabetical order. Living status (private home/community or secondary home care/NHs).

Author (date)	Age (years)	Dementia (*n*) / DLB (*n*)	Community / NH institution or both	Diagnostic criteria	Prevalence rate and comments
Aarsland *et al* (2008) [49]	≥70	196/39	Geriatric medicine, old age psychiatry and neurology outpatient clinics in Norway	2005	Probable DLB (*n*=31) 16% Probable and possible DLB (*n*=39) 20%
De Silva *et al* (2003) [68]	≥65	28/1	Community semi-urban Sri Lanka population	1996 + DSM-4	3.6%
Fernandez Martinez *et al* (2008) [69]	≥70	108/10	Community-dwelling Spanish elderly population	2005 + NPI + DSM-4	9.3%
Gascon-Bayarri *et al* (2007) [70]	≥70	165/15	Community-dwelling Spanish population	1996 + DSM-4	9.1%
Gurvit *et al* (2008) [71]	≥70	93/9	Community-dwelling Turkish elderly population	1996 + DSM-3	9.7%
Herrera *et al* (2002) [72]	≥65	118/2	Community-dwelling Brazilian elderly population	1996 + DSM-3	1.7%
Matsui *et al* (2009) [73]	≥65	275/16	Community-dwelling Japanese population	2005 + DSM-3	Probable DLB (*n*=12) 4.4% Probable and possible DLB (*n*=16) 10%
Rahkonen *et al* (2003) [74]	≥75	137/ 30	Community-dwelling Finish elderly population	1996 + DSM-4	Probable DLB (*n*=20) 7.3% Probable and possible DLB (*n*=30) 22%
Stevens *et al* (2002) [17]	≥65	72/ 22	Community-dwelling UK elderly population	1996 + DSM-3	Probable DLB (*n*=7) 9.7 %. Probable and possible DLB (*n*=22) 31%
Yamada *et al* (2001) [75]	≥65	142/4	Community-dwelling urban Japanese population	1996 + DSM-3	2.8%

Survival in people with DLB

In a large study, with more than 200 autopsy-confirmed DLB cases, the median survival time from onset of DLB symptoms was approximately five years. Results from a population-based study, comparing survival time in DLB individuals with the general population, presented data of 4 years earlier death, on average, among DLB individuals [24]. Predictors for shorter survival, beside older age, are fluctuating cognition and VH at onset of DLB [76].

Mueller et al recently published a systematic review and meta-analysis of studies that compared the survival between people with clinically diagnosed DLB or AD. They

confirmed higher and earlier mortality in people with DLB than in those with AD [77]. It is accepted that the presence of mixed pathology, as DLB+AD, is associated with a shorter survival time [78-80].

Stubendorff et al published the results of a prospective study that showed that early treatment with a positive clinical response to memantine predicted longer survival in patients with DLB/PDD [81].

Predictors of mortality in DLB individuals are beyond the scope of this thesis, but it is important to highlight the importance of e.g. risk factors for more suitable treatment strategies in DLB (Figure 7).

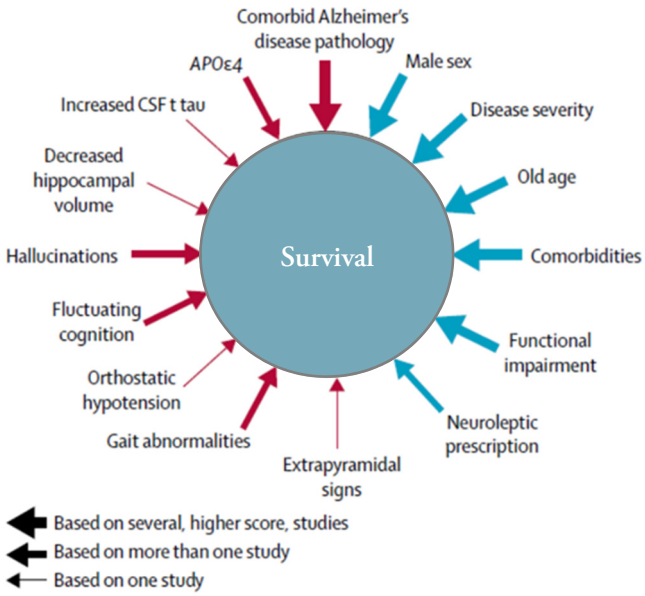

Figure 7) Predictors of mortality in individuals with dementia with Lewy bodies (DLB) [50].
Established predictors in dementia (blue), predictors studied in DLB (red), by permission of Elsevier

The survival time among NH residents with a DLB diagnosis was of interest for this thesis, which focused on survival among high-risk DLB individuals and possible areas for improvement. These topics are summarized in table 8 and discussed thoroughly in the Main Reflections section.

Table 8)
Mortality risk factors in older adults

Mortality risk factor	Strategies
Older age	
Inappropriate medication **Medication-related problems** **Adverse events**	Reduction in the use of inappropriate medication [82] Incorporation of clinical consensus for minimizing polypharmacy by, e.g., regular reviews of medicine [83, 84] Co-operation with pharmacists [83] Less use of anti-psychotic treatments [85] Incorporation of national guidelines in daily clinical work [86] Education [87]
Dementia	Faster dementia diagnostics followed by earlier anti-dementia treatments [88, 89] Focus on improving cognition (e.g., elimination of medicine with a cognitive burden or anti-cholinergic burden)[90, 91] Preventive strategies in dementia: cognitive training, preserved hearing, rich social network, exercise, and treatment of hypertension, diabetes and high cholesterol [12]
Poor physical health **ADL dependency [92]**	More active prevention of risk factors during all life stages (early, mid, late life) by all health-care providers, national guidelines [12] Earlier evaluation by a physiotherapist Multidisciplinary approach
Problematic neuropsychiatric symptomatology / BPSDs [93]	Prevention of NPSs Person-centred care [94] First-line treatment; suitable non-pharmacological treatment policy [94] Second-line treatment; suitable short-term pharmacological treatment in parallel Active investigation of earlier depression signs, sleep disturbances and dementia
Malnutrition [95]	Earlier evaluations of nutrition as a part of dementia investigation
Hospitalization [96]	Prevention of prolonged hospital days and rehospitalisation of DLB individuals

Quality of life

People with DLB have significantly lower quality of life (QoL) compared with those with AD [97]. The current studies and clinical research on DLB and QoL contain important information about the disease and its progress for patients and caregivers. These studies provide important information about the possible non-pharmacological treatment strategies, benefits of physical therapy or ADL support, and the importance of reporting neuropsychiatric symptoms (NPSs) that may appear and how they should be interpreted for good management [50, 98-100].

In a qualitative study, Larsson et al presented interview data obtained from DLB patients about their subjective experiences of living with DLB. Those interviews showed the importance of successful coping strategies for having a good QoL [100].

The Lewy Body Dementia Association conducted a web-based survey in which caregivers (family and friends) could grade and express their concerns and burdens. Eighty per cent of the caregivers felt that people around them did not understand their burden; 77% reported a fear about the future, 54% reported feeling stressed, and 52% reported experiencing loss of social life and isolation [98].

Treatment strategies in DLB

Cholinesterase inhibitors

The most common ChEIs are donepezil, rivastigmine and galantamine. As described below, ChEIs inactivate the enzyme acetylcholinesterase, which is involved in the termination of impulse transmission through the breakdown of the neurotransmitter acetylcholine in numerous cholinergic pathways in the central and peripheral nervous systems (Table 9) [101].

According to a Cochrane collaboration review on treatments with ChEI vs placebo, ChEIs have only a modest effect on cognition, ADL and global cognition in AD patients. However, in a double-blind clinical trial (DOMINO) of anti-dementia treatments, withdrawal of donepezil in AD patients led to increased risk of NH placement [102].

An international double-blind, placebo-controlled study on rivastigmine in people with DLB showed a positive effect on cognition and the NPSs apathy, anxiety, delusions and hallucinations [103]. A randomized clinical trial (RCT) of donepezil showed similar significant effects on cognitive and global and behavioural improvements in DLB/PDD patients [104, 105].

Memantine

Memantine is a specific, non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist that blocks or unblocks activation of NMDA receptors and targets the glutamatergic system. The efficacy of memantine has been shown in a population with moderate to severe AD (Table 9) [106].

In a double-blind, placebo-controlled RCT, Aarsland and colleagues found that memantine seemed to improve global clinical status as well as behavioural symptoms in DLB patients [107]. Subsequent studies have provided data showing that memantine is well tolerated in DLB patients and has showed some improvement of their cognition, VHs and QoL [107-109].

Table 9)
Summary of possible treatment areas in people with DLB

Treatment areas	Medicine group, name		Comments
Cognition	Acetylcholinesterase inhibitors	Rivastigmine [110] Donepezil [111]	Improvements in cognition, attention and memory as well as global improvement
	Memantine	Memantine [107, 112, 113]	Global improvement, some effect on NPSs
VHs	Acetylcholinesterase inhibitors	Rivastigmine [103]	Improvement in NPSs, delusions, VHs, apathy and depression
	Memantine	Memantine [106, 112]	Improvement in NPSs
	Anti-psychotics	Quetiapine [114, 115] Clozapine [116]	Quetiapine: limited efficacy Clozapine: high risk for agranulocytosis with treatment
		Pimavanserin [117]	Reduction in psychotic symptoms
Parkinsonism		Levodopa [118]	Variable effects, but may improve parkinsonism
RBD	Acetylcholinesterase inhibitors	Rivastigmine [25, 119]	Some improvement
		Melatonin [25]	
Depression and anxiety	Anti-depressants [13]	Venlafaxine Paroxetine	
Postural hypotension	Fludrocortisone [25]		Medicine may be a complement to non-pharmacological treatment policies
Medicine that should be avoided	Anti-cholinergic medication [13, 25] Antipsychotics [120]		Medicine with anti-cholinergic properties should be avoided because of cognitive burden and risk of cognitive worsening / delirium. Antipsychotics should be avoided e.g. because of worsening of mortality rate.

Other treatment areas

VHs and other NPSs are well-known central problems in many people with DLB; this topic is discussed later in the Neuropsychiatric symptoms section. Other clinical symptoms of interest that may be improved with suitable treatment include RBD, orthostatic intolerance and dysphagia/swallowing dysfunction (Figure 8). For example, RBD may be improved by memantine, followed by some positive effects with melatonin and lastly clozapine (Table 9) [25].

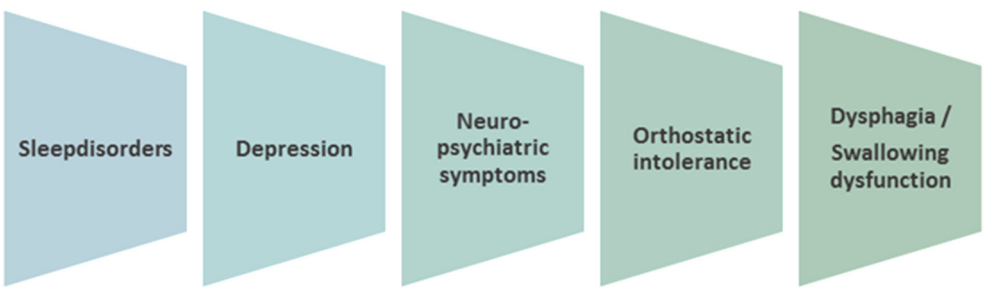

Figure 8)
Illustration of different symptoms that may present in individuals with DLB

The study by Londos et al on dysphagia and swallowing dysfunction assessed by videofluoroscopic examination in patients with DLB showed that >90% of the patients had swallowing dysfunction. However, a low percentage of the patients and their family/caregivers had reported dysphagia in these patients, which shows how difficult it is to diagnose this dysfunction clinically[121].

Neuropsychiatric symptoms

NPSs are common in people with dementia and become more prevalent as the dementia progresses (Figure 9). A person with DLB may have more severe NPSs such as worsening of VHs, depression, agitation, aggression, anxiety and irritability, and the prevalence ranges between 84% and 90% [122, 123].

