INTRODUCTION

The worldwide prevalence of dementia is currently estimated at 50 million.\(^1\) In the Netherlands, more than 270,000 people are diagnosed with dementia.\(^2\) The actual prevalence may be even higher as a result of under-diagnosis.\(^2\) The prevalence of dementia rises substantially with advancing age,\(^2\) affecting approximately 8% of the population aged over 65, 25% in those over 80 years of age, and more than 40% in those over 90 years of age.\(^2\) Major clinical symptoms of dementia include a decline in cognitive abilities and physical functions, as well as disturbances in sleep, behavior, and mood.\(^3\) These disturbances are sufficiently severe to interfere with daily independent functioning, eventually rendering a person dependent on care.\(^3\) Dementia is the leading cause of death in the Netherlands.\(^4\) There is no cure for dementia, and pharmacotherapy is limited to symptomatic treatment, but the effects are modest and may present adverse side-effects.\(^5\) With a worldwide ageing population, the number of persons with dementia in the Netherlands is expected to increase exponentially to over half a million in 2040.\(^2\) This increase will inevitably lead to a higher demand for long-term care.\(^6\) The enormous financial and social impact which dementia has on the persons affected, their families, and society make it a public health priority.\(^7\)

Characteristics of persons with dementia

Dementia-related neurodegenerative processes (e.g., neuronal damage and atrophy) result in cognitive, physical, and behavioral disturbances.\(^8\) Cognitive impairments, which are present in early stages of dementia, include memory, orientation, thinking, language, comprehension, and executive functions (EF).\(^9\) EF are a set of complex cognitive skills responsible for planning, inhibition, attentional control, goal-directed behavior, motivation, and taking initiative.\(^10\) In dementia, disturbances in the ability to take initiative is expressed in, among others, a reduced ability to perform self-care tasks or seek social activities. Therefore, EF is an important cognitive function required for independent functioning,\(^11\) and related deficits may increase the persons’ vulnerability to social isolation.\(^12\) Cognitive impairments in dementia are commonly accompanied by deterioration in motor functions, including a loss of mobility, muscle strength, balance, and endurance capacity.\(^13\) These disturbances increase fall risk and negatively affect a person’s ability to manage basic activities.\(^14\) Later stages of the disease are characterized by the presence of behavioral and psychological symptoms such as aggression, agitation, apathy, and depression. These symptoms affect almost all people with dementia,\(^15\)\(^16\) and negatively influence the quality of life of the persons with dementia and their caregivers.\(^17\)\(^18\)

Cognitive, physical, and behavioral disturbances severely impact a person’s ability to perform activities of daily living (ADL).\(^19\) ADLs are tasks which are performed on a daily
basis and are essential for independent functioning and self-care. There are two categories of tasks which describe the functional ability, i.e., ‘basic’ and ‘instrumental’ ADLs. Basic ADLs are simple self-care tasks learned at a young age (e.g., toileting, bathing, dressing, eating, and drinking). These tasks rely on motor skills and tend to be relatively spared in early stages of dementia. Instrumental ADLs (IADL) are complex tasks that are necessary to independently adapt to the environment (e.g., managing finances, medications, housekeeping, and transportation). These complex tasks rely more on cognitive skills, and are therefore more vulnerable in early stages of dementia. Studies show that older persons living in the community are more likely to be dependent in certain IADL tasks, while nursing home residents tend to be dependent in both IADL and basic ADL tasks. A general hierarchy in the sequence of decline of basic ADLs in older persons has been proposed. Specifically, the ability to bathe independently is lost first, followed by dressing, mobility, and at last feeding. It is evident that a decreased ability to independently perform ADLs is an important predictor for care dependency and nursing home admission.

