



# LUND UNIVERSITY

On Falls in the Elderly –Epidemiological Studies from the Longitudinal General Population Study ‘Good Aging in Skåne’ (GÅS), Sweden

Stenhagen, Magnus

2014

[Link to publication](#)

*Citation for published version (APA):*

Stenhagen, M. (2014). *On Falls in the Elderly –Epidemiological Studies from the Longitudinal General Population Study ‘Good Aging in Skåne’ (GÅS), Sweden*. [Doctoral Thesis (compilation)]. Division of Geriatric Medicine.

*Total number of authors:*

1

## General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

## Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117  
221 00 Lund  
+46 46-222 00 00

# On Falls in the Elderly

Epidemiological Studies from the Longitudinal General  
Population Study 'Good Aging in Skåne' (GÅS), Sweden

Magnus Stenhagen, M.D.



**LUND**  
UNIVERSITY

Cover photo published under the Creative Commons license

Copyright © Magnus Stenhagen

Lund University, Faculty of Medicine  
Doctoral Dissertation Series 2014:97  
ISBN 978-91-7619-026-5  
ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University  
Lund 2014



# Contents

Abstract	5
List of publications	7
Abbreviations	9
Background	11
The clinical problem	11
A greying world	11
Multimorbidity and frailty –a clinical challenge	12
A brief history of geriatrics in Malmö	13
Malmö –an epidemiological stronghold	14
Introduction	15
Definition of a fall	15
Epidemiology	15
Etiology and mechanisms	16
Consequences of falls	17
Risk factors for falls	18
Medical and psychological factors	18
Use of medications	19
Sensory and neuromuscular factors	20
Balance and mobility	20
Environmental and sociodemographic factors	21
Functional ability	21
Prevention of falls	21
Health-related quality of life and life satisfaction	23
Activities of daily living	24
Rationale of this dissertation	24
A changing demographic	25
Using a disease-oriented approach	25
A general elderly population	25
Using a prospective, long-term approach	26
Aspects of well-being and functional ability	26
Objectives	27
Methods	29
Study population	29
Paper I	30
Paper II	30
Paper III	31
Paper IV	31

Variables and data collection	32
Operationalization of falls	33
Medical and psychological factors	33
Use of medication	33
Sensory and neuromuscular factors	34
Balance and mobility	34
Environmental and sociodemographic factors	34
Functional ability	34
Health-related quality of life	35
Life satisfaction	35
Study design and statistical analysis	36
Paper I	36
Paper II	36
Paper III	37
Paper IV	38
Comparative analysis	38
Statistics	39
Ethics	39
Results	41
Initial baseline population	42
Paper I	42
Paper II	43
Paper III	45
Paper IV	46
Discussion	51
Main findings and clinical implications	51
Confirmatory findings	51
Use of neuroleptics	52
Heart failure and related factors	53
Deprivation of HRQoL and LS	53
Functional ability	54
Methodological considerations	55
Generalizability of results	55
Operationalization of falls	56
Reliability and validity of variables	57
Internal attrition	59
Statistical considerations	59
Internal validity and temporality	60
Limitations of a longitudinal design	60
Conclusions	61
Future perspectives	62
Populärvetenskaplig sammanfattning på svenska (General summary in Swedish)	63
Fallolyckor hos äldre -en tyst epidemi	63
Acknowledgements	67
References	69

# Abstract

In a 'greying world' with aging populations, falls in the elderly are a challenge to the health care system as they are associated with substantial mortality and morbidity. Apart from physical injuries, the consequences of falls are broad, with additional psychological and social consequences. The overall objective of this dissertation was to study falls and related risk factors, predictors, and consequences in a general elderly population, including the oldest-old (individuals aged over 85 years). Data were extracted from the longitudinal population study 'Good Aging in Skåne' (GÅS), in southern Sweden.

In Paper I, a cross-sectional study, it was concluded that falls were common in the population studied and that the risk was multifactorial. The results indicated that there was an overrepresentation of fallers in a distinct subgroup of the oldest-old, and a frail group with multiple risk factors. The risk of falling appeared to increase in a non-linear, almost exponential way with increasing number of risk factors.

Paper II used data from the baseline assessment and a 3- and 6-year follow-up assessment to study factors that could predict falls. Three independent components that predicted future falls were identified: reduced mobility, heart dysfunction, and functional impairment including nocturia. The use of neuroleptic drugs was the single most prominent individual risk factor for falls, although the prevalence was low in the population studied, and the confidence interval overlapped those of other significant predictors. Heart failure with symptoms was also a prominent, significant risk factor.

In Paper III, the long-term associations between falls, and the measurements of health-related quality of life (HRQoL), and life satisfaction (LS) were examined, using data from the baseline and 6-year follow-up assessment. Over six years, fallers had a notable, chronically reduced HRQoL and LS, compared to non-fallers. In an analysis adjusted for confounding factors, falls at baseline predicted a long-term reduction in the physical aspect of HRQoL after six years. This long-term deprivation in these aspects in elderly fallers may be more extent than previously assumed.

Paper IV used data from the baseline and 6-year follow-up assessment, with the objective of determining the relationship between long-term change in activities of daily living (ADL) and falls, and to identify characteristics of groups at risk of falling. Over six years, one in four had changed ADL status and this category had a higher risk for falls than those with no change in ADL. It was concluded that groups with different characteristics, with both deterioration and improvement in ADL, had an increased risk of falling. Those at risk who have improved ADL function may have a

history of sufficient burden of comorbidity, combined with obtained mobility for exposure to a fall event.

Falls seem to be a treat to successful and healthy aging as they are associated to a long-term reduction in well-being, especially in the physical aspect of HRQoL. Those prone to falling may therefore be an important target for interventional efforts, rehabilitation, and healthcare resources. Several findings in this dissertation were confirmatory, such as the intimate relationship between falls and advanced age, multimorbidity, frailty, and gait and balance disorders. It is important to highlight these conditions in interventional settings. However, the interplay between physical and functional rehabilitation and the risk for falls may be intricate, as some groups appear to have an increased risk of falling when they regain mobility and function. From a medical point of view, the findings that heart failure, a condition with increasing prevalence, and the use of neuroleptic drugs were prominent, significant predictors for falls in a general elderly population are of clinical interest, and may not have been widely reported.

# List of publications

This dissertation is based on the following papers, which are referred to in the text by their Roman numerals:

- I. Stenhagen M, Nordell E, Elmståhl S. Falls in elderly people: a multifactorial analysis of risk markers using data from the Swedish general population study 'Good Ageing in Skåne'. *Aging Clinical and Experimental Research*. 2013;25(1):59–67.
- II. Stenhagen M, Ekström H, Nordell E, Elmståhl S. Falls in the general elderly population: a 3- and 6-year prospective study of risk factors using data from the longitudinal population study 'Good Ageing in Skåne'. *BMC Geriatrics*. 2013;13:81.
- III. Stenhagen M, Ekström H, Nordell E, Elmståhl S. Accidental falls, health-related quality of life and life satisfaction: a prospective study of the general elderly population. *Archives of Gerontology and Geriatrics*. 2014;58(1):95–100.
- IV. Stenhagen M, Ekström H, Nordell E, Elmståhl S. Both deterioration and improvement in activities of daily living are related to falls: A 6-year follow-up of the general elderly population study 'Good Aging in Skåne' (GÅS). *Clinical Interventions in Aging*. 2014. In press.





# Abbreviations

ADL	Activities of Daily Living
ANOVA	Analysis of Variance
ATC	Anatomic Therapeutic Chemical classification system
BPSD	Behavioral and Psychological Symptoms of Dementia
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
cOR	crude Odds Ratio
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th version
GÅS	Good Aging in Skåne ("Gott Åldrande i Skåne")
HRQoL	Health-related Quality of Life
iADL	Instrumental Activities of Daily Living
ICD-10	International Classification of Diseases, 10th version
LS	Life Satisfaction
LSI-A	Life Satisfaction Index A
MCS	Mental Component Summary
MMSE	Mini-Mental State Examination
ns	not significant
NYHA	New York Heart Association
OR	Odds Ratio
pADL	Personal Activities of Daily Living
PCA	Principal Component Analysis
PCS	Physical Component Summary
ProFaNE	Prevention of Falls Network Europe
RCT	Randomized Controlled Trial
SF-12	12-item Short Form Health Survey
SF-36	36-item Short Form Health Survey
SNAC	Swedish National Study on Aging and Care
SUS	Skåne University Hospital
WHO	World Health Organization



# Background

## The clinical problem

In 1961, the World Health Organization (WHO) proclaimed that accidents were '*the world's third worst killer*'.<sup>1</sup> Even so, they had been less well studied than diseases of similar gravity. In the decades that followed, research, education, and prevention were implemented at all levels of society to try to reduce accidents. Today, unintentional injuries are the fifth leading cause of death in older adults, after cardiovascular, neoplastic, cerebrovascular, and pulmonary causes.<sup>2</sup> Accidental falls are responsible for two-thirds of the mortality from these injuries. In Sweden, with a population of nine million, 1,600 individuals were estimated to die from falls in the year 2010.<sup>3</sup> The majority of victims were elderly people. In comparison, in the same year approximately 2,400 individuals died from prostate cancer, 1,400 died from breast cancer, and 266 died from road traffic accidents.<sup>4,5</sup>

In a pioneering scientific paper in 1960, 'On the Natural History of Falls in Old Age', the British physician J.H. Sheldon stressed the importance of '*further investigate the natural history of falls in the elderly*', a then widespread clinical problem '*deprived of the exercise of curiosity*'.<sup>6</sup> Since then, a substantial body of work concerning falls in the elderly has been published in the medical literature.<sup>7</sup> Despite this, falls continue to be a major health problem, and are associated with considerable mortality and morbidity.<sup>2</sup> The severe consequences of falls in the elderly could qualify it as a 'Giant of Geriatrics', a term for the major geriatric syndromes 'instability', 'immobility', 'intellectual impairment', and 'incontinence' that was initially coined by B. Isaacs in 1965.<sup>8</sup>

## A greying world

Life expectancy is growing almost linearly in most developing countries, with no sign of deceleration.<sup>9</sup> Improvements in general living conditions, combined with medical advances in combating diseases of the young, have been followed by a marked reduction in old-age mortality.<sup>9,10</sup> When the Swedish pension system was introduced in 1913, the retirement age was 67 years. This was no bold proposition at the time, as the current life expectancy was slightly under 60 years.<sup>11</sup> From an international point of view, Sweden is one of the leading countries today regarding its aging population, which, historically, is a relative new phenomenon. In the coming decade, the post-war baby-boom generation will rapidly increase the proportion of the population that is

over 65 years of age. The oldest-old, a definition of ‘super seniors’ over 85 years old, have been the most rapidly expanding segment of the population in developed countries over the last decades.<sup>9,12</sup> This is a challenge to society, as this group is susceptible to disease and disability. It is an open question whether this demographic shift generates the scenarios ‘postponement’, ‘compression’, or ‘prolongation’ of morbidity.<sup>13</sup>

In Sweden, rural municipalities with poorer economies have the largest proportion of elderly individuals, due to the influx of younger people to urban and suburban areas.<sup>14</sup> Proportionately, the elderly have increased most in the inland parts of northern Sweden. In Skåne, the most southerly province of Sweden, the proportion of elderly inhabitants is highest in the small municipalities in the south-east.

## Multimorbidity and frailty –a clinical challenge

In an aging world, where the historical threats of tuberculosis, polio, and similar conditions have been defeated by modern medicine, acute diseases have been superseded by chronic diseases.<sup>13</sup> The aging process is characterized by a progressive loss of physiological and functional reserve in individual organs, with a diminished ability to compensate for disease and trauma.<sup>15</sup> This state of vulnerability can be described as ‘frailty’, one of the most challenging aspects of elderly individuals from a medical point of view.<sup>16</sup> Frequent clinical presentations of frailty are fatigue, weight loss, infections, falls, delirium, and fluctuating disability. In line with this, the burden of multimorbidity becomes more pronounced with age.<sup>17</sup> Simply put, advanced age is the strongest risk factor associated to acquire disease and injury.<sup>18</sup> Despite this development, most healthcare, medical research, and education is configured by a single-disease framework.

In the clinical setting, an accurate and timely diagnosis of the elderly and frail can be a challenge, because of unspecific and atypical presentations of symptoms.<sup>15</sup> A few clinical presentations, e.g. an acute state of confusion, can hide a range of underlying diseases. This challenge can result in frequent over- or underdiagnosis of conditions in the elderly. Large clinico-pathological studies in Malmö have shown that the diagnostic accuracy can be poor in cases of myocardial infarct, ulceration, and peritonitis in elderly inpatients.<sup>19</sup> Furthermore, older people with dementia or another form of cognitive impairment may not be able to communicate their symptoms accurately.<sup>15</sup> In this context, geriatric medicine is a broad, non-organ-specific specialty that requires knowledge of diseases of the elderly and of the normal aging process of the body.<sup>10</sup>

## A brief history of geriatrics in Malmö

Before the rise of the Swedish welfare state, the care of the elderly was mainly a concern of the family. Local poorhouses and hospitals, often managed by the church, were the only assisting institutions. In the first half of the twentieth century, the projections of an aging population started a socio-political debate in Sweden about management of the care of the elderly.<sup>20</sup> In a political reform in 1918, the municipalities formally took over responsibility for the care of old people.<sup>21</sup> The first modern senior facility in Malmö was established at Värnhem in 1928. As this had been the site of a former poorhouse, it could be socially stigmatizing for an older citizen in Malmö ‘to end up at Värnhem’. In Sweden, administration of the care of the elderly was formally separated from poor relief first in 1956.<sup>10</sup> In the wake of the post-war economic rise and development of the welfare state, care of the elderly grew widely in Sweden after 1960. The care of the chronically ill started to receive medical recognition, and the senior facility at Värnhem became a large hospital for the elderly patient.

The term ‘geriatrics’, derived from the word *geronte* (a council of elders in Sparta), was introduced by Dr Ignatz Leo Nascher in the early twentieth century.<sup>8</sup> Sweden acquired the world’s second academic chair in geriatric medicine in 1967, two years after the first chair was established in the United Kingdom.<sup>10</sup> ‘Långvårdsmedicin’ (long-stay medicine) became a medical specialty in Sweden in 1969. In 1988, it changed its name to the more internationally suitable term ‘geriatrik’. During its expansion during the 1970s and 1980s, clinical geriatric medicine and research in Sweden gained international recognition. Examples are the epidemiological study (H70) of an elderly cohort in Göteborg,<sup>8</sup> and the WHO study ‘Men born 1914’ in Malmö.<sup>22</sup> During the 1980s, Värnhem Hospital in Malmö had approximately 1,100 inpatients and was one of the largest long-stay hospitals in Europe.<sup>19,23</sup> A third of the beds were intended for geriatric assessment and rehabilitation, and two-thirds were in long-stay wards for the chronically disabled who were unable to live at home. The hospital had in-house dental and radiological clinics, and over a 20-year period (1968–87) the autopsy rate was 80%.

Somewhat abruptly, the Swedish political reform ‘Ädel-reformen’ in 1992 transferred the responsibility for the care of the elderly from an inpatient, hospital-centered environment of the county council to outpatient facilities in the municipality.<sup>24</sup> One ambition with this reform was to avoid institutionalization of the elderly and chronical ill, by acquiring better and more individualized housing conditions. Some argue that this reformation demedicalized the care of frail and elderly patients, and drained competence out of clinical geriatric medicine and research in Sweden.<sup>10</sup> In the beginning of the 2000s, Värnhem Hospital closed its doors, symbolizing the end of an era. Today, the old hospital buildings at Värnhem house a school and a student home. Altogether in Sweden, the number of geriatric inpatient beds decreased from

6,200 in 1994 to 2,200 in 2008, a 65% reduction.<sup>20</sup> With the aging population increasing in parallel, the Swedish healthcare system faces a challenge.

As the demographic shift is unequivocal, geriatric medicine is again expanding in southern Sweden. Large epidemiological studies have been launched to investigate the characteristics and needs of an aging population, and a new geriatric ward, specialized in the care of elderly patients who are acutely ill, opened at Skåne University Hospital (SUS) in Malmö in 2012. After a thriving rise and rather drastic fall, geriatric medicine in Malmö appears to be on the rise again.

## Malmö –an epidemiological stronghold

Epidemiology is an integral part of public health, and involves *'the study of the distribution and determinants of disease frequency'*.<sup>25</sup> The faculty of medicine at Lund University in Sweden has a strong tradition of epidemiological research.<sup>26</sup> The Lundby Study, started in 1947, monitored mental health in a cohort from a small municipality outside Lund.<sup>27</sup> This unique study was still active after 50 years.

When the faculty of medicine became established in Malmö in 1950, the city was found to be ideal for population-based research.<sup>26</sup> With approximately 200,000 inhabitants at the time, Malmö had one general hospital near the city center where all Malmö citizens were jokingly said to 'end up sooner or later'. At times, up to 90% of those who died underwent autopsy. As the council of Malmö was engaged in demographic issues, a fruitful collaboration became established between the city and the faculty.

Orthopedic epidemiology in Malmö has gained worldwide recognition, with an extensive radiological archive and leading research on osteoporosis. Other fields with prolific research are social medicine, geriatrics, diabetology, and ophthalmology. Furthermore, prominent cancer and cardiovascular research are represented in Malmö by the large cohort 'Diet and Cancer Study',<sup>28</sup> and the mentioned WHO study 'Men born 1914'.<sup>22</sup> The Malmö Preventive Project was established in 1974 for the screening of cardiovascular risk individuals.<sup>29</sup> At the department of social and preventive medicine, Leif Svanström carried out important studies on accidents, adopting epidemiological methods in traumatology research.<sup>30</sup> His work 'Falls on stairs' led to updated codes of practice for building of stairs in Sweden.

