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LEISURE ACTIVITIES AT OLD AGE AND THEIR INFLUENCE ON DEMENTIA DEVELOPMENT

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A Julyan et Larah,

"La chronologie empêche de faire des rapprochements entre les différentes époques.

En chacun de nous, il y a tous les temps"

Théodore ZELDIN, entretien avec Marianne Payot, octobre 1994

ABSTRACT

This thesis aims to describe the participation in leisure activities of elderly subjects and to detect their possible effect, if any, on the development of dementia. The data were derived from the Kungsholmen Project, which is a community-based prospective study on aging and dementia in people aged over 74 years, living in Stockholm, Sweden. The major findings are summarized below.

Study I. The pattern of participation in leisure activities was related to contextual factors as well as to mental and physical health conditions. In spite of the advanced age, the majority of the population was active, as 70% participated in at least one activity. Reading (19%) was the most prevalent individual activity, and mental activities (43%) the most prevalent activity type. Older age, female gender, low education, poor or limited social network, mental disorders, and physical limitation were all correlated with a decreased engagement in 'at least one activity'. Contextual factors and health-related factors were differentially associated with the five activity types.

Study II. We aimed to verify the hypothesis that mental, social and physical components are relevant protective factors against dementia, and that a combined beneficial effect may be present over a 6-year follow-up period. Multi-adjusted relative risks (RRs) of dementia for subjects with higher mental, physical and social component scores were 0.71 (95% CI: 0.49–1.03), 0.61 (95% CI: 0.42–0.87) and 0.68 (95% CI: 0.47–0.99), respectively. The most beneficial effect was present for subjects with high scores in all or in two of the components (RR of dementia=0.53; 95% CI: 0.36–0.78).

Study III. The hypothesis that an active lifestyle may protect against dementia development was further tested by using principal component analysis to characterize the exposure. Among a set of lifestyle variables, three underlying factors were identified: physical, mental and social factors. All the factors showed an independent protective effect on dementia development. The relative risks (RRs) ranged from 0.60 to 0.70. When these factors were integrated into an Active Lifestyle Index, a significant dose-response association was observed, Compared with low level of engagement (low in at least two of the factors), the RR of dementia was 0.66 (95% CI: 0.49-0.89) for the moderate level (high scores in two factors), and RR=0.51 (95% CI: 0.31-0.85) for the high level (high scores in all three factors).

Study IV. The hypothesis that an active lifestyle delays the dementia onset was verified over a 9-year follow-up period. The lifestyle factors of the mental, social and physical component scores estimated in a previous study (study II) were studied in relation to age at dementia onset. Results showed that dementia developed at a significantly later age in individuals who had a higher level of participation in activities with high physical, mental or social components. When the three components were integrated, we found that the broader spectrum of participation (higher levels in at least two of the components) the later the age at dementia onset (β 0.62; P<0.01).

Conclusions. Even in the advanced age, elderly persons are still active, being limited in their participation only by mental disorders or by physical limitation. An active lifestyle, defined as a higher level of participation in leisure activities with either mental, social or physical component may decrease the risk of dementia and postpone its onset.

Key words: leisure activities, dementia, components, dimensions, protective factor, onset.

SAMMANFATTNING

Syftet med denna avhandling är att beskriva äldres deltagande i fritidsaktiviteter och undersöka de eventuella effekterna av fritidsaktiviteterna på utvecklingen av demens. Data har hämtats från Kungholms-projektet som är en befolkningsbaserad, prospektiv undersökning om åldrande och demens hos personer över 74 år, boende i Stockholm. De huvudsakliga resultaten summeras nedan:

Studie I. Det fanns ett mönster för deltagande i fritidsaktiviteter som hängde samman både med omgivande faktorer och mentala och fysiska hälsotillstånd. Trots deltagarnas höga ålder var de flesta aktiva, och 70% utövade åtminstone en aktivitet. Att läsa (19%) var den vanligaste enskilda aktiviteten, och den vanligaste typen av aktivitet var mentala aktiviteter (43%). Högre ålder, kvinnligt kön, låg utbildning, svagt eller begränsat socialt nätverk, mental sjukdom och fysiska begränsningar var samtliga korrelerade med lägre deltagande i 'åtminstone en aktivitet'. Omgivningsfaktorer och hälsorelaterade faktorer var relaterade på olika sätt till de fem olika typerna av aktiviteter.

Studie II. Vi avsåg att testa hypotesen att mentala, sociala och fysiska komponenter utgör relevanta skyddsfaktorer för demens och att det kan finnas en kombinerad skyddande effekt över 6 års uppföljning. Den Relativa Risken (RR) för demens för personer med högre poäng på den mentala komponenten var 0.71 (95% CI: 0.49-1.03), när det gällde den fysiska komponenten var RR 0.61 (95% CI: 0.42-0.87) och för den sociala komponenten var RR 0.68 (95% CI: 0.47-0.99). Att ha höga poäng i två eller alla tre komponenterna hade den mest gynnsamma effekten (RR för demens = 0.53; 95% CI: 0.36–0.78).

Studie III. Hypotesen att en aktiv livsstil kan skydda mot utvecklingen av demens undersöktes vidare genom att använda Principal Component analys för att karaktärisera exponeringsvariabeln. Utifrån ett antal livsstilsvariabler kunde tre underliggande faktorer identifieras: en fysisk, en mental och en social faktor. Samtliga faktorer hade oberoende av varandra skyddande effekt mot utvecklingen av demens. De relativa riskerna (RRs) låg mellan 0.60 och 0.70. När faktorerena integrerades till ett index som mätte en aktiv livsstil, fann vi ett signifikant dos-respons samband. Jämfört med låg nivå av engagemang (låg poäng i åtminstone två av faktorerna) var RR för demens 0.66 (95% CI: 0.49-0.89) för måttlig nivå (hög poäng i två faktorer), och RR=0.51 (95% CI: 0.31-0.85) för hög nivå (hög poäng i alla tre faktorerna).

Studie IV. Hypotesen att en aktiv livsstil kan fördröja debuten av demenssjukdom undersöktes över en 9-års uppföljningsperiod. De mentala, sociala och fysiska livsstilsfaktorernas respektive poäng, som beräknats i Studie II, undersöktes i relation till ålder vid demensdebuten. Resultaten visade att demenssjukdomen utvecklades vid signifikant högre ålder hos dem som hade högre nivå av deltagande i aktiviteter med fysiskt, mentalt eller socialt innehåll. När de tre komponenterna integrerades, fann vi att ju bredare spektrum av aktiviteter (högre nivå i åtminstone två av komponenterna), desto högre ålder vid demensdebuten (β 0.62; P<0.01).

Konklusioner: Äldre personer är fortfarande aktiva vid hög ålder, om de inte begränsas av mentala sjukdomar eller fysisk funktionsnedsättning. En aktiv livsstil, definierat som högre nivå av deltagande i fritidsaktiviteter som är antingen mentala, sociala eller fysiska kan minska risken för demens och uppskjuta debuten av sjukdomen.

Nyckelord: fritidsaktiviteter, demens, komponenter, dimensioner, skyddsfaktor, insjuknande.

LIST OF PUBLICATIONS

This thesis is based on the following original papers, referred to in the text by their Roman numerals.

I.   Paillard-Borg S, Wang H-X, Winblad B, Fratiglioni L. Pattern of participation in leisure activities among older people in relation to their health conditions and contextual factors: A survey in a Swedish urban area. Ageing Soc 2009, (in press).

II.   Karp A, Paillard-Borg S, Wang H-X, Silverstein M, Winblad B, Fratiglioni L. Mental, physical and social components in leisure activities equally contribute to decrease dementia risk. Dement Geriatr Cogn Disord 2006; 21: 65-73.

III. Paillard-Borg S, Fratiglioni L, Winblad B, Wang H-X. Leisure activities in late life in relation to dementia risk: principal component analysis. (submitted)

IV.   Paillard-Borg S, Fratiglioni L, Winblad B, Wang H-X. Does a stimulating lifestyle postpone the onset of dementia? (manuscript)

CONTENTS

LIST OF ABBREVIATIONS

AD	Alzheimer's disease
ADL	Activity of Daily Living
ApoE ε4 allele	Apolipoprotein E ε4 Genotype
CES-D	Center for Epidemiological Studies-Depression survey
CI	Confidence Interval
CPRS	Comprehensive Psychopathological Rating Scale
DSM-III-R	Diagnostic and Statistical Manual of Mental Disorders, Third-Edition Revised
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Forth Edition
HSFR	Swedish Council for Research in the Humanities and Social Sciences
ICD-8	International Classification of Diseases, Eighth Revision
MMSE	Mini-Mental State Examination
NINCDS-ADRDA	National Institute of Neurological and Communicative Disorders-Alzheimer´s Disease and Related Disorders Association
NINDS-AIREN	National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences
NIH	National Institutes of Health
OR	Odds Ratio
RR	Relative Risk
SBU	Swedish Council on Health Care Assessment
SNACK	Swedish National Study of Aging and Care in Kungsholmen
VaD	Vascular Dementia
SPSS	Statistical Package for Social Sciences
MANCOVA	Multivariate analysis of covariance

1 INTRODUCTION

1.1 GLOBAL AGING

The world population is now living longer than ever before thanks to social, economic and medical advances. This phenomenon is accompanied by many new challenges that require strategical solutions. Young children have always outnumbered older people, but very soon for the first time in the history of human being, people aged 65 and over will outnumber children under age 5 (Figure 1) [1]. This reversal in the numerical proportions of the old and young reflects improved survival and reduced fertility [2]. This trend is emerging around the globe. Today almost 500 million people are older than 65 years, and they account for 8% of the world's population. By 2030, the world is likely to have one billion old people, which will represent 13% of the total population. While today's proportions of older people typically are highest in more developed countries, the most rapid increases in older populations are occurring in the less developed nations. From 2006 to 2030, the number of older people in less developed countries is projected to increase by 140% as compared to an increase of 51% in more developed countries [1].
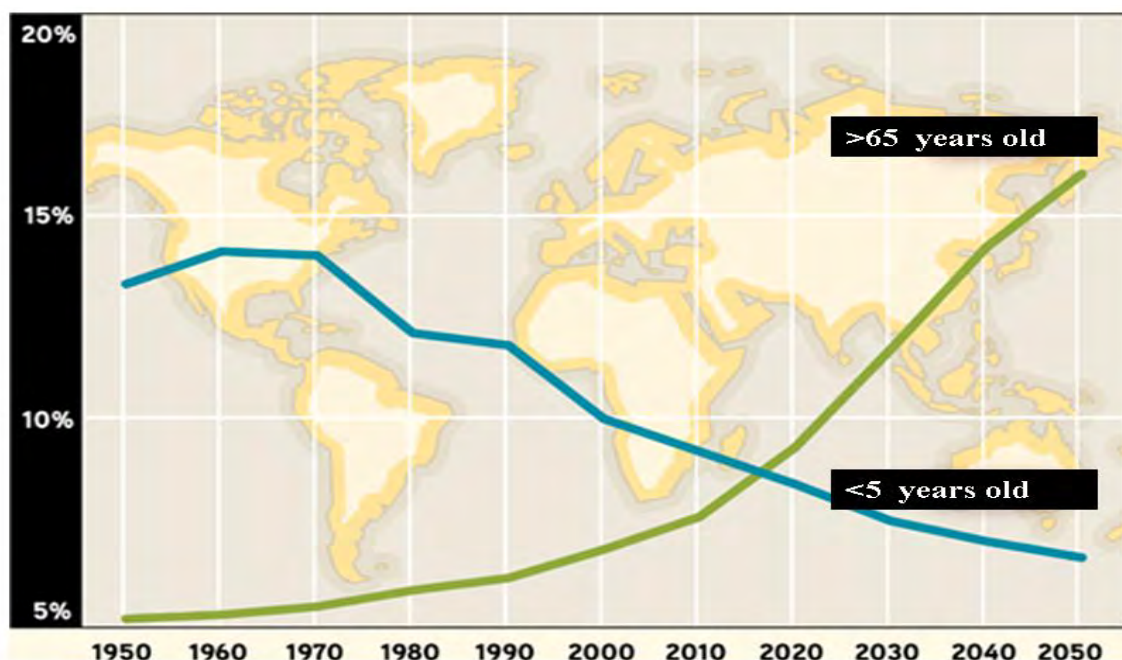

Figure 1. Young children and older people as a percentage of global population. (From World Population Prospects. United Nations. The 2004 Revision, 2005, modified).

1.1.1 Aging in Sweden

The twentieth century in Sweden was characterized by one of the highest increases in life expectancy in the world. A hundred years ago, a Swedish newborn could expect to live until the age of 56. Today, the average expected life span is about 81 years. In 2008, about 17% of the Swedish population (9.3 million inhabitants) are aged 65 or over [3]. This proportion will increase in the next 30 years. The increase will first be registered among the young-old (65 to 79 years), thereafter among the old-old (80 years and older). Older women will still constitute the majority among older people, but the female proportion in the population is expected to decrease from 64% in 2005 to 56% in 2050 [4]. Unless there is a remarkable improvement of the health situation among the old-old, the Swedish society will face an important challenge due to increasing number of subjects with chronic diseases. Dementia is one of the most common chronic disorders in the elderly [2] and one with highest impact in the quality of life of the individuals and their families.

1.2 DEMENTIA

Dementia is a syndrome characterized by progressive deterioration in multiple cognitive domains that are severe enough to interfere with daily functioning [5]. The cognitive deficits include primarily memory impairment and at least one of the other cognitive domains, such as aphasia, agnosia or disturbances in executive functioning [6]. Alzheimer's disease (AD) is the most common cause of dementia in the elderly, accounting for 60-70% of all dementia cases [7]. Vascular dementia (VaD) is the second most common cause of dementia. VaD is defined as impairment of cognitive functions resulting from ischemic, hypoperfusive or hemorrhagic brain lesions due to cerebrovascular disease or cardiovascular pathology [8] [9].

In this thesis, we refer to dementia as a syndrome, since the co-occurrence of AD and VaD pathological changes in the brain of older people is extremely common, making mixed dementia probably the most common type of dementia [10], although difficult to diagnose.

1.2.1 Prevalence and incidence of dementia

Dementia has become one of the major public health issues in both developed and less-developed countries due to the worldwide phenomenon of the aging population [11]. Several meta-analyses have resulted in similar estimates of dementia prevalence across regions [12]. The age-specific prevalence of dementia almost doubles every 5 years, from approximately 1.5% in persons aged 60–69 years to 40% in nonagenarians. An expert panel estimated that the global dementia prevalence in people aged 60+ years was 3.9%, with the regional prevalence being 1.6% in Africa, 3.9% in eastern Europe, 4.0% in China, 4.6% in Latin America, 5.4% in western Europe, and 6.4% in North America [13]. There is a similar pattern of dementia subtypes across the world, with the two most common forms of AD and VaD accounting for 50–70% and 15–25% of all dementia cases, respectively [14].

The global annual incidence of dementia is estimated to be around 7.5 per 1000 population [13], with no substantial variations across continents except Africa, where incidence rates are reported to be lower than other regions. The incidence rate of dementia increases exponentially with age, from approximately one per 1000 person–years in people aged 60–64 years to more than 70 per 1000 person–years in 90+ year-olds . The incidence rates of dementia across regions are quite similar in the younger–old group (<75 years), but greater variations are reported among the older ages . Pooled data from Europe suggest a geographical dissociation across Europe, but this variation may result from differences in methodology.

An expert panel estimated that in 2001 there were 24 million people with dementia in the world . Given the trend in population aging, the number of persons with dementia is expected to almost double every 20 years. Similar estimates have been previously reported [15]. The majority of people with dementia are living in developing countries. In 2008, China and other Asian countries have the highest number of people with dementia (6 million), followed by the European Union (5.0 million), USA (2.9 million), and India (1.5 million). The rate of increase in numbers of dementia patients varies substantially across various regions, with the rate being three to four times higher in developing areas than in developed regions. Further, the proportion of people with dementia in developing nations will rise from 61% in 2000 to 65% in 2020 and 71% in 2040. Thus, the demands

of healthcare and social services of the huge and rapidly growing numbers of dementia patients is a matter of great concern for policymakers in both developed and developing countries .