The nursing home environment

In the Netherlands, roughly 70,000 persons with dementia are institutionalized, and an estimated 90% of persons with dementia die in a long-term care setting rather than at home. As a result of the recently reformed Dutch long-term care sector, persons with dementia are stimulated to live at home as long as possible. Only when complex care needs arise and care burden becomes too high, the person is indicated for nursing home admission. This change in the care system means that once admitted, nursing home residents will have more severe dementia, more complex care problems, and more care dependency. Care dependency occurs when a persons’ self-care abilities have decreased to such an extent that they are, to varying degrees, dependent on nursing care. Care dependency is related to the development of dementia and can lead to reduced quality of life and high caregiver burden. The importance of the nursing home in supporting the needs of persons with dementia is evident, and despite changes in the care system, an increased demand for long-term care is expected.

However, there are indications that nursing home admission accelerates the progression of dementia symptoms. For instance, nursing home residents with dementia have a significantly lower quality of life and more cognitive impairment compared to home-dwelling persons with dementia. Nursing home residents also show an accelerated decline in their ability to independently perform ADL. Moreover, the nursing home may aggravate behavioral symptoms by not meeting the needs of persons with dementia. Agitation can arise when a person has unmet needs (e.g., physical discomfort or need for stimulation) which he or she is unable to explain or understand due to the cognitive impairments. The accelerated decline of dementia symptoms may be the result of the
impoverished (passive) nursing home environment.\textsuperscript{8} The passive environment in the nursing home is apparent in both ADL activities as well as physical activities. In Dutch nursing homes, nursing staff play a key role in assisting in the performance of activities, but also, where possible, in encouraging independent functioning in daily activities.\textsuperscript{36} Relatedly, there is evidence that dependence supportive behavior (e.g., taking over care tasks) is associated with higher levels of care dependency.\textsuperscript{37} Despite the negative consequences of taking over care tasks, a recent study found that, when nursing staff were involved in residents’ ADL and IADL, they completely took over care tasks 45\% of the time.\textsuperscript{38} This may be the consequence of time shortage and high workload often perceived by nursing staff. However, by taking over care tasks instead of offering assistance (e.g., verbal instructions) with ADLs, independent functioning and movement are not stimulated, perhaps further enabling functional decline and care dependence.\textsuperscript{39}

Besides care tasks being taken over in the nursing home, there is increasing evidence that most nursing home residents spend their days inactive (i.e., watching television, sleeping, or doing nothing).\textsuperscript{40,41} In a recent study, 85\%-91\% of psychogeriatric residents were observed in a sedentary position (i.e., lying or sitting).\textsuperscript{41} When residents were engaged in ADLs, they were most often engaged in activities related to mobility, eating, and drinking. This inactivity in the nursing home could be the result of patient-related (e.g., care dependency, mobility problems, chronic diseases, cognition), organizational (e.g., lack of relevant and meaningful activities, staff workload, or amount of staff), or environmental (e.g., facilities of the ward enable ADL performance) factors.\textsuperscript{41}

Consequences of physical inactivity
Physical inactivity is defined as ‘not performing at least 30 minutes of moderate intensive physical activity a single day in summer or winter.\textsuperscript{42,43} Physical inactivity has been identified as the fourth leading risk factor for global mortality.\textsuperscript{44} The rising incidence of inactivity has major implications for the general health of persons.\textsuperscript{44} There is evidence that physical inactivity is an important trigger for the development of many chronic health conditions, including cardiovascular diseases, stroke, atherosclerosis, hypertension, cancer, asthma, musculoskeletal disorders, and type 2 diabetes and its antecedents, such as insulin resistance and obesity.\textsuperscript{45,46} A physically inactive lifestyle is also associated with cognitive decline and neurodegenerative diseases, such as dementia.\textsuperscript{45} Not only has physical inactivity been related to an increased risk of developing dementia, but also to an accelerated progression of dementia.\textsuperscript{47}