In 2001, a national database on the aging population, 'Good Aging in Skåne' (GÅS), was launched as part of the 'Swedish National Study on Aging and Care' (SNAC), supported by the Ministry of Health and Social Affairs and Region Skåne.<sup>31</sup>

# Introduction

## Definition of a fall

An unintentional fall is coded as W00-W19 under ‘Accidents/External causes of morbidity and mortality’ in the International Classification of Diseases, 10th revision (ICD-10).<sup>32</sup> The ICD-10 presents a list of possible causes of falling, but does not define a fall.<sup>33</sup> As many may intuitively know what a fall is, the lack of a clear case definition has generated problems in research. The variations in an operational definition can reduce the validity of research and hinder meta-analyses between studies.<sup>33-35</sup>

One established definition of a fall is from the Kellogg International Working Group on the Prevention of Falls in the Elderly: ‘*unintentional coming to the ground or some lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke, or an epileptic seizure*’.<sup>36</sup> This definition explicit excludes the occurrence of syncope, which can be misleading. Recent research indicates that retrograde amnesia after syncope may be more common than previously assumed, particularly in the elderly, blurring the definition and anamnestic information.<sup>37</sup> In line with this, broader definitions of a fall can be useful in a medical context, addressing cardiovascular and neurological causes of falls.<sup>7</sup> A more recent definition is ‘*an unexpected event in which the participant comes to rest on the ground, floor or lower level*’, formulated by the Prevention of Falls Network Europe (ProFaNE), in an attempt to harmonize the methodical definition.<sup>35</sup> Despite efforts, there is still no universally accepted scientific definition of a fall.<sup>33</sup>

## Epidemiology

The true incidence of falls in the elderly is difficult to measure, due to its transient nature. Numerous population-based studies have tried to estimate the frequency, using different settings, age groups, and definitions of a fall.<sup>38,39</sup> The results have infrequent been reported in incidence rates (events per person at risk in a given time period), a measure commonly used in epidemiological research.<sup>25</sup> An often quoted estimation is that approximately one-third of community-living individuals over 65 years of age will fall at least once a year.<sup>40,41</sup> Large population studies in the 1980s and early 1990s have given us fairly concordant estimates of the incidence of falls in an elderly population.<sup>38</sup> In a review of 14 prospective, state-of-the-art studies involving subjects over 60 years of age, a mean proportion of 34% of the population fell during



a year.<sup>42</sup> In another meta-analysis of a general population, 28–35% of those aged over 65 years fell in a 1-year period, and 32–42% of those over 75 years of age had experienced falling.<sup>38</sup>

The number of falls increases with age and frailty.<sup>43</sup> Older people who are institutionalized fall more frequently, and their falls tend to result in more severe injuries and subsequent complications.<sup>39,44</sup> In Scandinavia, the epidemiology of falls in the oldest-old has been studied in depth. In a prospective study in Umeå, Sweden, 40% of those over 85 years fell a least once during a six-month period.<sup>45</sup> In a study of individuals over 85 years living at home in northern Finland, 49% fell during an 11-month period.<sup>46</sup>

According to a literature review, several studies have indicated that women are more prone to falling than men, while others have not found any sex difference.<sup>47</sup> In a Finnish study, women in the general population had a greater risk of falling repeatedly than men, but the gender difference evened out with advancing age.<sup>48</sup> Cold weather and winter season appear to increase the rate of falling in women, and the incidence of fractures.<sup>38</sup> Most falls occur during the day and approximately 20% occur during the night.<sup>49</sup>

## Etiology and mechanisms

Although falls are referred to as ‘unintentional’ in the ICD-10, their occurrence in an elderly population differs significantly from a normal Poisson distribution, discounting them as random events. This indicates that a causal process is involved.<sup>49</sup> The ability of humans to maintain a postural position in standing and walking depends on an interaction between numerous physiological systems, and the elderly individual is predisposed to falls from an interplay between accumulated disorders, organ dysfunction, age-related changes, and external factors.<sup>7,50</sup> The multifactorial nature of falls cannot be overemphasized.<sup>47</sup>

Despite the fact that there has been extensive overall research on the subject, there is limited objective or witnessed evidence for how and why a fall occurs. Due to the transient and elusive nature of a fall event, the direct causes that are known are imprecise at best. It has been estimated that up to 70% of falls in the elderly are not witnessed by anyone else.<sup>51</sup> In a 1-year prospective study of a general elderly population, trips and slips were the most prevalent causes of falls, accounting for 59% of the events recorded.<sup>52</sup> The time distribution and circumstances of injury-causing falls appear to differ between the elderly living at home and those living in institutionalized care.<sup>44</sup> In the oldest-old living at home, ongoing activity and the type of fall seem to play a minor role in falls causing injuries.<sup>53</sup>

Modern video-capture technology has given us the opportunity to gain new insights into the mechanisms of falling. A Canadian observational study installed video cameras in two long-term facilities, and captured 277 fall events over three years.<sup>54</sup> Incorrect weight shifting accounted for 41% of the events, followed by ‘trip and stumble’ (21%), ‘hit or bump’ (11%), and ‘loss of support’ (11%). Slipping accounted for only 3% of the incidents in this study.

In the Canadian study, syncope or ‘collapse or loss of consciousness’ by their definition, accounted for 11% of the falls.<sup>54</sup> The interplay between falls and syncope is not documented well in the literature. This uncertainty may stem from the transient nature of the event and poor recall in the elderly. The estimated proportion of falls attributed to syncope varies from 3% to 26%.<sup>42,55</sup> Accordingly, there may be a significant overlap between falls and syncope in the elderly.

## Consequences of falls

The potentially severe outcomes of falls in older people are not generated solely by the high incidence; young children and athletes fall more frequently than all but the frailest of old people.<sup>39</sup> Instead it is the combination of high frequency and increased susceptibility to injury. Older people have a higher prevalence of comorbidity, age-related physiological changes (e.g. osteoporosis), and diminished functional reserves.<sup>56</sup>

According to official data based on the ICD-10 classification, 935 deaths in Sweden in 2012 were primary coded as unintentional falls (W00-19).<sup>57</sup> This number is likely to be an underestimate; in a Swedish government report from 2010, 1,600 deaths were estimated to be caused by fall events in that year, 300,000 individuals were in need of acute hospital care after a fall, and falls were estimated to cost society 22 billion SEK per year.<sup>3</sup> The majority of those affected were elderly and frail.

Approximately 5–10% of falls result in a major injury such as a fracture, dislocation, laceration, serious soft tissue injury, or traumatic head injury.<sup>45,58–60</sup> Lying for a long time, caused by the inability to get up after a fall, may result in dehydration, pressure ulcers, or rhabdomyolysis.<sup>61</sup> Fractures may account for the greatest healthcare burden of all fall-related injuries.<sup>62</sup> A hip fracture is regarded as one of the most devastating consequences of a fall. This type of fracture is associated with 15% mortality during the hospitalization period, and one in three die within a year after the incident.<sup>63</sup> Approximately 19,000 elderly individuals suffer a hip fracture in Sweden each year, and 95% of them are caused by a fall.<sup>64</sup> There is evidence that fall-related injuries are accompanied by short- and long-term functional impairments, and consequent reduction in quality of life, in those affected.<sup>65</sup>

Apart from physical injuries, the outcomes of falls in the elderly are multifaceted, with additional psychological and social consequences.<sup>45,66</sup> Being prone to falling often

affects the relatives, and falls are an independent predictor of admission to sheltered housing.<sup>67</sup> Furthermore, falls are associated with higher anxiety and depression scores in those affected.<sup>68</sup> ‘Fear of falling’ is a concept where anxiety, loss of self-confidence, and avoidance of activity result in self-imposed functional limitations.<sup>69,70</sup> This term was coined by Murphy and Isaacs in a description of a post-fall syndrome in 1982.<sup>71</sup> About one-third of elderly people are assumed to develop fear of falling after a fall.<sup>72</sup> According to a systematic review, the main consequences of fear of falling are a decline in physical and mental performance, and a progressive loss of quality of life.<sup>70</sup>

## Risk factors for falls

A risk factor can be defined as a characteristic or set of circumstances which, on the basis of epidemiological evidence, is known to be associated with some health-related condition that one considers important to prevent.<sup>47</sup> A risk factor may not necessarily be directly causative, but rather a marker of increased probability of a particular outcome. For example, the use of a walking device may be strongly associated with falls, but may not be a cause of falling. Instead, it may be a marker of other problems that are causally related to falls, such as walking difficulties.<sup>73</sup> One way that one can divide risk factors is into modifiable factors and unmodifiable factors, where both can be used as markers of future falls, but only modifiable risk factors can be addressed using preventive strategies.<sup>74</sup>

In his pioneering study in 1960, J.H. Sheldon tried to systematically classify falls into different subtypes to identify circumstances predisposing to a fall; e.g. tripping, vertigo, or postural hypotension.<sup>6</sup> Much of his work has been confirmed in subsequent epidemiological studies, and hundreds of risk factors for falls have been identified.<sup>38</sup> Despite the heterogeneity of settings, sample populations, and risk factors studied, meta-analyses have revealed a coherent number of important risk factors for falls.<sup>68</sup> Several factors appear to be linked to the ‘Giants of Geriatrics’, which are associated with advanced age and general frailty. Impairment in gait and balance has repeatedly been associated with an increased risk of falling, and one of the most important individual risk factor is a history of previous falls.<sup>2,61,75</sup> As the cause of falls is multifactorial, the related factors can be divided into different categories. The following categorization is based on systematization by Lord et al. (2007).<sup>7</sup>

### *Medical and psychological factors*

Conditions with motor symptoms, such as arthritis and Parkinson’s disease, are known risk factors for falls.<sup>2,47,61,76</sup> This can be seen as intuitive, as these conditions have a direct effect on gait and mobility. The strong association between falls, advanced age, and frailty can explain the connection between falls and osteoporosis-related fractures.<sup>2,61,75,76</sup> Vitamin D deficiency has been reported to affect

predominantly the weight-bearing muscles of the lower limb, and a significant correlation between low levels of vitamin D and falls has been reported.<sup>77</sup> Vitamin D deficiency can also alter the outcome of falls, as it can lead to osteoporosis with an increased risk of sustaining fractures.<sup>78,79</sup> Furthermore, geronto-psychiatric conditions such as dementia, cognitive impairment, and clinical depression are associated with falls.<sup>2,38,39,47,61,75,76</sup> The underlying mechanisms may be related to disorientation, spatial dysfunction, or affected self-awareness, leading to an increased risk of exposure to a fall event. In line with this, psychotic disorders may be understudied yet important risk factors for falls.<sup>80</sup> Their association to falls may be related to altered perception or adverse effects of medication use.

The association between a history of stroke and falls could be complex, as the condition can generate both motor and cognitive sequelae.<sup>73,75</sup> Diabetes mellitus type 1 has been associated with falls, probably because of the risk of hypoglycemia.<sup>61,75,76</sup> There may also be an association with a higher prevalence of polyneuropathy and visual impairment in those affected. The association between cardiovascular risk factors and falls in the elderly is largely unknown, but there is evidence emerging of an overlap between cardiac disorders and falls.<sup>2</sup> The disorders of cardiac arrhythmias, structural heart disease and orthostatic hypotension are documented risk factors for syncope and falls.<sup>38,39,56,75</sup> For many of these conditions, there are established, effective treatments.<sup>55</sup> Epilepsy, another intermittent condition, has also been associated with an increased risk for falls and fractures.<sup>81</sup>

There have been conflicting results on whether anemia is an independent risk factor for falls in the general population.<sup>82</sup> The underlying mechanism may be a higher risk of dizziness and fainting. Sleeping disorders have been reported to be a potential risk factor for falls, probably related to reduced alertness during the day, or an increased risk of falling when it is dark.<sup>50,83</sup> Chronic obstructive pulmonary disease (COPD), an emerging condition in an aging population with a burden of multimorbidity, has been reported to be an independent risk factor, and a 'red flag' for future falls in the elderly.<sup>84</sup>

### *Use of medications*

Polypharmacy (the use of five or more drugs according to a common definition) and inappropriate drug use are a common phenomenon in elderly people.<sup>85</sup> Medication-related problems, such as improper use of drugs leading to adverse side effects or interactions, are common, costly, and often preventable in older adults.<sup>86</sup> Inappropriate use of medications can be one of the most modifiable risk factors for falls. The Swedish National Board of Health and Welfare has published a report that lists drugs that could increase the risk for falls in the elderly.<sup>87</sup> The drugs listed are opioids, neuroleptics, sedatives/hypnotics, sleep medications, antidepressants, and medications that can generate hypotension/orthostatic reactions. In line with this, there is a marked association between the use of psychotropic drugs such as

sedatives/hypnotics and falls.<sup>88-91</sup> Anticholinergic and antihypertensive drugs have shown a more modest association.<sup>75,88</sup> There is a general consensus that neuroleptic drugs contribute to falls in institutionalized care.<sup>7</sup> In the general population, this association is not widely reported, perhaps because of the low prevalence of use of this type of drug. Recent, large studies of a general elderly population have suggested that there may be a modest association between neuroleptics and falls.<sup>88,89</sup> There are conflicting results on whether there is a difference in risk between the use of typical and atypical neuroleptic drugs.<sup>90</sup>

### *Sensory and neuromuscular factors*

Dizziness and vertigo are symptoms that are frequently associated with falls.<sup>2,38,39,61,75,76</sup> These symptoms are common in the general elderly population and can have a multifaceted etiology, e.g. cardiac or neurological disorders, hypotension, adverse drug effects, or balance and vision impairments. The experience of pain, another common state in elderly people, is also associated with falls.<sup>61,75</sup> Pain from the musculoskeletal system may generate gait disorders or postural instability, and chronic pain may be associated with daytime tiredness and the use of inappropriate drugs with adverse effects.

Urine incontinence and nocturia (frequent micturition during the night) are other documented risk factors for falls.<sup>61,75,83</sup> These conditions can be markers of advanced age and general frailty. Their relationship with falls can also be more direct, as incontinence can generate orthostatic reactions. Frequent toilet visits, especially at night, can lead to hazardous situations with increased risk of falling. Finally, the broad condition of visual impairment in the elderly is commonly associated to an increased risk for falls.<sup>2,38,39,47,56,61</sup>

### *Balance and mobility*

The ‘Geriatric Giants’ instability and immobility are strongly associated with an increased risk of falling. Gait and balance disorders have consistently been identified in several reviews as being strong risk factors.<sup>2,38,39,56,61,75</sup> Vestibular dysfunction is common in older age, and may result in postural instability.<sup>56</sup> Mobility limitation, muscle weakness, and the use of a walking device are known risk factors for falls.<sup>2,38,39,56,61,75</sup> The association between these conditions and falls may seem intuitive, as they are directly related to an inability to maintain postural steadiness. They may also have a strong relationship with *sarcopenia*, an underdiagnosed condition in the geriatric population, presenting as progressive loss of muscle mass and strength with a risk of adverse outcomes.<sup>92</sup>

### *Environmental and sociodemographic factors*

Advanced age is a strong risk factor for falls, and institutionalized living is a distinct marker for future falls.<sup>39,44,47,56,61,75</sup> This association may be directly explained by the strong relationship between institutionalized living and general frailty and multimorbidity. Many studies have identified female sex as a risk factor for falls, but as mentioned earlier, there is a lack of agreement on the true association between falling and sex differences.<sup>47</sup>

Although not widely reported, the use of alcohol can be a common cause of falls.<sup>50</sup> This may seem logical, as alcohol intoxication affects balance and motor skills, combined with altered self-awareness. Living alone has been reported to be a risk factor for falls,<sup>50</sup> and the psychosocial factor of being married has been shown to be related to a reduced risk of hip fracture.<sup>41</sup> These findings demonstrate the broad range of risk factors associated with falls in the elderly. Furthermore, external factors in the home environment such as poor lighting, stairs, and loose rugs have been identified as risk factors for falls.<sup>47,56</sup>

### *Functional ability*

In meta-analyses, low physical activity and dependency in activities of daily living (ADL) have repeatedly been identified as risk factors for falls.<sup>2,38,39,61,75</sup> These impairments may be indirect markers of a general deterioration of health, multimorbidity, and musculoskeletal disorders. However, the relationship between physical activity, ADL, and falls can be intricate, as exposure to a fall event often requires some level of functional ability.<sup>93</sup> Falls are often related to changes in how the individual uses the environment,<sup>47</sup> and may have a close relationship with overall physical functioning combined with the cognitive aspect of self-awareness. Studies investigating the association between physical activity and the risk of falling have given equivocal results.<sup>47</sup>

## Prevention of falls

Falls in the elderly meet many of the criteria for prevention, with high frequency, heavy burden of morbidity, and evidence of preventability.<sup>94</sup> In the last decades, prevention of falls and injuries has been a major focus of research, with a substantial increase in the number of studies published.<sup>43,95</sup> There have been several attempts to translate research into clinical practice, in the form of fall prevention programs evaluated through randomized controlled trials (RCTs). These interventions have included exercise programs, education programs, optimization of medication, and modification of the environment. Some studies have used single interventions, others multifactorial interventions.<sup>66</sup>

According to meta-analyses, multi-component interventions have had some effect in preventing falls in the elderly.<sup>51,59,66,74,96,97</sup> Exercise programs involving strength, balance, and gait training have also been useful in reducing falls.<sup>43,51,66,74,96</sup> There is also evidence that home safety interventions can reduce falls, especially in frail elderly people.<sup>43,51,66,74</sup> There are divergent results on whether vitamin D supplementation reduces falls, but it is recommended to individuals with low levels of vitamin D.<sup>43,51,59,66,74</sup> Other effective preventive approaches are adjustment of psychotropic medication and modification of polypharmacy.<sup>43,51,59,66,74</sup>

Medical interventions such as cataract surgery to correct visual impairment and insertion of a pacemaker after falls associated with carotid sinus hypersensitivity have proven to be effective.<sup>43,66,74</sup> What the effective elements of cardiovascular programs for fall prevention actually are is still an open question.<sup>2</sup> Hip protectors may reduce the incidence of fractures in old people who are institutionalized. However, there is a lack of evidence for the benefit of hip protectors in a lower-risk population, and they are associated with compromised user compliance.<sup>59,98</sup>

Despite past research that has concentrated on prevention of falls, there may be quite a long way to go to optimize effective interventions, matching and recruiting populations, and maintaining adherence. There may be a substantial difference between optimal interventions in a general population and optimal interventions in those living in institutionalized care. Many subgroups, such as the frail and cognitively impaired, may require further investigation before optimal interventions can be implemented.<sup>59</sup> In a Swedish RCT focusing on fall and injury prevention in residential care, a group with higher cognitive abilities had fewer falls after a multifactorial intervention program. Those with lower cognitive ability did not respond as well to the interventions, but the incidence of hip fracture was reduced in this group.<sup>99</sup> At a 1-year follow-up of a multidisciplinary, multifactorial fall prevention program directed at older individuals who had suffered a hip fracture, the program was found to reduce falls and injuries in inpatients, but no significant effects could be detected after discharge.<sup>100</sup>

In all, there are equivocal estimations about the total effectiveness of fall prevention in the elderly. According to one review, there are strong evidence that structured fall-preventive programs can reduce the number of falls in both community-living elderly and those living in institutions.<sup>62</sup> Contradictory, a meta-analysis reports that the current evidence for the effectiveness of multifactorial fall risk assessments and interventions is modest at best.<sup>95</sup> According to this report, many studies have not been sufficiently powered to be able to detect clinically important effects such as the rate of falls, severity of injuries, and the impact on quality of life. There is also an uncertainty about the cost effectiveness of intervention programs.