The Neuropsychiatric Inventory (NPI) scale is used as a clinical tool to analyse different NPSs in dementia patients. The NPI has 12 domains (score 0–144), and is used to measure and visualize the psychological burden for individual patients. A higher total NPI score indicates more severe psychopathology [124].

A large factor analysis by the Alzheimer's Disease Consortium using the NPI scale categorized the most prevalent NPSs in dementia patients into four large sub-syndromes, as summarized in Figure 9 [125].

The most prevalent, apathy, was found in 65% of patients, followed by hyperactivity in 64%, affective disorders (anxiety and depression) in 59% and psychosis in 38% [125]. In NHs, an 87% prevalence of at least one NPS was found in the residents with dementia [126].

A comparison of NPSs between DLB and AD patients showed a significantly higher NPI total score and higher prevalence of difficult NPSs, such as hallucinations and apathy, in those with DLB, which led to greater distress for individuals and their caregivers [31].

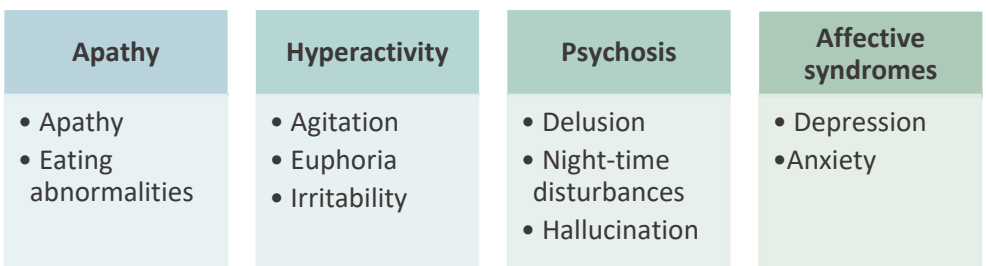

Figure 9) Neuropsychiatric symptoms in dementia
Examples of the most prevalent neuropsychiatric symptoms in elderly people with a dementia disorder

Hassler et al studied behavioural and psychological symptoms (BPSDs), a definition that contains the same symptoms as NPSs, in German general hospital patients with dementia. An increasing prevalence of BPSD symptoms was found with increasing dementia grade; the prevalence rates were 67%, 76% and 88% in patients with mild, moderate and severe dementia, respectively [127]. The most distressing BPSDs for the nursing staff were delusions, aggression and night-time disturbances.

Treatment strategies

Treatment of NPSs is divided into pharmacological and non-pharmacological strategies. There is increasing encouragement for the use of non-pharmacological treatments from professional organizations such as the European Medicines Agency, US Food and Drug Administration, Swedish NBHW and opinion-leading clinical research groups [128-131].

This thesis discusses several treatment strategies as a possible first-line approach for NPSs for all dementia disorders, especially DLB, in the section titled Non-pharmacological treatments.

Pharmacological treatments

Polypharmacy is a worldwide problem in the health-care system. Several countries report that polypharmacy increases the risk of adverse effects and other drug reactions and increases the risk of falls in NHs. There is especially strong evidence of an association between the use of anti-psychotics and/or anti-anxiety medicine and the risk of falls [83, 132-134].

When should pharmacological treatment (e.g. psychotropics) be used?

The recommendations by the Delphi Consensus Multidisciplinary Panel highlight three areas of importance: 1) major depression with or without suicidal ideation; 2) psychosis causing harm or with great potential for harm; and 3) aggression causing risk to self or others [135]. In these cases, minimal dosages and time to treat are important. Several studies have recommended a maximum of 12 weeks for medical treatment with anti-psychotics.

The medical treatment for NPS comprises different psychotropic medications, including hypnotics/sedatives, anxiolytics, anti-psychotics and anti-depressants.

The most negative impacts on patients and their caregivers are NPSs such as severe delusions/psychosis and agitation, which are often treated with anti-psychotics. However, the potential for improvement using both conventional and atypical anti-psychotics is questionable [136, 137].

Anti-psychotic medications

Large studies on anti-psychotics, especially conventional medications, have shown an association between their use and increased mortality in older people, especially those with dementia. In addition, use of these medications is associated with severe adverse reactions and events, including extrapyramidal symptoms, rigidity, cerebrovascular events, risk for falls and further cognitive decline [3, 85, 138-140].

Compared with risperidone, haloperidol has the greatest increase in risk of mortality mainly because of the risk of numerous and serious adverse events such as parkinsonism, somnolence/sedation and delirium [140-142]. Some studies have reported significant improvements in NPSs with risperidone or olanzapine, although these medications have modest efficacy and increase the risk of NH admission and mortality (Figure 10) [143].

In the past decade, anti-psychotics have been the subject of many regulatory risk communication methods and black box warnings worldwide. However, the use of psychotropics remains high and, according to several Swedish, Danish and Norwegian studies, varies greatly (39–71%). These variations have been reported in the elderly population with dementia, among institutionalized and non-institutionalized elderly patients and by primary care or specialist clinic health professionals [84, 144-147].

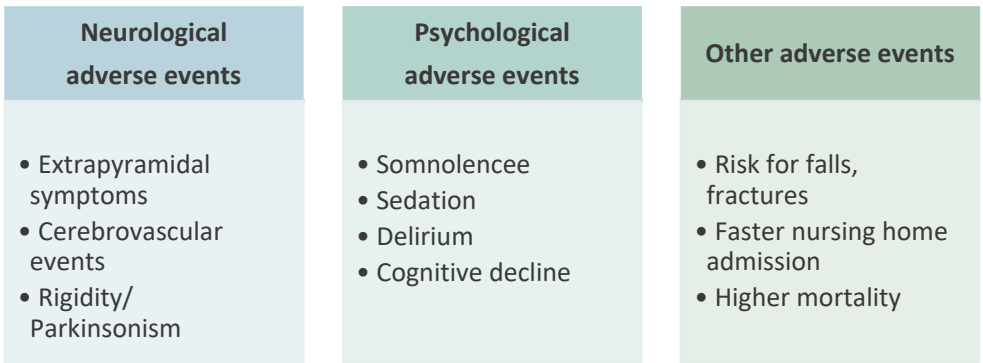

Figure 10) Adverse events
Examples of the most prevalent adverse events after usage of psychotropics in persons with dementia

Anti-psychotic medications and DLB

Sensitivity to anti-psychotics in DLB patients, also known as neuroleptic sensitivity, is a well-known problem that often leads to extrapyramidal signs, confusion, and increased risk of falls and mortality. This at the same time as the VHs and delusions in DLB individuals are highly occurring (50-70%) [148].

As mentioned earlier, treatment with donepezil or memantine has beneficial effects on VHs in DLB patients [111]. If an anti-psychotic needs to be used because of severe

symptomatology of VHs, agitation or psychosis, quetiapine has been shown to have some positive effects on agitation or psychosis in patients with dementia and parkinsonism [114]. Clozapine may also be effective in reducing VHs, although there is a risk of agranulocytosis and anti-cholinergic side effects [116].

Pimavanserin

Pimavanserin is among the newest drugs to treat NPSs. This drug is a selective 5-hydroxy-tryptamine 5-HT2A receptor inverse agonist/antagonist and has been approved in the US for the treatment of hallucinations and delusions associated with PD psychosis. Ballard et al recently published the results of a double-blind, placebo-controlled RCT on the efficacy of pimavanserin in treating symptoms of psychosis in patients with AD. Thirty per cent of the patients with the most severe NPSs, showed improvement graded on the NPI scale, and there were few adverse events such as urinary tract infection, falls and agitation [117].

Non-pharmacological treatments

Several RCTs and interventional studies have been published in the past 5 years on NPSs in elderly people with dementia, mainly those living in NH facilities. There are several interesting approaches to the use of non-pharmacological treatments for the most challenging and common NPSs such as agitation, aggression and psychosis. An international Delphi consensus by Kales and colleagues in 2019 presented a summary of the best treatment strategies for overall treatment of NPSs with a special focus on agitation and psychosis. Some of these treatment strategies are summarized in Table 10 [93].

Table 10)
Treatment strategies for individuals with neuropsychiatric symptoms

STEP I	**STEP II**	**STEP III**	
Identification of underlying causes	**First-line approach ; non-pharmacological treatment strategies**	**Second-line approach; pharmacological treatment strategies**	
Medical list reviews : Medical reason for the specific medicine? Investigate if there is existing untreated pain / infection? Psychotropics? Dosages? Duration?	Different strategies Caregiver training Environmental adaptations Person-centred care Tailored activities Music therapy [149] DICE [150]	Agitation Dextromethorphan Mirtazapine alatamine Melatonine	Psychosis Citalopram Analgesia Risperidone Pimavanserin [117]

Two interesting non-pharmacological approaches for identifying the underlying causes of NPSs are the multidisciplinary programmes Describe, Investigate, Create and Evaluate (DICE) and Well-Being and Health for People with Dementia (WHELD)

[150, 151]. Ballard and colleagues reported a large RCT on the beneficial effects of person-centred caring on NPSs using the WHELD intervention that comprises medical review (anti-psychotic use: yes/no) plus social interventions such as educating NH staff on dementia, person-centred care and cognitive behaviour principles [94, 151].

The health-care system

Dementia care in Sweden

According to the Swedish Dementia Registry (SveDem), there are 160 000 people living in Sweden with a dementia diagnosis, which represents an increase of 25 000 new dementia cases every year [152, 153].

According to Swedish statistics, 500 000 people aged over 80 years are living in Sweden today. In the year 2035, the population will pass 11 million and the greatest increase—75%—will be in ≥80 years older adults. The combination of the increase in life expectancy and the fact that dementia is an age-specific disorder means that dementia will become a demographic challenge for Swedish society and health care [154].

The early effective recognition of dementia is important for the effective application of suitable treatments and social care adjustments [10].

In a 2013 report, the government appointed the Swedish NBHW to identify a series of challenges that Sweden may confront because of the country's ageing population. In 2017, a national report on dementia care was presented that included 76 recommendations on dementia care relating to dementia investigation procedures, follow-up, multi-professional work, medical treatments and education [152]. The focus on better dementia care is organized around seven action areas, as summarized in Table 11.

Table 11)
Seven problem areas according to the Swedish national report on dementia care, 2017

Seven action areas for dementia care in Sweden	
1	Co-operation between the health-care system and social services
2	Knowledge and competence
3	Follow-up and evaluation (e.g., structured follow-up/evaluations of treatments as well as different possible neuropsychiatric symptoms in people with a dementia diagnosis)
4	Personnel
5	Family members and relatives
6	Society
7	Technology

Dementia friendly care

A well-known problem for Swedish medicine and hospital medical record (HMR) systems is the risk of medication errors and deficits in the transfer of medical information between hospitals and primary care settings [155-157]. According to a recent study by Reimers et al, the duration of Swedish geriatric hospital care is associated with the number of changes to a patient's prescriptions [158].

Table 12)
Dementia-friendly care

Dementia-friendly care	
Education about non-pharmacological and pharmacological treatment strategies [87, 94, 135, 150]	Dementia education: different stages, treatments, recognizable dementia symptomatology and further education about DLB features NPSs, symptoms and treatment strategies Education about delirium, depression and dementia
Communication [94, 152, 157] between different regions and clinics between different staff (e.g., physician and nursing staff)	Communication between medical staff Inclusion of discharge planners and physical therapists Inclusion of patients and family/caregivers Early initiation of interdisciplinary planning
Hospital environment [87, 94]	Patient safety interventions: falls prevention, pain assessment, evaluation, adverse events evaluation, less use of inappropriate medicine

According to statistics on drug use for the southern part (Region Skåne) of Sweden, the use of psychotropics has not decreased substantially. However, there may be less use of anti-psychotics in the oldest people (aged >85 years).