Several mechanisms have been proposed through which physical inactivity contributes to an increased risk of dementia. First, the chronic health conditions that arise as a result of inactivity (e.g., cardiovascular disease, stroke, hypertension, type 2 diabetes) are also
important risk factors for developing dementia.\textsuperscript{58} Second, physical inactivity is associated with a lower expression of important neuroprotective factors such as brain-derived neurotrophic factor (BDNF) and insulin-like growth factor-1 (IGF-1).\textsuperscript{59} BDNF and IGF-1 receptors are found in brain regions which are essential for cognitive performance (e.g., the hippocampus and the prefrontal cortex).\textsuperscript{50} The prefrontal cortex, hippocampus, and amygdala are brain regions which are especially vulnerable to dementia-related decline.\textsuperscript{51} However, deterioration of these areas negatively influences cognitive performance and behavior. For instance, degeneration of the hippocampus and the prefrontal cortex can contribute to memory impairments and executive dysfunction, respectively.\textsuperscript{8} Moreover, degeneration of the amygdala and the prefrontal cortex can contribute to agitated behavior.\textsuperscript{52} BDNF and IGF-1 play a key role in encouraging survival and growth of neurons (i.e., neurogenesis), synapses (i.e., synaptogenesis), and synaptic plasticity in these vulnerable brain regions.\textsuperscript{45} Therefore, adequate BDNF and IGF-1 levels are essential for cognitive performance.\textsuperscript{53} Besides the negative impact on neural functions, physical inactivity is related to lower cerebral blood flow, muscle atrophy, and a smaller volume of the hippocampus.\textsuperscript{54}

**Benefits of physical activity**

Despite the severe consequences of inactivity, there is evidence that regular engagement in physical activity can reduce the risk or delay the onset of dementia,\textsuperscript{55} and perhaps slow down the progression of dementia.\textsuperscript{56} Several neural and vascular pathways have been suggested to underlie the potentially protective effects of physical activity. First, physical activity reduces chronic health conditions such as diabetes, hypertension, and cardiovascular disease, factors which increase the risk for cognitive decline and dementia.\textsuperscript{55, 46} Second, physical activity has been found to improve brain vitality by altering brain structure and function.\textsuperscript{57} Studies show that brain regions which are vulnerable to dementia-related decline demonstrate positive structural and functional changes in response to physical activity.\textsuperscript{54, 57-59} For instance, physical activity can promote neurogenesis and angiogenesis, increase brain volume, and enhance cerebral blood flow of frontal and temporal brain regions.\textsuperscript{60, 61} Third, physical activity has been shown to increase levels of important neuroprotective factors that improve plasticity and neuronal survival, such as BDNF and IGF-1.\textsuperscript{49, 59, 62-66}

Different types of exercise influence brain function differently and may result in different levels of improvement. For instance, aerobic and strength training are thought to have distinct underlying mechanisms through which they influence cognitive function (Fig. 1). There is evidence that aerobic training can increase the neuroprotective BDNF levels in the hippocampus\textsuperscript{49} and improve cerebral blood flow, factors known to mediate effects on cognitive function.\textsuperscript{60} Strength training can increase concentrations of IGF-1 and lower homocysteine levels and oxidative stress.\textsuperscript{62-66} IGF-1 is strongly related to muscle mass
and strength\textsuperscript{67} as well as to cognitive performance.\textsuperscript{68} Elevated homocysteine has been associated with cerebral and hippocampal atrophy and is known to mediate positive effects of physical activity on cognitive function.\textsuperscript{69}