1.2.2 Risk and protective factors

Over the last 30 years, the accumulation of evidence in dementia research has gradually convinced most of the researchers that the disorder is not determined in a single time period of the lifespan, rather, it may be a result of complex interactions of genetic susceptibility, biological factors, and environmental exposures experienced over the life course (Figure 2) [16].
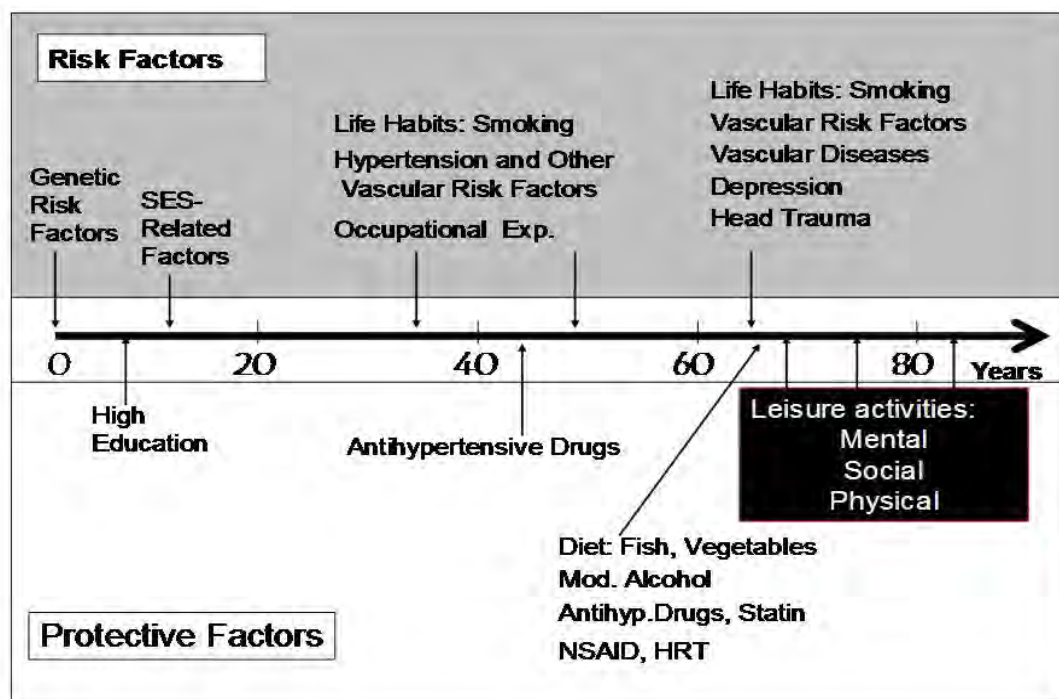
Figure 2. An active and socially integrated lifestyle in late life might protect against dementia. (From Fratiglioni L, Paillard-Borg S, Winblad B. 2004; modified).

Old age and genetic susceptibility are the only well-established risk factors for dementia. In addition to leisure activities, the following relevant risk factors are taken into account in this thesis:

- ➢ AGE: The incidence of dementia almost doubles every 5 years of age .

- ➢ GENDER: Female gender is often associated with a higher risk of AD than male gender, especially at the older-old age [5].

- ➢ EDUCATION: Low dementia prevalence and incidence among highly educated persons has been reported by numerous studies. Educational attainment and lifespan mental activity associated with childhood education may reduce the risk of dementia [17].

- ➢ SOCIAL NETWORK**:** Data from longitudinal studies (3 to 27 years of follow-up) have suggested that a poor social network is related to cognitive decline and dementia. The risk of dementia is decreased in old people with social integration and frequent contacts with relatives and friends .

- ➢ COMORBIDITY: There is strong evidence that comorbidity [18] and especially vascular risk factors and vascular disorders such as heart failure may play a role in the development of cognitive decline and dementia [19] [20].

- ➢ DEPRESSIVE SYMPTOMS: Depressive symptoms have been considered to be a response to cognitive decline or an early manifestation of dementia, but results of a recent meta-analysis suggest that depressive symptoms and depression could be a potential risk factor for dementia [21].

1.2.3 Delaying dementia onset

Delaying the onset of dementia is an alternative to primary prevention. Brookmeyer and colleagues reported that delaying the syndrome by 5 years would reduce the prevalence of 40% in 10 years and almost 50% in 50 years [22]. Delaying the onset of dementia can have a considerable impact in reducing the burden and costs related to this syndrome. Therefore, the identification of the protective and risk factors modulating the time at onset of dementia is crucial [23].

1.3 LEISURE ACTIVITIES

1.3.1 Why study leisure activities in the older population?

After retirement, leisure activities constitute a relatively large part of daily life. In addition, due to the aging of the population, the new generation of older people will live longer,

which means that they have more time to spend in leisure activity, albeit not necessarily in better health than their predecessors [24]. Older people need to cope with and adapt to new challenges related to their own aging as well as to contextual changes. They have to learn how to live with impairments, diseases and loss of energy, friends or significant others [25]. For that reason, in the last decades, increasing attention has been given to the relationship between participation in leisure activities and aging [26].

Some studies suggest that the "baby boom generation" is more active than their predecessors due to opportunities and resources earlier in life that influence the lifestyle in old age [27]. Furthermore, lifestyle changes allow a much greater variety of social and cultural activities than ever in the past. However, many of these relatively new opportunities, such as traveling and going to a restaurant can be costly and not accessible to all. Even if a general trend shows that many older people in the world are involved in leisure activities, it is important to remember regional differences, since climate, traditions, and infrastructure can influence the level of participation [28]. The findings of this thesis relate primarily to older urbanites of Northern Europe. Indeed, in Sweden since the 1950s, following a long tradition of social cohesion and solidarity, study circles and other organizational movements were commonly available in the community [29].

There is a general consensus that an active lifestyle and good health are probably mutually associated. Also, it is suspected that different types of activities may have different health benefits and that men and women might benefit differently from leisure activities. Consequently, leisure activities in old age have been a common focus for studies regarding different aspects of health status [30], such as depression [31], cognition [32] and mortality [33].

1.3.2 Theoretical perspectives on leisure activities and aging

In the early 1960s, the *Disengagement Theory* postulated that human aging involves an inevitable separation of relationship with others [34]. According to this theory, the social relationships that remain are altered in quality because of loss of roles, declines in abilities or sudden awareness of the proximity of death. However, the *Activity Theory* stated that life satisfaction decreased as activities decreased. This assumes that when changes occur, the typical response is to attempt to restore activity lost [35]. This theory

claims that it is important to uphold activity levels and replace lost activities and roles in order to maintain life satisfaction. As suggested by Bengtson and colleagues, both the *Disengagement Theory* and the *Activity Theory* are "first generation" theories in the context of social gerontology and sociology of aging [36]. The *Continuity Theory* that was developed about ten years later and considered as "second generation" theory is based on adaptation. According to this theory, older adults try to maintain this continuity of lifestyle by adapting strategies that are connected to their past experiences [36]. In other words, it assumes personal development and allows changes to be integrated into one's prior history without necessarily causing upheaval or disequilibrium [37]. The theory of *Selective Optimization with Compensation* (SOC) is similar to the continuity theory [38]. According to this theory, older people use three strategies to cope with changes due to old age: 1) selection: the choices and priorities older people make when they limit their activities due to losses in resources, 2) optimization: engagement in activities in order to increase and maintain physical and cognitive capacities necessary to an active lifestyle, 3) compensation: strategies that allow the older people to continue participation in the chosen activities despite losses. One of the most commonly used term to describe a good old age is *Successful Aging* which is based on three components: avoidance of disease, maintenance of high cognitive and physical function and active engagement with life [39].

1.3.3 Leisure activities, demographic, contextual and health factors

Many older persons explain their good health in terms of being active: "I am so busy and it keeps me in good health". Participation in leisure activities is influenced by many factors such as age, gender, level of education and socioeconomic status, mental and physical health (including physical limitation), as well as social network. It is important to be aware of the diversity of leisure activities available to a very diverse older population with many individual particularities. In addition, it is essential to consider the birth cohort effect when studying the behavioral pattern of a population. Contemporary older people, and probably to an even greater extent the future cohort of older people, will differ from previous generations due to significant changes during their earlier life stages . The relation between an active lifestyle and health has been carefully outlined in the activity theory as well as other theories, suggesting that to continue to be engaged with life is necessary for successful adjustment in old age.

The following factors most likely relate differently to participation in leisure activities:

> AGE: With advanced age more time and energy must be used in obligatory activities, such as IADL and ADL, which reduces the amount of time devoted to leisure activities but still allow the opportunity of an active lifestyle [40] [41].

> GENDER: Due to traditions, social norms, expectations or choices simply based on biological differences, women and men may enjoy different types of leisure activities. Commonly, women engage in more sedentary and indoor activities (handicrafts), while men engage in more physically challenging activities outside the home [42].

> SOCIO-ECONOMIC STATUS: Generally, a person's socioeconomic background influences what kind of leisure activities that person is interested in [43].

> EDUCATION: A higher education level has been found to increase social and productive activities [44]. Education is also closely related to occupation, which in turn is associated with income and socio-economic status. Participating in some leisure activities can be expensive, due to the cost of transportation or the costs associated with the appropriate equipment.

> SOCIAL NETWORK: A social network is made up of family members and friends, as well as regular contact with acquaintances. Not only the quantity but also the quality of the social connections is important. Having a large social network seems to be associated to a more active lifestyle [45] and other health-related behaviors [46]. It is likely that older persons with a limited social network have less incentive to participate in leisure activities and *vice-versa* .

> PHYSICAL AND MENTAL HEALTH: Decline in physical health (including physical limitation) and cognition is associated with normal aging. The sick, physically and cognitively impaired persons are less likely than healthy individuals to engage in leisure activities [44]. Depressive symptoms, decline in cognition, and dementia can impact the level of participation as some mental disorders can be connected to mental fatigue and physical exhaustion which naturally restrain participation in challenging activity types [47].

1.3.4 Leisure activities and occurrence of dementia

It is a widespread belief that staying active helps older people to maintain their physical and mental health. A number of studies have explored the association between leisure activities and risk of dementia/AD. Tables 1 to 3 describe the longitudinal studies that explored either the social, mental or the physical dimension of the activities in relation to dementia risk or onset, while Table 4 describes the studies that explored more than one dimension. The follow-up time of these studies range from one to 60 years. All the studies used similar diagnostic criteria for dementia diagnosis and have taken into account potential confounders. All associations were controlled for age, gender, and education. Some studies grouped leisure activities into different types according to the nature of activities such as physical, mental, and social activities. Others focused on leisure activities in general or specific individual activities. Ten studies that explored the social dimension of the activities, found a decreased risk of dementia [32 48-52 68 69 72 74]. There are 12 studies that have focused on the mental dimension. All of them reported a significant protective effect of mental activities on dementia [32 48 52-55 68-71 73 74]. Among leisure activities, the physical dimension is the most studied activity. Of the 19 studies, 12 reported a relation between participation in physical activities and lower risk of dementia [32 57-59 61 61-65 67 69 73]. A study from the Kungsholmen Project found that the physical dimension of the activities was not related to decreased risk of dementia; however, the study power was too small to detect a small effect [72].

Only two studies have investigated the relation between participation in leisure activities and its delaying effect on dementia onset [54 74]. Both studies explored the effect of participation in cognitive activities at midlife on dementia onset among monozygotic twin pairs (different study population), and found that midlife cognitive stimulation was related to later dementia onset. One of these studies additionally studied participation in social and physical activities at midlife and found an association between participation in social activities and later dementia onset [74]. However, no association was found in relation to physical activity and delayed onset.

1.3.5 Observational longitudinal studies

Table 1. Observational longitudinal studies on the association between social dimension of activities and dementia risk

Authors, (y), Country	n	Age at baseline (y)	Social dimension	Follow-up year	Covariates	Reported associations *
Bickel and Cooper, [48] (1994), Germany	422	>65	Social relations, social support, marital status	5-8		Being single or widow with increased risk of dementia †
Helmer et al, [49] (1999), France	3675	>65	Marital status, social network (social ties and satisfaction feeling), number of activities	5	Alc, dep, SN, LA	Never married with increased risk of dementia and AD; no association with social network and leisure activities
Fratiglioni et al, [50] (2000), Sweden	1203	>75	Marital status, living arrangement, social ties and satisfaction feeling, social network index	3	Cog, dep, ADL, VD, BP	Being single, living alone, or no satisfactory social network with increased dementia risk; poor and limited social network with increased dementia risk
Bennett et al, [51] (2006), USA	81	Mean age 84.3	Social network (size: number of children, family members, friends, number of children; frequency)	6	Dep, morb, LA	Inverse relation between cognitive function and all measures of disease pathology; social network as a modifier between pathology and cognitive function
Saczynski et al, [52] (2006), USA	2513	45-60	Social engagement: marital status, living arrangement, participation in an organization, and social events, and confident relationship	27	Cog, APOE, VD, morb	Participation in the lowest quartile with increased risk of dementia; decreased social engagement from midlife to late life with increased risk of dementia

Table 2. Observational longitudinal studies on the association between mental dimension of activities and dementia risk

Authors, (y), Country	n	Age at baseline (y)	Mental dimension	Follow-up year	Covariates	Reported associations *
Crowe et al, [53] (2003), USA	107	>75	Intellectual-cultural, self-improvement, and domestic activity	Middle adulthood		Overall activity with decreased dementia risk
Gatz et al, [54] (2005), Sweden	12,772	>65	"Choice" of leisure activities	Middle adulthood		Education significantly affects *dementia onset*, that is, occurrence and timing of dementia symptoms. Impact of education on in leisure activity choice
Fritsch et al, [55] (2005), USA	396	Mean 75	IQ scores at adolescence and mean number of activity level from high school year book	60		Higher adolescent IQ and greater activity with decreased risk of dementia
Wilson et al, [56] (2007), USA	700	Mean 80.4	Current and past frequency of cognitive activity	5	Cog, LA, soc	More frequent participation in cognitive activity was associated with decreased AD; cognitively inactive person with 2.6 times more risk of AD than a cognitively active.

Table 3. Observational longitudinal studies on the association between physical dimension of activities and dementia risk

Authors, (y), Country	n	Age at baseline (y)	Physical dimension	Follow-up year	Covariates	Reported associations *
Yoshitake et al, [57] (1995), Japan	828	>65	Leisure and at work physical activity	7	BP, CVD, alc, dia, cog,	Daily physical activity with lower risk of AD
Laurin et al, [58] (2001), Canada	4615	>65	Low, moderate, high physical activity level (time and intensity)	5	FA, smo, alc, NSAID, ADL, IADL, SPH, CD	High physical activity with lower risk of dementia and AD
Lindsay et al, [59] (2002), Canada	4615	>65	Regular exercise (not otherwise defined)	5		Regular physical activity with lower risk of AD
Yamada et al, [60] (2003), Japan	1774	>33	Physical activity	25 to 30		No association
Abbott et al, [61] (2004), USA	2257	71-93	Walking	3	APOE, smo	Men walking the least (<0.25 mile/day) with 1.8-fold greater risk of dementia compared with those walking more than two miles/day.
Podewills et al, [62] 2005, USA	3,375	>65	Leisure-time energy expenditure and an activity index	5.4	Eth, APOE, dep, occ, ADL,SN, ,IADL	Participation in > or =4 activities with a decreased risk of dementia compared with those engaging in 0-1 activity. More marked in APOE4 non-carriers but were absent in carriers
Rovio et al, [63] 2005, Finland	1449	65-79	Mid-life physical activity. Frequency of leisure-time physical activity that lasts at least 20-30 minutes and causes breathlessness and sweating.	21	FT; VD, PF, APOE, alc, smo	Leisure-time physical activity at midlife at least twice a week with decreased risk of dementia and AD. The associations were more pronounced among the APOE E^4 carriers.
Simons et al, [64] (2006), Australia	2805	>60	Physical activity	16	SN, VD, ADL	Daily gardening, and daily walking among men but not among women with reduced risk of dementia
Larson et al, [65] (2006), USA	1740	>65	Physical leisure time frequency	6.2	Alc, smo, APOE, dia, cog, morb, dep, CV,	Exercise three or more time each week with a lower risk of dementia than with exercise less than three times each week.
Rovio et al, [66] 2007, Finland	1449	65-79	The effects of occupational and commuting physical activity (physical activity at work and on the way to work)	21	FT, VD, PF, APOE, alc, smo	No association
Sumic et al, [67] (2007), USA	66	Mean 88.5	Physical activity (exercise)	4.7	APOE, cog	Effect of exercise modified by gender. No association for men. Less active women had two times increased risk.