Greater "dementia-friendly care" that focuses on improving the communication between different areas and/or medical staff as well as increased education and use of non-pharmacological treatment strategies is needed (Table 12).

Better communication strategies between medical staff, hospital and primary care as well as with family/caregivers are needed

Aims

Paper I

The aims were to identify and estimate the prevalence of observable DLB signs in a population covering all dementia NHs in a large Swedish city of 320 000 people.

Paper II

The aim was to investigate the use of psychotropic medication (anti-psychotics, hypnotics/sedatives, anti-depressants, anxiolytics and anti-dementia medication) in Swedish NHs with a special focus on patients with clinical signs of DLB.

Paper III

The aim was to determine the survival rates among older adults living with dementia in NHs in the third largest Swedish city in relation to the DLB core signs.

Paper IV

The main aim was to analyse the recognition of DLB core signs in residents of short-term NHs in the third largest Swedish city. A second aim was to investigate the conformity of clinical reports by nurses and physicians on DLB core signs.

Methods

The Methods section of this thesis presents the study designs separately for Papers I–III and Paper IV to provide a better overview of the two roughly similar study populations. The data were collected from NHs in 2012–2013 and from short-term NHs in 2018.

Papers I–III

Study population

Malmö is the third largest city in Sweden and is home to >300 000 people who have roots in >174 countries and speak 150 different languages [159].

According to the official registry for dementia NHs in the city of Malmö, in January 2012, there were 40 NHs specifically for dementia residents. From January 2012 to March 2013, all 40 dementia NHs in Malmö were invited to participate. All accepted and the data from these NHs were used in Papers I–III.

The inclusion criterion was all residents aged ≥65 years living in the NHs. The exclusion criteria were residents who declined to participate and/or were in a palliative state of treatment.

Nursing homes

The NHs in Malmö each housed an average of 15 residents with a range of 4–45 people per NH. The medical personnel included a physician (most often a specialist in general medicine), one or two registered nurses (with 3 years of university training) and a varying number (4–8) of assistant nurses (with 2 years of nursing care school).

Small pilot study

Before the start of the main study, a pilot study was performed at one of the 40 NHs, where a physician performed a complete examination of the residents' somatic and neurological status plus blood pressure measurements. The conclusion was that this procedure was time-consuming and could not be performed on 650 residents within the time frame needed.

Data collection

The data collection began after distribution of information about the study and education about the observable DLB core signs, the form content and data interpretation.

- The nurses collected electronic medication lists from the Swedish National Medication Dispensing System (NMDS) (Pascal®) for all participating residents.
- The Anatomical Therapeutic Chemical (ATC) Classification System was used to categorize medication: anti-psychotics (N05A), anxiolytics (N05B), hypnotics/sedatives (N05C), anti-depressants (N06A) and anti-dementia medicine (N06D) [160].
- Data on the dementia diagnosis (yes/no) were collected from electronic HMR systems (Melior®) simultaneously by the author of this thesis.
- Date of death was collected from HMR (WebPASiS) in August 2018, 6 years after the start of the study, and was used to analyse survival in Paper III.

The study form

Sätt Kryss i passande svar nedan :	JA	NEJ
Parkinson sjukdom, diagnos finns		
Lewy body sjukdom, diagnos finns		
Stelhet i kroppen och/eller skakningar. Bl.a. rör sig stelare och mera osmidigt		
Pratar tystare och kraftlöst		
Försämrad balans och faller lättare omkull		
Synhallucinationer Ex) berättar att de ser saker som inte finns		
Uttalad trötthet, sover dagtid		
Vilda oroliga drömmar Ex) kan plötsligt börja prata eller skrika under sömnen. Har mardrömmar		
Stroke (hjärninfarkt / blödning)		
Läkemedel mot Parkinson t ex Madopark®		
Medicinlista bifogad till frågeformuläret		

Figure 11)
Original study form from data collection in Papers I–IV.

The main clinical data were collected using a specifically designed form to record the observable clinical signs of DLB by the nursing personnel in each NH (Figure 11, figure 12).

- To maintain compatible data collection, we carefully chose three DLB core features and RBD (at that time only a suggestive feature), which are equivalent to the clinical criteria according to the third DLB Consortium report from 2005 [47]. RBD was added because a neuropathological validation study of the DLB criteria by Fujishiro et al showed that an increased number of core criteria plus RBD implied a higher likelihood of LB neuropathology [29].
- To make it easier for the nursing personnel to recognize the DLB features, we chose seven clinically observable DLB signs, which are presented in the form with no need for medical examination (Figures 13 and 14).
- For the data analysis, all seven clinical signs were fused into the four DLB core features: parkinsonism, VHs, fluctuating cognition and suspected RBD, as presented in Figure 12.
- In addition to the clinical DLB signs, demographic information such as age, sex, reported stroke, and use of anti-psychotics and PD medication were collected using the same form.

Definition of parkinsonism

To increase DLB sensitivity, it was important to use a plausible definition of parkinsonism because it is one of the DLB core features.

- The stricter definition of parkinsonism was used in which PD or parkinsonism as a diagnosis was reported in the form.
- The wider definition of parkinsonism included the presence of all three signs of rigidity, weak voice and balance problems, which were reported in the form.

In Paper I, these "stricter and wider" parkinsonism definitions together with VHs, fluctuating cognition and suspected RBD were used in the data analysis.

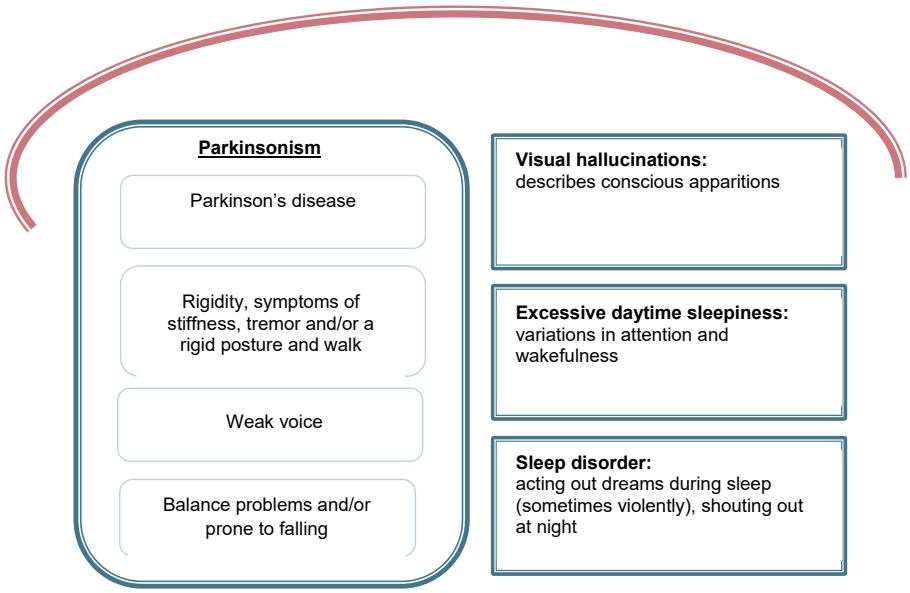

Figure 12) Seven observable clinical DLB signs, Paper I-II-III
Illustration over how all seven observable clinical DLB signs were fused into four DLB core features for the data analysis. Parkinsonism contains (Parkinson's disease, Rigidity, symptoms of stiffness, tremor and/or a rigid posture and walk, Weak voice and Balance problems and/or prone to falling).

Paper IV

The study population

In the city of Malmö in 2018, there were three large short-term NHs: A (n=56), B (n=44) and C (n=41). In September 2018, all three short-term NHs were invited to participate in the study presented in Paper IV.

The inclusion criteria were age ≥65 years and staying in a short-term NH in November and December 2018. The exclusion criteria were declining to participate and/or in a palliative state of treatment.

Short-stay NHs and their residents

A Swedish short-stay NH is often a post-acute care home for patients who require rehabilitation and nursing services after a hospitalization.

According to a Swedish NBHW statistical report on care and services for the elderly, in October 2017, there were nationally 9386 people aged >65 years staying in a short-term NH [161]. The Swedish NBHW's latest report on social welfare care and services for older people showed that rehabilitation was the main single reason for placement in a short-term NH (22%).

Thirty per cent of those staying in a short-term NH had a need related to updated health status (e.g., structural updating of the medical list, nutrition care, need for treatment for depression and anxiety and/or palliative care). Forty-eight per cent of the people in short-term NHs were there for updated social planning purposes by the municipality, for example, as patients moving back to their primary home or waiting for a new permanent NH placement [152].

Data collection

The focus of Paper IV was to identify the observable DLB core signs from the collected forms (nurses and physicians) and from the results of a medical examination by a physician (Figure 13).

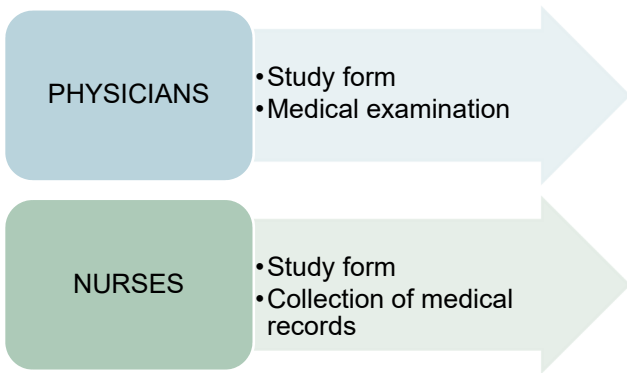

Figure 13)
The process of the data collection for Paper IV

The operation managers for separate short-term NHs were informed. After their approval and ethical approval, the study was presented followed by education of the active nursing personnel.

The study presentation separately to the nursing personnel in each of the short-term NHs by the author of this thesis. This included detailed information about the study and its focus, and the procedures for data collection. Twenty-four nurses (with 3 years of university) and a varying number of assistant nurses (with 2 years of nursing care school) actively participated in the data collection. The same introduction was given

separately to physicians who were also given details about the examination of neurological status and the anamnestic focus of the form, such as questions about existing parkinsonism, stroke, sleep disturbances and different NPSs.

There was also a unified discussion of the examination procedure among all involved physicians. This led to a consensus for the neurological examinations (to determine whether the patient exhibited clinical signs of parkinsonism and/or signs of cerebrovascular disease) and the anamnestic focus (used to collect data according to the form).

Nine physicians performed the medical examinations and completed the form. Five of the physicians were residents in geriatrics and had been working in the selected short-term NHs during 2018, one was a specialist in geriatric medicine, one a specialist in internal medicine, one a specialist in general medicine and one a specialist in rehabilitation medicine and psychiatry.

All data were collected simultaneously from the nursing personnel and physicians (Figure 13).

The study form

The study form for nurses and physicians in Paper IV was identical to that used in Papers I–III and contained the same seven observable DLB signs parkinsonism/PD, VHs, fluctuating cognition, RBD, rigidity, balance problems and weak voice (Figures 12, 13).

The differences between the forms for nurses and physicians were that physicians had a second page to record the results of the medical examination. During the medical examination, the physicians were asked to note the presence of parkinsonism (yes/no) and cerebrovascular disease (yes/no).

Definition of parkinsonism

Parkinsonism was considered present if the resident had one of the following:

- Parkinsonism found in the medical examination by the physician
- PD diagnosis according to HMRs
- Rigidity problems as recorded in the nurses' form in concordance with the revised DLB criteria [13].

