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Predictors and consequences of injurious falls among older adults: A holistic approach

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PREDICTORS AND CONSEQUENCES OF INJURIOUS FALLS AMONG OLDER ADULTS: A HOLISTIC APPROACH

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Till Vidar och Maj, till månen och tillbaka igen

ABSTRACT

The field of research on falls among older adults is well studied. Despite this, there are some knowledge gaps that need to be addressed: 1) research studying injurious falls, as opposed to any falls; 2) knowledge on sex differences, and specific risk profiles for injurious falls; 3) development of an effective screening tool for community-dwelling older adults, that can detect people at risk of first-time falls, who may be targeted by preventive interventions; and 4) what factors influence the risk of losing independence, in a long-term perspective, after an injurious fall.

The purpose of this thesis is to fill these gaps through the following aims: to detect risk profiles of injurious falls among older adults, to enable early detection of those at risk, and to examine the long-term consequences of fall injuries on everyday function. To reach these aims we used data from the ongoing population-based, Swedish National study on Aging and Care in Kungsholmen (SNAC-K). These are our main findings:

The results from **Study I** indicate that risk factors for injurious falls tend to cluster within individuals, forming specific risk profiles, rather than appearing one by one. It is possible to predict elevated fall risk up to 10 years in advance and it also seems possible to distinguish groups of people at different levels of risk.

In **Study II** we concluded that women and men share risk factors in many cases, but the levels of significance vary between the sexes. A few risk factors indeed seem to be sex specific. We also concluded that short-term (0–3 years) and long-term (4–10 years) risk factors differ, distinguishing specific acute and long-term risk profiles.

We developed a screening tool for first time injurious falls in **Study III**, consisting of: age, cohabitation status, IADL dependency, and a balance test. Scores on the screening tool were weighted according to sex-stratified coefficients. The predictive value (measured with Harrell's C statistics) of the scores were 0.75 and 0.77, for women and men, respectively. To be able to predict first time fallers up to 5 years in advance opens up for the possibility of primary prevention alongside with secondary prevention for recurrent fallers.

With **Study IV**, we showed that sociodemographic and health related factors (living alone, physical inactivity, and self-rated poor health) measured before an injurious fall modified disability trajectories up to 12 years after baseline. These results enable identification of extra vulnerable fallers, who might need extra rehabilitation and attention after an injurious fall, with the goal to maintain independence.

In **conclusion**, the results of this thesis suggest that 1) it might be more appropriate to study fall risk profiles, rather than risk factors in isolation; 2) risk factors for injurious falls may differ by sex and length of follow-up; 3) we created a screening tool for first time injurious falls, that is easy and quick to administer and has the possibility to predict falls up to 5 years in advance; and 4) sociodemographic and health related factors may help to identify extra vulnerable fallers, who might need extra rehabilitation and attention after an injurious fall, to maintain independence.

Key words: falls; fall risk factors; injuries; screening tool; sex differences; disability; trajectories; Swedish National study on Care and Aging in Kungsholmen; aging; epidemiology; cohort study.

SAMMANFATTNING

Fall bland äldre är väl studerat. Trots detta finns det några kunskapsluckor som behöver undersökas ytterligare; 1) forskning som studerar skadliga fall, i motsats till fall generellt. 2) könsskillnader och specifika riskprofiler för skadliga fall; 3) det saknas ett effektivt screeningverktyg för äldre hemmaboende, som kan upptäcka personer som är i risk för skadliga fall men som ännu inte fallit, och som kan rikta in förebyggande insatser; 4) lite är känt om vilka faktorer som påverkar risken för att bli hjälpberoende i ett långsiktigt perspektiv efter ett skadligt fall.

Denna avhandling syftade till att fylla dessa kunskapsluckor.

Syftet med denna avhandling var att upptäcka riskprofiler för skadliga fall hos äldre, för att möjliggöra tidig upptäckt av de som är i riskzonen och att undersöka de långsiktiga konsekvenserna av fallskador för hjälpberoende. För att besvara våra forskningsfrågor använde vi data från den pågående befolkningsstudien the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K). Dessa är resultaten, i korthet:

Resultaten från **Studie I** visar på att riskfaktorer för skadliga fall tenderar att samexistera hos individer och bilda specifika riskprofiler snarare än att existera för sig själva. Studien visade också att det är möjligt att förutsäga förhöjd fallrisk upp till tio år framåt i tiden och att det verkar vara möjligt att urskilja olika risknivåer för skadliga fall.

I **Studie II** såg vi att kvinnor och män delar riskfaktorer i många fall, men de verkar vara olika betydelsefulla för de olika könen. Några riskfaktorer tycks till och med vara könsspecifika. Vi drog också slutsatsen att kortsiktiga (0–3 år) och långsiktiga (4–10 år) riskfaktorer skiljer sig åt, vilket ger oss specifika akuta och långsiktiga riskprofiler.