Table 4. Observational longitudinal studies of the association between mixed social, mental and physical dimensions of activities and dementia risk

Authors, (y), Country	n	Age at baseline (y)	Social, mental, physical dimensions	Follow-up year	Covariates	Reported associations *
Fabrigoule et al, [68] (1995), France	2040	>65	Cultural, productive, and social activities; sport		Alc, cog, FF, soc	Travelling, odd jobs, knitting, or gardening with decreased risk of dementia; no association with sport§
Scarmeas et al, [69] (2001), USA	1172	>65	13 selected activities (physical, cultural, recreational, and social); leisure activity score; three factor scores	1-7 (mean 2.9)	Occ, FF, dep, VD, hyp, dia	Single activity and factor scores (intellectual, physical and social) with decreased risk of AD; higher leisure activity score with decreased risk
Wilson et al, [70] (2002), USA	801	>65	* Physical activity (duration) * Cognitive activity score (participation and frequency to seven mental activities)	Mean 4.5	SRH, dep, cog. PF	* No association * Higher cognitive activity score with lower AD risk
Wilson et al, [71] (2002), USA	842	Mean 76 (SD 6.3)	* Physical activity score (time in seven activities) * Cognitive activity score (frequency of seven information processing activities; physical activity score (time in seven activities)	4	SRH, dep, cog, PF	* No association * Higher cognitive activity score with lower AD risk
Wang et al, [72] (2002), Sweden	732	>75	Mental, social, physical, recreational, productive activities (reported); frequency of participation	6	FF, cog, morb, dep	Frequent engagement in mental, social and productive activities with lower dementia risk; no association with physical activity
Verghese et al, [73] (2003), USA	469	>75	* 11 physical activity scores (duration) * Six cognitive activities and eleven physical activities; cognitive and physical activity scores	Median 5.1	Eth, APOE, dep, occ, PMF	* Only dancing with low dementia risk * Reading and playing board games and musical instruments with lower risk of dementia and AD; cognitive-activity score with reduced risk of both
Karp et al, (2006), Sweden	776	≥75	Mental, physical and social component score estimated for 29 activities	6	Cog, morb, FF, dep	Higher mental, physical and social component score with decreased risk of dementia; most beneficial effect for subjects with high scores in all or in two of the components.
Carlson et al, [74] (2008), USA	147 Twin-pairs	Midlife	Physical, cognitive and social leisure activities	20-40	APOE	Cognitive and social leisure activities in midlife with reduced risk of dementia by *delaying the onset*, particularly among twin pairs at elevated genetic risk, possibly indicative of an enriched environment.; no association with physical activity

All associations were controlled for age, gender, and education. **Alc**=alcohol; **PF**=physical functioning; **soc**=social class; **dep**=depression; **SN**=social network; **LA**=leisure activity; **cog**=cognition; **APOE**= apoliprotein; **VD**=vascular diseases; **BP**=blood pressure; **occ**=occupation; **hyp**=hypertension; **dia**=diabetes; **morb**=morbidity. **SRH**=self-reported health status; **eth**=ethnicity; **PMF**=physical and mental functioning; **CD**=chronic diseases. **FA**=family aggregation; **smo**=smoking; **NSAID**=non-steroidal anti-inflammatory drugs; **ADL**=activity of daily living; **IADL**=instrumental activity of daily living; **CD**=chronic diseases; **morb**=morbidity; **SN**=social network; **FT**= follow-up time. **FF**=physical functioning. *Dementia diagnosed according to DSM III R criteria, AD diagnosed according to NINCDS-ADRDA criteria. †Diagnosed according to ICD 9 criteria.

2 AIMS

2.1 GENERAL AIMS

The general aims of this doctoral thesis are to explore leisure activities at old age and their influence on dementia development.

2.2 SPECIFIC AIMS

1. To describe the pattern of participation in leisure activities in an older population in relation to contextual factors as well as to mental and physical health *(Study I)*.

2. To verify the hypothesis that mental, social and physical components are relevant protective factors against dementia, and that a combined beneficial effect may be present *(Study II)*.

3. To explore the underlying dimensions of a set of interrelated lifestyle factors and test the hypothesis that an active lifestyle may protect against dementia development *(Study III)*.

4. To test the hypothesis that an active lifestyle may delay the dementia onset *(Study 1V)*.

3 METHODS

3.1 THE KUNGSHOLMEN PROJECT

All four studies are based on data from the Kungsholmen Project, a longitudinal population-based study on aging and dementia. The initial population consisted of all registered inhabitants who were 75 years and older and living in the Kungsholmen Parish in 1987 (n=2368). Of these eligible subjects, 181 individuals had died, 69 had moved out of the area, 308 refused to participate at the baseline examination.

Baseline survey (1987-1989) [75] [76]. A total of 1810 persons (76.4 %) participated in the initial survey, in which demographic, social, functional and cognitive data were collected. A Swedish version of the Mini-Mental State Examination (MMSE) was used as a screening test for possible dementia (Phase I) [77]. At the first clinical examination, 314 subjects with suspected dementia (MMSE<24) and a sample of subjects without cognitive impairment (n=354) underwent an extensive medical examination. This was the clinical phase of the baseline survey (Phase II). Of the 1810 participants who underwent the baseline examination, 1473 were diagnosed as non-demented. All participants were re-examined using the same extensive protocol at each follow-up, each at approximately three-year intervals.

Follow-up examinations (1991-2000). Four waves of follow-up have been completed, each with an average interval of three years. At every follow-up occasion, the surviving subjects underwent a structured interview by nurses, clinical examination by physicians, and neuropsychological assessment by psychologists. If the subject was not able to answer, an informant, usually a next-of-kin, was interviewed. For those subjects who had died before the follow-up examination, information regarding their health status was obtained from the Stockholm Computerized Inpatient Register System, which is a register of discharge diagnoses from all hospitals in Stockholm since 1969. The individual hospital records, discharge diagnoses, as well as the death certificates were examined.

3.1.1 Study population

The study populations of the four studies are illustrated in Figure 3.

Study I. Of the 1810 individuals who were surveyed at baseline, 110 subjects did not undergo clinical examination and 77 participants had missing information on leisure activities, leaving 1623 subjects available for the study.

Studies II and III. Of the 1473 subjects diagnosed as non-demented at the clinical phase of the baseline survey (phase II), 98 subjects whose MMSE scores were less than or equal to 23, or who were living in an institution were excluded from the study because institutionalization or impaired cognition may limit the person's activity. By the first follow-up examination, 269 subjects had died, 172 refused participation, and 934 participated. Of these, 158 were diagnosed as demented and were excluded from the analysis. Thus, the population for these studies was composed of those 776 persons still non-demented at the first follow-up examination. As 44 subjects refused to participate in the second follow-up, 732 dementia-free subjects were followed for another three years (study II) and six years (study III), and 123 and 212 cases were diagnosed as incident dementia, respectively.

Study IV. The study population consists of those 212 dementia incident cases detected at the second follow-up (123 incident cases) and third follow-up (89 incident cases) including dead subjects.
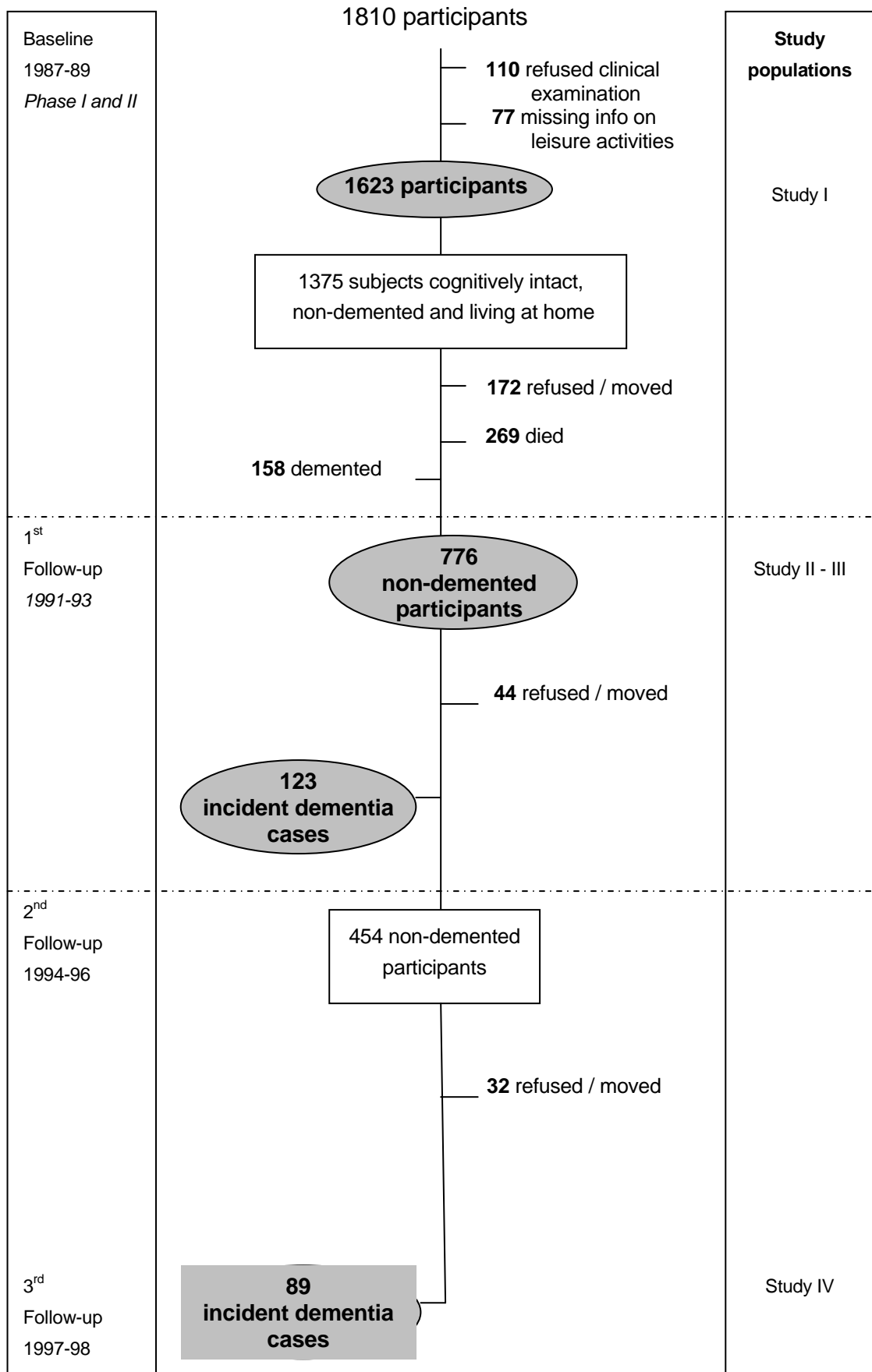
Figure 3. Study populations of studies I-IV.

3.2   DIAGNOSIS OF DEMENTIA

Dementia diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R) following a three-step diagnostic procedure [78].

First, a preliminary diagnosis was made by the examining physician. Second, all cases were independently reviewed by a specialized clinician and a second diagnosis was made. If the diagnoses were in disagreement, a third opinion was obtained and the concordant diagnosis was accepted.

For those participants who had died before the third follow-up examination of the project, information regarding their health status was obtained from the Computerized Inpatient Register System, which is a registry of discharge diagnoses from all hospitals in Stockholm since 1969. The individual hospital records, discharge diagnoses, as well as the death certificates were collected and extensively examined by a senior physician following the same three-step diagnostic procedure. When only discharge diagnoses from hospitals or death certificates were available, the reported diagnosis was accepted [79].

The age at dementia onset was assumed to be the age at midpoint between either the dates of two clinical examinations or the dates of clinical examination and death.

3.3 ASSESSMENT OF LEISURE ACTIVITIES AND LIFESTYLE FACTORS

Information on leisure activities and lifestyle factors was obtained from the participants through a personal interview by trained nurses at baseline of the project (1987-89).
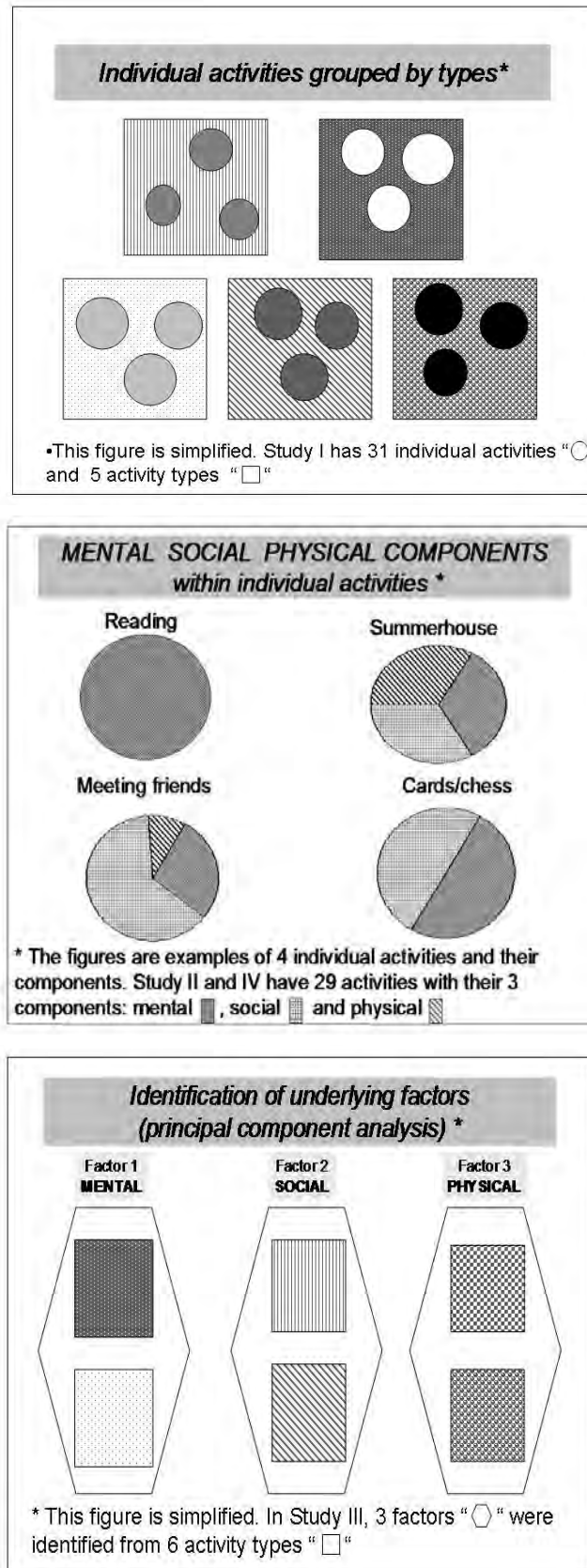
The subjects were asked the following questions:

1. a) Do you have any hobby(ies) in which you participate regularly?
b) If yes, which one? c) How often do you participate in your hobby(ies)?

2. a) Are you regularly participating in any professional association, pensioner's association, or other organizations? b) How often are you active in this organization/association?

3. a) Whether he/she has any children and close friends, respectively, and b) The frequency and satisfaction of contacts with them**.**

All four studies refer to questions 1.a) and b).

In **Study III**, the frequency of participation is taken into consideration as well as additional information on lifestyle factors (questions 2 and 3). Question 1.c) was coded: 1 = never, 2 = less than weekly, 3 = at least weekly; question 2.b) referring to *organizational activities* was coded: 1 = no or less than monthly participation, 2 = monthly, 3 = at least weekly; and question 3.b) referring to *social activities* was coded: 0 = less than weekly contact with friends or no children, or weekly unsatisfying contact, 1= at least weekly satisfying contact with friend(s) and/or family.