Statistics

- IBM Statistical Package for the Social Sciences (SPSS) for Windows (version 22.0; IBM Corporation, Armonk, NY, USA) was used for all statistical analyses.
- In the studies described in Papers I–IV, statistical methods such as Student's *t* test, one-way analysis of variance, Mann–Whitney *U* test, and chi-square test were applied to compare group differences.
- For all papers, the residents of the NHs and short-term NHs were divided into dichotomous groups according to age and the number of DLB signs (0–1 DLB and 2–4 DLB signs). All data are presented as mean 95% Confidence interval unless otherwise noted. Categorical data were analysed using the chi-square test. The significance level was set to $p<0.05$.
- In Paper II, NH residents were divided into dichotomous groups according to the presence of dementia (yes/no) or number of DLB signs (0–1 DLB and 2–4 DLB signs) and age (≤85 and ≥86 years).
- For Paper III, Kaplan–Meier graph were constructed to show the survival distribution for all residents, and log-rank tests were used to compare survival between groups.
- Multivariate Cox regression analysis was performed to identify possible covariates of survival. Age and sex were controlled for in the Cox regression analysis. $p<0.05$ was considered to be significant.

Ethics

- For all papers, informed consent forms were given to the nurses at the 40 NHs and the three short-term NHs. Thereafter, the nurses collected oral informed consent from the residents and/or their family members. If a resident lacked the capacity to consent because of fragility, a family member and/or trustee made this decision together with the nurse before inclusion in the study.
- For Paper IV, all data were collected simultaneously from nursing personnel and physicians. The nurse and/or physician gave the same study information to each resident separately, and verbal consent was collected.
- The Regional Ethical Review Board in Lund approved all four studies.

Main results

Demographic data for Papers I–III

For Paper I, there were 650 older adults living in 40 NHs; 30 were excluded because they had declined participation or had missing data, which left 620 (95%) participants with a high response rate for the collected study data (Figure 14,15). The mean age for the total population was 86 (±7.5) years, and the range was 65 to 105 years; 467 (75%) were women.

For Papers II and III, 10 residents had incomplete medicine data and were excluded, leaving data for 610 residents. The medical lists were identified in 576 (94%), HMRs for 594 (97%) and completed forms for 610 (100%) of the 610 residents.

Of the 610 residents, 440 (72%) had a formal, International Classification of Diseases (ICD) coded dementia diagnosis, as shown in Figure 14.

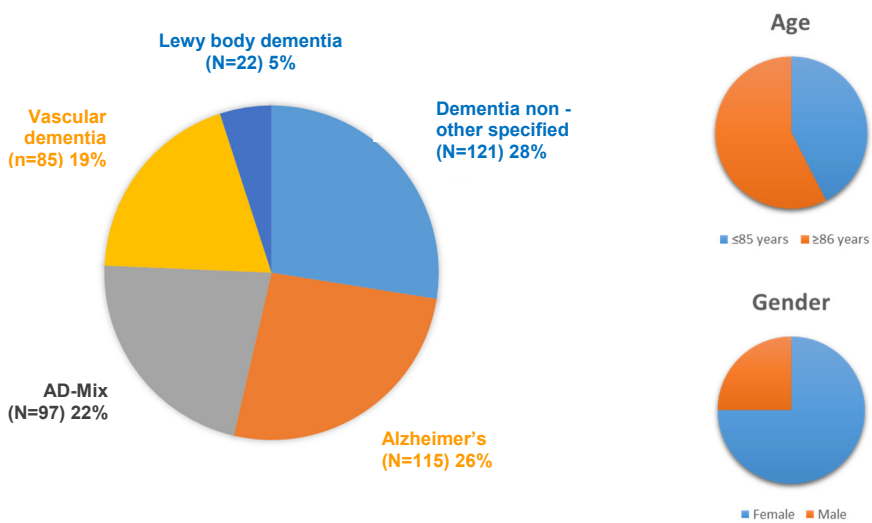

Figure 14) Demographics
Dementia diagnosis according to ICD-10 coding, age and sex. Data from hospital medical records, Paper(s) I - II

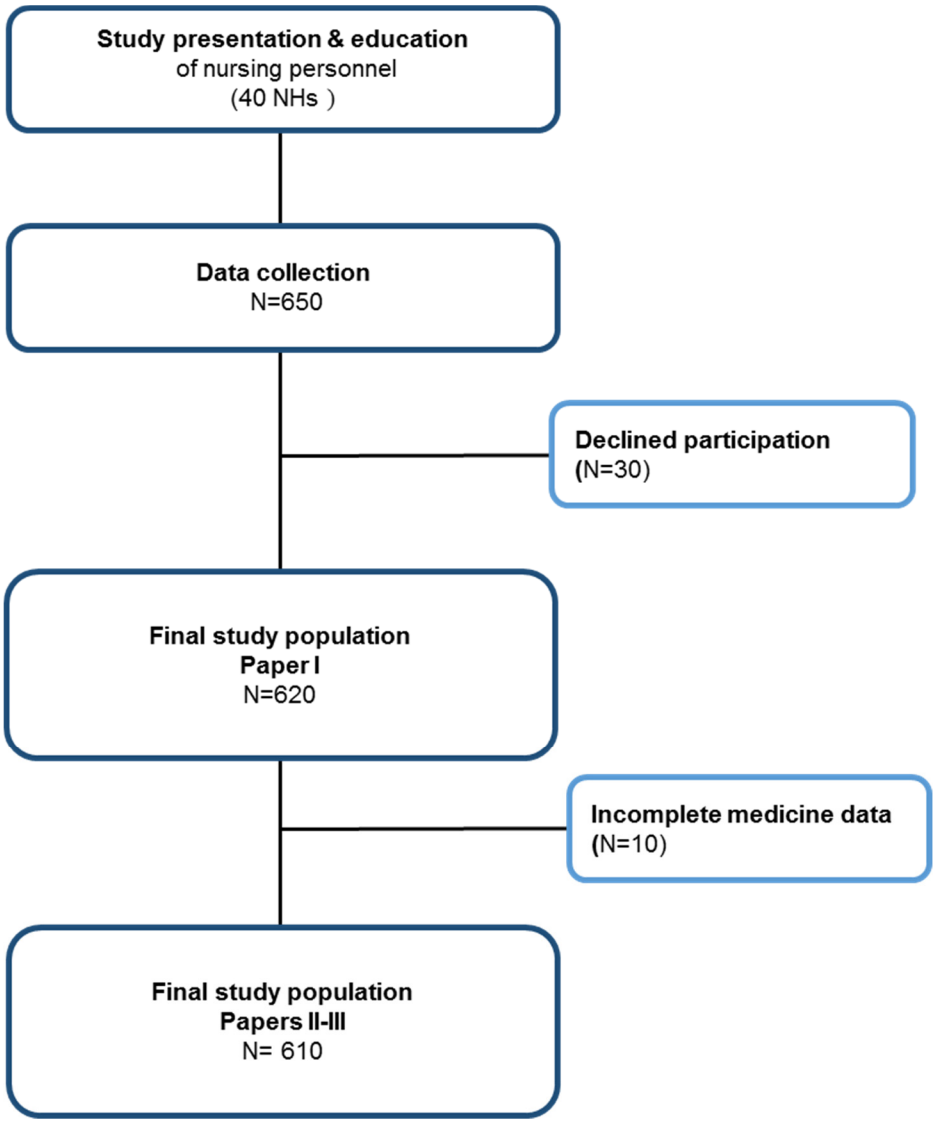

Figure 15) Flowchart of the study population Paper(s) I–III
Flow chart of the study population residing in all 40 NHs in the local region from January 2012 to March 2013

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Results included in Paper I

Prevalence

The seven clinical signs recorded in the collected forms were fused into the four DLB core features of parkinsonism, VHs, fluctuating cognition and suspected RBD (Table 13).

- In Paper I, the prevalence of ≥2 DLB core signs was 16% among the NH residents. However, when the wider more inclusive parkinsonism variable was used, the prevalence of DLB core signs increased to 20%.
- The most prevalent DLB signs in the residents with 2–4 DLB signs were fluctuating cognition followed by VHs, suspected RBD and parkinsonism. The most prevalent combination of only two DLB signs was VHs and fluctuating cognition, which was found in 30 residents (Table 13).
- Forty-two residents (7%) had 3–4 DLB signs, and 14 residents (2%) had all four DLB signs. The 91% of residents already diagnosed with DLB/PDD were classified within the group with 2–4 DLB core signs.

Table 13)
Summary of the seven observable DLB signs from the study form for Paper I

Clinically observable DLB signs	All residents n(%) 620(100%)	Residents with 0-1 core DLB sign n(%) 520(84%)	Residents with 2-4 core DLB signs n(%) 100(16%)
Visual hallucinations	123(20)	44(8)	79(79)
Fluctuating cognition	232(37)	143(27)	89(89)
Suspected RBD	55(9)	7(1)	48(48)
Parkinsonian signs			
Parkinson, *stricter*	42(7)	8(2)	34(34)
Parkinson, *wider*	90(15)	41(8)	49(49)
Rigidity	203(33)	138(27)	65(65)
Balance	245(40)	176(34)	69(69)
Weak voice	133(21)	83(16)	50(50)

Comments

Prevalence of DLB core signs

The focus in Paper I was to describe the prevalence of observable DLB signs in NH residents. At the start of the study, there was a 6% prevalence of ICD-diagnosis DLB/PDD among the NHs residents.

DLB is associated with both psychological and neurological symptoms, which makes it difficult to diagnose and may lead to underestimation of the prevalence [162, 163]. At the time of this study, no studies had reported the DLB prevalence in NHs, although some clinical and pathological studies had reported a DLB prevalence of 12–22% [74, 164, 165].

Herein, I present an increasing sensitivity of finding possible people at risk of DLB by using observable DLB signs from nursing personnel with the best knowledge of the residents. The found prevalence rates were 7% in the residents with 3–4 DLB signs and 16–20% in the residents with 2-4 DLB signs.

Visual hallucinations

VHs were found in 20% of all the NH residents, in 79% of participants in the group with 2–4 DLB signs and in 80% of those who had been formally diagnosed with DLB (Table 13).

Other studies show a wide range of prevalence (40–63%) of VHs in patients with DLB. This wide range may reflect the difficulty identifying these clinical signs in DLB patients since many have good insights and do not admit this symptom [148, 166]. However, it is important to identify and categorize VHs because there are several good treatment strategies to lower the frequency and burden on QoL in people with DLB and their family members.

Combination of different DLB core signs

The most frequent combination of two DLB signs in the residents was VHs and fluctuating cognition. Some studies have also shown these two symptoms to be the most common combination. This suggests that our DLB grouping may be representative of this patient population [167].

Given that fluctuating cognition is often seen in combination with other symptoms, questions about fluctuating cognition is a possible "opening" in the clinical medical history taking, after which questions about VHs and vivid dreams and neurological investigation regarding parkinsonism could follow. This might improve the recognition of combinations of core signs and reduce the risk of underestimating the prevalence in DLB patients.

Results included in Paper II

Psychotropic medication

The data collected in 2012–2013 showed that 86% of the residents used psychotropic medication (N05A/N05B/N05C/N06A). The medication data in this study included medicines used only on a daily basis (Table 14).

- The use of all four psychotropics was found in 6% of participants, use of three in 17%, use of two in 31% and use of one in 32% of residents. The most frequently used psychotropic ATC groups were anxiolytics followed by anti-depressants, hypnotics/sedatives and anti-psychotics (Figure 16).
- Anti-dementia medication was used by 33% of all NH residents and only by those with a formally registered dementia diagnosis.