It has been suggested that to be effective, evidence-based preventive strategies should be used throughout all levels of the healthcare system<sup>74</sup>, and be part of everyday life in fall-prone elderly people.<sup>100</sup> There are in Sweden no current, national guidelines on

fall prevention, although The Swedish National Board of Health and Welfare mentions fall prevention in their national guidelines for the diseases of the musculoskeletal system.<sup>101</sup> According to this text, an individualized multi-professional fall prevention approach is recommended. The level of evidence for preventing falls using this method is estimated as moderate. In Denmark and Norway, the healthcare system have established special outpatient clinics at key hospitals for elderly patients suffering from falls, instability and syncope.<sup>102,103</sup> This concept is not implemented in Sweden.

## Health-related quality of life and life satisfaction

The WHO has defined health as being *'not only the absence of disease and infirmity, but also the presence of physical, mental, and social well-being'*.<sup>104</sup> It is now widely acknowledged that the personal burden of illness cannot be described fully by measures of disease, such as size of infarction or tumor load.<sup>105</sup> Psychosocial factors such as functional impairments, pain, and difficulty in fulfilling personal and family responsibilities must be taken into account. Falls and associated complications appear to generate substantial and possibly long-term reduction in the quality of life of elderly people.<sup>65,106</sup>

Since the Second World War, the term 'quality of life' has been widely established, especially in healthcare practice and research.<sup>107,108</sup> Improved quality of life can be seen as the most desirable outcome of all healthcare policies, especially in an elderly population.<sup>109,110</sup> In those with chronic multimorbidity and frailty, perceived health and well-being can be more adequate apposed medically defined diagnoses. Although quality of life originally lacked a consistent definition, the WHO has conceptualized it as *'individuals' conceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns'*.<sup>111</sup> Health-related quality of life (HRQoL) refers to the physical, psychological, and social domains of health. This concept has been widely used in surveys of health status in clinical practice.<sup>112</sup> Concerning falls, there is evidence that their main burden regarding morbidity, measured as impact on HRQoL, stems from fear of falling rather their physical sequelae.<sup>106</sup>

Overlapping the concept of quality of life, the concept of life satisfaction (LS) was developed in the 1960s by Bernice Neugarten, who wanted to measure general mental well-being in an elderly population.<sup>113</sup> LS can be defined as *'a cognitive judgemental global evaluation of one's life, or not just an absence of disease or disability but also includes the satisfaction of social and psychological needs'*.<sup>113,114</sup> In comparison, HRQoL can be seen as measuring present health and health in the past month, and LS corresponds to a global instrument measuring life satisfaction in a life perspective. Several studies in Malmö on the GÅS population have identified circumstances that



affect LS, especially in the oldest-old.<sup>115</sup> Burden of symptoms, functional capacity, marital status, and cognitive ability appeared to be factors that proved important for maintenance of LS in advanced age. In relation to falls, there has been limited research encompassing the concept of LS.

## Activities of daily living

In geriatric medicine, clinical practitioners have long recognized the importance of assessing physical function and disability, alongside traditional diagnosis of diseases.<sup>116</sup> The concept of the comprehensive geriatric assessment has been used in this context, and determines a person's medical, psychosocial, functional, and environmental resources and problems.<sup>117</sup> From the point of view of the affected individual (e.g. after a hip fracture), the most central aspect of quality of life may be the ability to remain independent in the home environment.<sup>118</sup> The concept of ADL, measuring the individual's functional status, is a cornerstone of geriatric rehabilitation and has been developed and refined since the 1950s.<sup>119</sup>

The original ADL index was developed after the observation that functional recovery in disabled patients was similar to the order of development of primary functions in children. The initial index was based on primary biological and psychosocial functions, categorized as six tasks: bathing, dressing, going to the toilet, transferring, continence, and feeding.<sup>119,120</sup> Besides being useful in evaluating an individual's rehabilitation progress, ADL can be used to study the progression of disability in the aging process.<sup>116,120</sup> According to several studies, falling is an independent determinant of a general functional decline, dependency in ADL, and a reduction in physical activity.<sup>121–123</sup>

## Rationale of this dissertation

Research aimed at understanding falls in the elderly dates back 50 years.<sup>76</sup> In the last decade, the pendulum of the state-of-the-art research has shifted to intervention studies evaluated through RCTs. Despite these efforts, falls still generate a heavy burden of mortality and morbidity in the elderly.<sup>2</sup> The overall rationale of this dissertation was to gain knowledge about risk factors and consequences of falls in a general elderly population, with reference to the following aspects.

### *A changing demographic*

In light of the rapidly changing demographic distribution in the last century, the health of the elderly population of today is different from that 50 years ago. For example, due to substantial interventions regarding risk factors and a revolution in treatment, the death rates from coronary heart disease in the United States have undergone a profound decline.<sup>124</sup> After peaking in 1968, the age-adjusted death rates have now been reduced by 50%. In line with this, there is a need for continuous research on the dynamic, elderly segment of the population. With an aging population and overextended healthcare systems, further insight on factors and circumstances that would explain falls is needed. For example, little is known and published about falls and risk factors in the oldest-old,<sup>45</sup> an expanding segment of the population with a significant morbidity burden. This may be because of the difficulty in recruiting the oldest and frail individuals to studies. The population studied in this dissertation includes a significant proportion of the oldest-old.

### *Using a disease-oriented approach*

According to Delbaere et al. (2010), there has been a tendency to use a physiological impairment approach rather than a disease-oriented approach in evaluating risk factors for falls.<sup>76</sup> Attributing fall risk to a specific medical diagnosis has been problematic, because the conditions may vary considerably in a population.<sup>125</sup> For example, as mentioned, the relationship between cardiovascular conditions and falls in the elderly is largely unknown.<sup>2</sup> Several other potentially clinically relevant conditions related to falls, such as anemia and the use of neuroleptics drugs, have not been widely studied in the general population.<sup>75</sup> The first two studies of this dissertation included a broad spectrum of medical conditions, evaluated by a physician in a medical examination setting.

### *A general elderly population*

According to a review of the literature, several studies on falls have used small and often highly selected, and sometimes non-random, sample populations.<sup>47</sup> The generalizability may therefore not have been appropriate. Furthermore, small sample sizes generate low statistical power, and important clinical associations can remain undetected. For example, Lord et al. (2007) stated that individuals using neuroleptics in the general population may not constitute sufficient numbers to be able to detect any significant relationship to falls.<sup>7</sup> In a review of 74 studies investigating risk factors for falls in a general population, 60% had a sample size of less than 1,000 subjects.<sup>75</sup> In contrast, this dissertation includes studies with larger sample sizes, randomly selected from a *general* elderly population. This approach may generate sufficient statistical power to allow detection of potential important associations between falls and conditions with low prevalence.

### *Using a prospective, long-term approach*

Other methodological issues occur in the published research on falls in the elderly. Some earlier findings were based on studies with retrospective or cross-sectional design.<sup>47</sup> This approach does not provide the ability, as in prospective studies, to show a temporal relationship in the association, i.e. to assess outcome after exposure. This is an absolute criterion when explaining causal relationships.<sup>126</sup> Several prospective studies have used a short follow-up period. Three systematic reviews of studies on risk factors for falls in individuals over 64 years of age included 23 prospective studies from 1988 to 2009.<sup>68,73,127</sup> The follow-up period ranged from 16 days to a maximum of 16 months, with the majority having a 1-year design. In line with this, according to a recent meta-analysis of 74 prospective studies on risk factors for falls, only 30% had a follow-up period of over 1 year.<sup>75</sup> Three of the four studies included in this dissertation were prospective in design, with lengthy follow-up periods of three and/or six years. This long-term approach may generate findings that are relevant in a prevention setting, where long-term reductions in risk are desirable outcomes. A risk factor with long-term consequences identified may be of extra value in interventional efforts. A long-term approach may also detect factors associated to ill-health, which the healthcare system may not optimally assess and rehabilitate over an extended period of time.

### *Aspects of well-being and functional ability*

As many studies have focused on the physical consequences of falls, there is an explicit need for studies evaluating falls in other measurements, such as the concepts of HRQoL and LS.<sup>65</sup> A literature review from 2012 assessing what we know about quality of life and falls in the elderly revealed gaps in knowledge, unclear definition of the concept, and an abundance of descriptive studies.<sup>128</sup> Although LS is established in measurement of well-being in later life, to our knowledge, there have been no studies investigating the association between LS and falls in the general elderly population.

In an aging population, an increasing proportion of individuals with functional disability and loss of independence can be expected.<sup>118,129</sup> With an impending increase in falls, it is relevant to study the interaction between a longitudinal change in ADL and falls. This consideration could be helpful in identifying groups that are at risk of falling, and to gain a better understanding of the natural course of disability over time.

# Objectives

The specific objectives of the studies included in this dissertation were as follows:

**Paper I:** To describe the prevalence of falls in a general elderly population, especially in the oldest-old, and to identify risk factors associated with falls. In addition, to analyze the relationship between increasing number of risk factors and falls.

**Paper II:** To identify risk factors that predict falls in a general elderly population after three and six years, using a multifactorial approach, and to present significant predictors in thematic components.

**Paper III:** To prospectively examine the long-term relationships between falls and HRQoL and LS over a 6-year period in a general elderly population.

**Paper IV:** To determine the relationship between change in ADL and falls over a 6-year period in a general elderly population, and to identify characteristics of groups at risk for falls.



# Methods

## Study population

The longitudinal, long-term, multi-purpose population study ‘Swedish National Study on Aging and Care’ (SNAC) involves four research centers that collect data in four different areas of Sweden.<sup>130</sup> The main goal of the study is to characterize the aging process, health, and care of the general elderly population in different aspects. The part of SNAC that operates in the province of Skåne is called ‘Good Aging in Skåne’ (GÅS). Skåne is the most southerly province in Sweden; in the beginning of 2014 it had 1,277,000 inhabitants.<sup>131</sup> It is divided into 33 municipalities, and Malmö, Sweden’s third largest city, has 314,000 inhabitants. Approximately 17% of the inhabitants of Skåne were born outside Sweden.

This dissertation is based on data from the GÅS population study, which involves five municipalities in Skåne, covering both urban and rural areas: Malmö, Hässleholm, Ystad, Eslöv, and Osby.<sup>31</sup> The subjects invited to participate were randomly selected from the National Population Register using a computerized random number generator. Proportions were weighted so that more subjects came from urban areas than from rural areas, and a higher proportion of the elderly was included, in relation to the background population. Citizens from all areas of the towns were invited to try to avoid any selection bias due to socioeconomic status. The only exclusion criterion was inability to speak and understand the Swedish language in absence of a relative that could interpret. There was no exclusion of subjects living in institutionalized care or sheltered housing. Home visits were offered to subjects who were unable to get to the research center. Approximately one in ten of the assessments were performed this way. Help to fill in the questionnaires was offered to subjects with difficulties in reading or writing. Subjects with cognitive impairment were invited to participate in the study with the help of others.

Initially, 5,370 subjects were invited to participate by letter. The GÅS population study included men and women from nine age cohorts: 60, 66, 72, 78, 81, 84, 87, 90, and 93 years. Altogether, 2,931 individuals agreed to participate, giving a response rate of 60% of those eligible at the time.<sup>132</sup> These subjects were recruited to a baseline assessment, which took place between February 2001 and July 2004; a lengthy inclusion period was needed due to the scope of the study. The older cohorts, aged over 78 years at baseline, were invited to a 3-year follow-up assessment between January 2005 and June 2006. All cohorts were invited to a 6-year follow-up between March 2007 and December 2011. The response rate at the follow-up assessments was 80% of those eligible.<sup>132</sup> Those who only participated in the baseline assessment were

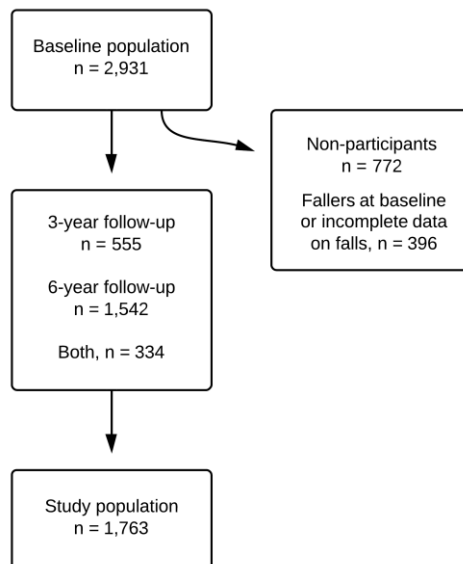
categorized as non-participants. A complementary, descriptive dataset of the characteristics of the initial GÅS study population at the baseline assessment is presented in Table 1.

### *Paper I*

This study used data from the baseline assessment. Altogether, 2,865 subjects had complete data on falls and were included in the study population.

### *Paper II*

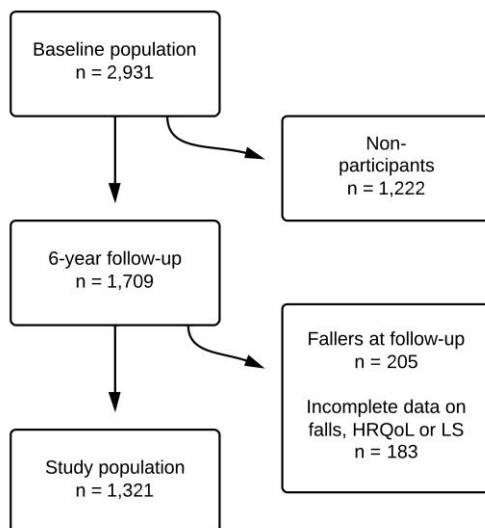
The second study used data from the baseline assessment and the 3- and 6-year follow-up assessments. The 772 subjects who did not participate in the follow-up were excluded. Furthermore, the 396 subjects who had a history of falling at baseline, or who had incomplete data on falls, were excluded. The study population consisted of a mixture of those participating in the 3- and/or 6-year follow-up; 334 subjects who were over 78 years of age at the baseline assessment participated in both follow-up assessments. In total, 1,763 subjects from the baseline assessment, enrolled in the 3- and/or 6-year follow-up with complete data, were included in the study population (Figure 1).



**Figure 1.** Flow chart of the inclusion of the study population in Paper II.

### *Paper III*

This study used data from the baseline and 6-year follow-up assessments. The 1,222 subjects who did not participate in the follow-up were excluded. Furthermore, the 205 fallers at the follow-up assessment, together with 183 subjects with incomplete data on falls, HRQoL, and LS, were excluded. In total, 1,321 subjects from the baseline assessment, enrolled in the 6-year follow-up with complete data, were included in the study population (Figure 2).

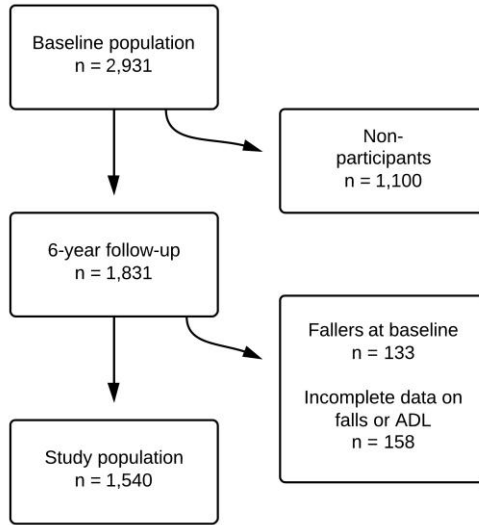


**Figure 2.** Flow chart of the inclusion of the study population in Paper III.

### *Paper IV*

The fourth study used data from the baseline and 6-year follow-up assessments. The 1,100 subjects who did not participate in the follow-up were excluded, a lower proportion than in Paper III, as data had been added to over time. The 133 fallers at the baseline assessment, together with 158 subjects with incomplete data on falls and ADL, were excluded. In total, 1,540 subjects from the baseline assessment, enrolled in the 6-year follow-up assessment with complete data, were included in the study population (Figure 3).





**Figure 3.** Flow chart of the inclusion of the study population in Paper IV.

## Variables and data collection

At the baseline and follow-up assessments, the subjects underwent a day-long comprehensive examination and evaluation by a purpose-trained physician, a registered nurse, and a test-leader. Medical, functional, and cognitive assessments were complemented with self-reported questionnaires. Identical protocols were used at the baseline and follow-up assessments. Since the examination was rather extensive, subjects were offered the possibility of splitting up the assessment in different sessions. Subjects with incomplete data were contacted after the assessment in order to obtain missing information.<sup>31</sup>

### *Operationalization of falls*

In the medical examination at the baseline and follow-up assessments, a physician recorded data on falls during a face-to-face interview with the subject. Using a structured questionnaire, the subject was asked: 'Have you fallen once or more in the last six months?' The answer was categorized as 'No', 'Once or twice', or 'More than twice'. This operationalization of falls was used in Papers I–IV. The circumstances, severity, or outcome of the fall event were not recorded. In Paper I, falls were used as the dependent variable recorded at the baseline assessment. In Papers II and IV, falls were used as the dependent variable assessed at the 3- and/or 6-year follow-up. In Paper III, falls were used as an independent variable recorded at the baseline assessment.

Papers I and II included the following variables:

### *Medical and psychological factors*

The physician's assessment was based on three components: physical examination, medical history, and medical records. The categorization of somatic diseases was based on the ICD-10.<sup>32</sup> The factor heart disease included the prevalence of angina, myocardial infarction, and arrhythmia. Congestive heart failure with symptoms was identified using the New York Heart Association (NYHA) Functional Classification criteria together with the ICD-10 diagnosis, and included subjects with NYHA class II–IV symptoms.<sup>133</sup> These classes include symptoms ranging from slight limitation of physical activity to inability to carry on any physical activity without discomfort. The factor stroke included cerebral infarction, hemorrhage, and transient ischemic attack. COPD, diabetes type 1, osteoporosis-related fracture, hip fracture, osteoarthritis of hip and/or knee, epilepsy, Parkinson's disease, and dementia were categorized using the ICD-10.<sup>32</sup> Anemia was classified using a venous blood sample (Hemoglobin <134 g/L for men, Hemoglobin <117 g/L for women).<sup>134</sup>

Depression and psychosis was coded using the Diagnostic and Statistical Manual of Mental Disorders, 4th version (DSM-IV).<sup>135</sup> A score below 24 points on the Mini-Mental State Examination scale (MMSE, range 0–30 points) defined cognitive impairment.<sup>136</sup> The prevalence of sleeping disorders was assessed using a self-reported questionnaire based on the research of Livingston et al. (1993).<sup>137</sup>

### *Use of medication*

The subject's ongoing medication was recorded by a physician using the Anatomical Therapeutic Chemical classification system (ATC).<sup>138</sup> The use of sedatives/hypnotics, neuroleptics, anticholinergic drugs, antihypertensive drugs (beta-blockers, ACE

inhibitors, calcium-channel blockers), and diuretic drugs (thiazide and loop diuretics) was categorized separately. The use of one or more of these medications was also categorized as ‘use of fall risk drugs’, with reference to earlier research.<sup>85-87</sup> The use of other drugs was categorized as ‘use of other drugs’.