Leisure activities were analyzed and explored in different ways depending on the aim of the study. The different models used in this thesis are shown in Figure 4 and Table 5.

Individual activities grouped by types*

•This figure is simplified. Study I has 31 individual activities "○" and 5 activity types "□"

In **Study I**, the leisure activities were first reported into 31 activities and then grouped into five types (**mental, social, physical, productive** and **recreational**) according to their major characteristic. The categorisation of activity types was determined by two independent raters who had an agreement of 90% in the activity type groupings. The remaining 10% of the activities were discussed by the two raters until a consensus was reached.

MENTAL SOCIAL PHYSICAL COMPONENTS within individual activities *

Reading   Summerhouse

Meeting friends   Cards/chess

* The figures are examples of 4 individual activities and their components. Study II and IV have 29 activities with their 3 components: mental ▮ , social ▦ and physical ▨

In **Studies II** and **IV**, the leisure activities were first reported into 29 activities. A **mental, social** and **physical** component score was assigned to each of the activities by the researchers and a sample of elderly persons. The correlation between the researchers' and the elderly subjects' ratings was 0.86. The grading of the 3 components was coded as: 0 = none, 1 = low, 2 = moderate, 3 = high.

Identification of underlying factors (principal component analysis) *

Factor 1 MENTAL   Factor 2 SOCIAL   Factor 3 PHYSICAL

* This figure is simplified. In Study III, 3 factors "⬡" were identified from 6 activity types "□"

In **Study III**, lifestyle factors were grouped as follows: *1. Intellectual activities*: e.g., reading books; *2. Outdoor Cultural activities*: e.g., attending theater; *3. Fitness activities*: e.g., practicing active sports; *4. Productive activities*: e.g., gardening; *5. Social activities*: e.g., contacting children/friends; *6. Organizational activities*: e.g., participating in association. Three dimensions were identified with principal component analysis: **mental** (1 & 6), **social** (4 & 5), and **physical** (2 & 3).

Figure 4. Three different models analyzing leisure activities.

Table 5. Classification of leisure activities in the four studies

Study I	Study II and IV			Study III
*31 activities * grouped in 5 types* according to their major component	*29 activities * with their components,* *each scored by a 4-grade scale* (0 = none, 1 = low, 2 = moderate, 3 = high)			*6 activity types grouped in 3 factors* *identified* by principal component analysis

Study I	Study II and IV	MENTAL SCORE	PHYSICAL SCORE	SOCIAL SCORE	Study III
MENTAL ACTIVITIES: reading, cultural interest, cultivating cultural and political interests, doing cross-words, attending courses, painting, writing, playing music, playing the stock market, playing solitaire	Literature	3	0	0	**MENTAL FACTOR**
	Handicraft	2	1	1	**Intellectual**: reading books/newspapers, writing, studying, doing crosswords, painting, drawing and card/game playing
	Crossword or puzzle	3	0	0	
	Political/cultural interests	3	1	3	
	Cards/chess	3	0	3	**Organizational**: participating in any professional association, pensioner association, or other organizations
	Summerhouse	2	2	2	
PHYSICAL ACTIVITIES: walking, playing sports	Courses	3	1	2	
	TV	2	0	0	**SOCIAL FACTOR**
	Theatres/concerts	3	1	2	
SOCIAL ACTIVITIES: playing cards, going to the theatre, attending cultural events, meeting friends, travelling, collecting, singing, attending church activities, rehabilitation therapy	Sport	1	3	2	**Productive**: gardening, housekeeping, cooking, working after retirement, doing volunteer work, sewing, knitting, crocheting, and weaving
	Exhibitions /museums	3	1	1	
	Friends	2	1	3	
	Walks	1	3	1	**Social**: contacting children and close friends frequently and with satisfaction
	Radio	2	0	0	
	Travels	3	2	2	
PRODUCTIVE ACTIVITIES: making handicrafts, working, practicing outdoor activities, taking care of family and others, gardening, cooking, housekeeping	Gardens/flowers	2	2	1	**PHYSICAL FACTOR**
	Paintings/photo	3	0	0	
	Family/charity	2	2	3	
	Outdoor activities	2	3	2	**Outdoor cultural**: attending theater, concert and art exhibition, travelling
	Collections	3	0	0	
RECREATIONAL ACTIVITIES: watching TV, listening to the radio, playing bingo, reminiscing	Cooking	2	1	1	
	Writing	3	0	1	**Fitness**: practicing active sports, swimming, walking, and gymnastics
	Housekeeping	1	2	0	
	Church activities	2	1	3	
	Music	2	1	2	
	Solitaire	2	0	0	
	Stock market	3	0	0	
	Bingo	2	1	3	
	Singing	2	1	2	

* **As Study I** consisted of institutionalized, demented and non-demented participants, it included two leisure activities (rehabilitation therapy, reminiscing) that were not included in **study II**.

3.4 ASSESSMENT OF COVARIATES

Information about age and gender was derived from the National Population Register. Information about the highest level of formal education was collected through personal interview. Cognitive function was measured with the MMSE [77]. Physical function or dependence was defined as disability in at least one of the basic activities of daily living (ADL): bathing, dressing, toileting, continence, feeding, or transfer [80]. Depressive symptoms were assessed by two self-reported symptoms and assessed as: often being in a low mood and/or feeling lonely. These two symptoms are included in the Center for Epidemiological Studies-Depression Scale (CES-D) Scale [81].

Data concerning diseases occurring before baseline were obtained by reviewing hospital discharge diagnoses through the Stockholm Computerized Inpatient Register System. These diseases were diagnosed according to the International Classification of Disease, 8th edition [82]: coronary heart disease (ICD-8: 410-414), cerebrovascular disease (ICD-8: 430-438), diabetes mellitus (ICD-8: 250), malignancy (ICD-8: 140-208 and 230-239) and hip fracture (ICD-8: 820). Comorbidity was defined as having one of these diseases.

Information on marital status, living arrangement, parenthood, close social ties, and frequency of satisfaction with these connections were obtained in a personal interview by trained nurses at baseline of the project. A four-item social network index was constructed in a previous study [83]. Both quantitative and qualitative aspects of the social network were assessed. In **Study I**, this social network index was used, but reduced to three items (poor or limited, moderate, rich) since only a few people had a poor social network. In **Study IV,** the index was further aggregated to rich and moderate vs. poor and limited since a limited number of participants had a rich social network. In **Study III**, living arrangement was defined as living with a spouse/partner vs. living alone since the social activity in this study included contact with children and friends.

Age, gender and education were collected at baseline and considered as basic potential confounders in all four studies. Additionally, cognitive function, physical function, depressive symptoms, and comorbidity were considered as additional potential confounders in all studies. In **Study III**, additional adjustment for living arrangement,

and in **Study I** and **IV** for social network, was performed. All covariates were collected at baseline of the project, contemporary to leisure activity assessment.

3.5   STATISTICAL ANALYSES

Table 6 summarizes the specific analyses for each study, the outcome variables, the determinants, and the potential confounders that were considered in the four studies.

Table 6. Statistical models used in the four studies

Studies	Major determinants	Outcome	Covariates	Statistical model	Analytical strategy*
Study I	No determinant as the design is cross-sectional	Participation in leisure activities	Age, gender, education, social network, mental disorders, somatic diseases, physical limitation	Logistic regression	First, the mean and standard deviation of the number of activities for each studied factors were calculated. Logistic regression analyses were performed to estimate the participation in 'at least one activity' and in mental, social, physical, productive, and recreational activities in relation to the contextual and health factors.
Study II	Leisure activities (mental, physical, social components)	Incident dementia	Age, sex, education, MMSE, comorbidity, depressive symptoms, ADL	Cox proportional hazards models	The first set of analyses were performed for each of the mental, physical and social components, contrasting subjects with one or more moderately/highly scored activities with subjects without any moderately/highly scored activity to the median value. Second, the sum of scores for each component was analyzed as a) continuous variables, b) four groups with a similar number of cases, c) then, two groups dichotomized according to the median value, and d) finally, to capture the combined effect of the three components, combinations were created using the sum score for each component after dichotomization according to the median value.
Study III	Leisure activities/Lifestyle factors: mental, organizational, productive, social and fitness, outdoor cultural activities (mental, physical, social factors)	Incident dementia	Age, sex, education, MMSE, comorbidity, depressive symptoms, ADL, living arrangement	Factor analysis (principal component analysis), Cox proportional hazards models	First, principal component analysis was used to identify the internal structure of interrelated lifestyle factors including engagement in mental, fitness, productive, organizational, social and outdoor cultural activities. Second, the identified three underlying lifestyle factors (mental, social, physical) were analyzed as a) continuous variables, b) quartile and tertile categorizations, c) then the tertiles were dichotomized, and d) finally, the three identified factors were integrated into an Active Lifestyle Index based on the previous dichotomization.
Study IV	Leisure activities (mental, physical, social components)	Age at dementia onset	Age, sex, education, MMSE, comorbidity, depressive symptoms, ADL, social network	Linear regression	First, the mental, social and physical component scores assessed in study II were analyzed as a) continuous variables, b) quartile and tertile categorizations, and c) then the tertiles were dichotomized, and d) finally, the three components were integrated into an index based on the previous dichotomizations

3.6 ETHICAL CONSIDERATIONS

All eligible persons living in the Kungsholmen district were contacted personally with an individualized letter explaining the content, duration, purpose of the study, as well as the importance of participation, but clearly stating that it was voluntary and that at any time they could discontinue participation. A nurse in order to check their availability and to book the first visit then directly contacted them via telephone. For all participants, informed consent was requested directly at the screening evaluation. The aims of the project were explained and confidentiality of the information provided by the subjects or informants was stressed. If the persons were severely cognitively impaired, a proxy was asked for consent (usually a close family member). It was agreed, as a rule, that the examination or interview should be interrupted if the person in any way expressed anguish or discomfort, regardless of whether informed consent had been given directly by the person or by a proxy.

All four studies included in this thesis used data collected from Phase I to Phase V of the project as well as data from medical records, death certificates, and the inpatient register database. For each phase, approval from the Ethics Committee at the Karolinska Institutet was obtained.

Death certificates and the Stockholm Inpatient Register data: Dnr. 99:025; 01:020.

| Baseline survey (Phase I and II): | Dnr. 87:148 |

Baseline survey (Phase I and II):   Dnr. 87:148

First Follow-up (Phase III):   Dnr. 90:251

Second follow-up (Phase IV):   Dnr. 94:122

Third follow-up (Phase V):   Dnr. 97:413

In addition, all researchers working with the Kungsholmen Projects database follow the guidelines of the Swedish Council for Research in the Humanities and Social Sciences (HSFR); the principles of autonomy and integrity, the rule of consent, and the demand for research [84].

4 RESULTS

All four studies explored participation in leisure activities in an urban Scandinavian population born 1914 or earlier, 75 years-old or older at the beginning of the project and living in the Kungsholmen area, which is an island in Stockholm inner city. At baseline of the study, the mean age of the eligible participants was 82-years old (SD ± 5 years). They were mostly women (76%), and relatively highly educated (only two with less than 2 years education).

4.1 STUDY I

The pattern of participation in leisure activities in relation to contextual factors as well as to mental and physical health was described among the 1623 eligible participants at baseline of the project, including the demented and institutionalized participants.

The participants listed all the leisure activities they were engaged in. These activities were successively organised into 31 major categories. About 16% of the young-old (75-79 years old) participated in 'challenging' activities, such as working and making handicrafts, but the participation rate in these activities declined with increasing age. On the contrary, some activities such as gardening, travelling or writing kept a steady, although low, level of participation (3%). Activities that are more passive were more popular among the oldest-old (85+). About 6% reported watching TV or listening to the radio. In general, men were more active than women were. Several activities were gender-specific. About 17.5% of the men engaged in political and cultural interests or professional activities, whereas 16% of the women made handicrafts or did crosswords (Figure 5).
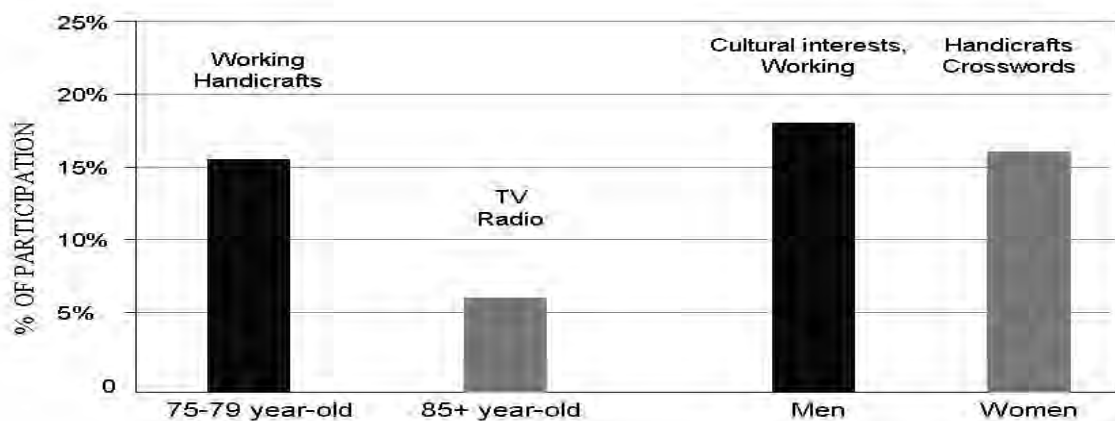

Figure 5. Participation in the most popular activities by age and gender.

The leisure activities were further grouped into mental, social, physical, productive and recreational activity types. The most common activity type was mental activity (43%), whereas the least common activity type was physical activity (9%) (Figure 6). The most common individual activities included one productive activity (making handicrafts) and two mental activities (reading, cultivating political and cultural interests) and these were enjoyed by at least 10% of our study population.
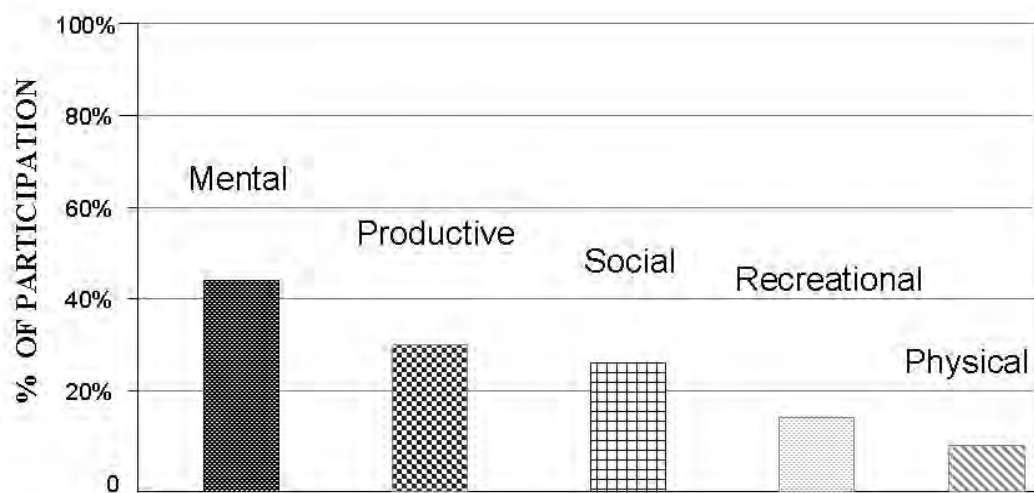

Figure 6. Percentage of subjects participating in different leisure activities according to activity types. The cumulative percentage is over 100% as the participants can be active in more than one activity type.