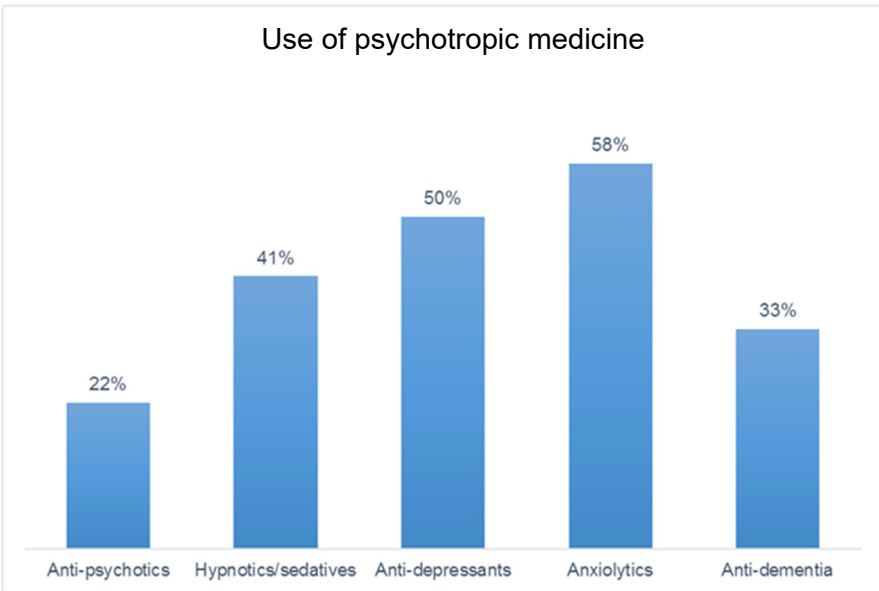

Figure 16)
The prevalence of use of different psychotropic medications in all NH residents in 2012–2013

Prevalence of the use of anti-psychotic medications

- One-fifth of the residents had used some anti-psychotics, most prevalently risperidone, followed by haloperidol and other atypical anti-psychotics (clozapine, olanzapine and quetiapine).
- The prevalence of use of anti-psychotic treatment did not differ between men and women or according to the existing dementia diagnosis. However, the use of anti-psychotics differed by age and was significantly more frequent in younger residents aged ≤85 years than in those aged ≥86 years.
- The main finding for anti-psychotic use was the increasing prevalence, from 25% to 43%, with an increasing number of DLB core signs (Figure 17). Comparison of all NH residents showed that those with ≥2 DLB core signs had the highest use of any anti-psychotics (33%) and haloperidol (14%) (Table 14).

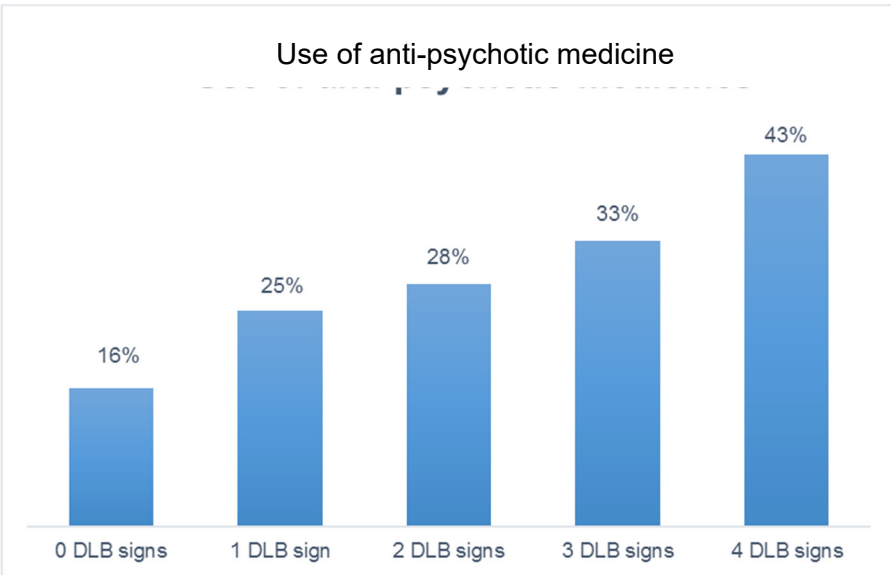

Figure 17)
The prevalence of anti-psychotic medicines in all NH residents in 2012–2013

Prevalence of the use of anti-dementia medications

- The results for anti-dementia medications showed that almost half of the residents with a formal dementia diagnosis used an anti-dementia medication. A higher percentage of younger residents aged ≤85 years (43%) used anti-dementia medications than those aged ≥86 years (26%) (Figure 18).
- Comparison of the use of anti-dementia medication according to the number of DLB core signs showed no differences between the types of ChEIs. However, a higher percentage of patients with ≥2 DLB core signs used memantine.

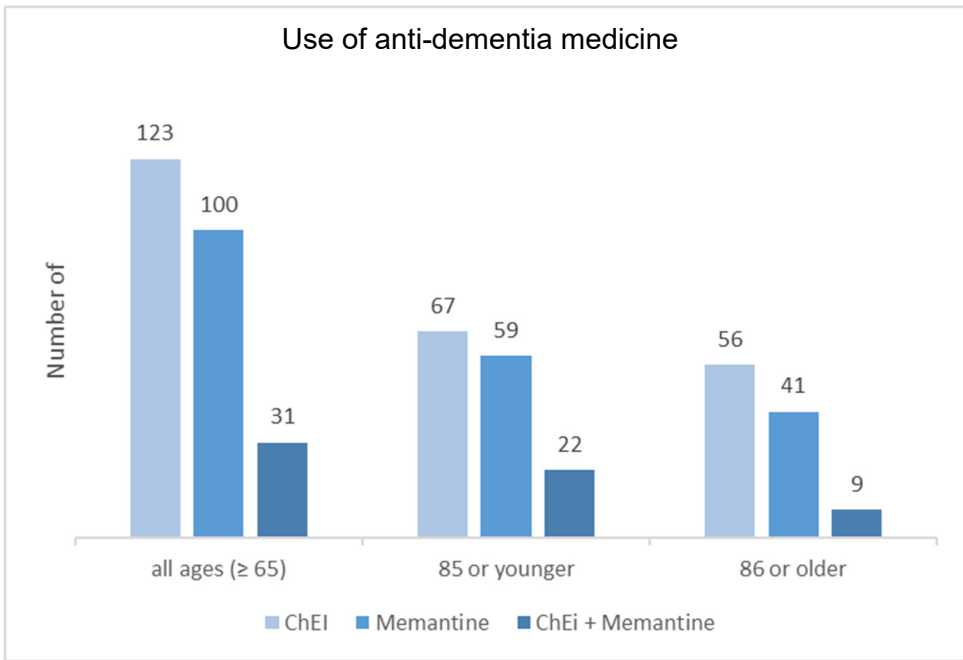

Figure 18)
Use of anti-dementia medication in all NH residents in 2012–2013

Table 14)
Prevalence of psychotropic medication

	Study population [a] 576 (100%)	**Dementia diagnosis** [b]		*P*-value	**DLB signs** [c]		*P*-value	**Age groups** [d]		*P*-value
		yes 440(100%)	**no** 154(100%)		**0–1** 458(100%)	**2–4** 118(100%)		**≤85 years,** 259(100%)	**≥86 years,** 351(100%)	
Anti-psychotics	132 (23)	102 (23)	30 (19)		93 (20)	39 (33)	*	71 (27)	61 (17)	**
Haloperidol	42 (7)	28 (6)	14 (9)		25 (5)	17 (14)	**	23 (9)	19 (5)	
Risperidone	57 (10)	49 (11)	8 (5)		45 (10)	12 (10)		29 (11)	28 (8)	
Other anti-psychotics [e]	11 (2)	9 (2)	2 (1)		7 (2)	4 (3)		6 (2)	5 (1)	
Anxiolytics	336 (58)	263 (60)	73 (47)	*	250 (55)	86 (73)	***	136 (53)	200 (57)	
Oxazepam	308 (53)	248 (56)	60 (39)	**	227 (50)	81 (69)	***	125 (48)	183 (52)	
Diazepam	44 (8)	31 (7)	13 (8)		25 (5)	19 (16)	***	22 (8)	22 (6)	
Hypnotics	234 (41)	176 (40)	58 (38)		186 (41)	48 (41)		103 (40)	131 (37)	
Zopiclone	189 (33)	139 (32)	50 (32)		145 (32)	44 (37)		78 (30)	111 (32)	
Other [f]	77 (13)	67 (15)	10 (6)	**	68 (15)	9 (8)	**	39 (15)	38 (11)	
Anti-depressants	290 (50)	225 (51)	65 (42)	**	220 (48)	70 (59)	*	129 (50)	161 (46)	
SSRI	204 (35)	156 (35)	48 (31)		156 (34)	48 (41)		88 (34)	116 (33)	
Mirtazapine	127 (22)	103 (23)	24 (16)	*	90 (20)	37 (31)		58 (22)	69 (20)	
Venlafaxine	18 (3)	14 (3)	4 (3)		14 (3)	3 (3)		13 (5)	5 (1)	*
Anti-dementia medicine	192 (33)	192 (44)	0 (0)	***	149 (33)	43 (36)		104 (40)	88 (25)	***
ChEI	123 (21)	123 (28)	0 (0)	***	104 (23)	19 (16)		67 (26)	56 (16)	**
Memantine	100 (17)	100 (23)	0 (0)	***	69 (15)	31 (26)	**	59 (23)	41 (12)	***

a Prevalence N(%) of Psychotropics among residents with existing medical list All participants: 610 (100%), with registered medical lists for 576 (94%) participants.
b Prevalence N(%)of Psychotropics among residents with existing dementia diagnoses.
There were (N= 440) with a dementia diagnosis and (N=154) without a dementia diagnosis
c Prevalence N(%) of Psychotropics among residents (610 (100%); with 0-1 (N=485) and 2-4 (N=125) core DLB signs. DLB groups according to a wider parkinsonism variable.
d Age group total 610 (100%): ≤85 years (N=259) and ≥86 years (N=351)
e Other (N05A): Clozapine (n=1), Olanzapine (n=8), Quetiapine (n=2)
f Other (N05C): Melatonine (n=21), Klometiazol (n=58), Nitrazepam (n=6), Propriomazin (n=5)
*P-value <0.05 **P-value< 0.005 ***P-value <0.001

Comments

Psychotropic medication

Almost 90% of all NH residents received some psychotropic treatment, and more than half used at least one anxiolytic medication, most often oxazepam. One possible explanation for this dominant prescription of anxiolytics in a geriatric/older population in NHs is the "milder" adverse events associated with these drugs compared with haloperidol. There is a well-known high prevalence of different NPSs in older people, especially in those with dementia [168].

Anti-psychotic medication

Anti-psychotics, which are further grouped into atypical or typical anti-psychotics, are one of the most medicine used to treat several NPSs including severe agitation, psychosis and hallucinations [131, 169]. In the geriatric population, anti-psychotic treatment often results in several difficult adverse effects, especially in those with a dementia diagnosis [143, 170].

With this in mind, residents with ≥2 DLB core signs may also be those with hypersensitivity to anti-psychotics. An increased risk of adverse events such as somnolence, falls, extrapyramidal symptoms, malignant neuroleptic syndrome and finally increased mortality, may follow [136, 171].

Residents with ≥2 DLB core signs had the highest percentage of using anti-psychotics and haloperidol. In addition, the anti-psychotic use increased up to 43% with an increasing number of clinical DLB core signs, which indicated that the most fragile residents received the less beneficial treatment.

The association between drug use and the number of DLB signs was difficult to establish because potential side effects of anti-psychotics are identical to some DLB signs. This is an important limitation of this study.

However, one favourable finding is that those residents with ≤1 DLB core feature had the highest haloperidol doses (1.5–2.0 mg) compared with those with ≥2 DLB core signs. This suggests that the symptoms in patients with ≥2 DLB core signs were less influenced by anti-psychotic side effects.

Anti-dementia medication

Anti-dementia medication was taken by 44% of the residents with a dementia diagnosis but by none without a formal dementia diagnosis. This suggests that the diagnoses obtained from HMRs were valid because no resident without a dementia diagnosis was being treated with anti-dementia medication. It could also mean that a basal dementia

investigation was planned or taking place in parallel within primary care and the result was unavailable during the period of data collection.

The use of anti-dementia treatment also differed by age; residents aged ≤85 years had higher frequency anti-dementia medication compared with those aged ≥86 years. In some aspects, this situation may be disadvantageous because the older population with dementia can also have both a good short-term cognitive response as well as a positive long-term response to ChEIs [172].