### *Sensory and neuromuscular factors*

The prevalence of vertigo, current pain, urine incontinence, and nocturia was assessed using self-reported questionnaires.

### *Balance and mobility*

Information on a self-perceived tendency to fall and pain during movement was obtained from self-reported questionnaires. Impaired mobility was defined as using a walking aid. Walking speed was measured by timing the subject’s walking speed over 15 meters without running. Low walking speed was defined as obtaining a time above the median value for the study population. A score of 1 or 2 on the 6-grade Mattiasson-Nilo scale for the classification of physical activity was classified as low physical activity.<sup>139</sup> A maximum score of 6 corresponds to ‘hard or very hard exercise regularly’, and a score of 1–2 corresponds to an activity level of ‘hardly no physical activity’, or ‘mostly sitting, sometimes a walk, easy gardening or similar tasks’.

### *Environmental and sociodemographic factors*

Age and sex were recorded at recruitment to the study. Higher education was defined as completion of at least one year of higher education after secondary school. Information about the subject’s housing situation was obtained from a questionnaire. Living in a residential home or a retirement or nursing home was defined as living in sheltered housing. Outdoor adaptation of housing was defined as the provision of improved accessibility for people with mild or severe disabilities, or for those in wheelchairs. Indoor adaptation was defined as having thresholds removed, the bath being replaced by a shower, all rooms being made accessible by wheelchair, and/or the installation of a contact alarm or a stair-lift.

Apart from the variables described above, Papers I and II included data on independence/dependency regarding ADL. Paper IV used this assessment in more depth, complemented with the ADL staircase.

### *Functional ability*

ADL was assessed through self-reported questions according to the revised ADL scale of Sonn and Åsberg, using identical protocols at the baseline and follow-up

assessments. This instrument is a development of Katz' ADL index.<sup>140,141</sup> The instrument comprises ten activities, which can be divided into four instrumental activities (iADL: cleaning, grocery shopping, transportation, and cooking) and six personal activities (pADL: bathing, dressing and undressing, use of the toilet, mobility, incontinence, and food intake).

These activities can be arranged hierarchically in the form of the ordinal 10-step ADL staircase, where a higher score indicates dependency in a more basic activity, and an overall lower functional ability. Those who are dependent in activities with a higher score (e.g. food intake) are estimated to be dependent in activities with a lower score. Dependency in iADL was defined as independence in the activities of pADL while being dependent in at least one activity in iADL. Dependency in pADL was defined as being dependent in at least one activity in pADL.

Paper III included data on HRQoL and LS:

### *Health-related quality of life*

The 36-item Short Form Health Survey (SF-36) has been constructed to survey health status in clinical practice. It is multidimensional in its form and consists of eight dimensions covering physical, mental, emotional, and social components.<sup>112</sup> In Paper III, HRQoL was evaluated using the 12-item Short Form Health Survey (SF-12). This is a shorter version of the established SF-36, which can be useful in large population studies. High consistency between the SF-12 and the SF-36 has been demonstrated.<sup>142</sup> SF-12 is a generic instrument that includes 12 items finalized into a physical and mental component summary (PCS and MCS). The SF-12 PCS includes the components general health, physical function, physical role limitation, and bodily pain, while SF-12 MCS involves mental role limitation, vitality, social function, and mental health. The total score for SF-12 PCS/MCS ranges from 0 to 100 in both, with a higher score indicating higher HRQoL.<sup>142,143</sup>

### *Life satisfaction*

LS was measured using the Life Satisfaction Index A (LSI-A), used in a questionnaire format of 20 questions. The index was developed by Neugarten, Havighurst, and Tobin (1961) and was aimed at measuring general mental well-being in an elderly population.<sup>113</sup> At its core, LSI-A is multidimensional in character and it covers five components of life satisfaction: (1) zest versus apathy, taking pleasure in activities that make up a normal life; (2) resolution and fortitude, considering life to be meaningful and accepting how life has been; (3) congruence between desired and achieved goals, feeling successful in having achieved major goals; (4) self-concept, having a positive

self-image; and (5) mood tone, having a positive, optimistic attitude and mood. The total score ranges from 0 to 40 with a higher score indicating a higher LS.<sup>113</sup>

## Study design and statistical analysis

In Papers I–IV, all variables were dichotomized according to either being or not being exposed to the factor, except for the following: Age was categorized according to the ordinal cohorts at the baseline assessment: 60, 66, 72, 78, 81, 84, 87, 90, and 93 years. In the descriptive analyses, age was presented in terms of decades. The score of HRQoL, LS, and the ADL staircase was used as a continuous variable. The cut-off values for the dichotomization of anemia, cognitive impairment, low walking speed, and low physical activity were described above.

### *Paper I*

By design, this was a cross-sectional study. The study population was divided into non-fallers, occasional fallers (with one or two falls during the previous six months), and frequent fallers (with more than two falls in the same period). Thirty-eight factors (described above) were included as independent variables.

The association between the three groups and the independent variables was analyzed using a multiple logistic regression model adjusted for age. The results were presented as odds ratios (OR). Also, the risk of falling with increasing number of significant, accumulated risk factors was analyzed with a logistic regression model, using the group with no risk factors as the reference group.

### *Paper II*

This was a prospective study. The study population was dichotomized into ‘fallers’ (who had experienced one or several falls six months before the 3- and 6-year follow-up assessments), or ‘non-fallers’ (who had not experienced any falls in the same period). The same 38 independent variables from Paper I were used, as recorded at the baseline assessment.

The association between falls recorded at the follow-up assessment and exposure to the independent variables at baseline was initially analyzed using a logistic regression model. The results were presented as crude odds ratios (cOR). Also, a multiple logistic regression model, adjusted for age and sex, was used to predict the risk of falling when exposed to the individual factors. The results were presented as OR.

As a large set of variables was analyzed, a principal component analysis (PCA) was used to group significant factors into smaller thematic and manageable components. This approach was used to reduce multicollinearity in the explanatory variables, and

to produce a smaller number of uncorrelated components predicting falls. Before performing the PCA, the suitability of the data was assessed as described in the Results section. The factors in each retained component were dichotomized into a 'dummy variable', representing the whole component. The risk of falling associated with the components was analyzed in a final multiple regression analysis, with the components adjusted for each other. The results were presented as OR.

An attrition analysis was made to compare the characteristics of sociodemographic, comorbidity and use of medication of the non-participants after the baseline assessment, with the study population. Pearson's chi-squared test was used to analyze statistical differences within the factors included.

For a more comprehensive interpretation of the findings, a complementary, descriptive analysis was made of the pharmaceutical indications and characteristics of those using neuroleptic drugs in the GÅS baseline population (Table 4).

### *Paper III*

By design, this was a prospective study. Falls were dichotomized in the same way as in Paper II, but in contrast, this measure was used as an independent variable at the baseline assessment. The dependent outcome variables, the scores of the SF-12 PCS/MCS and LSI-A, were recorded at the 6-year assessment. All other variables included were recorded at the baseline assessment. The score of the SF-12 PCS/MCS and LSI-A was also recorded at the baseline for a descriptive analysis. Comorbidity included the prevalence of heart disease, heart failure with symptoms, COPD, osteoporosis-related fracture, cancer, and cognitive impairment. Social factors included the prevalence of higher education, cohabitation, and urban/rural living. Prevalence of low walking speed was used to adjust for general frailty.

Initially, the statistical differences between non-fallers and fallers at the baseline assessment in the categories age, sex, social factors, low walking speed, and comorbidity were analyzed using Pearson's chi-squared test and Analysis of Variance (ANOVA). The differences in mean scores of SF-12 PCS/MCS and LSI-A between non-fallers and fallers at the baseline and follow-up assessment, and the changes over time (the value of  $\Delta$ ), were analyzed using independent-samples t-test.

Furthermore, a multiple linear regression model adjusted for age, sex, social factors, the baseline score of SF-12 PCS/MCS and LSI-A, and the prevalence of low walking speed and comorbidity, was used to predict the outcome of falls at the baseline assessment, on the variables SF-12 PCS/MCS and LSI-A at the follow-up assessment. The results were presented as B-coefficients.

## *Paper IV*

This was a prospective study. Falls was used as the dependent variable; it were recorded at the 6-year follow-up assessment and dichotomized in the same way as in Papers II and III. The study population was divided into eight groups related to the subject's change or no change in ADL independence/dependency from the baseline to the 6-year follow-up assessment. Furthermore, the study population was divided into four groups according to change or no change in the ADL staircase over the same period.

The association between falls and each group, was initially analyzed using a logistic regression model, with the results presented as cOR. In the analyses of the groups with change in ADL status, the group that stayed independent in ADL was used as the reference, and for the ADL staircase the corresponding reference group was those with no change in score. To adjust for confounding factors, a multiple logistic regression model was used, adjusted for age, sex, and comorbidity. This model was based on the components predicting falls in Paper II. As the components 'reduced mobility' and 'functional impairment' were assumed to be intimately associated with ADL, only the component 'heart dysfunction' (including the factors heart disease, heart failure with symptoms, and the use of fall risk drugs), was used to reduce multicollinearity in the exploratory variables. The results were presented as OR.

Finally, a descriptive analysis was made of characteristics of clinical interesting groups with significant risk of falling. The characteristics of sociodemographic, comorbidity and the use of medication were separately compared to those who remained independent in ADL. The statistical significance of differences was analyzed using Pearson's chi-squared test, complemented with Fischer's exact test when sample sizes were small.

### *Comparative analysis*

For an analytical interpretation of the operationalization of falls in this dissertation, a complementary, comparative analysis was made of the proportions of fallers in the GÅS baseline population, according to age and sex. Data were extrapolated from a 6-month period to a 12-month period, and compared to the 12-month study of fallers in a general population by Prudham et al. (1981).<sup>144</sup> This was a survey study recording falls over one year in a general population over 65 years in northern England (Figure 7).

### *Statistics*

The IBM® SPSS® software package version 18 and 20 were used for the statistical analyses in Papers I–IV.<sup>145</sup> A 95% confidence interval (CI) and a p-value of <0.05 defined statistical significance. All p-values were two-sided.

### **Ethics**

All studies were approved by the Ethics Committee of Lund University, Sweden, and were conducted in accordance with the Declaration of Helsinki. All the subjects gave their written informed consent.





# Results

**Table 1.** Characteristics of the GÅS baseline population (n = 2,931).

	n	%
Men	1,294	44.2
Women	1,636	55.8
Age, years		
60–69	1,383	47.2
70–79	559	19.1
80–89	753	25.7
90–94	236	8.1
Municipality		
Malmö	1,846	63.0
Hässleholm	382	13.0
Ystad	309	10.5
Eslöv	270	9.2
Osby	124	4.2
Urban living	2,502	88.2
Rural living	335	11.8
Cohabiting	1,521	53.6
Living in apartment	1,714	60.6
Living in own house	896	31.7
Sheltered housing	107	3.8
Higher education*	494	16.9
Born outside Sweden	280	9.6
Dementia†, 60–79 years	39	2.0
Dementia†, 80–94 years	104	10.8
Suspected cognitive impairment‡, 80–94 years	204	24.3
Data on falls	2865	97.7

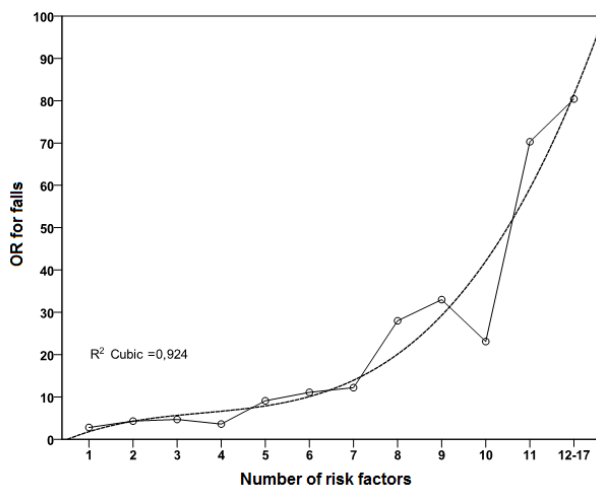
\*At least one year of higher education after secondary school.  
†Certain or suspected diagnosis.  
‡A score of < 24 points in the Mini-Mental State Examination test.

### *Initial baseline population*

There were slightly more women than men in the initial baseline population of the GÅS study (Table 1). One in three were 80 years or older, and almost nine out of ten lived in an urban setting. Over 90% lived in their own apartment or house, and almost 4% lived in sheltered housing. Approximately one in ten were born outside Sweden. About 11% of those 80 years or older had a certain or suspected dementia diagnosis. According to the MMSE test, slightly over 24% of the same age group had suspected cognitive impairment. A vast majority of the baseline population had data on falls (97.7%).

### *Paper I*

About one in ten of the study participants had fallen during the previous six months: 9.8% ( $n = 281$ ) had fallen once or twice, and 1.7% ( $n = 49$ ) had fallen more than twice. The incidence of falls increased distinctly with advanced age, and was very common in the oldest-old. Over one in three of the frequent fallers were in the category  $\geq 90$  years old. Women fell more than men; there were more women in the group of occasional fallers and frequent fallers, 64.4% and 65.3%, respectively, than men. In the adjusted analysis, 21 risk factors were found to be significantly associated with falls. The five risk factors with the most prominent risk for falls in frequent fallers were a subjective tendency to fall (OR = 37.9,  $p = <0.001$ ), low walking speed (OR = 12.8,  $p = 0.017$ ), use of neuroleptics drugs (OR = 10.9,  $p = <0.001$ ), impaired mobility (OR = 10.0,  $p = <0.001$ ), and living in a residential home (OR = 8.4,  $p = <0.001$ ). Fall risk appeared to increase in a non-linear, almost exponential way with increasing number of accumulated risk factors (Figure 4).



**Figure 4.** Risk of falling (expressed as odds ratios, OR) with increasing number of risk factors, plotted with an interpolated curve ( $n = 2,865$ ).

## *Paper II*

At the 3-year follow-up assessment with the older cohort (age over 78 years at the baseline assessment), 19.1% (n = 106) of the subjects had fallen during the previous six months. The corresponding proportion at the 6-year follow-up was 13.3% (n = 205). After adjustment for age and sex, 11 factors carried a significantly increased risk of falling, with OR ranging from 1.35 to 3.30. The use of neuroleptics drugs (OR = 3.30, 95% CI 1.15 to 9.43) and heart failure with symptoms (OR = 1.88, 95% CI 1.17 to 3.04) were the most prominent individual risk factors, although their confidence intervals overlapped those of other significant risk factors. Use of neuroleptics had low prevalence in the study population (1.2% of those with recorded medication).

All statistically significant factors except the use of neuroleptics drugs, being a part of fall risk drugs, were included in the PCA. Examination of the correlation matrix revealed the presence of nine coefficients of 0.3 and above, indicating a moderately positive relationship according to our definition. The analysis revealed four independent components with eigenvalues exceeding 1, explaining 51.7% of the variance. Inspection of the screen plot revealed a clear break after the third component. As the fourth component consisted of a single variable, a three-component solution was chosen (Table 2). Direct oblim rotation was used to calculate the factor loadings of the variables, and no correlation over 0.3 was found between the components. Finally, the PCA revealed three independent components predicting falls:

Reduced mobility, OR = 2.12 for falls (95% CI 1.54 to 2.91), including the factors indoor adaptation, osteoarthritis of hip and/or knee, low walking speed, and impaired mobility.

Heart dysfunction, OR = 1.66 for falls (95% CI 1.26 to 2.20), including heart disease, heart failure with symptoms, and fall risk drugs.

Functional impairment, OR = 1.38 for falls (95% CI 1.01 to 1.88), including dependency in pADL and nocturia.

According to the data extracted from the attrition analysis (Table 3), the non-participants (n = 772) were significantly older compared to the study population (n = 1,763), with a greater burden of somatic disease, cognitive impairment, consumption of fall risk drugs, immobility, and dependency in ADL.

**Table 2.** Principal component analysis with eligible components and their predicted risk for falls, expressed as odds ratios, OR (n = 1,763).

Risk factors	Component and factor loading		
	Reduced mobility	Heart dysfunction	Functional impairment
Indoor adaptation	.66		
Osteoarthritis of hip and/or knee	.63		
Low walking speed	.58		
Impaired mobility	.41		
Heart disease		-.78	
Heart failure with symptoms		-.71	
Use of fall risk drugs		-.59	
Dependency in pADL			.87
Nocturia			.85
OR for falling	2.12	1.66	1.38
(95% CI)	(1.54 to 2.91)	(1.26 to 2.20)	(1.01 to 1.88)

**Table 3.** Data extracted from attrition analysis. Comparison of various characteristics in non-participants and participants. Statistical differences were analyzed with Pearson's chi-squared test.

Age (decade)	Non-participants (n = 772)		Study population (n = 1,763)		p-value
	n	%	n	%	
80	222	28.8	379	21.5	<0.001
90	89	11.5	55	3.1	<0.001
Risk factors					
Heart disease	204/766	26.6	387/1,759	22.0	0.012
Stroke	98/771	12.7	135/1,758	7.7	<0.001
Hip fracture	27/760	3.6	31/1,742	1.8	0.007
Dementia	52/733	7.1	37/1,701	2.2	<0.001
Cognitive impairment	127/695	18.3	139/1,715	8.1	<0.001
Use of fall risk drugs	393/772	50.9	635/1,763	36.0	<0.001
Urine incontinence	149/690	21.6	267/1,720	15.5	<0.001
Impaired mobility	153/700	21.9	154/1,730	8.9	<0.001
Low physical activity	238/717	33.2	293/1,739	16.8	<0.001
Residential home	28/727	3.9	19/1,744	1.1	<0.001
Dependency in pADL	222/686	32.4	390/1,714	22.8	<0.001

The complementary analysis of those using neuroleptic drugs in the GÅS baseline population (Table 4, n = 59) showed that two-thirds used typical neuroleptics and one-third used atypical drugs, respectively. The latter group was older, with signs of a greater burden of cognitive impairment. The most common indication was anxiety/sedation followed by psychotic symptoms. Almost one in five had an unclear indication for using neuroleptics. Almost 12% had the indication behavioral and psychological symptoms of dementia (BPSD). This was an elderly group, and all lived in sheltered housing and had signs of cognitive impairment according to their dementia diagnosis.