The pattern of participation in the five activity types varied depending on the demographic and contextual factors, and health conditions. In summary, the findings of Figure 7 reveal the unique relation of each of the studied factors to the specific activity types. Participation in mental activities was impacted by older age, lower education, mental disorders and physical limitation, whereas participation in physical activities was influenced only by physical limitation.
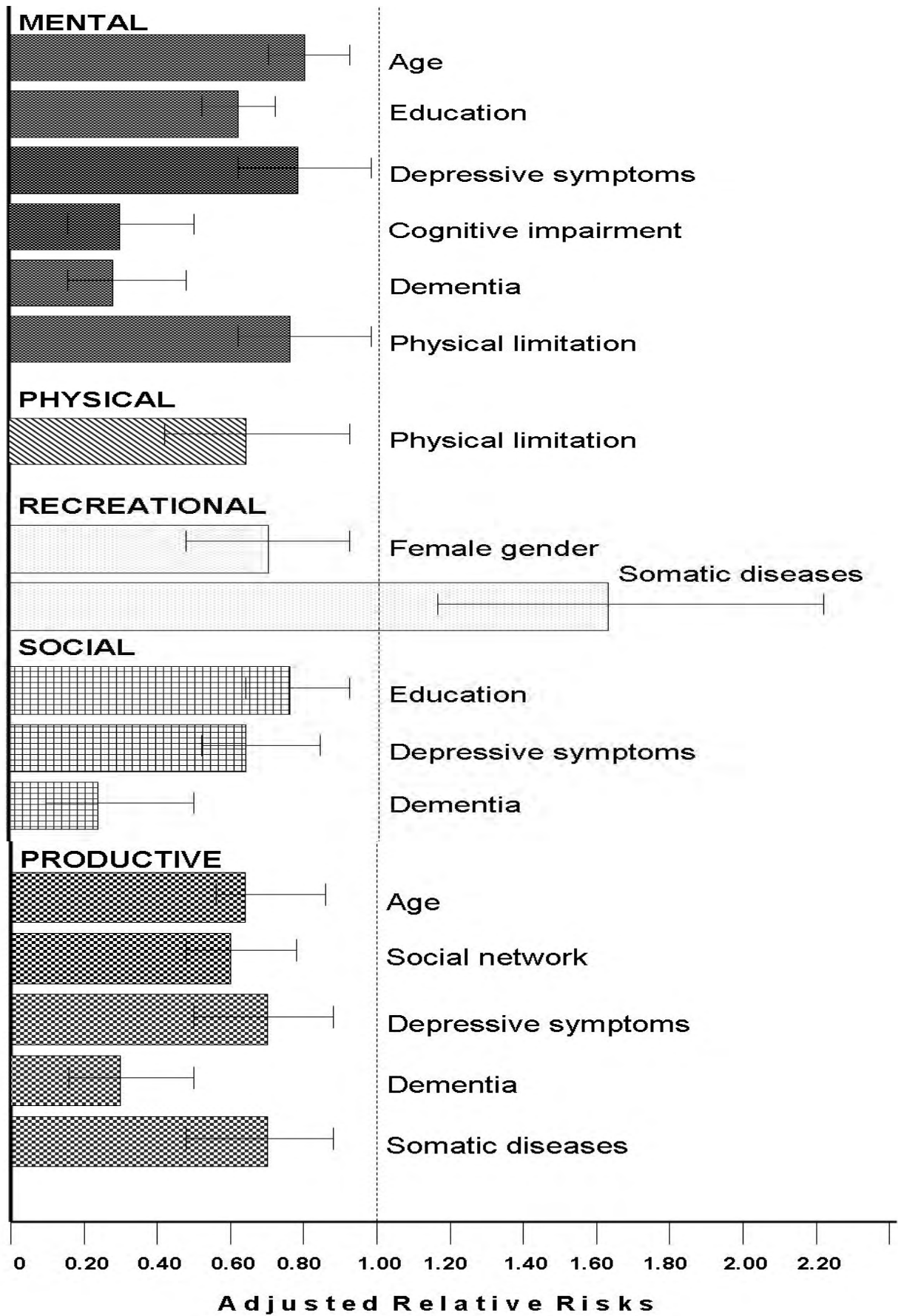
Figure 7. Participation in the five activity types in relation to demographic, contextual and health factors. The bars represent the significant adjusted Relative Risks (95% CI).

4.2   STUDY II

Studies II, III and **IV** are longitudinal studies with a period of six (**Study II**) and nine years of follow-up (**Study III and IV**). The baseline characteristics of the study population and the incident dementia cases are reported in Table 7.

Table 7. Baseline (1987-1989) characteristics of the cohort subjects and distribution of the incident dementia cases occurring during the second follow-up (1994-1996) and the third follow-up (1997-98)

Baseline characteristics	BASELINE Participants (n=732)		2ND FOLLOW-UP Incident dementia cases (n=123)		3RD FOLLOW-UP Incident dementia cases (n=212)	
	n	%	n	%	n	%
Age (years)						
75-79	364	49.7	36	29.3	89	42.0
80-84	232	31.7	55	44.7	77	36.3
≥85	136	18.6	32	26.1	46	21.7
Sex						
Female	543	74.2	93	75.6	167	78.8
Male	189	25.8	30	24.4	45	21.2
Education*						
0-7 years	386	52.5	70	56.9	119	56.1
8-10 years	164	22.6	24	19.5	43	20.3
>10 years	179	24.9	29	23.5	49	23.1
MMSE score						
27-30	554	75.7	85	69.1	149	70.3
24-26	178	24.3	38	30.9	63	29.7

* For three subjects, information was missing.

In Study II, a mental, social and physical component score was estimated for each leisure activity. The sum score was analyzed first as continuous variable, then in four groups with similar number of cases and then in two groups dichotomized according to the median value of the total scores of each of the three components. The cutoffs differed as the mental score ranged from 0 to 18, the physical score from 0 to 12 and the social score sums from 0 to 13. The mental component differed from the physical and social components in that it had no persons with a 0 score, aside from the group of subjects who participated in no activities at all. All of the three components' scores distributions were positively skewed. The higher cutoffs for each of the components were associated with lower risk of dementia (Table 8).

Table 8. Relative risks* and 95 % CI of dementia in relation to degree of estimated mental, physical and social component score in baseline leisure activities

High score in	No. of subjects	No. of cases	RR (95 % CI)*
MENTAL component (0-3 vs. 4-18)	372	48	0.71 (0.49-1.03)
PHYSICAL component (0 vs. 1-12)	447	56	0.61 (0.42-0.87)
SOCIAL component (0-1 vs. 2-13)	368	48	0.68 (0.47-0.99)

* Adjusted for age, sex, education, baseline MMSE, comorbidity, physical functioning and depressive symptoms.

The mental, physical and social components were further merged into an index with four categories: 1) low score in all three components, 2) high score in one component, 3) high score in two components, and 4) high score in all three components. Having high scores in two or three of the components was associated with a significant reduction in risk of dementia (Figure 8). Having high scores on two or more of the components (categories three and four together) had a RR=0.53, 95% CI: 0.36-0.78, compared to high score in one or none of the components.
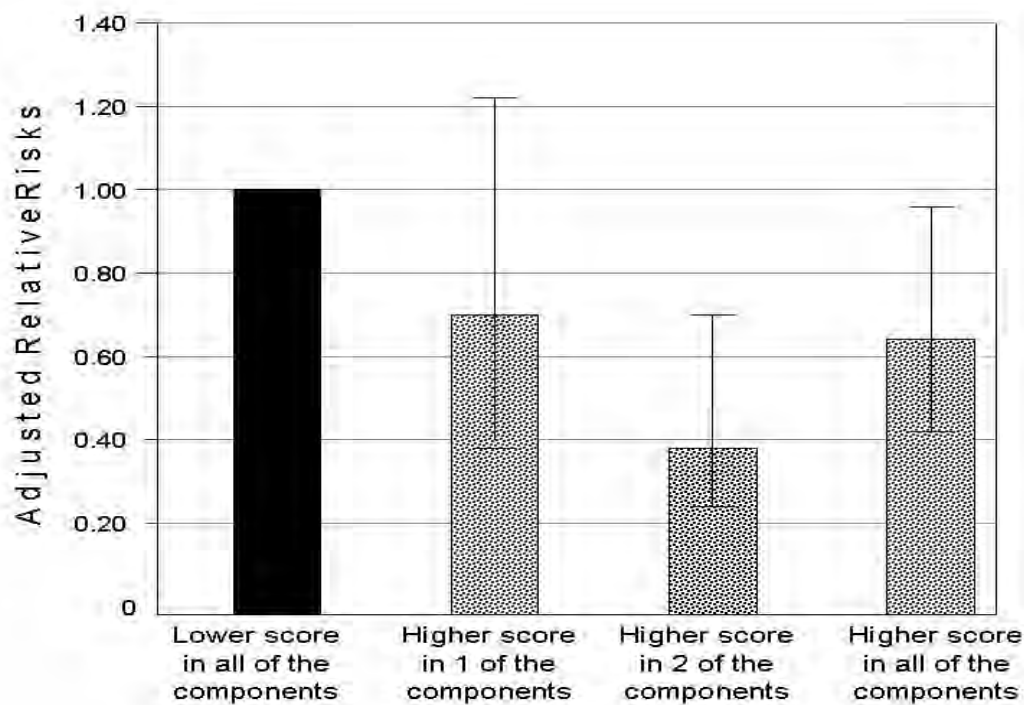
Figure 8. Relative risks* 95 % CI of dementia associated with combinations of higher or lower mental, physical and social score (index).

* Adjusted for age, sex, education, baseline MMSE, comorbidity, physical functioning and depressive symptoms.

4.3 STUDY III

In **Study III**, principal component analysis was used to identify underlying factors from six interrelated lifestyle variables. Three factors were identified: p*hysical* factor including: fitness and outdoor cultural activities; *mental* factor including intellectual and organizational activities; and *social* factor including social and productive activities.

An independent protective effect of social factor (RR=0.79; 95% CI: 0.69-0.99) and a trend of physical (RR=0.96; 95% CI: 0.83-1.11) and mental (RR=0.92; 95% CI: 0.80-1.06) factors on dementia risk were observed when the factor scores were analysed as continuous variables, after controlling for age, sex, education, comorbidity, cognitive and physical functioning, living arrangement and depressive symptoms.

The cutoffs used in this study were based on the continuous factor scores generated with principal component analysis. A clear pattern of protective effects of physical, mental and

social factors on dementia risk was observed when using a categorisation based on tertile distributions of the factor scores in the multivariate regression models (Figure 9).
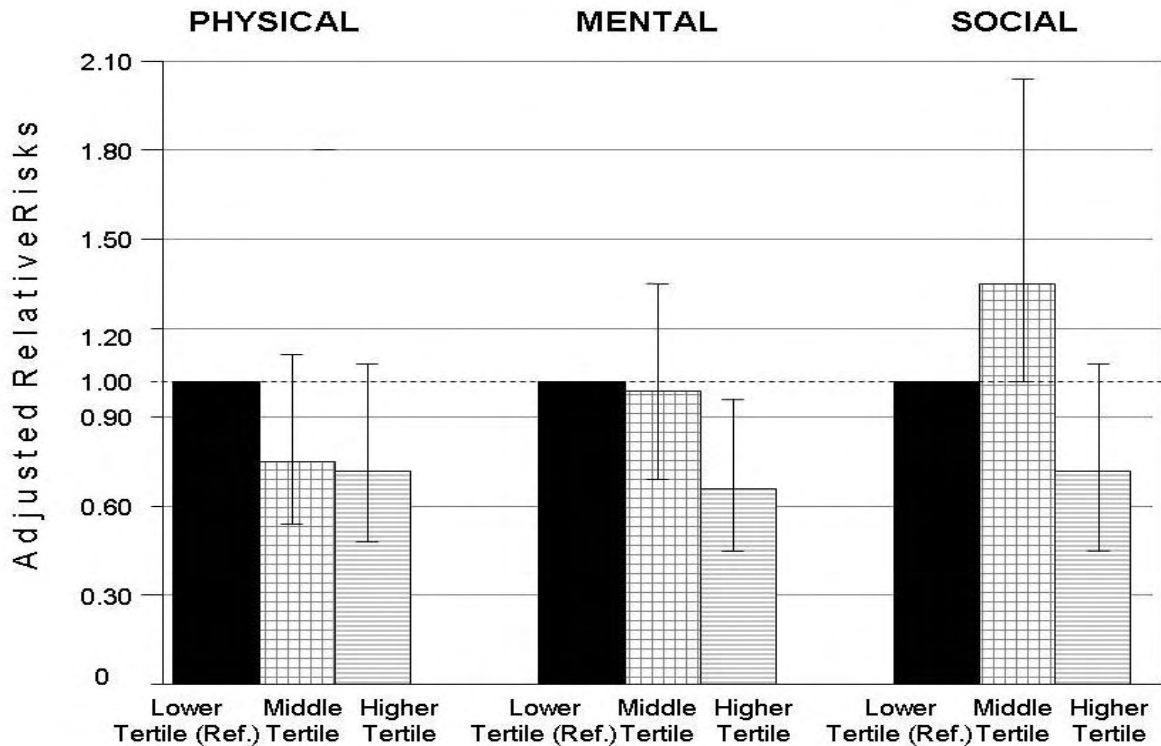

Figure 9. Relative risks* and 95% CI of incident dementia in relation to the tertile distributions (factor scores) of physical, mental and social factors.

* Adjusted for age, sex, education, MMSE, comorbidity, physical functioning, depressive symptoms and living arrangement at time of exposure assessment.

According to the results, we grouped the variables based on the tertile distributions into dichotomized variables. Higher physical (upper two tertiles) (RR=0.69; 95% CI: 0.49-0.97) and social (higher tertile) (RR=0.63; 95% CI: 0.46-0.87) factor scores were significantly associated with reduced risks of dementia adjusting for all covariates, while the higher mental (upper two tertiles) (RR=0.79; 95% CI: 0.57-1.09) factor scores showed a tendency towards protection. No interactive effect was found between APOE genotype and physical, mental, or social factors on risk of dementia.

The dichotomized physical, mental and social factors were further integrated into a four category index according to their possible combinations. A three level *Active Lifestyle Index* was created: 1) *Low level*: low scores in physical, mental and social factors, or one high score in either one of the three factors; 2) *Moderate level*: high scores in two of the three factors; and 3) *High level:* high scores in all the three factors. This index was then related to incident

dementia in a Cox regression model including several covariates as possible confounders (Figure 10).
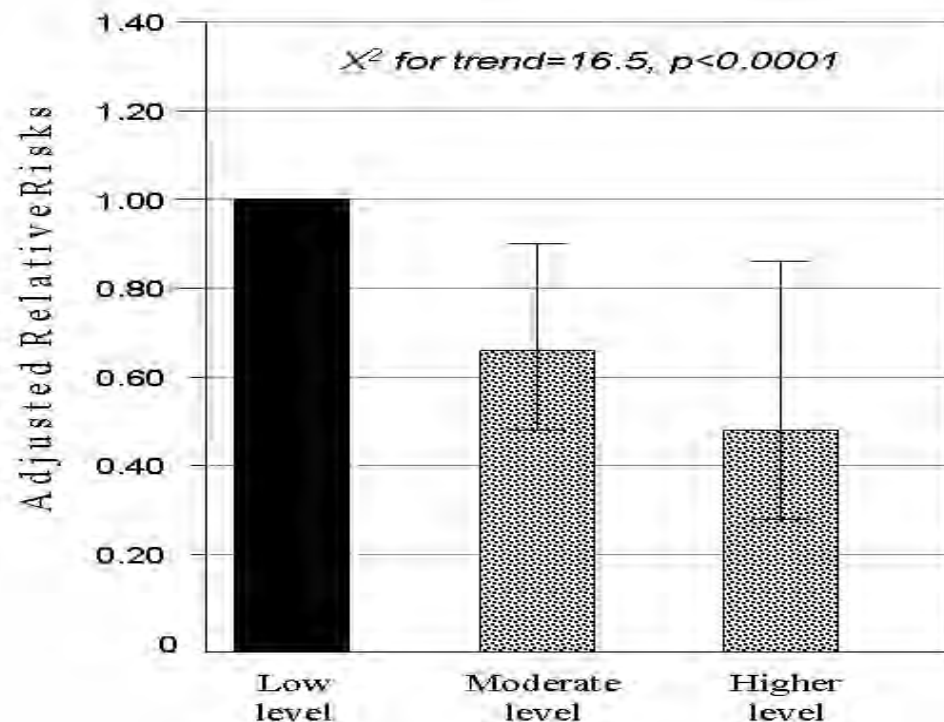

Figure 10. Relative risks* and 95% CI, for dementia in relation to the Active Lifestyle Index.