Vi utvecklade ett screeningsverktyg för förstagångsfall med skadlig utgång i **Studie III**, bestående av; ålder, samboendestatus, IADL-beroende och ett balanstest. Värdena på poängen vägdes enligt könsstratifierade koefficienter. Det prediktiva värdet (mätt med Harrell's C-statistics) för verktyget var 0,75 respektive 0,77 för kvinnor och män. Att kunna identifiera förstagångsfallare upp till 5 år i förväg öppnar upp för möjligheten till primärt preventiva insatser vid sidan av sekundärprevention för återfallare.

Med **Studie IV** visade vi att sociodemografiska och hälsorelaterade faktorer (att leva ensam, fysisk inaktivitet och självskattad dålig hälsa), mätt före ett skadligt fall, modifierar hjälpberoende upp till 12 år efter baslinjemätningen. Dessa resultat möjliggör identifiering av extra sårbara fallare, som kan behöva extra rehabilitering och uppmärksamhet efter ett skadligt fall, med målet att bibehålla självständighet.

Sammanfattningsvis pekar resultaten från denna avhandling på att 1) det kan vara lämpligare att studera fallriskprofiler, snarare än riskfaktorer en och en; 2) riskfaktorer för skadliga fall kan variera beroende på kön och uppföljningens längd; 3) det är möjligt att förutse förstagångsfall med skadlig utgång upp till 5 år i förväg, med ett enkelt och snabbt screeningverktyg utvecklat inom ramen för denna uppsats; 4) sociodemografiska och hälsorelaterade faktorer kan hjälpa till att identifiera extra utsatta individer som fallit, som kan behöva extra rehabilitering och uppmärksamhet efter ett skadligt fall, för att bibehålla individers oberoende.

Nyckelord: fall; fallrisk-faktorer; skador; screeningverktyg; könsskillnader; hjälpberoende; Swedish National study on Care and Aging in Kungsholmen; åldrande; epidemiologi; kohortstudie

LIST OF SCIENTIFIC PAPERS

I. **Ek S**, Rizzuto D, Fratiglioni L, Johnell K, Xu W, Welmer AK. Risk Profiles for Injurious Falls in People Over 60: A Population-Based Cohort Study. J Gerontol A Biol Sci Med Sci. 2018 Jan 16;73(2):233-239. doi: 10.1093/gerona/glx115.*

II. **Ek S**, Rizzuto D, Fratiglioni L, Calderón-Larrañaga A, Johnell K, Sjöberg L, Xu W, Welmer AK. Risk Factors for Injurious Falls in Older Adults: The Role of Sex and Length of Follow-Up. J Am Geriatr Soc. 2019 Feb;67(2):246-253. doi: 10.1111/jgs.15657. Epub 2018 Nov 29.**

III. **Ek S**, Rizzuto D, Calderón-Larrañaga A, Franzén E, Xu W, Welmer AK. Predicting First-Time Injurious Falls in Older Men and Women Living in the Community: Development of the First Injurious Fall Screening Tool. J Am Med Dir Assoc. 2019 Apr 3. pii: S1525-8610(19)30249-X. doi: 10.1016/j.jamda.2019.02.023. [Epub ahead of print]***

IV. **Ek S**, Rizzuto D, Xu W, Calderón-Larrañaga A, Welmer AK. Sociodemographic and health-related predictors for functional decline after an injurious fall: a population-based cohort study. *Under review*

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Trevisan C, Crippa A, **Ek S**, Welmer AK, Sergi G, Maggi S, Manzato E, Bea JW, Cauley JA, Decullier E, Hirani V, LaMonte MJ, Lewis CE, Schott AM, Orsini N, Rizzuto D.Nutritional Status, Body Mass Index, and the Risk of Falls in Community-Dwelling Older Adults: A Systematic Review and Meta-Analysis. J Am Med Dir Assoc. 2019 May;20(5):569-582.e7. doi: 10.1016/j.jamda.2018.10.027. Epub 2018 Dec 13. Review.

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CONTENTS

ABBREVIATIONS

ADL – Activities of Daily Living
ANOVA – Analysis of Variance
ATC – Anatomical Therapeutic Chemical
AUC – Area under the ROC curve
BMI – Body Mass Index
CI – Confidence Intervals
DALY – Disability Adjusted Life Years
ED – Emergency Department
FRAST – Fall Risk Assessment & Screening Tool
FRAT – Fall Risk Assessment Tool
FRAT-up – Web based Fall Risk Assessment Tool
FRID – Fall Risk Increasing Drug
FROP-com – Falls Risk for Older People in the Community assessment
GDP – Gross Domestic Product
HR – Hazard Ratio
IADL – Instrumental Activities of Daily Living
ICD-10 International Classification of Diseases, Tenth Revision
LASA – Longitudinal Aging Study Amsterdam
MADRS – Montgomery-Åsberg Depression Rating Scale
MICE – Multiple Imputations Chained Equations
mmHg – Millimeters of mercury
MMSE – Mini-Mental State Examination
OR – Odds Ratio
PAR – Population Attributable Risk
PIN – Personal Identification Number
PPV – Positive Predictive Value
SEK – Swedish crowns
SNAC-K – Swedish National study on Aging and Care in Kungsholmen
SPPB – Short Physical Performance Battery
STEADI – Stopping Elderly Accidents, Deaths, & Injuries
Thai-FRAT – Thai Fall Risk Assessment Tool
USD – United States Dollars
WHO – World Health Organization