### *Paper III*

At the follow-up assessment, the male population had a general higher mean score in SF-12 PCS/MCS and LSI-A than the female population ( $p = <0.001$ ). All mean scores decreased significantly with advancing age, but SF-12 MCS had a less pronounced decline. Subjects with prevalence of co-morbidity, low walking speed and absence of co-habiting and higher education had significantly reduced scores in all outcomes ( $p = <0.001$ ), except in SF-12 MCS with the absence of higher education ( $p = 0.159$ ).

**Table 4.** Pharmaceutical indications and characteristics of those using neuroleptic drugs in the GÅS baseline population (n = 59).

Indication	n (%)	Sheltered housing, %	Age over 80 years, %	MMSE† < 24, %
Psychotic symptoms	17 (28.8)	46.7	47.1	50
BPSD*	7 (11.9)	100	85.7	100
Anxiety/Sedation	22 (37.3)	17.6	54.5	37.5
Bipolar disorder	2 (3.4)	0	0	0
Other/Unknown	11 (18.6)	25	54.5	37.5
Typical neuroleptics	39 (66)	33.3	46.2	37.5
Atypical neuroleptics	19 (32)	61.5	73.7	62.5
No data	1 (2)	0	0	0

\*Behavioral and psychological symptoms of dementia.  
†Mini-Mental State Examination test.

Fallers scored significantly lower in SF-12 PCS/MCS and LSI-A at the baseline assessment and 6-year follow-up than non-fallers, especially in the SF-12 PCS ( $p < 0.001$ ) (Table 5).

The values of  $\Delta$  were minimal in the SF-12 MCS and LSI-A instruments, for both fallers and non-fallers. In SF-12 PCS, the values of  $\Delta$  were notably different, with a mean reduction of 2.5 points in fallers as compared to 1.6 in non-fallers, although the difference was not statistically significant.

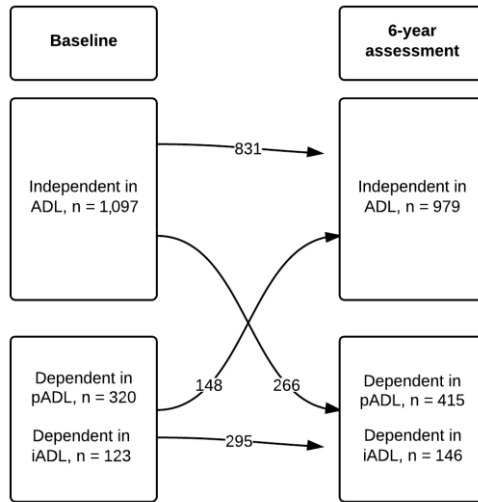
In the adjusted linear multiple regression analysis, one or more falls at the baseline assessment predicted a significant reduction in SF-12 PCS at the follow-up assessment (B-coefficient -1.8, 95% CI -3.4 to -0.2).

**Table 5.** Mean scores at the baseline and 6-year follow-up assessments in non-fallers and fallers in the SF-12 physical component summary (PCS, 0–100), mental component summary (MCS, 0–100), and Life Satisfaction Index A (LSI-A, 0–40). Changes over time described as the value of  $\Delta$ . Statistical differences were analyzed with independent-samples t-test ( $n = 1,321$ ).

	Baseline	p-value	6-year follow-up	p-value	Value of $\Delta$	p-value
SF-12 PCS						
Non-fallers	48.2		46.6		1.6	
Fallers	41.8	<0.001	39.3	<0.001	2.5	ns
SF-12 MCS						
Non-fallers	55.3		55.3		0	
Fallers	52.5	0.001	52.4	0.004	0.1	ns
LSI-A						
Non-fallers	28.4		28.3		0.1	
Fallers	25.4	<0.001	25.3	<0.001	0.1	ns

### *Paper IV*

Slightly more than one in four (26.9%,  $n = 414$ ) of the study population had changed ADL status over six years. Seventeen percent ( $n = 266$ ) went from independence in ADL to dependency in iADL or pADL (Figure 5). Almost one in ten (9.6%,  $n = 148$ ) went from dependency in iADL or pADL to independence in ADL.



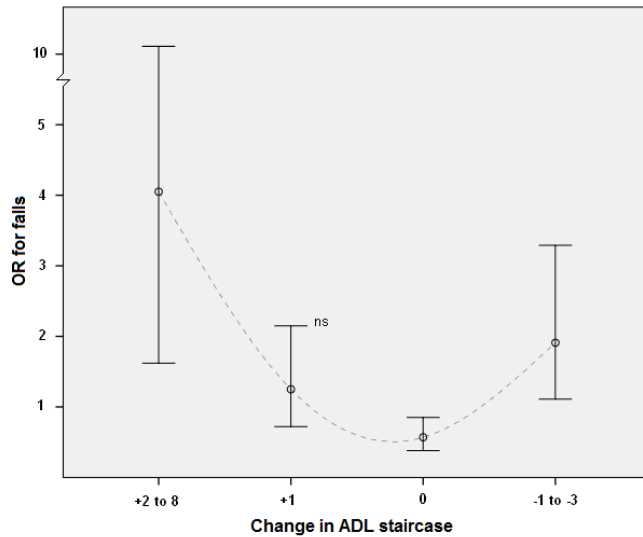
**Figure 5.** Status in activities of daily living (ADL) at baseline and 6-year follow-up assessment (n = 1,540).

According to the adjusted multiple logistic regression analysis, those who became dependent in ADL had an increased risk of falling compared to the reference group (those remained independent in ADL, n = 831), particularly the group who became dependent in pADL (OR = 2.31, 95% CI 1.42 to 3.76, n = 181). In line with this, the group with a marked functional reduction in the ADL staircase (2–8 steps) had an increased risk for falls compared to their reference group (no change in ADL staircase, n = 883), with OR 4.05 (95% CI 1.62 to 10.11, n = 29).

The group who became independent in ADL, from ADL dependency, also had a higher risk of falling than the reference group, particularly the group who became independent from iADL (OR = 4.13, 95% CI 1.89 to 9.00, n = 44). The group with an 1- to 3-step improvement in the ADL staircase had a higher risk for falls (OR = 1.91, 95% CI 1.11 to 3.29, n = 122) than the reference group. The trend in the association between change in the ADL staircase and falls is shown in Figure 6.

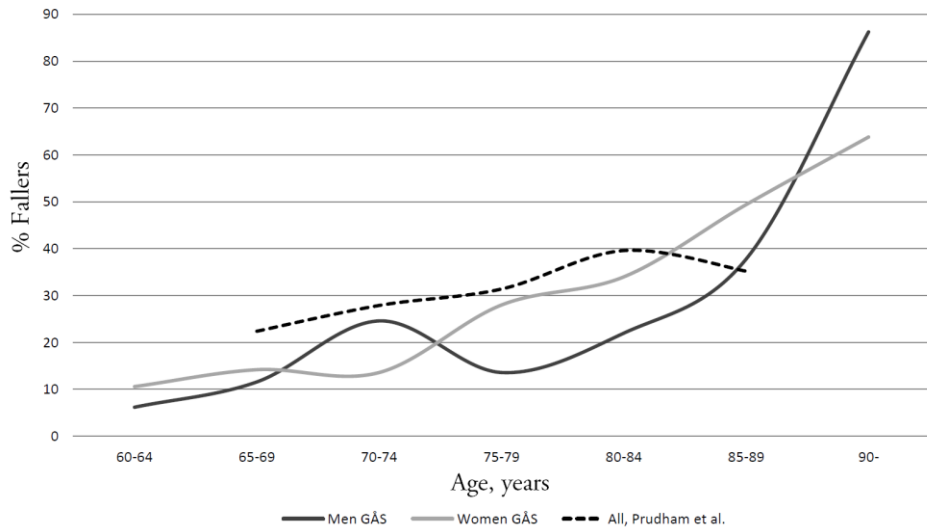
According to the analysis of the characteristics of groups with marked risk for falls, the group with a marked decline in the ADL staircase were significantly older, with greater burden of cognitive impairment, gait disability, arrhythmia, and use of fall risk medications than the group who stayed independent in ADL. The group who became independent from iADL dependency, had a higher prevalence of low walking speed and ischemic heart disease (angina and myocardial infarction) than those who stayed independent in ADL. This group included proportionately more men, but the difference was not statistically significant (p = 0.157).





**Figure 6.** Association between change in the ADL staircase (0–10 steps) over six years and the risk of falling, as recorded at the follow-up assessment. An increased score corresponds to a functional decline. Risk expressed as odds ratios (OR), with 95% confidence intervals shown by whiskers (n = 1,200).

According to the complementary, comparative analysis of the proportions of fallers (Figure 7), the ratio of fallers increased with advancing age in both populations (n = 2,865/2,357). The study population of Prudham et al. (1981) included 41% men and 59% women, a fairly concordant sex ratio to the GÅS baseline population. The proportions of fallers were slightly higher throughout the study by Prudham et al. although it did not include subjects over 90 years of age. Women fell generally more than men in the GÅS study, although male fallers were overrepresented among the oldest-old.



**Figure 7.** Proportions of fallers in the GÅS baseline population (n = 2,865), according to age and sex. Data extrapolated from a 6-month period to a 12-month period, and compared to the 12-month study of fallers in a general population by Prudham et al. (1981) (n = 2,357). Lines are interpolated between data points to show overall trend.



# Discussion

## Main findings and clinical implications

Falls seem to be a treat to successful and healthy aging as they are associated to a long-term reduction in HRQoL and LS, especially in the physical aspect of HRQoL. The diverse risk factors for falls identified in this dissertation confirm that falls in a general elderly population are a multifaceted health problem, and require concern at many levels of the healthcare system. Many risk factors appear to be adjustable, although there were strong associations between falls and advanced age and general frailty.

According to the findings of the first study, falls are common in a general elderly population, and the risk is multifactorial. There appears to be an overrepresentation of fallers in a distinct subgroup of the oldest-old, and a frail group with multiple risk factors. There was a strong, positive association between the number of accumulated risk factors and the risk of falling. The trend was apparently non-linear, almost exponential, with a marked rise after eight accumulated risk factors. This finding partly contradicts earlier research, where the fall risk increased linearly with accumulation of risk factors.<sup>41</sup> A more recent prospective study of 8,378 women from a general elderly population showed a similar association to the findings in Paper I, where the incidence of falls increased sharply after eight accumulated risk factors.<sup>146</sup>

### *Confirmatory findings*

A significant part of the independent risk factors that were found to predict falls were related to the musculoskeletal system: impaired mobility, osteoarthritis of the hip and/or knee, and low walking speed. These are confirmatory findings, as gait and balance impairment, muscle weakness, and musculoskeletal pain have been widely reported to be risk factors for falls.<sup>38,39,47,61,73,75</sup> These findings are already integrated into a variety of intervention programs for prevention of falls. According to a Cochrane review, various RCTs have shown that group and home-based exercise programs effectively reduce falls in a general elderly population.<sup>66</sup> According to guidelines from the American and British geriatric societies, older people who have had recurrent falls should be offered long-term exercise and balanced training.<sup>2</sup> Some trials that included this type of training showed a significant reduction in falls in addition to other benefits in gait, balance, and reduced fear of falling.<sup>51</sup> An additional British guideline recommends muscle-strengthening and balance programs for prevention of falls.<sup>147</sup> Those most likely to benefit are elderly people from the general population, with a history of falls and/or gait and balance deficits.

Although exercise as a single intervention has given positive outcomes, the optimal type, duration, and intensity of the exercise is still unclear. Although proven to be beneficial, exercise programs must be initiated with caution as some studies have shown that exercise may increase the rate of falling in people with limited mobility.<sup>51</sup>

### *Use of neuroleptics*

In the first study, the use of neuroleptic drugs had a strong association with falls. This association was confirmed in the following study, where neuroleptics were the single most prominent predictor for falls, although the confidence interval overlapped those of other significant risk factors. The prevalence of the use of neuroleptics was relatively low. Two percent of the baseline population in GÅS used neuroleptics drugs (Table 4).

As the use of psychotropic, and especially sedative/hypnotic drugs are a well-known risk factor for falls, an interaction between neuroleptic drugs and falls in a general elderly population may not have been as widely reported. This association was not found in community-living populations in studies from the 1990s.<sup>125,148</sup> This may have been due to milder symptoms or doses, or that the studies were not sufficiently powered to detect a relationship. More recent studies have found a moderate association between neuroleptics and falls in a general population.<sup>88-91,149</sup> Neuroleptic drugs are a heterogenic pharmaceutical group, but their main therapeutic action is dopamine receptor blockade.<sup>150</sup> The adverse effects of typical neuroleptics can emulate parkinsonism (dystonia, rigidity and tremors). The newer, atypical drugs can generate anticholinergic effects, combined with sedation and orthostatic reactions.

The finding that the use of neuroleptic drugs is a strong predictor for falls may be clinically significant, as they are used to medicate confusional states and BPSD in non-psychiatric, elderly patients. In the context of an aging population, the condition of dementia has been described as a silent epidemic, which is projected to increase worldwide.<sup>151</sup> In the GÅS population, the most common indication for neuroleptics was anxiety/sedation. In current medical practice, both older typical and newer atypical neuroleptic drugs are used to treat symptoms associated with dementia, confusional states and anxiety, although the proven positive effects have been limited.<sup>152</sup> Almost one in five who took neuroleptics had an unclear indication. According to data presented in Table 4, one in three of the users of neuroleptic drugs in the GÅS baseline population used typical neuroleptics. These individuals were seemingly younger and more cognitive intact than those using atypical drugs. You can hypothesize that these individuals used neuroleptics for psychotic symptoms, and atypical drugs were more commonly used for the 'geriatric indications' anxiety, sedation and BPSD. Inappropriate drug use may be one of the most adjustable risk factors for falls in the elderly. In a randomized controlled trial of an elderly cohort, withdrawal of psychotropic medication reduced the risk of falling, with a relative hazard risk of 0.34.<sup>153</sup> Even so, the strong association between the use of neuroleptics

drugs and falls may be confounded by a high prevalence of cognitive impairment in this group, a condition known to increase the likelihood of falling.<sup>2,56,61</sup>

### *Heart failure and related factors*

The finding that heart dysfunction is an independent predictor for falls is partly a confirmatory finding, and the most common cardiovascular disorders associated with falls are carotid sinus hypersensitivity, vasovagal syndrome, and brady- and tachyarrhythmias.<sup>51</sup> The finding that heart failure with symptoms was a predictor for falls, is an association that has not been widely reported. This risk factor may be relevant in a clinical geriatric setting, as heart failure is the only cardiovascular disease to have an increasing worldwide incidence, which is projected to rise significantly in the coming decades.<sup>154,155</sup> Today, heart failure is already the number one hospital discharge diagnosis for older adults in the United States.<sup>155</sup> At the same time, there has been a relative lack of published clinical trials in which the efficacy of heart failure treatment has been assessed exclusively in elderly individuals.<sup>154</sup>

The association between heart failure and an elevated risk for falls may be explained by adverse effects of the pharmacotherapy (e.g. diuretics, ACE inhibitors, and beta-blockers), although these medications taken individually did not predict falls in these studies. Response to pharmacotherapy for heart failure varies in elderly individuals, who are susceptible to adverse events such as orthostatic hypotension, incontinence, dehydration, electrolyte disturbance, and drug-drug interactions.<sup>154</sup> One common side effect of diuretics is hyponatremia, a very common condition in the elderly, which is associated with impairment of gait and attention.<sup>156</sup> In a case-control study, Renneboog et al. (2006) observed a higher number of falls in subjects with mild hyponatremia than in controls.<sup>157</sup> Subjects with moderate chronic hyponatremia fell considerably more frequently than subjects with normal sodium levels.

Furthermore, nocturia was found to be an independent predictor for falls. It may be explained by incontinence as a symptom of a general deterioration of health. Another mechanism may be that night-time visits to the toilet in the dark provide a high-risk environment for falls.<sup>83</sup> Diuretics or fluid treatment might be restricted late in the day, to avoid frequent toilet visits with risk of orthostatic reactions, dizziness, and other adverse events at night.

### *Deprivation of HRQoL and LS*

Falls predicted a long-term reduction in the physical aspect of HRQoL. These results contradict the theory that the mental consequences and fear of falling, rather than physical sequelae, dominate the reduction in HRQoL after a fall.<sup>106</sup> Severe injury after a fall is a rather rare event, even though some cases can be fatal.<sup>38,123</sup> Instead of actual physical harm, the long-term reduction in the physical aspect may result from insecurity and avoidance of activity, which indirectly may cause a decline in the

individual's physical function. The studies included in this dissertation have not considered the concept of fear of falling, but one could hypothesize that those prone to falling in the population studied would have a high score in this respect.

Overall, fallers scored significant lower in SF-12 PCS/MCS and LSI-A at the baseline assessment, than non-fallers, and continued to do so after six years. Fallers appear to be in a chronic, continuous deprived state regarding both HRQoL and the more global concept of LS, compared to non-fallers. This long-term reduction of well-being in fallers may be more extent than previously assumed. However, no direct causal relationship to falls can be proven as these associations may be confounded by advanced age and frailty. More research is needed on fallers' seemingly long-term reduction in this respect and its intimate association with general frailty, physical and functional decline, and comorbidity. As the need for prevention of falls is well-established, one clinical implication of this finding may be the need for a more continuous, physically and mentally-oriented follow-up of elderly people who are prone to fall.

### *Functional ability*

Over six years, 17% of the study population became dependent in ADL, and 16% had a functional decline in the ADL staircase. These results correspond well to a previous cohort study of the elderly, where 19% became more dependent in functional ability after 5 years.<sup>158</sup> One-quarter of the study population in Paper IV had a change in ADL status over six years, and this category included the groups with the highest risk of falling. The distinct group with a marked decline in the ADL staircase (2–8 steps) had a prominent risk for falls, although the confidence interval was wide. This appeared to be a group with impairments in several domains, consistent to frailty with a reduced ability to compensate. This group fulfilled many of the criteria of a 'geriatric syndrome', with a higher prevalence of advanced age, female gender, gait disability, arrhythmia, cognitive impairment, and consumption of fall risk medications.