Results included in Paper III

Survival among NH residents

One aim of the study in Paper III was to analyse survival in relation to the number of DLB core signs identified in Paper I and the influence of medication identified in Paper II in the same NH population. The survival data from NHs were collected 6 years after the study was initiated (January 2012–August 2018), at which time 558 (96%) of the residents had died, with a mean survival time of 29 (28–31) months after the study began. Other population characteristics contained in Paper III are presented in more detail in the section on demographics.

- The survival analyses showed a significant difference in mean survival time; survival was 8 months shorter in residents with ≥2 DLB core signs than in those with ≤1 DLB core feature (P=0.0004).
- The Kaplan–Meier survival curve confirmed the shorter survival time over an 80-month period in residents with ≥2 DLB core signs than in those with ≤1 DLB core signs (Figure 19).
- Mortality risk was also significantly higher among residents with signs of fluctuating cognition, RBD, balance problems and rigidity than in those without these signs (Table 15).
- Survival in relation to treatment with anti-dementia medication showed longer survival (mean, 95% CI) among those treated with anti-dementia medication (34, 31–37) compared with those without treatment) (30, 28–32) (P=0.037). However, older residents were less likely to use anti-psychotics, and older age was a risk factor for mortality.

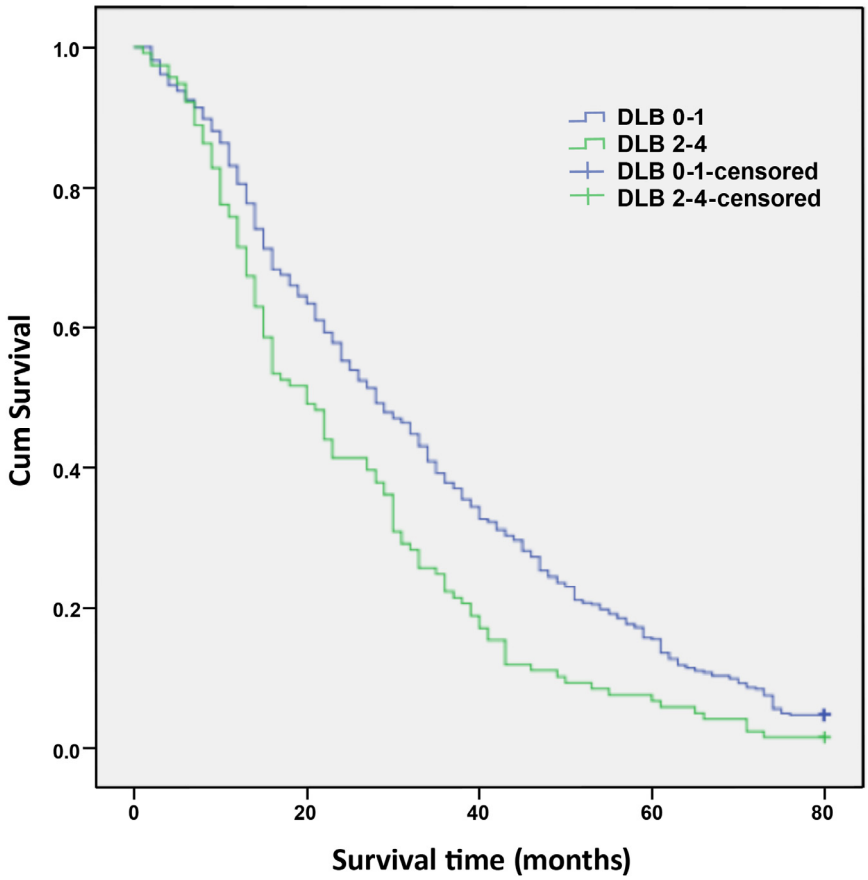

Figure 19) Kaplan–Meier survival curves
Kaplan–Meier estimates of 80-month survival time from the reported time of onset for the two groups according to the number of DLB core signs (DLB 0–1 and DLB 2–4). Log rank X^2 (df =1, *n*=583) =14.8, *p*=0.0001.

Table 15)
Mortality risk based on DLB core signs (*set as the reference value)

	Hazard ratio (95% CI)			
Clinical signs recorded in the study form	**Model 1 (crude estimates)**	**P value**	**Model 2 (estimates adjusted for age and sex)**	**P value**
Parkinsonism ***(no*, yes)***	1.20 (0.86–1.66)	0.280	1.41 (1.01–1.95)	0.043
Fluctuating cognition ***(no*, yes)***	1.36 (1.15–1.62)	0.0004	1.35 (1.13–1.60)	0.001
Visual hallucinations ***(no*, yes)***	1.10 (0.90–1.36)	0.330	1.23 (0.99–1.52)	0.052
RBD ***(no*, yes)***	1.49 (1.11–1.98)	0.007	1.65 (1.23–2.21)	0.001
Balance problems ***(no*, yes)***	1.36 (1.14–1.61)	0.0005	1.31 (1.11–1.56)	0.002
Rigidity ***(no*, yes)***	1.41 (1.18–1.68)	0.0002	1.45 (1.21–1.74)	<0.001

Comments

Importance of recognizing high-risk DLB individuals vs survival

People with DLB/PDD have intensive medical and nursing care needs as well as shorter survival [24, 173, 174]. This highlights the importance of recognizing high-risk DLB individuals, more rapidly; hence, a suitable medical treatment and nursing care can be applied earlier and more effectively, even for older individuals living at NHs.

The study described in Paper III identified a significantly shorter survival time among residents with ≥2 DLB core signs, who are also at high risk of a possible DLB diagnosis. These patients had an 8-month shorter mean survival time (from the beginning of the study) even though they were older (mean age of 86 years) and were near the end stage of their life.

Anti-dementia treatment

Anti-dementia treatment has several benefits, which is why a basal dementia investigation to provide a correct diagnosis is vital [12]. This study showed a longer survival among residents treated with anti-dementia medication. However, important limitations of Paper II are the cross-sectional nature of the data collection and the lack of data about the duration and dosages of anti-dementia and other psychotropic medicine.

Results included in Paper IV

Demographics

In the study reported in Paper IV, new data were collected from residents staying in a short-term NH (Figure 20, Table 16).

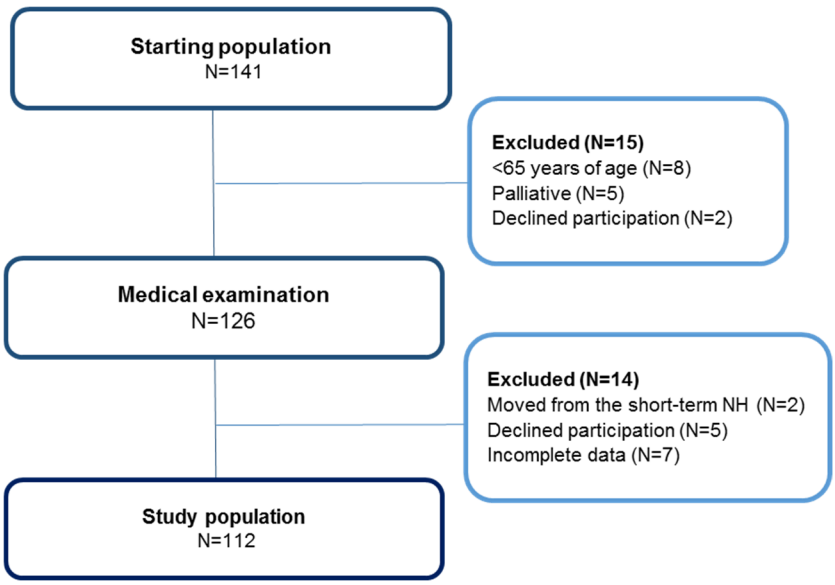

Figure 20)
Flowchart presenting the data collection process, Paper IV

Table 16)
Prevalence of DLB core signs recorded at all short-term NHs

Core DLB signs	4 core DLB signs by Nurses *n* (%)	4 core DLB signs by Physicians *n* (%)	4 core DLB signs by Physicians and Nurses *n* (%)
Visual hallucinations[1]	14 (13)	16 (14)	25 (22)
Parkinsonism	33(30)	32 (29)	46 (41)
Fluctuating cognition	39 (44)	33 (30)	54 (48)
RBD[2]	10 (9)	18 (16)	25 (22)

[1] The physicians could not decide/interpret visual hallucination in *n*=3 and nurses in *n*=1.
[2] The physicians could not decide/interpret RBD in *n*=3.
Dementia with Lewy bodies (DLB); REM sleep behaviour disorder (RBD); *n*=number; *n* total= 112 (100%)

Prevalence of DLB core signs

During the data collection, nursing personnel completed the study form and physicians performed medical examinations according to the study procedures (Figure 13).

- The data collected by nurses and medical examinations by physicians showed parkinsonism in 41% of all short-term NH residents. All seven (100%) residents diagnosed with PD were identified and included with those with parkinsonism.
- A formal dementia diagnosis was found in 36 residents, eight of whom had a DLB diagnosis. Seven (88%) formally diagnosed DLB residents were identified as high-risk DLB patients and were classified in the group with 2–4 DLB core signs (Table 17).
- When nurses and physicians recognized DLB signs in the residents separately, the prevalence rates of 2–4 DLB signs were 20% and 21% of the population, respectively.
- When the nurses' and physicians' identification of residents with 2–4 DLB signs was combined, the prevalence was 32% (Table 17, Figure 21).

Table 17)
Study population characteristics in residents with 0–1 and 2–4 DLB core signs

Characteristics at baseline	**All short-term NHs residents,** *n* = 112 (100%)	**Residents with 0-1 core DLB signs,** *n* = 76 (68%)	**Residents with 2-4 core DLB signs,** *n* = 36 (32%)
Age, *mean/median (SD)*	83/83 (7.9)	83/85 (7.8)	82/81 (8.3)
Sex, *female n (%)*	70 (63)	52 (68)	18 (50)
Diagnoses	***n* (%)**	***n* (%)**	***n* (%)**
PD	7 (6)	1 (1)	6 (17)
MCI	10 (9)	8 (11)	2 (6)
Dementia	36 (32)	19 (25)	17 (47)
AD/AD-Mix	*8 (7)*	5 (7)	3 (8)
Vascular dementia	*14 (12)*	9 (12)	5 (14)
Dementia NOS	*6 (5)*	4 (5)	2 (6)
DLB	*8 (7)*	1 (1)	7 (19)
Medicine			
Anti-dementia	13 (12)	8 (11)	5 (14)
Anti-psychotics	6 (5)	3 (4)	3 (8)

Parkinson disease (PD), dementia with Lewy bodies (DLB). Mild cognitive impairment (MCI). Anti-dementia and anti-psychotic medications were classified according to the Anatomical Therapeutic Chemical Classification (ATC) System.

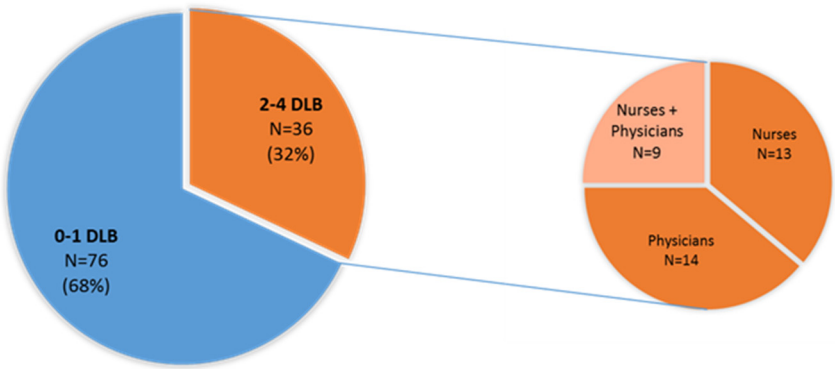

Figure 21) Recognition of high-risk DLB individual
Summary of identification of residents with 2–4 DLB core signs by nurses and physicians separately, and by both combined.