* Adjusted for age, sex, education, MMSE, comorbidity, physical functioning, depressive symptoms and living arrangement at time of exposure assessment.

4.4 STUDY IV

In **Study IV**, linear regression was used to examine the associations between the lifestyle factors (mental, social and physical component scores) and age at dementia onset. General linear models were used to estimate the mean age at dementia onset in relation to the activity level. When first analyzed as continuous variables, the multi-adjusted model indicated that only greater score sums in the physical component appeared to postpone dementia ($\beta=0.22$, $P=0.04$) after controlling for age, sex, education, comorbidity, cognitive and physical functioning, social network, and depressive symptoms.

In order to estimate the effect of the three components on dementia onset, each of the component scores was categorized into tertiles. Based on the results, each of the three factors

was contrasted as "upper two tertiles vs. lower tertile". Higher physical (β=0.59, P<0.01) and social (β=0.53, P<0.01) component scores were associated with delayed dementia onset, while the mental component showed only a tendency towards a protective association (β=0.43, P=0.06).

The dichotomized physical, mental and social factors were further integrated into a three-category index: 1) Low activity lifestyle: lower level in all three components - mental, physical and social; 2) Moderately active lifestyle: higher level in one of the components; 3) Highly active lifestyle: higher levels in at least two of the components. The highly active lifestyle was significantly related to later dementia onset (β=0.62, P<0.01) compared to low activity and the *test for trend* revealed a clear significant difference between the levels of activity (P<0.01).

The mean age at dementia onset in relation to the index was also assessed. After adjustment for age, gender, education, social network, comorbidity, depressive symptoms, and cognitive and physical functioning. The effect was not so strong as the delay reached a maximum of 8 months. However, we have to consider that this is an old population with an average age at dementia onset of 86 years and 5 months (standard deviation 4.1) (Table 8).

Table 8. Mean age at dementia onset for the mental, physical and social components (combination of higher, mid- or lower tertiles)

INDEX	Mean age		
	n=212	(SD)*	*P*
LOW ACTIVITY Lower levels in the mental, physical and social components	51	86 years *and* 2 months (4.0)	
MODERATELY ACTIVE LIFESTYLE Higher level in one of the components	36	86 years *and* 4 months (4.1)	
HIGHLY ACTIVE LIFESTYLE Higher levels in at least two of the components	125	86 years *and* 10 months (4.1)	
Test for trend			*<0.01*

*Adjusted for age, gender, education, social network, comorbidity, depressive symptoms, cognitive and physical functioning.

5 DISCUSSION

In this thesis, pattern of participation in leisure activities and their influence on dementia development was investigated using cross-sectional as well as six- and nine-year follow-up data derived from the Kungsholmen Project, which included an urban community cohort of 75+ years old persons. The main findings are summarized in the following points:

- Older age, female gender, low education, poor or limited social network, mental disorders, and physical limitation were the factors correlated with a decreased engagement in 'at least one leisure activity'. Demographic, contextual and health related factors were differentially associated with the specific activity types (mental, social, physical, productive or recreational).

- Engagement in leisure activities with higher scores in the mental, social or physical component was associated with a decreased dementia risk, and being involved in a broad spectrum of activities appears to be the most beneficial.

- We confirm the same inverse association between active life and dementia risk by using activity factors derived from principal component analysis. A higher level of either mental, social or physical factor score was associated with a decreased risk of dementia, and a dose-response association was observed when dementia risk was related to the combined effect of the three factors.

- When the mental, social and physical components were integrated into an index, we found that the broader the spectrum of participation (higher levels in at least two of the components) the later the age at dementia onset.

5.1 INTERNAL VALIDITY

5.1.1 Selection bias

A dementia-free cohort was identified by a two-phase design at baseline of the Kungsholmen Project, through a screening phase for all participants and a clinical phase for those who screened positive (MMSE<24) and a sample of those who screened negative (MMSE≥24) [75]. In the screening phase some very mild dementia cases, in particularly those with high

education, may have been missed and consequently been classified as non-demented. A syndrome such as dementia influences lifestyles; thus, misclassification in the identification of the dementia-free cohort may have led to an overestimation of the association between dementia and participation in leisure activities. However, in a previous paper we estimated a low false negative rate of 2.5% that should introduce only a small bias, if any [76].

The dropouts are another source of potential selection bias. Of the 2368 older inhabitants of the Kungsholmen Parish invited to participate, 558 (24%) never took part in the project due to death (32%), refusal (53%), or moving from the area (15%). In comparison with those who participated in the screening phase, the dropouts due to death were older and more often men. The ones who refused or moved did not differ from the participants with regard to age and gender. As the level of participation among the non-participants was unknown to the researchers, we can only hypothesize that there may have been a systematic bias if the persons in the prodromal phase of dementia were more likely to refuse participation to the project. This may have led to an underestimation of the association between inactivity and risk of dementia as there is a high probability that participants with prodromal dementia will develop dementia at follow-up [85].

Also, the participants that were lost at follow-up have a tendency to have different probabilities of developing dementia than the ones who stayed in the cohort. Out of the 1473 non-demented participants identified at baseline, 172 (12%) were lost to follow-up due to refusal or moving out of the area. The dropouts were not different with respect to baseline demographic features except for that they were older and affected by vascular disease [86]. Among those who remained free of dementia at the first follow-up, only 44 (6%) and 32 (7%) participants refused the second and third follow-ups, respectively. Due to this low dropout rate it is probable that the dropout bias did not greatly affect the findings of **Studies II, III, and IV.**

5.2   MISCLASSIFICATION OF DISEASE

All dementia diagnoses were clinically based, as neuroimaging was not feasible in a large population-based study like the Kungsholmen Project. This may have affected the diagnostic accuracy, but the diagnostic procedure was made through consensus among three independent physicians and has been validated with a relatively high overall agreement

(κ=0.70) on diagnosis [78]. Although misclassification of disease may have occurred, it is likely that it was non-differential. However, there might be a "diagnostic bias" due to education since the participants with lower education might have been diagnosed earlier which might have influenced marginally the results in all studies [85].

5.2.1 Misclassification of the leisure activities

The exposure may also be biased by misclassification. Open-ended questions were used to obtain information concerning participation in leisure activities. There is always a risk of a systematic difference in how people report activities, which may be related to the outcome or some other confounders. In **Study I**, information from informants may be less accurate than from subjects themselves. However, our findings are in line with two earlier studies, using activity specific questionnaires, suggesting that demented elderly are less active [87] [88]. In **Studies II**, **III** and **IV**, we repeated the analyses excluding the participants who did not report any activities at all (as well as treating them as a separate group), and the results were similar [85]. In addition, we have used different estimations of the exposure, first using the predominant components of each specific activity [72], then scoring the different physical, mental and social component in each activity (Study II) and finally using factor scores from the principal component analysis (Study III). We obtained the similar results.

5.2.2 Possible confounders and inverse causality

The observed associations may have several explanations other than the beneficial effect of an active life on dementia risk. First, the premorbid cognitive capability of an individual to engage in certain activities might mediate or confound the reported associations [89] [90]. Indeed, no studies specifically controlled for this potential confounder, but most of them explored this association and controlled for baseline mental function and education, which should be appropriate surrogates. In addition, in our studies the associations are adjusted for cognitive functioning at baseline and education. Second, participation in mental, social and physical activities might be a sign of a good lifestyle in general, which could be linked to better overall physical and mental-health. Third, although the relationship between participation in leisure activities in late-life and dementia risk has been explored longitudinally, the reduced social network and activity could be determined by the prodromal cognitive and depressive

symptoms that have been reported in early phases of dementia [91] [92]. In order to exclude the inverse causality we have excluded all incident dementia cases between baseline and first follow-up, we have excluded subjects with MMSE$\leq$23 and the persons leaving in an institution, and we have adjusted for baseline cognitive performances. Finally, some analyses have been repeated in a subsample of subjects with MMSE$\geq$26.

5.2.3 Strengths

This thesis has many strengths. First, the cohort of the Kungsholmen Project involved all older people living in an urban community. Second, an open-ended question was used to obtain information about leisure activities directly from the participants and informants in case of cognitive impairment or dementia. This method of ascertainment allows the gathering of a large range of answers based on the personal perception of what is a leisure activity for the participants, and capture a wide variety of possible and sometimes unexpected answers [93].

In **Studies II, III** and **IV**, the influences of impaired cognition and institutionalization on leisure activities and dementia have been eliminated by including only participants who lived at home and with good cognitive functioning. In addition, lifestyle variables were assessed at least 6 years before dementia diagnosis to reduce the influence of preclinical dementia. Finally, additional analyses were performed in a sub-population with intact cognition and physical health, for all three studies, and the results were confirmed.

5.3 INTERPRETATIONS OF THE FINDINGS

In **Study I**, the various patterns of participation in leisure activities among the baseline population of the Kungsholmen Project (including the demented, cognitively impaired and institutionalized participants) were described cross-sectionally in relation to demographic, contextual and health related factors. It was found that the activity pattern is influenced by several interrelated factors.

First, we assessed participation in "at least one leisure activity". As expected, we found decreased participation in activies among the older participants. At older ages, more time might be spent in obligatory activities, such as IADL and ADL, which constrains the amount of time devoted to leisure activities [94] [95]. In regards to gender differences, we found that

women were less active, so we can speculate that they might not report certain activities, such as cooking or household chores, as they do not perceive these activities as leisurely. It is important to note that elderly women may have reduced opportunities for leisure activities due to lower socio-economic status [96]. In addition, lower education was found to be associated with decreased activity. In fact, low education can be an indicator of lower socio-economic status, and limited financial means may lead to a more restricted choice of leisure activities [97] [98] and influence lifestyle choices [99]. In addition, our findings revealed that persons with a limited social network are less active; it is likely that these individuals have less incentive to participate in leisure activities. Finally, as expected, people with physical limitation and mental disorders were less active [100].

When we assessed participation in leisure activities in relation to the five activity types, surprisingly, advanced age was related to decreased participation in mental activities, regardless of health conditions including sight. As this type of activities is suitable even in the very old age [101], this finding can be explained by a general decrease of interest with increasing age. In contrast, less participation in productive activities in advanced age is expected since these activities are rather demanding by nature [102]. Our finding that women participate less in recreational activities is consistent with an earlier report showing that women tend to spend (or report) more time in housework and cooking activities rather than recreational activities [41]. Lower education was found related to less participation in mental and social activities. These types of activities probably attract participants with a level of education beyond elementary, due to the intellectual component of most of these activities. A limited social network was related to less participation in productive activities, which is in line with our previous study suggesting that a number of these activities have an important social component since their "product" is for others or made to be shared with others [85].

Participants with depressive symptoms and dementia were less active in mental, social and productive activities. We can speculate that either living with dementia or experiencing loneliness and/or feeling in low mood are mental states that prevent the elderly person from being fully active. Some mental disorders are often connected to mental fatigue and physical exhaustion which naturally restrain a person from participation in challenging activity types [103]. However, the cognitively impaired persons had less participation only in mental activities suggesting that their cognitive limitation was no obstacle towards a relatively active life. In line with a previous report [104], a decrease participation in productive (30%) and an increased

participation in recreational activities (60%) were related to presence of somatic disease. Productive activities are rather challenging for an elderly person and some of them (e.g., cooking and housekeeping) need to be done regularly, which could be difficult in the presence of illness. On the other hand, recreational activities are static in nature and less cognitively and physically challenging, therefore it is sensible to think that these activities involved more people with somatic diseases. Finally, the participants with physical limitation were less active in physical and mental activities, which is in line with the finding that physical functioning is associated with cognitive functioning of older adults [105].

In **Studies II, III** and **IV**, we assessed longitudinally the relation between an active lifestyle and decreased dementia risk as well as delayed dementia onset. In **Study II**, we found that engagement in late-life in leisure activities with mental, social, and physical components is associated with decreased risk of dementia and that being involved in a broad spectrum of activities appears to be the most beneficial [32]. Although other researchers have acknowledged the fact that most leisure activities consist of several overlapping components, nobody to our knowledge, has attempted to separate the different components from each other [106]. As few older people engaged in vigorous exercise, the benefit of light physical components in activities that are not primarily physical, is especially noteworthy.

In **Study III**, we confirmed the results of paper II by using a different aggregation modality of the leisure activities. We found that the component, type and variety of the activities might be important [68]. In addition, this study included also participation in organizational activities, and contact with friends and family members. The results showed that the higher the score in mental, social or physical factors the higher the protection against dementia. Previous studies have predominantly focused on the impact of different types of activities on the risk of dementia [68 69 72 107]. Our results are in line with a previous review which concludes that an active and socially integrated lifestyle in late life may protect older people against dementia.

In **Study IV**, we found that higher level of participation in activities that have physical, mental and social components was associated with later dementia onset. The results showed that the highest level of participation was significantly associated with a delaying effect. Even though the mean age at dementia onset was not dramatically older for the ones with the highest level of participation, the effect was still significant. Many studies have investigated lifestyle as a protective factor on dementia incidence, but only a few have looked at lifestyle as

a delaying factor on dementia onset. Level of education has been found to affect the choice of leisure activities during the life course. Education might significantly affect dementia onset in term of occurrence and timing of dementia symptoms [90]. In line with our findings, a previous study of twin pairs showed that cognitive and social leisure activities in midlife probably reduce the risk of dementia by delaying its onset. However, no association was found with physical activity [74].

How might mental, social and physical leisure activities protect against dementia or delay the disease? Three etiological hypotheses may explain the beneficial effect of an active lifestyle on dementia risk. *The brain reserve hypothesis* might be the primary hypothesis explaining the effect of an active lifestyle as a protective delaying factor on dementia onset. This hypothesis speculates that some lifestyle factors, such as participation in leisure activities, delay the detection of dementia since the person is able to cope with cognitive demands longer despite the accumulated pathological lesions in the brain. Indeed, pathological processes in the brain need to accumulate to a certain extent in order to cause cognitive impairment sufficiently severe to become a clinically manifested dementia syndrome [108]. This level of cognitive impairment constitutes a threshold that marks the clinical onset of dementia. Avoiding or postponing this threshold represents one of the possible objectives of preventative strategies [85]. Animal studies suggest that different experiences can affect the structure of the brain, including vasculature, number of cells and synapses, and connections between cells even in the adult life [109] [110]. Although the extent to which this occurs in humans is still unknown, scientists generally believe in the existence of a 'reserve' in the brain that can explain the individual differences in coping with the dementing pathological processes [85]. The *vascular hypothesis* proposes that an active lifestyle may have a beneficial effect on cardiovascular diseases and stroke. Vascular factors and related disorders may be involved in the pathogenesis and progression of dementia [111] [112], supporting both a direct or indirect effect of severe atherosclerosis on dementia in old people [113]. *The stress hypothesis* suggests that active individuals have more opportunities to engage with others and to be physically active, leading to positive emotional states and lower stress [52]. According to the glucocorticoid cascade hypothesis, stress downregulates the hippocampal corticosteroid receptors and leads to corticosterone hypersecretion, which in turn dampens the feedback inhibition of the adrenocortical axis leading to further hypersecretion, that finally causes permanent loss of hippocampal neurons [114], resulting in dementia [115].

6 CONCLUSIONS

In conclusion, most people over 75 years of age report participation in at least one leisure activity. However, demographic, contextual and health factors influence differently on the activity types, suggesting that the older population cannot be regarded as an homogenous community in terms of dementia prevention and that many factors may impact the opportunity to enjoy an active lifestyle. Finally, our findings support the hypothesis that an active lifestyle in late life protects against dementia risk or delays the age of dementia onset and that the higher the level of engagement in a variety of activities, the stronger the protection. These findings highlight the public health importance of encouraging older persons to have an active lifestyle in order to reduce the risk or delay the onset of dementia.

7 GENERALIZABILITY

All populations have their own unique specificities and characteristics that need to be considered before generalizing the findings to different populations. The Kungsholmen Parish is a geographically-defined central area of Stockholm. Its population differed from other urban areas in Sweden since it had a higher proportion of pensioners, women, highly educated persons, and unmarried or divorced older persons. On the other hand, it was quite similar in terms of the health care system as other parts of the city. We may speculate that our findings are generalizable beyond Sweden and Scandinavia to older urban Western populations. However, some caution is needed in regards to the cohort effect since many societal changes took place during the 20th century that could have influenced the participation in leisure activities.