Somewhat paradoxically, the group that improved their functional ability and became independent, from ADL dependency, had an increased risk for falls. Thus, the risk for falls in relation to the change in ADL could be plotted as a U-shaped curve (Figure 6). According to reviews, this pattern has been described in the literature regarding the association between physical ability and falls in the elderly, where the risk of falling has been suggested to be generally reduced in physically active people, with a potentially increased risk in the most active and least active individuals.<sup>47,159</sup> In a large prospective cohort study of a general population of elderly men, the most active quartile had a significantly greater risk for falls than the least active quartile.<sup>93</sup> This result confirms the previous findings that exercise may increase the rate of falling in subgroups with limited mobility, who are not accustomed to physical activity.<sup>51</sup>

The small group that became independent, from iADL dependency, had the most marked risk for falls, although the confidence interval was wide and overlapped those of other groups at risk. This group was generally younger with a predominance of men. Characteristically, they were physically and cognitively intact, with moderate consumption of risk medications, but with a higher prevalence of ischemic heart disease. In a study of 9,259 elderly individuals from a general population, the risk of falling peaked at an intermediate ADL limitation stage, an assumed point where the individual had significant disabilities but sufficient function to remain partially active.<sup>160</sup> In line with this, this particular at-risk group may consist of subjects with a history of comorbidity combined with sufficient mobility for exposure to a fall event.

These findings indicate that there are groups with different characteristics who are at risk for falls in a general elderly population. Thus, preventive measures may require different strategies. A meta-analysis of six studies reported that physical training reduced the number of older adults who fell.<sup>161</sup> In contrast, according to a literature review, it seemed questionable whether any intervention program with physical activity could reduce the number of falls in elderly individuals living in institutions.<sup>162</sup> This intervention may be too risky in this particular group, leading to falls during exercise.

## Methodological considerations

### *Generalizability of results*

One implicit aim of these studies was to generalize the results to the target population, a general elderly population. Forty percent of those initially invited to the GÅS study choose not to participate for various reasons.<sup>132</sup> No data were available on these subjects, but one could imagine that the more frail, immobile, and cognitively impaired would choose not to participate. Approximately 10% of those recruited at the baseline assessment were born outside Sweden (Table 1). In the total population of Skåne, 17% are born outside Sweden, and the city of Malmö has a higher proportion of foreign-born citizens (31%).<sup>131</sup> This possible underrepresentation of ethnic diversity may be due to language difficulties and cultural differences. However, as the older population of Skåne consists of fewer individuals born outside Sweden than in the younger generations, the ethnic diversity in the GÅS study may be adequate. The GÅS study had also a fairly balanced sex ratio at the baseline assessment (44% men, 56% women).

There are uncertainties about the precise prevalence of dementia in the general population of Sweden. A Swedish literature review estimated that the prevalence of dementia was 1–6% in a 60- to 79-year old population, and 12–37% in 80- to 94-year-olds.<sup>151</sup> In the baseline population of the GÅS study, 2% of those 60–79 years



old, and almost 11% of those 80 years and older, had a certain or suspected dementia diagnosis (Table 1). According to these numbers, subjects with dementia seem to be underrepresented in the study population compared to the background population. However, cognitive function was screened at the assessment using the MMSE test. Slightly over 24% of those 80 years and older had a score less than 24 points (Table 1), a cut-off value for suspected cognitive impairment. This result indicates that the GÅS study may have recruited an adequate sample population in including the cognitively impaired.

Twenty percent of those who had not died or moved during the GÅS study chose not to participate in the follow-up assessments.<sup>132</sup> Various characteristics of these non-participants were compared to the study population included in Paper II (Table 3). This attrition analysis showed that the non-participants were significantly older with a greater burden of somatic disease, cognitive impairment, consumption of fall risk drugs, immobility, and dependency in ADL. This analysis did not include age stratification, and a significant part of the inter-group differences may be explained by a higher mean age in the non-participants.

Despite efforts such as offers of home visits in the GÅS study, selection bias could not be excluded, which would affect the external validity and generalizability of the results. As falls are intimately associated with advanced age and general frailty, there may have been an underrepresentation of fallers in the sample population compared to the target population. This misrepresentation, of including more healthy subjects that seem to fall less, could be classified as a negative or 'toward the null' bias,<sup>163</sup> which may have systematically diluted the results throughout these studies.

### *Operationalization of falls*

The assessment of falls had various limitations in these studies. The subjects were asked if they had fallen in the previous six months. A longer period was not used, to try to minimize recall bias. As falls are a common event in the elderly, the ProFaNE network recommends that they should be recorded using prospective daily recordings, and a notification system with a minimum of monthly reporting.<sup>35</sup> Telephone or face-to-face interviews should be used to complement missing data. Due to the scope of the GÅS study, being a long-term, longitudinal study, the use of this method was not practicable.

In the GÅS study, the absolute number of falls during the previous six months was not recorded. Thus, an incidence ratio commonly preferred in epidemiological research, expressed as fall rate per person year, could not be calculated. The severity or consequences of a fall were not identified, which can be seen as a limitation, as the outcome of a fall event can be diverse in the elderly. Despite this, a dichotomized outcome variable such as falls versus no falls might be adequate, as any fall could be a serious event for the older individual, where low-impact falls can have serious consequences.<sup>164</sup>

A standard definition of a fall event was not used, as recommended by the ProFaNE network.<sup>35</sup> However, there is no unanimously accepted method of recording falls, and existing definitions may be impractical to use in a lay perspective. In a small study in an accident and emergency department in Wales, 107 subjects aged over 50 years were initially asked ‘Did you fall?’ after a suspected fall event.<sup>165</sup> After a detailed history of the events surrounding the fall was taken, the ‘Did you fall?’ question was estimated to have a sensitivity of 91.5%, and a specificity of 100% in assessing falls. The simplified approach to recording falls in the GÅS study appears to have good face validity, and may be able to identify non-fallers with a high degree of confidence. There may be underreporting of fallers, mainly because of recall bias. In line with this, fallers may find it difficult to estimate the exact number of falls retrospectively. Therefore, the use of the dichotomization faller/non-faller may be rational with the data at hand.

The distribution of falls in the GÅS study seems to be in fairly good agreement with the previous literature. The proportions of fallers increased with advanced age and women fell proportionally more than men (Figure 7), but the difference receded in the oldest-old – a trend seen in previous epidemiological research.<sup>48,144</sup> The overall proportion of fallers was lower in the GÅS baseline population in the age range 65–84 years than the Prudham et al. study (1981).<sup>144</sup> This may have been because of systemic underreporting and misclassification of falls, or because the study sample in the GÅS study was healthier overall.

There was a higher proportion of fallers in the oldest-old in the GÅS study, compared to Prudham et al., but this study only included 4% of those 85 years and older. The corresponding proportion for the oldest-old was 16% in the GÅS baseline population. In a prospective Swedish study from Umeå University, 40% of a cohort over 85 years of age fell during a 6-month period.<sup>45</sup> In GÅS, the corresponding proportion of fallers in the oldest-old was 28.4% in the same period. The higher frequency of fallers in the Umeå study may have been due to different sample characteristics; half of the study population lived in sheltered housing, a marker of general frailty. In the GÅS population, approximately 80% of the oldest-old lived in their own homes. In a Finnish study of individuals over 85 years of age living at home, 49% fell during an 11-month period.<sup>46</sup> Extrapolated to 11 months, 52.1% of the oldest-old would have fallen in the GÅS study.

In an international multi-center study of community-living men aged 65 years or older (n = 10,998), 18.7% reported that they had fallen during the 12 months preceding the baseline evaluation.<sup>166</sup> The corresponding, extrapolated proportion of male fallers in the GÅS baseline assessment was 18.4%.

### *Reliability and validity of variables*

The validity of the recording of medical diagnoses and medications in the GÅS study could be estimated as good, as the data were collected in a medical examination by a

purposed-trained physician. The operationalization of these variables was based on the international, established classifications ICD-10, DSM-IV, and ATC.<sup>32,135,138</sup> The physician had access to the subjects' computerized medical records. However, the prevalence of a diagnosis did not explain whether the subject was affected by the condition at the assessment. For example, a hip fracture may have had surgical intervention without complications, or earlier symptoms of angina pectoris could have been medically well-treated at the time. On the other hand, congestive heart failure was assessed using the established NYHA functional classification, as a complement to the ICD-10 diagnosis. The NYHA classification assessed the severity of symptoms from heart failure during physical activity at the examination.<sup>133</sup> The gold standard of heart failure diagnostics, echocardiography with an estimation of the heart's ejection fraction, was outside the scope of the GÅS study.

MMSE was used to assess cognitive function. It is an established instrument for screening of cognitive impairment in the elderly. It has shown good reliability in 24-hour and 28-day retests by single or multiple examiners.<sup>136</sup> It has also proven to be valid, and could separate the diagnostic groups of dementia, depression with cognitive impairment, and isolated depression in the elderly. Used in a serial order, the MMSE has proven to be able to follow changes in the cognitive state of a population.

HRQoL was measured using the SF-12, which is a shorter version of the SF-36 health survey. In a Swedish study, there was satisfactory empirical evidence that the SF-36 proved reliable in a non-English speaking country, with desired results for internal consistency reliabilities (Cronbach's  $\alpha > 0.70$ ).<sup>167</sup> The SF-36 health survey has proven to be useful for a variety of purposes, but it can be too long for inclusion in large-scale health measurement.<sup>143</sup> The use of SF-12 is justified in studies with large sample sizes, such as the GÅS study. The downsizing to the SF-12 has generated minimal loss of measurement precision, with studies showing a high degree of correspondence in reproducing SF-36 PCS and MCS measures using SF-12 items. The validity of SF-12 has usually been about 10% below that of the SF-36.<sup>168</sup>

LSI-A is one of the most widely used scales to measure LS in older people.<sup>169</sup> The index was developed to measure the psychological well-being of older people, using lengthy interview material. The scale was constructed and validated against the judgements of a clinical psychologist who re-interviewed some of the subjects.<sup>113</sup> Neugarten et al. (1961) originally tested the internal consistency of the index, and its validity and reliability have been evaluated over the years.<sup>113,170</sup> A meta-analysis of 34 studies that examined its generalizability found evidence for adequate reliability.<sup>169</sup> However, the measurement of subjective well-being is complex, and its conceptualization and measurement are somewhat controversial.<sup>171</sup> Neugarten's original index with five domains was used in Paper III, but subsequent research has offered models with less domains, which have provided a better fit for data from heterogeneous groups of elderly people.<sup>171,172</sup> The research concerning the optimal dimensionality of LS is in no way conclusive.

ADL is an internationally established instrument for assessment of functional ability. It can be measured through self-reporting, in an interview setting, or as a performance test. In the GÅS study, ADL was measured by self-reporting. The responses were assessed by the examining nurse, to verify that they were reasonably in line with the subject's functional status. The Sonn and Åsberg ADL scale used in these studies has shown high inter-observer reliability and good construct validity.<sup>141</sup> The internal consistency and the internal reliability of the instrument have proven to be satisfactory.<sup>140</sup> A high score in the ADL staircase has correlated well with a high level of assistance care or with the type of the individual accommodation, relationships that have indicated good external validity of the instrument.

### *Internal attrition*

Despite efforts to minimize internal attrition by re-contacting subjects with incomplete data, some variables included in these studies did have significant internal missing. In Paper III, 12.2% of the study population had to be excluded because of incomplete data on falls, HRQoL, and LS. In Paper IV, 9.3% of the study population had to be excluded due to incomplete data on falls and ADL. Furthermore, 340 subjects had no data on the ADL staircase, due to sensitivity of missing data in computing the score. One could hypothesize that the older, frail, and cognitively impaired subjects would not have completed the full assessment to the same extent as the healthier subjects, excluding subjects with possible deterioration in ADL. Despite this, no attempt to impute data was made in order to reduce possible misclassification.

### *Statistical considerations*

Due to the multifactorial approach and the exploratory characteristics of these studies, multiple statistical calculations on several variables were carried out. This approach increased the risk of multiple comparisons, i.e. an increased risk of type-I errors where false-positive results are generated by chance. No method, such as Bonferroni correction, was used to counteract this problem. The rationale behind this approach was that adjustment for type-I errors would increase the risk of type-II errors. This could generate false-negative results, whereby clinically significant associations with conditions with low prevalence might be rejected.

Although the statistical calculations used throughout these studies could identify numerical, significant associations and differences between variables, they do not provide any evidence if the relationship is significant in a clinical setting.

### *Internal validity and temporality*

Internal validity reflects the degree to which a study is free from bias or systematic error, or the extent to which a causal conclusion based on a study is warranted.<sup>173</sup> It thereby reflects the extent to which the independent variables are the actual cause of change in the dependent variable. Falls in the elderly clearly qualify as having a ‘multifactorial web of causation’, as the etiology is multifaceted, consisting of both internal and external factors. The mechanism of a fall could depend on both chronic and transient conditions. In line with this, these studies had a limited ability to explain causal relationships between identified risk factors and falls. Multiple regression analyses and a PCA were used in an attempt to control for confounding factors, and to identify independent explanatory variables. As falls in the elderly appear to be intimately associated with general frailty and multimorbidity, it was not possible to control for all factors affecting a fall.

Throughout the statistical analyses, the explanatory power was limited in interpreting the variance in the outcome variables – a common feature in this type of studies. This means that a significant part of the sum of the explanatory variables behind a fall was not identified in these studies. For example, possible important risk factors such as visual impairment, alcohol use and orthostatic reactions, were not included. A fall may also be a purely accidental, transient event, with few identifiable causes. Papers II–IV had prospective designs, the ‘gold standard approach’ in identifying risk factors in epidemiological research.<sup>147</sup> This design makes it possible to study outcome after exposure, fulfilling the criterion of showing temporality in a causal mechanism. According to the Bradford Hill criteria for causation, this condition is obligatory in trying to find a causal relationship.<sup>126</sup> Despite this, the risk factors identified in these studies may by no means be direct causative factors for falls, and should above all be interpreted as individual markers of an increased probability for falls.

### *Limitations of a longitudinal design*

The 3- and 6-year assessments provided valuable data on long-term trends and outcomes in the population studied. However, the lengthy scope of the GÅS study is at the expense of a more detailed study of the participants. Data on falls could only be assessed in the limited time frame of six months before the assessments. This approach limited the ability to study transient, non-chronic and acute physiological changes that could lay behind a fall. It also generated long periods with unknown history of falls and other adverse events. Furthermore, a fall could have taken place just before the follow-up assessment, affecting the subject at the examination. A sequence like this could affect the interpretation of temporality. These limitations may have been the most marked methodological biases in the prospective design of Papers II–IV.

The values of HRQoL and LS appeared to be stable over time, and showed little change over six years. The elderly individual may have conserved these measurements at this point in life. The lack of dynamic change over time could also be explained by floor and ceiling effects. Those with an extreme score in a continuous measurement, e.g. the SF-12 PCS/MCS, may not be able to decline or increase any further. Over time, the phenomenon ‘regression toward the mean’ could have counteracted dramatic changes over time in the study population. A variable that shows an extreme value on its first assessment will tend to be closer to the center of its distribution on a later measurement.<sup>163</sup>

## Conclusions

The risk of falling appears to increase in a non-linear, almost exponential way with increasing number of accumulated risk factors. There appears to be an overrepresentation of fallers in a distinct subgroup of the oldest-old, and a frail group with multiple risk factors.

Several identified predictors for falls in a general elderly population were confirmatory, and linked to the musculoskeletal system and general frailty: impaired mobility, low walking speed, osteoarthritis, dependence in ADL, and nocturia. These findings highlight the clinical relevance of identifying and recruiting these individuals to rehabilitation and fall-preventive interventions.

The use of neuroleptic drugs was the single most prominent predictor for falls, although the prevalence was low in these studies, and the confidence interval overlapped those of other significant predictors. This finding may be clinically relevant, as these drugs are used to medicate BPSD, confusional states, and anxiety in the elderly – conditions that can be expected to increase in an aging population.

Heart dysfunction and specifically heart failure with symptoms were significant predictors for falls. This may be clinically important, as heart failure is increasing worldwide. The elderly are sensitive to adverse effects of its pharmacotherapy and the treatment is poorly documented in this group.

Falls predict a long-term reduction in the physical aspect of HRQoL in a general elderly population. Over six years, fallers had a notable, chronically reduced score in both HRQoL and LS compared to non-fallers. This long-term deprivation in fallers in this respect may be more extent than previously assumed.

Both deterioration and improvement in ADL over six years increased the risk for falls in a general elderly population. Those with improved ADL function who are at risk of falling may have a history of comorbidity combined with sufficient mobility for a fall event. Preventive efforts may require different strategies, as groups of different characteristics were at risk for falls.

Falls seem to be a threat to successful and healthy aging as they are associated to a long-term reduction in well-being, especially in the physical aspect of HRQoL. Those prone to falling may therefore be an important target for interventional efforts, rehabilitation, and healthcare resources. The diverse risk factors for falls identified in this dissertation confirm that falls are a multifaceted health problem, and require concern at many levels of the healthcare system. Many risk factors appear to be adjustable, although there were strong associations between falls and advanced age and general frailty. A continuous, comprehensive care and professional assessment may be vital for the fall-prone elderly individual.

## Future perspectives

There may be a long and winding road ahead to create and optimize effective interventional programs and rehabilitation settings for elderly individuals who tend to fall. The challenge lies in the nature of the fall event; it is a transient, elusive, and multifactorial condition, ultimately related to the inevitable degenerative processes of human aging. As physiotherapists and occupational therapists have a tradition of assessing and studying individuals who are prone to falling, falls in the elderly may be a somewhat neglected health problem in the every-day life of the clinical physician. This is unfortunate, as falls in the elderly generate a heavy burden of mortality and morbidity, straining the healthcare system. One explanation may be that preventive efforts to reduce accidents are not a high priority in the everyday work in an acute healthcare setting. Many physicians are trained in a single-organ specialty and work in a healthcare system with a long tradition of a single-disease framework. In light of this, it is of importance to increase general knowledge of falls and their associated factors, not only in the general public, but also in the medical profession. The concept of comprehensive geriatric assessment may be vital in the care and interventional efforts involving elderly fallers.

There is an explicit need for studies that focus on falls using a disease-oriented approach, examining acute medical conditions such as cardiac- and neurally-induced syncope, as well as emerging chronic conditions in the elderly, e.g. the interplay between falls and the severe condition of chronic heart failure. Furthermore, more research is needed on the relationship between falls, inappropriate drug use, and the treatment of behavioral and confused states in the cognitively impaired.