Medication data

The study reported in Paper IV focused on the use of anti-psychotics and anti-dementia medication.

Anti-dementia medication was used by 13 (12%) residents (two took a ChEI and 11 took memantine) and anti-psychotics were used by six (5%) residents (one took risperidone and five took quetiapine).

The use of anti-dementia or anti-psychotic medication did not differ between the residents with 0–1 and 2–4 DLB core signs.

Short-term NHs

The residents were staying in short-term NHs most often because of unsustainable medical status followed by fractures, infections, rehabilitation, delirium and palliation.

Among residents with 2–4 core DLB signs, the three main reasons for staying in a short-term NH were an unsustainable medical condition in 23 patients (64%), infections in six (17%) and rehabilitation needs in five (14%) (Figure 22).

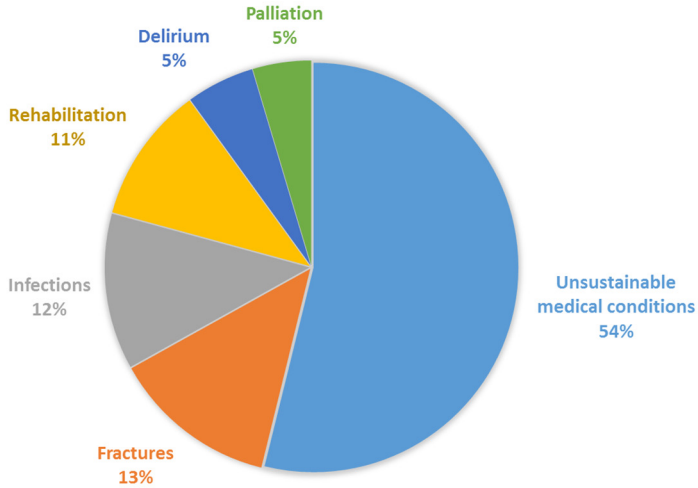

Figure 22) Reasons for placement in short-term NHs
Summary of all ICD diagnoses found in all residents in short-term NHs

Comments

In this relatively large clinical study that included all short-term NHs covering a total geographic area of the third largest Swedish city, the prevalence of high-risk DLB individuals was 32% in all short-term NH residents compared with 7% in previously formally diagnosed DLB residents.

The nurses and physicians all evaluated the same residents, but only nine residents with 2–4 core DLB signs were identified by both groups. This suggests the need for different levels of competence and teamwork between nurses and physicians.

There may be differences between nurses' and physicians' understanding of residents' symptoms and signs, medical needs and medical history. In addition, the work of nurses and physicians can take different approaches; although many findings are similar, there is the risk that these different approaches may result in differences in the identification of medical needs in the same patient. Therefore, close teamwork between the nurses and physicians is beneficial to provide continuity in the reports on different medical signs and NPSs to guide physicians.

According to data from the medical lists, there was a less beneficial, low use of ChEIs and memantine in residents with a dementia diagnosis and in those with a known DLB diagnosis. By contrast, the low prevalence of anti-psychotic use was promising; no patient was taking haloperidol and only six patients were treated with atypical anti-psychotics.

The physicians in short-term NHs were responsible for medical health and medical prescriptions during the residents' stay in the short-term NH. The responsible physicians in this study population were specialists in geriatric medicine. This acknowledges that understanding the geriatric patient is important and leads to good pharmacological treatments such as the low usage of anti-psychotics. However, the treatment strategy in residents with diagnosed dementia may have been less beneficial because of the low prevalence of the use of anti-dementia medication.

Among residents with 2–4 DLB core signs, the main reason for staying in a short-term NH was because of an unsustainable medical condition (64%), which indicated a greater need for medical care. This finding is consistent with studies showing greater need for assistance in people with a DLB diagnosis [80, 175, 176].

Conclusions

Paper I

Elderly people with DLB signs may constitute 16–20% of all residents in NHs. This result indicates that it is important for general practitioners to identify this fragile patient group to help clinicians deliver more appropriate treatment.

Paper II

Residents from Swedish NHs with 2–4 clinical DLB signs receive unfavourable medical treatment with high use of anti-psychotic and insufficient prescription of anti-dementia medication. These findings show the importance of more effectively identifying older adults with DLB signs and improving collaboration with nursing personnel to provide more appropriate medical prescription.

Paper III

The main study finding was that elderly NH patients with ≥2 DLB signs are at significantly increased mortality risk relative to other elderly NHs residents and it is therefore important to identify this group. The identification of possible DLB is beneficial for more appropriate medical treatment, nursing care and prevention of unnecessary hospital admissions.

Paper IV

This paper showed that applying the new DLB core features and educating nurses and physicians about DLB increased the sensitivity for finding observable DLB signs and possible DLB residents in short-term NHs.

Main reflections

Representativeness

Figure 23)
Illustration of the city of Malmö,Shutterstock

Study population

Gender

Most studies have identified a sex difference by showing that men have a higher prevalence of DLB than women [177]. In this thesis research, the frequency of having ≥2 DLB core signs did not differ significantly between men and women living in NHs. One possible reasons for this lack of difference is the older mean age of this population; previous studies have shown a higher prevalence of DLB in men in the 70–79-year-old age group and more equal prevalence rates in those aged >80 years [38, 65].

Age

The mean age of the residents in this thesis research was 86 years, which indicates that the study population was suitable for investigating Lewy body symptoms because the prevalence of Lewy body pathology increases with age [38, 49, 178]. For example, Rahkonen et al reported a 20% DLB prevalence in a similar population and age group (≥85 years); the prevalence was 16–20% in the patients with 2–4 DLB signs in Paper I [74, 179].

Dementia diagnosis

In Papers I–III, it was assumed that the basal dementia investigation (as described by the Swedish NBHW) was performed before dementia was diagnosed. Those residents without a diagnosis were either under a dementia investigation or did not have dementia. However, the ICD-10 definition of severe dementia is the need for permanent support and caregiving from others, and all residents in these studies were classified as having severe dementia.

The incidence of dementia increases with age, and age is a known risk factor for the development of DLB/PDD. This indicates that the NH population studied here, whose mean age was 86 years, was a suitable sample for prevalence analysis [177, 180].

Data collection

Why did we choose to design our own study form?

The main reason why the specially designed form was used in the data collection (rather than, e.g., the NPI scale) to investigate DLB signs was the need for an easily applicable instrument that would fit well in the clinical work in the NHs and short-term NHs.

Using the clinical DLB signs from the study form as an observation manual for NH personnel allowed those personnel to identify residents with ≥2 DLB signs and to categorize them as at-risk or high-risk patients for inappropriate medication. This provided valid information about the actual symptoms of the residents of the NHs and short-term NHs.

Strengths and limitations

Papers I–III

- A strength of Papers I–III was the data collected from a large population of NH residents by nursing personnel who followed a consistent study form and a long follow-up of 6 years (80 months).
- Another strength is the use of the Swedish NMDS and HMR, together with the actual clinical signs reported by nursing personnel who knew the residents best, which provided accurate information about the use of medication at the time of data collection. A limitation is that dosages of given medicine (except anti-psychotics for Paper II) and the starting point for use of medicine were not recorded.
- In earlier studies, parkinsonism has been found to be present in 55–60% of DLB patients [74]. In Paper I, parkinsonism was found in 34% of NH residents; this may be a limitation because clinical examinations could not be performed on the residents, and this study may have underestimated the prevalence of parkinsonism. However, use of the wider parkinsonism variable showed that in those with 2–4 DLB signs, 49% of all residents had at least one parkinsonism feature. This suggests that inclusion of the signs weak voice, balance problems and rigidity improved the identification of parkinsonism and possible DLB.
- The results of survival analysis among older people must be interpreted with caution, mainly because of the presence of coexisting chronic diseases, which vary in severity, as well as the unknown treatment duration for different medicines, about which there was insufficient information. This is another limitation.
- The use of an unvalidated form may also be considered a limitation. However, 90% (n=13) of the residents with a formal DLB diagnosis from Paper I were included in the residents who had been evaluated as having ≥2 DLB core signs.

Paper IV

- In Paper IV, nursing personnel were educated about DLB and its core signs at specific times as well as continuously during the data collection. Therefore, there were opportunities to discuss specific clinical symptoms in individual patients during the medical examination. This is a strength of this study.

- A strength of this study was that the complete medical examinations of all short-term NH residents were performed simultaneously with the rest of the data collection (study forms, HMR and medicine lists). Another strength is that the medical examinations performed on all residents led to an improved diagnosis of parkinsonism and/or signs of a cerebrovascular disease.
- One of the limitations of Papers I–IV was the cross-sectional nature of the initial data collection. In addition, the participants were at different stages of their disease, and it was not possible to collect complete data on the severity of dementia, co-morbidities and function in all residents.
- In the study included in Paper IV, the recognition of parkinsonism by either nurses or physicians increased the sensitivity and improved the identification of high-risk DLB patients, which was a strength of the study. Both nurses and physicians identified 100% of residents with previously known PD and 88% of all previously diagnosed DLB residents; this shows good accuracy.

Implications of the main results

Interest in dementia and LBD is increasing every year. As mentioned above, the updated DLB diagnostic criteria and DSM-5 have improved the sensitivity for identifying people with DLB. However, DLB is still an underdiagnosed neurocognitive disorder with complex clinical signs, and this complexity means that there is a wide variety of cognitive profiles and panorama of psychological, neurological and cognitive symptoms [13, 50, 181].

Identifying high-risk DLB patients

Why is it important to find residents with DLB core signs?

Several studies have emphasized the importance of identifying DLB/PDD patients; identifying these patients may help to reduce the risk of an incorrect diagnosis, unsuitable medication or worsening of QoL [98, 102, 176]. People with DLB have worse physical and psychological health, need more medical help, and have more hospital days and earlier nursing home admission (Figure 24) [96].

The thesis research shows that co-operation and promotion of close work between nurses and physicians can help to improve the identification of DLB core signs and high-risk DLB patients. These will make it possible to apply more suitable treatment strategies, both pharmacological and non-pharmacological.

Preventing inappropriate medication

Several large studies have shown shorter survival times among residents with dementia, especially DLB, treated with anti-psychotics. All of these studies concluded by encouraging less use of psychotropics, which has also been a consistent message in important clinical guidelines and in this thesis [128, 130, 152].

There have been some changing trends in anti-psychotic treatments over the past decade, but these have produced only minor results [146, 168]. This thesis research found that almost 90% of all NH residents used some form of psychotropics; 23% of the dementia population used anti-psychotics, and only one-third used anti-dementia medication. This thesis research also showed that high-risk DLB residents had been given unsuitable prescriptions involving high use of anti-psychotics and low use of anti-dementia medication. These findings suggest that efforts are needed to reduce the prescription of anti-psychotic treatment especially because people with DLB have an increased risk of neuroleptic sensitivity and a higher risk of adverse events and mortality, as described earlier.

Preventing neuropsychiatric symptoms

In clinical practice, identification of high-risk DLB patients should make it easier to understand and treat difficult NPSs. Identifying high-risk DLB patients in an NH may help to prevent NPSs and inappropriate treatment of severe NPSs such as VHs, delirium and psychosis.

Although ChEIs are not the first-line medical treatment of NPSs, they may reduce the emergence of NPSs in elderly people with dementia and may play a positive role in treating these symptoms [111].'

Preventing injuries and improving medical care

In clinical practice, identification of high-risk DLB patients should make it easier to understand and treat somatic difficulties such as orthostatic hypotension. Measuring orthostatic blood pressure as part of a focused medical review and appropriate measurement of both supine and standing blood pressure may help to identify those at risk and to minimize the risk of falls, fractures, need for surgery and pain.

Non-pharmacological treatments, such as compression stockings and increasing dietary salt intake, may be beneficial for people with orthostatic hypotension and can be easily applied in an NH.