8 RELEVANCE

The findings of this thesis represent a contribution to the understanding of the etiology of dementia development. Our description of the leisure activity patterns in older persons is needed and relevant at a public health level. Our results consistently found that participation in a variety of activities covering more than one of the mental, physical and social dimensions is more beneficial than the participation in only one type of activity. Such results emphasize the importance of promoting and giving access

to a large diversity of activities to older persons, which may reduce their risk to develop dementia or postpone the onset of the disease. At the individual level, awareness that an active lifestyle is associated with a reduced risk of developing dementia is important. It stimulates engagement with life, which, in the process, might also prevent other diseases such as depression and vascular disorders.

9 FUTURE DIRECTIONS

The four studies in this thesis have the potential to provide a basis for future exploration of different lifestyles at old age. However, it would be interesting in future studies to also consider activity patterns at different periods of life. In fact, The Swedish National Study of Aging and Care in Kungsholmen (SNACK) included a list of specific leisure activities in different life periods. The "SNACK" project follows a 60 year old or older population. At each follow-up, the participants were asked about their participation in leisure activities. Therefore, in the near future, the possibility will be given to observe any change over time in the leisure activity pattern in this population.

In the past ten years, several studies on this topic have shown that an active lifestyle in late-life protects against dementia. However, there are still remaining questions such as whether premorbid personality or intelligence may explain the reported association [116] [117]. Furthermore, the leisure activity "industry" is evolving rapidly and future cohorts of older persons are already exposed to "types" of technological stimulation that differ greatly from past cohorts, such as video games and daily use of computers. Also, inequitable opportunities between socio-economic classes have decreased. As predicted by Lawton in 1978, an increasing number of leisure activities that were then class dependent (playing golf), have been made more accessible to the general elderly population [118]. A recent study simulated activity patterns based on economic and demographic scenarios among the elderly Dutch population in 2020. The results showed that the future elderly will need to work longer, but will also increase their time spent in social/leisure activities [119].

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11 REFERENCES

1. United Nations Department of Economic and Social Affairs, Population Division. World Population Prospects. The 2004 Revision. New York: United Nations, 2005.

2. Marengoni A. Prevalence and impact of chronic diseases and multimorbidity in the aging population. Dissertation for doctoral degree. Karolinska Institutet, Stockholm, Sweden, 2008.

3. Statistiska Centralbyrån. Sweden's population, preliminary figures: largest population increase in nearly 40 years: Nr:362, 2008.

4. Westerholm B. Health and aging in Sweden. In Robinson M, Novelli W, Pearson, C. Norris, L (eds). Global health and global aging. San Francisco: Jossey-Bass: 157-8, 2007.

5. Qiu C, De Ronchi D, Fratiglioni L. The epidemiology of the dementias: an update. Curr Opin Psychiatry 2007; 20: 380-5.

6. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised (DSM-III-R). Washington, DC: American Psychiatric Association, 1987.

7. Fratiglioni L, Winblad B, von Strauss E. Prevention of Alzheimer's disease and dementia. Major findings from the Kungsholmen Project. Physiol Behav 2007; 92: 98-104.

8. Roman GC. Vascular dementia: distinguishing characteristics, treatment, and prevention. J Am Geriatr Soc 2003; 51: S296-304.

9. Xu W. Diabetes Mellitus and the risk of dementia. A population –based study. Dissertation for doctoral degree. Karolinska Institutet, Stockholm, Sweden, 2008.

10. Korczyn AD, Vakhpova V. The prevention of the dementia epidemic. J Neurol Sci 2007; 257: 2-4.

11. Jorm AF, Jolley D. The incidence of dementia: a meta-analysis. Neurology 1998; 51: 728–33.

12. Fratiglioni L, von Strauss E, Qiu C. Epidemiology of the dementias of old age. In Jacoby R, Dening T, Thomas A, and Oppenheimer C (eds). The Oxford Textbook of Old Age Psychiatry. London: Oxford University Press, 2007.

13. Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, Hall K, Hasegawa K, Hendrie H, Huang Y, Jorm A, Mathers C, Menezes PR, Rimmer E, Scazufca M. Global prevalence of dementia: a Delphi consensus study. Lancet 2005; 366: 2112–7.

14. Zhang ZX, Zahner GE, Román GC, Liu J, Hong Z, Qu QM, Liu XH, Zhang XJ, Zhou B, Wu CB, Tang MN, Hong X, Li H. Dementia subtypes in China: prevalence in Beijing, Xian, Shanghai, and Chengdu. Arch Neurol 2005; 62: 447-53.

15. Wimo A, Winblad B, Agüero-Torres H, von Strauss E. The magnitude of dementia occurrence in the world. Alzheimer Dis Assoc Disord 2003; 17: 63–7.

16. Fratiglioni L, Paillard-Borg S, Winblad B. An active and socially integrated lifestyle in late life might protect against dementia. Lancet Neurol 2004; 3: 343-53. Review.

17. Stern Y. Cognitive reserve and Alzheimer disease. Alzheimer Dis Assoc Disord 2006; 20: 112–7.

18. Agüero-Torres H, Fratiglioni L, Guo Z, Viitanen M, von Strauss E, Winblad B. Dementia is the major cause of functional dependence in the elderly: 3-year follow-up data from a population-based study. Am J Public Health 1998; 88: 1452-6.

19. Lyketsos CG, Toone L, Tschanz J, Rabins PV, Steinberg M, Onyike CU, Corcoran C, Norton M, Zandi P, Breitner JC, Welsh-Bohmer K, Anthony J, Østbye T, Bigler E, Pieper C, Burke J, Plassman B, Green RC, Steffens DC, Klein L, Leslie C, Townsend JJ, Wyse BW, Munger R, Williams M; Cache County Study Group. Population-based study of medical comorbidity in early dementia and "cognitive impairment, no dementia (CIND)": association with functional and cognitive impairment: The Cache County Study. Am J Geriatr Psychiatry 2005; 8: 656-64.

20. Newson RS, Kemps EB. General lifestyle activities as a predictor of current cognition and cognitive change in older adults: A cross-sectional and longitudinal examination. J Gerontol B Psychol Sci Soc Sci 2005; 60: 113-20.

21. Ownby RL, Crocco E, Acevedo A, John V, Loewenstein D. Depression and risk for Alzheimer disease: systematic review, meta-analysis, and metaregression analysis. Arch Gen Psychiatry 2006; 63: 530-8.

22. Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. Am J Public Health 1998; 88: 1337-42.

23. Mortimer J. Prospects for prevention of dementia and associated impairments. In Promoting successful and productive aging. Bond LA, Cutler SJ, & Grams A (eds.). Thousand Oaks. CA: Sage publications, 131-47, 1995.

24. Agahi N, Parker M. G. Are today's older people more active than their predecessors? Participation in leisure-time activities in Sweden in 1992 and 2002. Ageing Soc 2005; 25: 925-41.

25. Baltes MM, Wahl HW, Schmid-Furstoss U. The daily life of elderly Germans: activity patterns, personal control, and functional health. J Gerontol 1990; 45: 173-9.

26. Kelly JR, Ross J-E. Later-life leisure: Beginning a new agenda. Leis Sci 1988; 11: 47-59.

27. Huber J, Skidmore P. The New old: Why baby boomers won't be pensioned off, from http: //www.demos.co.uk/files/thenewold.pdf, 2005.

28. Mollenkopf H, Marcellini F, Ruoppila I, Széman Z, Tacken M (eds). Enhancing mobility in later life – Personal coping, environmental resources, and technical support. The out-of-home mobility of older adults in urban and rural regions of five European countries. IOS Press, Amsterdam, 2005.

29. Agahi Neda. Leisure in late life. Pattern of participation and relationship with health. Dissertation for doctoral degree. Karolinska Institutet, Stockholm, Sweden, 2008.

30. Seeman TE, Berkman LF, Charpentier PA, Blazer DG, Albert MS, Tinetti, ME. Behavioral and psychosocial predictors of physical performance: MacArthur studies of successful aging. J Gerontol A Biol Sci Med Sci 1995; 60: 177-83.

31. Glass TA, Mendes de Leon C, Marottoli RA, Berkman LF. Population based study of social and productive activities as predictors of survival among elderly Americans. BMJ 1999; 319: 478-83.

32. Karp A, Paillard-Borg S, Wang HX, Silverstein M, Winblad B, Fratiglioni L. Mental, physical, and social components in leisure activities equally contribute to decrease dementia risk. Dement Geriatr Cogn Disord 2006; 21: 65-73.

33. Kaplan GA, Strawbridge WJ, Cohen RD, Hungerford LR. Natural history of leisure-time physical activity and its correlates: Associations with mortality from all causes and cardiovascular disease over 28 years. Am J Epidemiol 1996; 144: 793-7.

34. Cumming E, Henry W. 1960. Growing Old. Basic Books: New York.

35. Havighurst RJ. Successful aging. Gerontologist 1961; 1: 8–13.

36. Bengtson VL, Burgess EO, Parrott TM. Theory, Explanation, and a Third Generation of Theoretical Development in Social Gerontology. J Gerontol B Psychol Sci Soc Sc 1997; 52B: S72-88.

37. Atchley RC. Retirement and leisure participation: Continuity or crisis? Gerontologist 1971; 11: 13-7.

38. Baltes PB, Baltes MM. (1990). Psychological perspectives on successful aging: the model of selective optimization with compensation. In Baltes PB & Baltes M.M (eds.), Successful Aging: Perspectives from the Behavioral Sciences. Cambridge: University Press. New York.

39. Rowe J, Kahn RL. Successful Aging. Gerontologist 1997; 37: 433-40.

40. Horgas AL. Wilms HU, Baltes MM. Daily life in very old age: Everyday activities as expression of successful living. Gerontologist 1998; 38: 556-68.

41. Lawton MP, Moss M, Fulcomer M. Objective and subjective uses of time by older people. Int J Aging Hum Dev 1987; 24: 171-88.

42. O'Brien Cousins S. Exercise, aging and health: Overcoming barriers to an active old age. Bristol, Pa. London: Brunner/Mazel; Taylor & Francis, 1998.

43. Bourdieu P. (1984). Distinction: A social critique of the judgement of taste. Cambridge, Mass: Harvard University Press.

44. Bukov A, Maas I, Lampert T. Social participation in very old age: Cross sectional and longitudinal findings from BASE. Berlin Aging Study. J Gerontol B Psychol Sci Soc Sci 2002; 57: P510-7.

45. Vance DE, Ross LA, Ball KK, Wadley VG, Rizzo M. Correlates of Individual Physical Activities in Older Adults. Act Adapt Aging 2007; 31: 1-21.

46. Litwin H. The association of disability, sociodemographic background, and social network type in later life. J Aging Health 2003; 15; 391-408.

47. Berger AK, Fratiglioni L, Forsell Y, Winblad B, Bäckman L. The occurrence of depressive symptoms in the preclinical phase of Alzheimer's disease: A population-based study. Neurology 1999, 53, 1998-2002.

48. Bickel H, Cooper B. Incidence and relative risk of dementia in an urban elderly population: findings of a prospective field study. Psychol Med 1994; 24: 179–92.

49. Helmer C, Damon D, Letenneur L, Fabrigoule C, Barberger-Gateau P, Lafont S, Fuhrer R, Antonucci T, Commenges D, Orgogozo JM, Dartigues JF. Marital status and risk of Alzheimer's disease: a French population-based cohort study. Neurology 1999; 53: 1953–8.

50. Fratiglioni L, Wang HX, Ericsson K, Maytan M, Winblad B. Influence of social network on occurrence of dementia: a community-based longitudinal study. Lancet 2000; 355: 1315–9.

51. Bennett DA, Schneider JA, Tang Y, Arnold SE, Wilson RS. The effect of social networks on the relation between Alzheimer's disease pathology and level of cognitive function in old people: a longitudinal cohort study. Lancet Neurol 2006; 5: 406-12.

52. Saczynski JS, Pfeifer LA, Masaki K, Korf ES, Laurin D, White L, Launer LJ. The effect of social engagement on incident dementia: the Honolulu-Asia Aging Study. Am J Epidemiol. 2006; 163: 433-40.

53. Crowe M, Andel R, Pedersen NL, Johansson B, Gatz M. Does participation in leisure activities lead to reduced risk of Alzheimer's disease? A prospective study of Swedish twins, J Gerontol B Psychol Sci Soc Sci 2003; 58: P249–55.

54. Gatz M, Prescott CA, Pedersen NL. Lifestyle risk and delaying factors. Alzheimer Dis Assoc Disord. 2006 ; 20: S84-8.

55. Fritsch T, Smyth KA, McClendon MJ, Ogrocki PK, Santillan C, Larsen JD, Strauss ME. Associations between dementia/mild cognitive impairment and cognitive performance and activity levels in youth. J Am Geriatr Soc 2005; 53: 1191-6.

56. Wilson RS, Scherr PA, Schneider JA, Tang Y, Bennett DA. Relation of cognitive activity to risk of developing Alzheimer disease. Neurology 2007; 69: 1911-20.

57. Yoshitake T, Kiyohara Y, Kato I, Ohmura T, Iwamoto H, Nakayama K, Ohmori S, Nomiyama K, Kawano H, Ueda K. Incidence and risk factors of vascular dementia and Alzheimer's disease in a defined elderly Japanese population: the Hisayama Study. Neurology 1995; 45: 1161–8.

58. Laurin D, Verreault R, Lindsay J, MacPherson K, Rockwood K. Physical activity and risk of cognitive impairment and dementia in elderly persons. Arch Neurol 2001; 58: 498–504.

59. Lindsay J, Laurin D, Verreault R, Hébert R, Helliwell B, Hill GB, McDowell I. Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health on Aging. Am J Epidemiol 2002; 156: 445–53.

60. Yamada M, Kasagi F, Sasaki H, Masunari N, Mimori Y, Suzuki G. Association between dementia and midlife risk factors: the Radiation Effects Research Foundation Adult Health Study. J Am Geriatr Soc 2003 51: 410–4.

61. Abbott RD, White LR, Ross GW, Masaki KH, Curb JD, Petrovitch H. Walking and dementia in physically capable elderly men, JAMA 2004; 292: 1447–53.

62. Podewils LJ, Guallar E, Kuller LH, Fried LP, Lopez OL, Carlson M, Lyketsos CG. Physical activity, APOE genotype, and dementia risk: findings from the Cardiovascular Health Cognition Study. Am J Epidemiol 2005; 161: 639-51.

63. Rovio S, Kåreholt I, Helkala EL, Viitanen M, Winblad B, Tuomilehto J, Soininen H, Nissinen A, Kivipelto M. Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. Lancet Neurol 2005; 4: 705-11.

64. Simons LA, Simons J, McCallum J, Friedlander Y. Lifestyle factors and risk of dementia: Dubbo Study of the elderly. Med J Aust 2006; 184: 68–70.

65. Larson EB, Wang L, Bowen JD, McCormick WC, Teri L, Crane P, Kukull W. Exercise is associated with reduced risk for incident dementia among persons 65 years of age and older. Ann Intern Med 2006; 144: 73–81.

66. Rovio S, Kåreholt I, Viitanen M, Winblad B, Tuomilehto J, Soininen H, Nissinen A, Kivipelto M. Work-related physical activity and the risk of dementia and Alzheimer's disease. Int J Geriatr Psychiatry 2007; 22: 874-82.

67. Sumic A, Michael YL, Carlson NE, Howieson DB, Kaye JA. Physical activity and the risk of dementia in oldest old. J Aging Health 2007; 19: 242-59.

68. Fabrigoule C, Letenneur L, Dartigues JF, Zarrouk M, Commenges D, Barberger-Gateau P. Social and leisure activities and risk of dementia: a prospective longitudinal study. J Am Geriatr Soc 1995; 43: 485–90.

69. Scarmeas N, Levy G, Tang MX, Manly J, Stern Y. Influence of leisure activity on the incidence of Alzheimer's disease. Neurology 2001; 57: 2236–42.

70. Wilson RS, Mendes De Leon CF, Barnes LL, Schneider JA, Bienias JL, Evans DA, Bennett DA. Participation in cognitively stimulating activities and risk of incident Alzheimer disease. JAMA 2002; 287: 742–8.