**Fig. 1.** Neural and vascular pathways involved in the effect of aerobic and strength training on dementia.

**Movement interventions to slow down the dementia process**

With accumulating evidence for the protective effects of physical activity, and a cure for dementia being absent, one of the proposed strategies for slowing down dementia-related decline is stimulating movement. In the nursing home, common methods used to stimulate movement are through physical activity interventions or ADL interventions.
Aerobic and strength exercises are physical activity interventions commonly studied in nursing home residents with dementia, and while the benefits for physical function,\textsuperscript{70} cognition,\textsuperscript{71, 72} and mood and behavioral problems\textsuperscript{73, 74} are well-established in healthy adults, results are inconsistent and less convincing in persons with dementia.\textsuperscript{75, 58, 75-85} Considerable variation exists with regard to the optimal type, duration, length, frequency, and intensity of physical activity interventions.\textsuperscript{75} However, there is some agreement that the strongest cognitive and physical effects can be reached following a combination of strength and aerobic exercise training.\textsuperscript{77, 86, 87} Considering the distinct underlying mechanisms through which aerobic and strength training can each affect dementia symptoms, it is indeed plausible that a combination of aerobic and strength training could be most beneficial for improving or maintaining function in persons with dementia.

The second method, ADL training, imbeds movement into daily care tasks. The focus is on restoring or maintaining residents’ highest level of functional independence by encouraging residents to perform their ADLs as independently as possible.\textsuperscript{33, 88, 89} Since most basic ADLs (e.g., bathing and toileting) are overlearned behaviors, it is argued that these functions can still be trained and stimulated in persons with dementia.\textsuperscript{90, 91} By embedding movement into daily care tasks, ADL training enables continuous stimulation of movement throughout the day. Since persons with dementia show a reduced ability to initiate activities, external stimulation and motivation to engage in activities is important to avoid inactivity. There is evidence that participation in daily activities can positively influence physical functioning and quality of life.\textsuperscript{41} Several nursing homes have attempted to implement such care interventions (e.g., function focused care or restorative care), but the impact upon resident outcomes is inconsistent and unclear.\textsuperscript{88, 89, 92-97}

In conclusion, physical activity and ADL interventions have a common goal: to maintain or improve function and quality of life by stimulating movement. More insight into the effect of movement stimulation, as well as factors that contribute to independent functioning and a better quality of life could benefit persons with dementia and their caregivers. Results from previous studies emphasize the need for structural changes in nursing homes in order to reduce resident inactivity. This gave rise to the aims in this thesis, which are described in the following section.
AIMS AND OUTLINE OF THE THESIS

The main aim of this thesis is to examine the effectiveness of different movement stimulation interventions on ADL ability, quality of life, cognitive and physical functions, and mood and behavioral problems in nursing home residents with dementia. Additionally, cross-sectional studies strive to examine factors associated with care dependency, ADL ability, and quality of life. The cross-sectional studies are described in Part I and the intervention studies are described in Part II.

PART I: Cross-sectional studies in nursing home residents with dementia
Chapter 2 of this thesis examines which demographic, cognitive, physical, behavioral, and disease related factors are associated with care dependency and the ability to perform ADLs. Chapter 3 examines which demographic, cognitive, behavioral, and disease related factors are associated with quality of life. In doing so, nine domains of quality of life are investigated separately, to take into account the multidimensional nature of quality of life.

PART II: Movement stimulation interventions in nursing home residents with dementia
This part of the thesis is focused on the effects of different movement stimulation interventions on ADL ability, quality of life, cognitive functioning, physical functioning, mood, and behavior. Chapter 4 explores the effectiveness of 12 months of movement-oriented restorative care (MRC); an intervention which aims to integrate movement into the daily lives of nursing home residents with dementia using a multidisciplinary approach. Chapters 5 and 6 examine and compare the effects of 6 months of ADL training, multicomponent aerobic and strength training, and combined ADL and multicomponent aerobic and strength training in nursing home residents with moderate to severe dementia. More specifically, chapter 5 investigates and compares the effect of the three interventions on quality of life and ADL performance. Chapter 6 investigates and compares the effects of the three interventions on cognitive functions, physical functions, and mood and behavioral problems.

To conclude the thesis, chapter 7 provides a summary and general discussion of the main findings. The chapter provides a reflection on the findings, a discussion of methodological considerations, and implications for future policy, practice, and research.
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General introduction