# Populärvetenskaplig sammanfattning på svenska (General summary in Swedish)

## Fallolyckor hos äldre -en tyst epidemi

Fallolyckor hos äldre är idag ett omfattande men underreporterat hälsoproblem. Cirka 1,600 individer, en huvuddel äldre, avlider årligen i Sverige till följd av ett fall. Detta kan jämföras med 1,400 respektive 2,400 individer som avlider årligen av bröst- och prostatacancer. Strax under 300 individer dör årligen i trafiken i Sverige. Vid sidan av risk för allvarliga skador som skalltrauma eller höftfraktur, är konsekvenserna av fallolyckor mångfacetterad. Forskning har visat att fall, vid sidan av kroppsliga men, ofta ger sociala och psykologiska konsekvenser hos äldre med minskad självständighet, oro och sänkt livskvalitet. I dagens 'grånande värld', där både andelen yngre äldre och de allra äldsta (över 85 år) växer, är fortsatt forskning kring fallolyckor betydelsefullt. Dagens äldre är en föränderlig och heterogen grupp med ett annorlunda hälso- och sjukdomspanorama jämfört med ett halvsekel sedan.

Ett fall beror vanligtvis på en mängd samspelande faktorer, och det övergripande syftet med denna avhandling var att med epidemiologisk metod studera orsaker och konsekvenser av fallolyckor i en allmän äldre befolkning. Epidemiologi kan beskrivas som studiet av sjukdomars distribution och orsaker. Avhandlingens samtliga delstudier baserades på data från äldrestudien 'Gott Åldrande i Skåne' (GÅS). Denna studie omfattade initialt 2931 slumpvis utvalda män och kvinnor i åldrarna 60-93 år, från fem kommuner i Skåne, vilka genomgick en större hälsoundersökning. Samtliga deltagare inviterades till en uppföljande undersökning tre och/eller sex år senare. Hembesök erbjöds för att kunna inkludera de allra äldsta och sjukliga. Få tidigare studier av fallolyckor hos äldre är baserat på ett motsvarande material.

I den första delstudien studerades sambandet mellan fall och 38 medicinska, psykologiska, sociala, funktionella och demografiska riskfaktorer. Kvinnor föll mer än män. Risken att falla ökade markant med stigande ålder. En upplevd känsla av ostadighet och fall, medicinering med neuroleptiska läkemedel, nedsatt rörlighet och låg gånghastighet var betydande riskfaktorer för att falla. Hos deltagare med flera individuella riskfaktorer ökade risken för att falla i en nästan exponentiell trend.

Delstudie 2 inkluderade motsvarande 38 riskfaktorer från den första delstudien. Individens fallbenägenhet följdes upp efter tre och/eller sex år. Denna studiedesign



kan ge mer ingående information om orsakssamband bakom ett fall. Då ett flertal faktorer analyserades, kompletterades studien med en analys som delade upp de mest betydande riskfaktorerna för fall i tre tematiska komponenter: 1) Reducerad rörlighet (vilket inkluderade riskfaktorerna nedsatt rörlighet, låg gånghastighet, artros i höft och/eller knäled samt anpassat boende) 2) Nedsatt hjärtfunktion (hjärtsjukdom, symtomatisk hjärtsvikt samt medicinering med läkemedel som ökar risken för fall 3) Nedsatt funktionsförmåga (beroende i Aktiviteter i Dagligt Liv (ADL) samt inkontinens nattetid). Vid sidan av dessa komponenter, var den enskilt starkaste riskfaktorn för fall i studien pågående medicinering med neuroleptiska läkemedel.

I den tredje delstudien studerades hur fall påverkade hälsorelaterad livskvalitet och livstillfredsställelse. Ett eller flera fall vid startpunkten av studien gav en betydande försämring i den fysiska aspekten av hälsorelaterad livskvalitet efter sex år, jämfört med de som inte föll. Studien visade att de som föll hade en markant, kronisk försämrad hälsorelaterad livskvalitet och livstillfredsställelse både vid starten och efter sex år, jämfört med de som inte föll. Hög ålder och multisjuklighet kan dock vara faktorer som till stor del förklarar dessa samband.

I delstudie 4 undersöktes om förändring av funktionsförmåga över sex år ökade risken för fall. Funktionsförmågan bedömdes med instrumentet ADL, som beskriver individens förmåga att kunna vara självständig i dagliga aktiviteter. En fjärdedel av deltagarna förändrade deras ADL-förmåga över sex år. Denna kategori hade högre risk för att falla, jämfört med de utan förändring. Grupper med både försämring och förbättring i ADL-förmåga hade en betydande ökad risk för fallolyckor. Individer med en förbättring i funktionsförmåga kan ha fått en återhämtad rörelseförmåga som ökat risken för att utsättas för ett fall.

Sammanfattningsvis visar avhandlingen att fallolyckor verkar vara ett betydande hot mot ett friskt och aktivt åldrande, då de som faller hade en långvarigt sänkt hälsorelaterad livskvalitet och livstillfredsställelse, särskilt i den fysiska aspekten av hälsorelaterad livskvalitet. Det är därför viktigt att uppmärksamma dessa individer för preventiva och rehabiliterande åtgärder. Flera resultat i avhandlingen konfirmerar tidigare forskning; flera riskfaktorer för fall var associerade med hög ålder, multisjuklighet och besvär från rörelseapparaten. Detta belyser vikten av fysisk träning för att förebygga fallolyckor. Detta preventiva arbete kan dock vara komplicerat; något paradoxalt hade individer med både försämrad och förbättrad funktionsförmåga ökad risk för att falla. Detta pekar på att dagens äldre är en bred, heterogen grupp där preventiva åtgärder för att förhindra fallolyckor kan kräva olika strategier.

Ur ett medicinskt perspektiv var symtomatisk hjärtsvikt en betydande riskfaktor för fall. Detta fynd är sparsamt rapporterat tidigare och kliniskt relevant då hjärtsvikt är en sjukdom som ökar markant i en åldrande befolkning. Äldre är samtidigt känsliga för bieffekter från läkemedel som används för att behandla hjärtsvikt, och det finns få större, högkvalitativa studier som har kartlagt den optimala sviktbehandlingen för

äldre individer. Vidare var medicinering med neuroleptiska läkemedel den enskilt mest markanta riskfaktorn för fallolyckor. Fyndet är kliniskt relevant då flera av dessa preparat används för att medicinera orostillstånd hos äldre och dementa, trots att medicinsk behandling av dessa tillstånd har tvivelaktig effekt.



# Acknowledgements

I wish to express my sincere thanks to:

Professor Sölve Elmståhl, my main supervisor, for initial encouragement, continuous support, steady supervision and loads of genuine optimism. Thank you for the rare and generous achievement of recruiting and introducing a young doctor to *both* scientific and clinical positions at SUS Malmö;

Eva Nordell, co-supervisor and co-author, for continuous support from the very first day and throughout the whole project, for valuable scientific inputs, and an eye for detail;

Henrik Ekström, co-supervisor and co-author, for great hands-on supervision, wise and valuable inputs, and for interesting discussions about methodological and scientific issues;

All the men and women throughout Skåne, and all the staff, who voluntary and professionally dedicated their time and effort to the great GÅS project;

Hats off to Ghassan Salameh and Daniel Lindström for computer support;

Lund University Libraries, for financial endorsement of Open Access publication;

Madeleine Nilsson, for genuine support at the Geriatric Clinic;

Dr. Jolanta Nobis and Dr. Peter Lind, for initial encouragement at SUS Malmö;

The staff of Lund University and SUS Malmö for creating a stimulating environment that supports young doctors pursuing scientific careers. Thank you for flexible scheduling, economic support, and great educational programs;

My family, always supporting.

Financial supports were given by:

Region Skåne

The Medical Faculty of Lund University

The Swedish Ministry of Health and Social Affairs

The Vårdal Institute



# References

1. Candau MG. Accidents: world's third worst killer. *Unseco Cour.* 1961(4):4–5.
2. American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. Guideline for the prevention of falls in older persons. *J Am Geriatr Soc.* 2001;49(5):664–72.
3. Myndigheten för samhällsskydd och beredskap. Statistik från MSB. Fallolyckor 2010. (In Swedish). Karlstad, Sweden; 2010.
4. The National Board of Health and Welfare. Causes of death 2010. Official statistics of Sweden. Stockholm, Sweden; 2011.
5. Transportstyrelsen. Nationell statistik. (In Swedish). (Internet) <https://www.transportstyrelsen.se/sv/Press/Statistik/Vag/Olycksstatistik/Polisrapporterad-statistik/Nationell-statistik/>. Accessed August 2014.
6. Sheldon JH. On the natural history of falls in old age. *Br Med J.* 1960;2(5214):1685–90.
7. Lord SR. Falls in older people: risk factors and strategies for prevention. 2nd ed. Cambridge, New York, USA: Cambridge University Press; 2007.
8. Morley JE. A brief history of geriatrics. *J Gerontol A Biol Sci Med Sci.* 2004;59(11):1132–52.
9. Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: the challenges ahead. *Lancet.* 2009;374(9696):1196–208.
10. Steen B. Guldår för svensk geriatrik under 1900-talet. Från kronikervård till modern specialitet –och internationell förebild. (In Swedish). *Läkartidningen.* 2004;101(26-27):2252–5.
11. Parker MG, Thorslund M. Health trends in the elderly population: getting better and getting worse. *The Gerontologist.* 2007;47(2):150–8.
12. Suzman R, Riley MW. Introducing the "oldest old". *Milbank Mem Fund Q Health Soc.* 1985;63(2):177–86.
13. Fries JF. Aging, natural death, and the compression of morbidity. *N Engl J Med.* 1980;303(3):130–5.
14. Stenflo GA. Äldres omsorgsbehov och närhet till anhöriga. Rapport. Statistiska Centralbyrån. (In Swedish). Stockholm, Sweden; 2006.
15. Emmett KR. Nonspecific and atypical presentation of disease in the older patient. *Geriatrics.* 1998;53(2):50–2, 58–60.
16. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet.* 2013;381(9868):752–62.

17. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet*. 2012;380(9836):37–43.
18. Tinetti ME, Fried TR, Boyd CM. Designing health care for the most common chronic condition—multimorbidity. *JAMA*. 2012;307(23):2493–4.
19. Wroblewski M. Clinical diagnosis in geriatric medicine. Clinical and clinico-pathological studies of myocardial infarction, ulcer disease and peritonitis in long-stay elderly patients. PhD diss., Lund University, Sweden, 1990.
20. Thorslund M. Åldrandet och äldreomsorgens utveckling. (In Swedish). *Socialmedicinsk Tidskr*. 2010;87(5-6).
21. Bjurling O. Malmö stads historia. Band 7. (In Swedish). Malmö, Sweden: Allhems förlag; 1994.
22. Reinprecht F. Hypertension, blood pressure, cognition and cerebral blood flow in the cohort of "Men born 1914". PhD diss., Lund University, Sweden, 2006.
23. Elmståhl S. Personal communication. Malmö, August 2014.
24. Socialstyrelsen. Lägesrapport 2010. (In Swedish). Stockholm, Sweden; 2010.
25. Rothman KJ. *Modern epidemiology*. 3rd ed. Philadelphia, USA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008.
26. Westling H. Medicinska fakulteten vid Lunds universitet 1668-2003. (In Swedish). Lund, Sweden: Medicinska Fakulteten; 2003.
27. Esson-Möller E, Larsson H, Uddenberg CE, White G. Individual traits and morbidity in a Swedish rural population. *Acta Psychiatr Neurol Scand Suppl*. 1956;100:1–160.
28. Manjer J, Elmståhl S, Janzon L, Berglund G. Invitation to a population-based cohort study: differences between subjects recruited using various strategies. *Scand J Public Health*. 2002;30(2):103–12.
29. Berglund G, Eriksson KF, Israelsson B, Kjellström T, Lindgärde F, Mattiasson I, et al. Cardiovascular risk groups and mortality in an urban Swedish male population: the Malmö preventive project. *J Intern Med*. 1996;239(6):489–97.
30. Svanström L. Falls on stairs: an epidemiological accident study. *Scand J Soc Med*. 1974;2(3):113–20.
31. Ekström H, Elmståhl S. Pain and fractures are independently related to lower walking speed and grip strength: Results from the population study "Good Ageing in Skåne". *Acta Orthop*. 2006;77(6):902–11.
32. World Health Organization. *International Classification of Diseases (ICD)*. (Internet) <http://www.who.int/classifications/icd/en/>. Accessed August 2014.
33. Zecevic AA, Salmoni AW, Speechley M, Vandervoort AA. Defining a fall and reasons for falling: comparisons among the views of seniors, health care providers, and the research literature. *The Gerontologist*. 2006;46(3):367–76.

34. Hauer K, Lamb SE, Jorstad EC, Todd C, Becker C, PROFANE-Group. Systematic review of definitions and methods of measuring falls in randomised controlled fall prevention trials. *Age Ageing*. 2006;35(1):5–10.
35. Lamb SE, Jørstad-Stein EC, Hauer K, Becker C, PROFANE-Group. Development of a common outcome data set for fall injury prevention trials: the prevention of falls network Europe consensus. *J Am Geriatr Soc*. 2005;53(9):1618–22.
36. Kellogg International Work Group. The prevention of falls in later life. A report of the Kellogg international work group on the prevention of falls by the elderly. *Dan Med Bull*. 1987;34 Suppl 4:1–24.
37. Moya A, Sutton R, Ammirati F, Blanc J-J, Brignole M, Dahm JB, et al. Guidelines for the diagnosis and management of syncope: the task force for the diagnosis and management of syncope of the European society of cardiology (ESC). *Eur Heart J*. 2009;30(21):2631–71.
38. Masud T, Morris RO. Epidemiology of falls. *Age Ageing*. 2001;30 Suppl 4:3–7.
39. Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategies for prevention. *Age Ageing*. 2006;35 Suppl 2:ii37–ii41.
40. O’Loughlin JL, Robitaille Y, Boivin JF, Suissa S. Incidence of and risk factors for falls and injurious falls among the community-dwelling elderly. *Am J Epidemiol*. 1993;137(3):342–54.
41. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. *N Engl J Med*. 1988;319(26):1701–7.
42. Rubenstein LZ, Josephson KR. The epidemiology of falls and syncope. *Clin Geriatr Med*. 2002;18(2):141–58.
43. World Health Organization. WHO global report on falls prevention in older age. Geneva, Switzerland: World Health Organization; 2008.
44. Luukinen H, Koski K, Honkanen R, Kivelä SL. Incidence of injury-causing falls among older adults by place of residence: a population-based study. *J Am Geriatr Soc*. 1995;43(8):871–6.
45. Von Heideken Wågert P, Gustafson Y, Kallin K, Jensen J, Lundin-Olsson L. Falls in very old people: the population-based Umeå 85+ study in Sweden. *Arch Gerontol Geriatr*. 2009;49(3):390–6.
46. Iinattiniemi S, Jokelainen J, Luukinen H. Falls risk among a very old home-dwelling population. *Scand J Prim Health Care*. 2009;27(1):25–30.
47. Berglund A. Fall risk factors in community-dwelling elderly people. *Nor J Epidemiol*. 2012;22(2):151–64.
48. Luukinen H, Koski K, Hiltunen L, Kivelä SL. Incidence rate of falls in an aged population in northern Finland. *J Clin Epidemiol*. 1994;47(8):843–50.
49. Campbell AJ, Borrie MJ, Spears GF, Jackson SL, Brown JS, Fitzgerald JL. Circumstances and consequences of falls experienced by a community population 70 years and over during a prospective study. *Age Ageing*. 1990;19(2):136–41.



50. Fuller GF. Falls in the elderly. *Am Fam Physician*. 2000;61(7):2159–68, 2173–4.
51. Panel on Prevention of Falls in Older Persons, American Geriatrics Society and British Geriatrics Society. Summary of the updated American geriatrics society/British geriatrics society clinical practice guideline for prevention of falls in older persons. *J Am Geriatr Soc*. 2011;59(1):148–57.
52. Berg WP, Alessio HM, Mills EM, Tong C. Circumstances and consequences of falls in independent community-dwelling older adults. *Age Ageing*. 1997;26(4):261–8.
53. Lehtola S, Koistinen P, Luukinen H. Falls and injurious falls late in home-dwelling life. *Arch Gerontol Geriatr*. 2006;42(2):217–24.
54. Robinovitch SN, Feldman F, Yang Y, Schonnop R, Leung PM, Sarraf T, et al. Video capture of the circumstances of falls in elderly people residing in long-term care: an observational study. *Lancet*. 2013;381(9860):47–54.
55. Davies AJ, Kenny RA. Falls presenting to the accident and emergency department: types of presentation and risk factor profile. *Age Ageing*. 1996;25(5):362–6.
56. Ambrose AF, Paul G, Hausdorff JM. Risk factors for falls among older adults: a review of the literature. *Maturitas*. 2013;75(1):51–61.
57. The National Board of Health and Welfare. Causes of death 2012. Official statistics of Sweden. Stockholm, Sweden; 2013.
58. Kannus P, Parkkari J, Koskinen S, Niemi S, Palvanen M, Järvinen M, et al. Fall-induced injuries and deaths among older adults. *JAMA*. 1999;281(20):1895–9.
59. Kannus P, Sievänen H, Palvanen M, Järvinen T, Parkkari J. Prevention of falls and consequent injuries in elderly people. *Lancet*. 2005;366(9500):1885–93.
60. Saari P, Heikkinen E, Sakari-Rantala R, Rantanen T. Fall-related injuries among initially 75- and 80-year old people during a 10-year follow-up. *Arch Gerontol Geriatr*. 2007;45(2):207–15.
61. Tinetti ME, Kumar C. The patient who falls: "It's always a trade-off". *JAMA*. 2010;303(3):258–66.
62. Karlsson MK, Vonschewelov T, Karlsson C, Cöster M, Rosengen BE. Prevention of falls in the elderly: a review. *Scand J Public Health*. 2013;41(5):442–54.
63. Rose S, Maffulli N. Hip fractures. An epidemiological review. *Bull Hosp Jt Dis N Y N*. 1999;58(4):197–201.
64. Nyberg L, Gustafson Y, Berggren D, Brännström B, Bucht G. Falls leading to femoral neck fractures in lucid older people. *J Am Geriatr Soc*. 1996;44(2):156–60.
65. Hartholt KA, van Beeck EF, Polinder S, van der Velde N, van Lieshout EMM, Panneman MJM, et al. Societal consequences of falls in the older population: injuries, healthcare costs, and long-term reduced quality of life. *J Trauma*. 2011;71(3):748–53.
66. Gillespie LD, Robertson MC, Gillespie WJ, Sherrington C, Gates S, Clemson LM, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev*. 2012;9:CD007146.