71. Wilson RS, Bennett DA, Bienias JL, Aggarwal NT, Mendes De Leon CF, Morris MC, Schneider JA, Evans DA. Cognitive activity and incident AD in a population-based sample of older persons. Neurology 2002; 59: 1910–4.

72. Wang H-X, Karp A, Winblad B, Fratiglioni L. Late-life engagement in social and leisure activities is associated with a decreased risk of dementia: a longitudinal study from the Kungsholmen project. Am J Epidemiol 2002; 155: 1081–7.

73. Verghese J, Lipton RB, Katz MJ, Hall CB, Derby CA, Kuslansky G, Ambrose AF, Sliwinski M, Buschke H. Leisure activities and the risk of dementia in the elderly. N Engl J Med 2003; 348: 2508–16.

74. Carlson MC, Helms MJ, Steffens DC, Burke JR, Potter GG, Plassman BL. Midlife activity predicts risk of dementia in older male twin pairs. Alzheimers Dement 2008; 4: 324-31.

75. Fratiglioni L, Viitanen M, Backman L, Sandman PO, Winblad B. Occurrence of dementia in advanced age: the study design of the Kungsholmen Project. Neuroepidemiology 1992; 11 Suppl 1: 29-36.

76. Fratiglioni L, Grut M, Forsell Y, Viitanen M, Grafstrom M, Holmen K, Ericsson K, Backman L, Ahlbom A, Winblad B. Prevalence of Alzheimer's disease and other dementias in an elderly urban population: relationship with age, sex, and education. Neurology 1991; 41: 1886-92.

77. Folstein MF, Folstein SE, McHugh PR.. "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12: 189-98.

78. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 3rd ed, revised (DSM-III-R): 97-163, 1987.

79. Fratiglioni L, Grut M, Forsell Y, Viitanen M, Winblad B. Clinical diagnosis of Alzheimer's disease and other dementias in a population survey. Agreement and causes of disagreement in applying DSM-III-R criteria. Arch Neurol 1992; 49: 927-32.

80. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffee MW. The index of ADL: A standardized measure of biological and psychosocial function. JAMA 1963; 185: 914-19.

81. Radloff LS, Teri L. Use of the Center for Epidemiological Studies-Depression Scale with older adults. Clin Gerontol 1986; 5: 119-36.

82. World Health Organization. International Classification of Diseases. Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death. Eighth Revision (ICD-8). Vol. 1. Geneva, Switzerland: World Health Organization, 1967.

83. Fratiglioni L, Wang H-X, Ericsson K, Maytan M, Winblad B. Influence of social network on occurrence of dementia: a community-based longitudinal study. Lancet 2000; 355: 1315-9.

84. Swedish Council for Research in the Humanities and Social Sciences (HSFR). (1991). Ethical principles in research. Stockholm, Sweden: Swedish Council for Research in the Humanities and Social Sciences (HSFR).

85. Karp A. Psychosocial factors in relation to development of dementia in late-life: a life course approach within the Kungsholmen project. Dissertation for doctoral degree. Karolinska Institutet, Stockholm, Sweden, 2005.

86. Qiu C. The relation of blood pressure to dementia in the elderly. A community-based longitudinal study. Dissertation for doctoral degree. Karolinska Institutet, Stockholm, Sweden, 2004.

87. Resnick HE, Fries BE, Verbrugge LM. Windows to their world: the effect of sensory impairments on social engagement and activity time in nursing home residents. J Gerontol B Psychol Sci Soc Sci 1997; 52: S135-S44.

88. Schroll M, Jonsson PV, Mor V, Berg K, Sherwood S. An international study of social engagement among nursing home residents. Age Ageing 1997, 26 (Suppl. 2), 55-59.

89. Snowdon DA, Kemper SJ, Mortimer JA, Greiner LH, Wekstein DR, Markesbery WR. Linguistic ability in early life and cognitive function and Alzheimer's disease in late life: findings from the Nun Study. JAMA 1996; 275: 528–32.

90. Whalley LJ, Starr JM, Athawes R, Hunter D, Pattie A,Deary IJ. Childhood mental ability and dementia. Neurology 2000; 55: 1455–59.

91. Small BJ, Fratiglioni L, Viitanen M, Winblad B, Backman L. The course of cognitive impairment in preclinical Alzheimer disease: three- and 6-year follow-up of a population-based sample. Arch Neurol 2000; 57: 839–44.

92. Berger AK, Small BJ, Forsell Y, Winblad B, Backman L. Preclinical symptoms of major depression in very old age: a prospective longitudinal study. Am J Psychiatr 1998; 155: 1039–43.

93. Kerlinger FN. Foundations of Behavioral Reasearch (2nd ed). New York: Holt, Rinehart and Winston: 484, 1981.

94. Horgas AL. Wilms HU, Baltes MM. Daily life in very old age: Everyday activities as expression of successful living. Gerontologist 1998; 38: 556-68.

95. Lawton MP, Moss M, Fulcomer M. Objective and subjective uses of time by older people. Int J Aging Hum Dev 1986-1987; 24: 171-88.

96. Larsson K. (2007).The social situation of older people in Sweden - The National Social Report 2006. International Journal of Social Welfare.

97. Kelly JR, Ross JE. Later-life leisure: Beginning a new agenda. Leis Sci 1988; 11: 47-59.

98. Strain LA, Grabusic CC, Searle MS, Dunn NJ. Continuing and ceasing leisure activities in later life: a longitudinal study. Gerontologist 2002; 42: 217-23.

99. Pohjolainen P, Heikkinen E, Lyyra AL, Helin S, Tyrkko K. Socio-economic status, health and life-style in two elderly cohorts in Jyvaskyla. Scand J Soc Med 1997; 52 (Suppl.): 1-65.

100. Everard KM, Lach HW, Fisher EB, Baum CM. Relationship of activity and social support to the functional health of older adult. J Gerontol B Psychol Sci Soc Sci 2000; 55: S208-S12.

101. Baltes PB, Baltes MM. Psychological perspectives on successful aging: The model of selective optimization with compensation. In Baltes PB & Baltes MM (eds.), Successful aging: Perspectives from the behavioral sciences. Cambridge: University Press, 1990.

102. Glass TA, Mendes de Leon C, Marottoli RA., Berkman LF. Population based study of social and productive activities as predictors of survival among elderly Americans. BMJ 1999; 319: 478-83.

103. Berger AK, Fratiglioni L, Forsell Y, Winblad B, Bäckman L. The occurrence of depressive symptoms in the preclinical phase of Alzheimer's disease: A population-based study. Neurology 1999; 53: 1998-2002.

104. Herzog AR, Kahn R, Morgan JN, Jackson JS, Antonucci TC. Age differences in productive activities. J Gerontol 1989; 44: S129-S38.

105. Newson RS, Kemps EB. General lifestyle activities as a predictor of current cognition and cognitive change in older adults: A cross-sectional and longitudinal examination. J Gerontol B Psychol Sci Soc Sci 2005; 60: P113-P20.

106. Richards M, Hardy R, Wadsworth ME. Does active leisure protect cognition? Evidence from a national birth cohort. Soc Sci Med 2003; 56: 785-92.

107. Crowe M, Andel R, Pedersen NL, Johansson B, Gatz M. Does participation in leisure activities lead to reduced risk of Alzheimer's disease? A prospective study of Swedish twins. J Gerontol B Psychol Sci Soc Sci 2003; 58: 249-55.

108. Katzman R. Can late life social or leisure activities delay the onset of dementia? JAGS 1995; 43: 583-4.

109. Kempermann G, Kuhn HG, Gage FH. More hippocampal neurons in adult mice living in an enriched environment. Nature 1997; 386: 493–5.

110. Rundek T, Bennett DA. Cognitive leisure activities, but not watching TV, for future brain benefits. Neurology 2006; 66 : 794–5.

111. Kivipelto M, Helkala EL, Laakso MP, Hänninen T, Hallikainen M, Alhainen K, Iivonen S, Mannermaa A, Tuomilehto J, Nissinen A, Soininen H. Apolipoprotein E epsilon4 allele, elevated midlife total cholesterol level, and high midlife systolic blood pressure are

independent risk factors for late-life Alzheimer disease. Ann Intern Med 2002; 137: 149–55.

112. Qiu C, Winblad B, Fastbom J, Fratiglioni L. Combined effects of APOE genotype, blood pressure, and antihypertensive drug use on incident AD. Neurology 2003; 61: 655–60.

113. Launer LJ. Demonstrating the case that AD is a vascular disease: epidemiologic evidence. Ageing Res Rev 2002; 1: 61–77.

114. Sapolsky RM, Krey LC, McEwen BS. The neuroendocrinology of stress and aging: the glucocorticoid cascade hypothesis. Endocr Rev 1986; 7: 284–301.

115. Belanoff JK, Gross K, Yager A, Schatzberg AF. Corticosteroids and cognition. J Psychiatr Res 2001; 35: 127–45.

116. Wang H-X, Karp A, Herlitz A, Crowe M, Kåreholt I, Winblad B, Fratiglioni L. Personality and lifestyle in relation to dementia incidence. Neurology 2009; 72: 253-9.

117. Bracco L, Piccini C, Baccini M, Bessi V, Biancucci F, Nacmias B, Bagnoli S, Sorbi S. Pattern and progression of cognitive decline in Alzheimer's disease: role of premorbid intelligence and ApoE genotype. Dement Geriatr Cogn Disord 2007; 24: 483-91.

118. Lawton MP. Leisure Activities for the Aged. Ann Am Activity Pol Soc Sci 1978; 438: 71-80.

119. Arentze T, Timmermans H, Jorritsma P, Olde Kalter MJ, Schoemakers A. More gray hair—but for whom? Scenario-based simulations of elderly activity travel patterns in 2020. Transportation 2008; 35: 613–27

12 APPENDIX

List of dissertations from the Aging Research Center and the Stockholm Gerontology Research Center, 1991-2008.

1991

Herlitz Agneta. Remembering in Alzheimer's disease. Utilization of cognitive support. (Umeå University)

1992

Borell Lena. The activity life of persons with a dementia disease.

1993

Fratiglioni Laura. Epidemiology of Alzheimer´s disease. Issues of etiology and validity.

Almkvist Ove. Alzheimer´s disease and related dementia disorders: Neuropsychological identification, differentiation, and progression.

Basun Hans. Biological markers in Alzheimer´s disease. Diagnostic implications.

1994

Grafström Margareta. The experience of burden in care of elderly persons with dementia. (Karolinska Institutet and Umeå University)

Holmén Karin. Loneliness among elderly - Implications for those with cognitive impairment.

Josephsson Staffan. Everyday activities as meeting-places in dementia.

Stigsdotter-Neely Anna. Memory training in late adulthood: Issues of maintenance, transfer and individual differences.

Forsell Yvonne. Depression and dementia in the elderly.

1995

Mattiasson Anne-Cathrine. Autonomy in nursing home settings.

Grut Michaela. Clinical aspects of cognitive functioning in aging and dementia: Data from a population-based study of very old adults.

1996

Wahlin Åke. Episodic memory functioning in very old age: Individual differences and utilization of cognitive support.

Wills Philippa. Drug use in the elderly: Who? What? & Why? (Licentiate thesis)

Lipinska Terzis Beata. Memory and knowledge in mild Alzheimer's disease.

1997

Larsson Maria. Odor and source remembering in adulthood and aging: Influences of semantic activation and item richness.

Almberg Britt. Family caregivers experiences of strain in caring for a demented elderly person. (Licentiate thesis)

1998

Agüero-Eklund Hedda. Natural history of Alzheimer's disease and other dementias. Findings from a population survey.

Guo Zhenchao. Blood pressure and dementia in the very old. An epidemiologic study.

Björk Hassing Linda. Episodic memory functioning in nonagenarians. Effects of demographic factors, vitamin status, depression and dementia. (In collaboration with the Department of Psychology, University of Gothenburg, Sweden)

Hillerås Pernilla. Well-being among the very old. A survey on a sample aged 90 years and above. (Licentiate thesis)

1999

Almberg Britt. Family caregivers caring for relatives with dementia – Pre- and post-death experiences.

Robins Wahlin Tarja-Brita. Cognitive functioning in late senescence. Influences of age and health.

Zhu Li. Cerebrovascular disease and dementia. A population-based study.

2000

Hillerås Pernilla. Well-being among the very old. A survey on a sample aged 90 years and above. (In collaboration with H. M. Queen Sophia University College of Nursing, Stockholm, Sweden)

von Strauss Eva. Being old in our society: Health, functional status, and effects of research.

2001

Jansson Wallis. Family-based dementia care. Experiences from the perspective of spouses and adult children.

Kabir Nahar Zarina. The emerging elderly population in Bangladesh: Aspects of their health and social situation.

Wang Hui-Xin. The impact of lifestyles on the occurrence of dementia.

2002

Fahlander Kjell. Cognitive functioning in aging and dementia: The role of psychiatric and somatic factors.

Giron Maria Stella T. The rational use of drugs in a population of very old persons.

2003

Jönsson Linus. Economic evaluation of treatments for Alzheimer's disease.

2004

Berger Anna-Karin. Old age depression: Occurrence and influence on cognitive functioning in aging and Alzheimer´s disease

Cornelius Christel. Drug use in the elderly - Risk or protection? Findings from the Kungsholmen project

Qiu Chengxuan. The relation of blood pressure to dementia in the elderly: A community-based longitudinal study

Palmer Katie. Early detection of Alzheimer's disease and dementia in the general population. Results from the Kungsholmen Project.

Larsson Kristina. According to need? Predicting use of formal and informal care in a Swedish urban elderly population. (Stockholm University)

2005

Derwinger Anna. Develop your memory strategies! Self-generated versus mnemonic strategy training in old age: Maintenance, forgetting, transfer, and age differences.

De Ronchi Diana. Education and dementing disorders. The role of schooling in dementia and cognitive impairment.

Passare Galina. Drug use and side effects in the elderly. Findings from the Kungsholmen Project.

Jones Sari. Cognitive functioning in the preclinical stages of Alzheimer's disease and vascular dementia.

Karp Anita. Psychosocial factors in relation to development of dementia in late-life: a life course approach within the Kungsholmen Project.

Nilsson Jan. Understanding health-related quality of life in old age. A cross-sectional study of elderly people in rural Bangladesh.

2006

Klarin Inga. Drug use in the elderly – are quantity and quality compatible.

Nilsson Erik. Diabetes and cognitive functioning: The role of age and comorbidity.

Ngandu Tiia. Lifestyle-related risk factors in dementia and mild cognitive impairment: A population-based study.

Erika Jonsson Laukka. Cognitive functioning during the transition from normal aging to dementia.

2007

Ferdous Tamanna. Prevalence of malnutrition and determinants of nutritional status among elderly people. A population-based study of rural Bangladesh. (Licentiate thesis)

Westerbotn Margareta. Drug use among the very old living in ordinary households-Aspects on well-being, cognitive and functional ability.

Rehnman Jenny. The role of gender in face recognition. (Stockholm University)

Beckman Gyllenstrand Anna. Medication management and patient compliance in old age.

Nordberg Gunilla. Formal and informal care in an urban and a rural population. Who? When? What?

2008

Gavazzeni Joachim. Age differences in arousal, perception of affective pictures, and emotional memory enhancement. (Stockholm University)

Marengoni Alessandra. Prevalence and impact of chronic diseases and multimorbidity in the aging population: A clinical and epidemiological approach.

Rovio Suvi. The effect of physical activity and other lifestyle factors on dementia, Alzheimer's disease and structural brain changes.

Weili Xu. Diabetes mellitus and the risk of dementia. A population-based study.

Meinow Bettina. Capturing health in the elderly population – complex health problems, mortality, and the allocation of home help services. (Stockholm University)

Agahi Neda. Leisure in late life. Patterns of participation and relationship with health.

Haider Syed Imran. Socioeconomic differences in drug use among older people. Trends, polypharmacy, quality and new drugs.

2009

Thilers Petra. The association between steroid hormones and cognitive performance in adulthood.

Rana AKM Massud. The impact of health promotion on health in old age: results from community-based studies in rural Bangladesh