In addition, it may be helpful if clinicians incorporate assessment of swallowing function in the medical history to identify those at risk of dysfunction that may lead to aspiration. Applying simple treatment policies, such as offering carbonated liquid at meals, may improve swallowing function and lower the risk of choking and aspiration [182].

Finally, it is crucial for physicians to update the medical list regularly and, if needed, to stop the prescription of psychotropic, anti-hypertensive and anti-cholinergic medicine [99, 183].

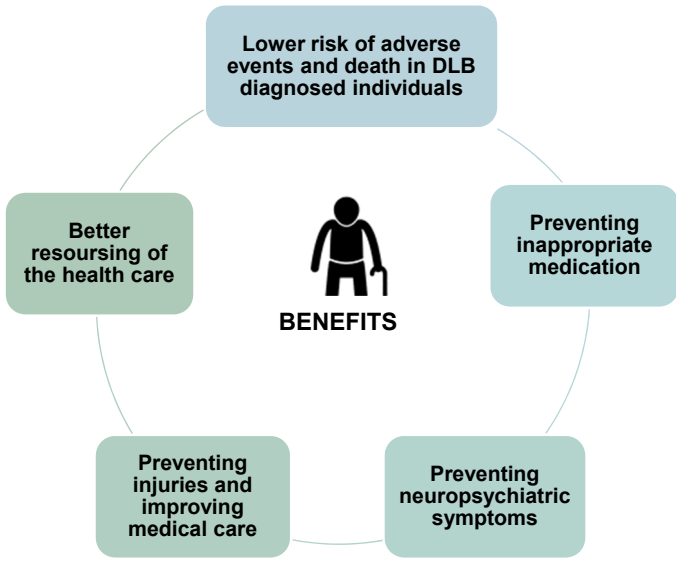

Figure 24)
Summary of different benfits with finding high-risk DLB individuals

How can the DLB identification in NHs be improved?

One of the main questions in this thesis was whether the residents with ≥2 DLB core signs might be high-risk patients for an undiagnosed DLB/PDD diagnosis and, if so, how can medical personnel identify them earlier and more effectively.

According to statistical reports from the SveDem, in 2017 the summarized percentage of different dementia diagnoses showed a 6% prevalence of DLB/PDD [67, 89]. The study included in Paper I found a prevalence of DLB signs of 16–20% of all NH residents; however, this study did not include a medical examination. This finding prompted the collection of the new data presented in Paper IV, which showed a 32% prevalence.

Updated DLB criteria's and suitable cognitive testing

Using the definitions of core and supportive clinical DLB signs simplifies the diagnostic procedure. However, the inclusion of both psychological and neurological symptoms makes it more difficult to separate DLB from other dementia disorders or diseases. Using autopsy results from AD and DLB patients, Tiraboshi et al reported that the presence of VHs was the best positive predictor of DLB followed by lack of visuospatial

impairment as a negative predictor [60]. It may also be beneficial to include questions on RBD in the clinicians' medical history taking from family and patients early in the dementia investigation. Polysomnography may be a good complement during the dementia investigation (Figure 25) [59].

The current cognitive tests such as the MMSE may be less optimal for identifying people with DLB. One approach might be to optimize the "basal dementia investigation" by adding other cognitive tests to separate DLB from coexisting AD more easily [4, 52, 57, 60].

Awareness of multimorbidity

Summarizing the results from several studies is difficult. The common NH symptoms are the "three Ds": delirium, dementia and depression. Under-recognition of DLB may reflect the difficulty in recognizing and distinguishing the DLB core signs from the three Ds and, in NHs, from other common NPSs [69, 135]. Being aware of the known multimorbidity of different dementia pathologies in the same patient may allow for a broader investigation in the beginning, even in the older old aged >80 years [6, 162].

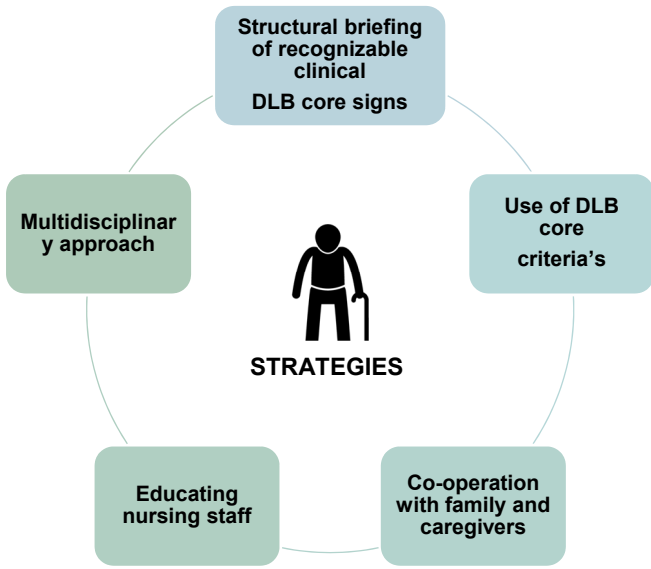

Figure 25)
Summary of different strategies for improvement of finding high-risk DLB individuals

Educating nursing staff

The updated DLB consensus criteria are detailed and complex, and are not easily applicable in the routine clinical work of nursing personnel. This may be

disadvantageous for identifying NH residents with DLB, mainly because nursing staff can best observe a patient on an everyday basis.

Educating nursing staff about the DLB core signs and applying these as clinically observable signs in an NH may help to increase the recognition of DLB. For example, a nurse who has learned about DLB and recognizes signs such as VHs in a patient will report this faster to the physician for further examination of the patient for other signs of DLB.

Multidisciplinary approach

By incorporating a multidisciplinary approach, suitable person-centred care using non-pharmacological followed by pharmacological treatment strategies may be applied effectively.

The health-care system would benefit from a geriatric medicine multidisciplinary approach involving active investigation of early depression signs, sleep disturbances, the cognitive profile and dementia, followed by evaluations of nutrition, co-operation with pharmacists on medical reviews and earlier evaluations by physiotherapists.

By using a structural briefing of each resident's symptomatology in the context of recognizable clinical DLB core signs and by having the nurses and physicians working closer together, we increased the percentage of potential residents with DLB and possibly the sensitivity of DLB recognition.

In other words, it is unlikely that all 32% of the residents with 2–4 DLB core signs had an actual DLB diagnosis; however, we increased the number of high-risk residents identified in the first step. This understanding should help to increase the ability to find more suitable medical treatments such as the use of more anti-dementia and less anti-psychotic medication.

The future perspective

Today, there are about 169 000 people with dementia in Sweden, and 66 000 NH placements/homes actively in use, which means that ~100 000 people with dementia still live at home, often with some type of home care. In 2030, there will be 250 000 people with some type of dementia diagnosis [184]. The dementia cost in Sweden for 2012 was approximately €16 billion [184].

Nursing home admission

NH and short-term NH places are scarce, and the health-care system is not fully ready for this challenge and the future increased need for dementia care in Sweden. There can be noticeable cost savings by postponing NH admission; for example, the costs of delaying NH admission for one person are €15 000 for a 3-month delay, €30 000 for a 6-month delay and €60 000 for a 1-year delay.

Figure 26)
Illustration over European countries, Shutterstock

Among all dementia subgroups, people with DLB have a shorter time to NH admission, especially in connection with severe NPSs and high caregiver burden. It is possible that earlier DLB screening, followed by the DLB diagnosis and suitable pharmacological and non-pharmacological strategies will postpone the need for NH admission.

Hospital care

One day of care at hospital, costs €500. According to Mueller et al, patients with DLB consume 4 additional hospital days, mainly because of NPSs and poorer physical health

compared with AD patients [96]. Theoretically, preventing rehospitalization once per year and taking the 5 plus 4 days needed by the average DLB patient would save €4500/year by preventing hospitalization.

Today, the biggest challenge is making an early DLB diagnosis and differentiating DLB from AD. Knowing that costs and different resources are higher per person in DLB patients than in AD patients, improving the ability to identify DLB is very important (176, 185). Improving nursing personnel's understanding of DLB and its different symptoms and fluctuating course may help to reduce the need for unnecessary visits to acute medical care and hospitalization.

Cost savings and their application to dementia care are beyond the scope of this thesis, but it is important to highlight the importance of DLB screening and suitable NPS treatments.

Patients, family and caregivers

A study of caregivers' burden shows that receiving knowledge about the disease progression from health-care professionals makes it more manageable to care for someone with DLB in their home and improves the patient's QoL [98].

Some of the dementia challenges might be more manageable with improvements in co-operation and involvement of the family and caregivers living with someone with DLB. A meta-analysis of non-pharmacological interventions for NPSs of dementia summarized the best treatment strategies and concluded that good family knowledge of the disease progression prevented unnecessary rehospitalization [186]. This may be applicable in the Swedish health-care system, especially for high-risk DLB patients, who are often undiagnosed, and may translate to cost saving.

Short-term NHs as "a safety net"

Better co-operation between nursing personnel and physicians may improve the efficiency of identifying patients at high risk of DLB according to their core signs.

Primary care has the main responsibility for correctly applying dementia investigations when needed. However, short-term NHs may provide a good "safety net". After a hospitalization, for NH residents with high fragility and a highly unsustainable medical condition as the reason for short-term NH placement, short-term NH may be a good starting point for follow-up of both recognizable DLB signs and dementia in general including all its subtypes.

Co-operation

It is crucial to promote the use of continuous medical evaluations, diagnoses and medical treatments of residents in short-term NHs. Co-operation within and networking between short-term NHs, NHs, researchers and physicians in both primary and hospital care should be improved.

Faster application of new knowledge about dementia care, non-pharmacological treatments and the current medications for treating dementia is needed.

Table 18) Summary of improvement strategies for dementia and DLB care

STRATEGIES TO IMPROVE DEMENTIA AND LEWY BODY DEMENTIA CARE		**PATIENTS BENEFITS**	**HEALTH-CARE & SOCIAL BENEFITS**
Education [151]	Medical staff (NHs and hospitals) Education of society, patients and caregivers	Improved QoL Increased survival Less NPSs (depression, delirium, hallucinations, psychosis) Less polypharmacy Less adverse events Less unnecessary hospitalization Improved time to nursing home admission	Better survival of people with dementia Better usage of anti-dementia medication Better medical treatments of dementia patients Less hospitalization of already fragile patients Less inappropriate medication Less medication-related problems Less anti-psychotics Improved possibilities for more home care than NH admissions Improved costs of dementia care Better dementia care
More active prevention of risk factors during all life stages (early, mid and late in life) [12]	Preventive strategies in dementia: cognitive training, preserved hearing, rich social network, exercise, and treatment of hypertension, diabetes and high cholesterol.		
Prevention [93]	Active BPSD approach to prevent difficult NPSs Prevention of prolonged hospital days and rehospitalization		
Incorporation of national guidelines in routine clinical work [86, 152]	Reduced use of inappropriate medication and anti-psychotic treatments [85]. Incorporation of clinical consensus for minimizing polypharmacy by, e.g., regular reviews of medicine [83, 84].		
Faster dementia diagnosis [67]	Earlier anti-dementia treatments. Focus on improving cognition (e.g., elimination of factors/medicine that give cognitive burden).		
Gero-psychiatric approach [147] [95]	Multidisciplinary approach Earlier evaluations by a physiotherapist Active investigation of earlier depression signs, sleep disturbances and dementia Earlier evaluations of nutrition/malnutrition Co-operation with pharmacists on medical reviews		
Person-centred care [94] [143]	First-line treatment; suitable non-pharmacological treatment policy Second-line treatment; suitable or short-term pharmacological treatment parallel		
Easily accessible patient and caregiver support	Education of society, patients and caregivers Accessible support contact by health-care		

BPSD: behavioural and psychological symptoms of dementia, NPSs: neuropsychiatric symptoms, NHs: nursing homes, QoL: quality of life

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Recognition of dementia with Lewy bodies

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