67. Tinetti ME, Williams CS. Falls, injuries due to falls, and the risk of admission to a nursing home. *N Engl J Med.* 1997;337(18):1279–84.
68. Oliver D, Daly F, Martin FC, McMurdo MET. Risk factors and risk assessment tools for falls in hospital in-patients: a systematic review. *Age Ageing.* 2004;33(2):122–30.
69. Jørstad EC, Hauer K, Becker C, Lamb SE, ProFaNE Group. Measuring the psychological outcomes of falling: a systematic review. *J Am Geriatr Soc.* 2005;53(3):501–10.
70. Scheffer AC, Schuurmans MJ, van Dijk N, van der Hooft T, de Rooij SE. Fear of falling: measurement strategy, prevalence, risk factors and consequences among older persons. *Age Ageing.* 2008;37(1):19–24.
71. Murphy J, Isaacs B. The post-fall syndrome. A study of 36 elderly patients. *Gerontology.* 1982;28(4):265–70.
72. Vellas BJ, Wayne SJ, Romero LJ, Baumgartner RN, Garry PJ. Fear of falling and restriction of mobility in elderly fallers. *Age Ageing.* 1997;26(3):189–93.
73. Ganz DA, Bao Y, Shekelle PG, Rubenstein LZ. Will my patient fall? *JAMA.* 2007;297(1):77–86.
74. Karlsson MK, Magnusson H, von Schewelow T, Rosengren BE. Prevention of falls in the elderly—a review. *Osteoporos Int.* 2013;24(3):747–62.
75. Deandrea S, Lucenteforte E, Bravi F, Foschi R, La Vecchia C, Negri E. Risk factors for falls in community-dwelling older people: a systematic review and meta-analysis. *Epidemiol Camb Mass.* 2010;21(5):658–68.
76. Delbaere K, Close JCT, Heim J, Sachdev PS, Brodaty H, Slavin MJ, et al. A multifactorial approach to understanding fall risk in older people. *J Am Geriatr Soc.* 2010;58(9):1679–85.
77. Stein MS, Wark JD, Scherer SC, Walton SL, Chick P, Di Carantonio M, et al. Falls relate to vitamin D and parathyroid hormone in an Australian nursing home and hostel. *J Am Geriatr Soc.* 1999;47(10):1195–201.
78. Melin AL, Wilske J, Ringertz H, Sääf M. Vitamin D status, parathyroid function and femoral bone density in an elderly Swedish population living at home. *Aging Milan.* 1999;11(3):200–7.
79. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *BMJ.* 1996;312(7041):1254–9.
80. Knight M, Coakley C. Fall risk in patients with acute psychosis. *J Nurs Care Qual.* 2010;25(3):208–15.
81. Souverein PC, Webb DJ, Weil JG, Van Staa TP, Egberts ACG. Use of antiepileptic drugs and risk of fractures: case-control study among patients with epilepsy. *Neurology.* 2006;66(9):1318–24.
82. Thaler-Kall K, Döring A, Peters A, Thorand B, Grill E, Koenig W, et al. Association between anemia and falls in community-dwelling older people: cross-sectional results from the KORA-Age study. *BMC Geriatr.* 2014;14(1):29.

83. Voermans NC, Snijders AH, Schoon Y, Bloem BR. Why old people fall (and how to stop them). *Pract Neurol*. 2007;7(3):158–71.
84. Sibley KM, Voth J, Munce SE, Straus SE, Jaglal SB. Chronic disease and falls in community-dwelling Canadians over 65 years old: a population-based study exploring associations with number and pattern of chronic conditions. *BMC Geriatr*. 2014;14:22.
85. Elmståhl S, Linder H. Polypharmacy and inappropriate drug use among older people—a systematic review. *Healthy Aging Clin Care Elder*. 2013;(5):1–5.
86. American Geriatrics Society Beers Criteria Update Expert Panel. American geriatrics society updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2012;60(4):616–31.
87. Fastbom, J, Schmidt, I. Indikatorer för god läkemedelsterapi hos äldre. (In Swedish). Stockholm, Sweden: Socialstyrelsen; 2010.
88. Berdot S, Bertrand M, Dartigues J-F, Fourrier A, Tavernier B, Ritchie K, et al. Inappropriate medication use and risk of falls—a prospective study in a large community-dwelling elderly cohort. *BMC Geriatr*. 2009;9:30.
89. Bloch F, Thibaud M, Dugué B, Brèque C, Rigaud A-S, Kemoun G. Psychotropic drugs and falls in the elderly people: updated literature review and meta-analysis. *J Aging Health*. 2011;23(2):329–46.
90. Huang AR, Mallet L, Rochefort CM, Egualé T, Buckeridge DL, Tamblyn R. Medication-related falls in the elderly: causative factors and preventive strategies. *Drugs Aging*. 2012;29(5):359–76.
91. Woolcott JC, Richardson KJ, Wiens MO, Patel B, Marin J, Khan KM, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. *Arch Intern Med*. 2009;169(21):1952–60.
92. Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc*. 2011;12(4):249–56.
93. Chan BKS, Marshall LM, Winters KM, Faulkner KA, Schwartz AV, Orwoll ES. Incident fall risk and physical activity and physical performance among older men: the osteoporotic fractures in men study. *Am J Epidemiol*. 2007;165(6):696–703.
94. Tinetti ME, Williams CS. The effect of falls and fall injuries on functioning in community-dwelling older persons. *J Gerontol A Biol Sci Med Sci*. 1998;53(2):M112–119.
95. Gates S, Fisher JD, Cooke MW, Carter YH, Lamb SE. Multifactorial assessment and targeted intervention for preventing falls and injuries among older people in community and emergency care settings: systematic review and meta-analysis. *BMJ*. 2008;336(7636):130–3.
96. Chang JT, Morton SC, Rubenstein LZ, Mojica WA, Maglione M, Suttorp MJ, et al. Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ*. 2004;328(7441):680.

97. Moyer VA, U.S. Preventive Services Task Force. Prevention of falls in community-dwelling older adults: U.S. preventive services task force recommendation statement. *Ann Intern Med.* 2012;157(3):197–204.
98. Rubenstein LZ, Josephson KR. Falls and their prevention in elderly people: what does the evidence show? *Med Clin North Am.* 2006;90(5):807–24.
99. Jensen J, Nyberg L, Rosendahl E, Gustafson Y, Lundin-Olsson L. Effects of a fall prevention program including exercise on mobility and falls in frail older people living in residential care facilities. *Aging Clin Exp Res.* 2004;16(4):283–92.
100. Berggren M, Stenvall M, Olofsson B, Gustafson Y. Evaluation of a fall-prevention program in older people after femoral neck fracture: a one-year follow-up. *Osteoporos Int.* 2008;19(6):801–9.
101. Socialstyrelsen. Nationella riktlinjer för rörelseorganens sjukdomar 2012. (In Swedish). Stockholm, Sweden; 2012.
102. Odense Universitetshospital, Geriatrisk afdeling, Faldklinik. (In Danish). (Internet) <http://www.ouh.dk/wm125117>. Accessed August 2014.
103. Smebye KL, Granum S, Wyller TB, Mellingsæter M. Medisinske funn i en tverrfaglig geriatrisk fallpoliklinikk. (In Norwegian). *Tidsskr Den Nor Legerforening.* 2014;134(7):705–9.
104. World Health Organization. Constitution of the world health organization. Basic documents. 45th ed. Geneva, Switzerland; 2005.
105. Muldoon MF, Barger SD, Flory JD, Manuck SB. What are quality of life measurements measuring? *BMJ.* 1998;316(7130):542–5.
106. Iglesias CP, Manca A, Torgerson DJ. The health-related quality of life and cost implications of falls in elderly women. *Osteoporos Int.* 2009;20(6):869–78.
107. Farquhar M. Elderly people's definitions of quality of life. *Soc Sci Med.* 1995;41(10):1439–46.
108. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. *N Engl J Med.* 1996;334(13):835–40.
109. Farquhar M. Definitions of quality of life: a taxonomy. *J Adv Nurs.* 1995;22(3):502–8.
110. Lin M-R, Wolf SL, Hwang H-F, Gong S-Y, Chen C-Y. A randomized, controlled trial of fall prevention programs and quality of life in older fallers. *J Am Geriatr Soc.* 2007;55(4):499–506.
111. The WHOQOL Group. Development of the world health organization WHOQOL-BREF quality of life assessment. *Psychol Med.* 1998;28(3):551–8.
112. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473–83.
113. Neugarten BL, Havighurst RJ, Tobin SS. The measurement of life satisfaction. *J Gerontol.* 1961;16:134–43.
114. Diener E. Subjective well-being. *Psychol Bull.* 1984;95(3):542–75.

115. Enkvist Å. Life Satisfaction and the Oldest-Old. Results from the longitudinal population study "Good Aging in Skåne". PhD diss., Lund University, Sweden, 2013.
116. Guralnik JM, Branch LG, Cummings SR, Curb JD. Physical performance measures in aging research. *J Gerontol.* 1989;44(5):141–6.
117. Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment: a meta-analysis of controlled trials. *Lancet.* 1993;342(8878):1032–6.
118. Wang L, van Belle G, Kukull WB, Larson EB. Predictors of functional change: a longitudinal study of nondemented people aged 65 and older. *J Am Geriatr Soc.* 2002;50(9):1525–34.
119. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. *JAMA.* 1963;185:914–9.
120. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *The Gerontologist.* 1970;10(1):20–30.
121. Sekaran NK, Choi H, Hayward RA, Langa KM. Fall-associated difficulty with activities of daily living in functionally independent individuals aged 65 to 69 in the United States: a cohort study. *J Am Geriatr Soc.* 2013;61(1):96–100.
122. Stel VS, Smit JH, Pluijm SMF, Lips P. Consequences of falling in older men and women and risk factors for health service use and functional decline. *Age Ageing.* 2004;33(1):58–65.
123. Tinetti ME, Mendes de Leon CF, Doucette JT, Baker DI. Fear of falling and fall-related efficacy in relationship to functioning among community-living elders. *J Gerontol.* 1994;49(3):140–7.
124. Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980–2000. *N Engl J Med.* 2007;356(23):2388–98.
125. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther.* 2003;83(3):237–52.
126. Hill AB. The environment and disease: association or causation? *Proc R Soc Med.* 1965;58:295–300.
127. Vieira ER, Freund-Heritage R, da Costa BR. Risk factors for geriatric patient falls in rehabilitation hospital settings: a systematic review. *Clin Rehabil.* 2011;25(9):788–99.
128. Nicolussi AC, Fhon JRS, Santos CAV, Kusumota L, Marques S, Rodrigues RAP. Quality of life in elderly people that have suffered falls: integrative literature review. *Cien Saude Colet.* 2012;17(3):723–30.
129. Stuck AE, Walthert JM, Nikolaus T, Büla CJ, Hohmann C, Beck JC. Risk factors for functional status decline in community-living elderly people: a systematic literature review. *Soc Sci Med* 1982. 1999;48(4):445–69.

130. Lagergren M, Fratiglioni L, Hallberg IR, Berglund J, Elmståhl S, Hagberg B, et al. A longitudinal study integrating population, care and social services data. The Swedish national study on aging and care (SNAC). *Aging Clin Exp Res*. 2004;16(2):158–68.
131. Statistiska centralbyrån. Befolkningsstatistik. (In Swedish). (Internet) <http://www.scb.se/>. Accessed August 2014.
132. Douhan J, Elmståhl S. Fysisk aktivitet & bra matvanor för det goda åldrandet - Resultat från forskningsprojektet Gott Åldrande i Skåne (GÅS). Rapport. (In Swedish). Geriatriska kliniken, Skånes universitetssjukhus, Malmö, 2013; 1-34.
133. American Heart Association. Classes of Heart Failure. (Internet) [http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure\\_UCM\\_306328\\_Article.jsp](http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp). Accessed August 2014.
134. Labmedicin Skåne. Analysportalen. (In Swedish). (Internet) <http://www.analysportalen-labmedicin.skane.se/viewAnalys.asp?Nr=2224>. Accessed August 2014.
135. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. 4th ed. Washington, DC, USA: American Psychiatric Association; 2000.
136. 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(3):189–98.
137. Livingston G, Blizard B, Mann A. Does sleep disturbance predict depression in elderly people? A study in inner London. *Br J Gen Pract J R Coll Gen Pract*. 1993;43(376):445–8.
138. WHO Collaborating Centre for Drug Statistics Methodology. WHOCC - Structure and principles. (Internet) [http://www.whooc.no/atc/structure\\_and\\_principles/](http://www.whooc.no/atc/structure_and_principles/). Accessed August 2014.
139. Mattiasson-Nilo I, Sonn U, Johannesson K, Gosman-Hedström G, Persson GB, Grimby G. Domestic activities and walking in the elderly: evaluation from a 30-hour heart rate recording. *Aging Milan*. 1990;2(2):191–8.
140. Sonn U, Åsberg KH. Assessment of activities of daily living in the elderly. A study of a population of 76-year-olds in Gothenburg, Sweden. *Scand J Rehabil Med*. 1991;23(4):193–202.
141. Åsberg KH, Sonn U. The cumulative structure of personal and instrumental ADL. A study of elderly people in a health service district. *Scand J Rehabil Med*. 1989;21(4):171–7.
142. Sullivan M, Karlsson J, Taft C. SF-12 Health Survey: Swedish manual and interpretation guide (SF-12). Sahlgrenska University Hospital, Gothenburg. 1997.
143. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220–33.
144. Prudham D, Evans JG. Factors associated with falls in the elderly: a community study. *Age Ageing*. 1981;10(3):141–6.

145. IBM. SPSS software. (Internet)  
<http://www-01.ibm.com/software/analytics/spss/>. Accessed August 2014.
146. Faulkner KA, Cauley JA, Studenski SA, Landsittel DP, Cummings SR, Ensrud KE, et al. Lifestyle predicts falls independent of physical risk factors. *Osteoporos Int*. 2009;20(12):2025–34.
147. National Collaborating Centre for Nursing and Supportive Care (UK). Clinical practice guideline for the assessment and prevention of falls in older people. NICE clinical guidelines, no. 21. London, UK: Royal College of Nursing; 2004.
148. Cumming RG, Miller JP, Kelsey JL, Davis P, Arfken CL, Birge SJ, et al. Medications and multiple falls in elderly people: the St Louis OASIS study. *Age Ageing*. 1991;20(6):455–61.
149. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. *J Am Geriatr Soc*. 1999;47(1):30–9.
150. Läkemedelsverket. Läkemedelsbehandling vid schizofreni - behandlingsrekommendation. (In Swedish). Information från Läkemedelsverket 2013;24(5):15–27.
151. Statens beredning för medicinsk utvärdering, SBU. Demenssjukdomar: en systematisk litteraturöversikt. Sammanfattning och slutsatser. (In Swedish). Stockholm, Sweden; 2006.
152. Läkemedelsverket. Behandling och bemötande vid beteendemässiga och psykiska symtom vid demenssjukdom – ”BPSD”. (In Swedish). Information från Läkemedelsverket 2008;19(5):15–24.
153. Campbell AJ, Robertson MC, Gardner MM, Norton RN, Buchner DM. Psychotropic medication withdrawal and a home-based exercise program to prevent falls: a randomized, controlled trial. *J Am Geriatr Soc*. 1999;47(7):850–3.
154. Cheng JWM, Nayar M. A review of heart failure management in the elderly population. *Am J Geriatr Pharmacother*. 2009;7(5):233–49.
155. Ahmed A. American college of cardiology/American heart association chronic heart failure evaluation and management guidelines: relevance to the geriatric practice. *J Am Geriatr Soc*. 2003;51(1):123–6.
156. Decaux G. Is asymptomatic hyponatremia really asymptomatic? *Am J Med*. 2006;119(7 Suppl 1):S79–82.
157. Renneboog B, Musch W, Vandemergel X, Manto MU, Decaux G. Mild chronic hyponatremia is associated with falls, unsteadiness, and attention deficits. *Am J Med*. 2006;119(1):71.e1–8.
158. Schroll M, Avlund K, Davidsen M. Predictors of five-year functional ability in a longitudinal survey of men and women aged 75 to 80. The 1914-population in Glostrup, Denmark. *Aging (Milan)* 1997;9(1-2):143–52.
159. Moayyeri A. The association between physical activity and osteoporotic fractures: a review of the evidence and implications for future research. *Ann Epidemiol*. 2008;18(11):827–35.

160. Henry-Sánchez JT, Kurichi JE, Xie D, Pan Q, Stineman MG. Do elderly people at more severe activity of daily living limitation stages fall more? *Am J Phys Med Rehabil.* 2012;91(7):601–10.
161. Gregg EW, Pereira MA, Caspersen CJ. Physical activity, falls, and fractures among older adults: a review of the epidemiologic evidence. *J Am Geriatr Soc.* 2000;48(8):883–93.
162. Karlsson MK, Nordqvist A, Karlsson C. Physical activity, muscle function, falls and fractures. *Food Nutr Res.* 2008;52.
163. Delgado-Rodríguez M, Llorca J. Bias. *J Epidemiol Community Health.* 2004;58(8):635–41.
164. Sterling DA, O'Connor JA, Bonadies J. Geriatric falls: injury severity is high and disproportionate to mechanism. *J Trauma.* 2001;50(1):116–9.
165. Dickens J, Jones M, Johansen A. Falls definition—reliability of patients' own reports. *Age Ageing.* 2006;35(4):450–1.
166. Karlsson MK, Ribom E, Nilsson J-Å, Ljunggren Ö, Ohlsson C, Mellström D, et al. Inferior physical performance tests in 10,998 men in the MrOS study is associated with recurrent falls. *Age Ageing.* 2012;41(6):740–6.
167. Sullivan M, Karlsson J, Ware JE Jr. The Swedish SF-36 Health Survey—I. Evaluation of data quality, scaling assumptions, reliability and construct validity across general populations in Sweden. *Soc Sci Med* 1982. 1995;41(10):1349–58.
168. Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, et al. Cross-validation of item selection and scoring for the SF-12 health survey in nine countries: results from the IQOLA Project. *International quality of life assessment. J Clin Epidemiol.* 1998;51(11):1171–8.
169. Wallace KA, Wheeler AJ. Reliability Generalization of the Life Satisfaction Index. *Educ Psychol Meas.* 2002;62(4):674–84.
170. Shmotkin D. The structure of the Life Satisfaction Index A in elderly Israeli adults. *Int J Aging Hum Dev.* 1991;33(2):131–50.
171. Liang J. Dimensions of the life satisfaction index a: a structural formulation. *J Gerontol.* 1984;39(5):613–22.
172. Fagerström C, Lindwall M, Berg AI, Rennemark M. Factorial validity and invariance of the life satisfaction index in older people across groups and time: addressing the heterogeneity of age, functional ability, and depression. *Arch Gerontol Geriatr.* 2012;55(2):349–56.
173. Porta M. *A dictionary of epidemiology.* 6th ed. Oxford, UK: Oxford University Press; 2014.