1 INTRODUCTION

1.1 Epidemiology and costs

Falls among older people are an urgent public health concern due to their medical and economic consequences, especially in light of an increasing older population. About 30% of people above the age of 65 fall every year, of which around 10% require medical care (1). Some long-term consequences are a lower activity level, a higher risk of dependency, institutionalization, and an earlier death (2–4). Several studies have shown a decrease in quality of life after a fall injury, with probable causes being the aforementioned consequences (4–6). For individuals over the age of 75, falls are one of the leading causes of disability, measured with Disability Adjusted Life Years (DALY) (7).

Incidence trends of fall-related injuries among older adults seem to vary across geographical regions. One review (8) showed a slight increase of injuries among older people in Spain between 2000 and 2010, while an Australian study showed an increase in injuries but a decrease in fractures (9). On the contrary, Nilson et al. showed slightly decreasing incidence rates of injuries overall in Sweden between 2001 and 2010 (10). Results from these studies indicate that among younger-old the trends are more stable while among older-old incidence is increasing (8, 10). This increase is potentially rather due to an increasing older population and an increasing life-expectancy rather than due to any real change in incidence per capita (7).

The cost of falls is affecting society, the community, and the people close to the one who falls. The costs of fall injuries can be divided into two categories: direct costs, which refer to health care costs adjacent to a fall, and indirect costs, which may include loss of income and productivity for the person who falls or relatives that take care of that person. Indirect costs are, by nature, difficult to monitor and measure (1). There are a few studies conducted to estimate the direct costs of falls, their estimates range between 1,059 USD to 10,913 USD (≈ 8700 to 89500 SEK) for an injurious fall and 5,654–42,840 USD (≈ 46,500–35,1500 SEK) for hospitalization after a fall (11–13). In Sweden, the estimated cost for a hip fracture was around 250 000 SEK in 2009 (14). Only one review from 2010 also calculated the indirect costs by loss of gross domestic product (GDP). Results showing a loss of GDP ranging between 0.2 and 0.7% of the total (11).

Considering the impact on the quality of life for the individuals, the increasing older population worldwide, and the high costs of fall injuries, falls among older adults is a public health issue that deserves the highest priority.

1.2 Risk Factors

The World Health Organization (WHO) classifies fall risk factors in four categories: 1) socioeconomic (e.g., education level and social interactions); 2) biological (e.g., sociodemographic factors, diseases, and impairments); 3) behavioral (e.g., medication use and physical activity level); and 4) environmental (e.g., poor lightning, slippery floors, and uneven sidewalks) (1).

In this project we will concentrate on socioeconomic, biological, and behavioral risk factors. The focus in this thesis is on injurious falls, although, because of the small number of previous studies distinguishing between injurious falls and any falls, the below section is concerning risk factors for falls in general.

Socioeconomic/sociodemographic risk factors. As for many other health outcomes, low socioeconomic status is related to an increased risk of falls (15). In our study we use **education** level as a proxy measure for socioeconomic status. Also, **living alone** has been shown to be positively associated with falls (16).

Biological risk factors. Older **age** is one of the most prominent risk factors (17). Yet, whether age is an individual risk factor or just a proxy for a decrease in many different functions and systems is debated. One could argue that other risk factors are likely to increase their impact with increasing age, and that age itself is not a risk factor.

Being **underweight** has been shown to be associated with a higher risk of fractures (17–19), while being overweight or obese has shown conflicting results. However, mainly obesity is shown to be risk increasing (20). In fact, Kim et al. concluded that there is a U-shaped association between body mass index (**BMI)** and the risk of falls (21), and a recent meta-analysis from our research group has confirmed that association (22).

Furthermore, impaired **vision** is a risk factor for falling (16, 23). Self-rated vision is shown to be a valid proxy for an actual vision acuity test when studying health outcomes among older individuals (24, 25).

Pain is also associated with an increased risk of falls, both general pain and in specific parts of the body (17, 26, 27). It has, however, been suggested that there are sex differences in the association of pain and falls. Even though women experience more pain and falls, pain has been shown to be more strongly associated to falls in men than women (27).

The presence of two or more chronic diseases, termed **multimorbidity** (28), increases the risk for falls. Although, the number of chronic diseases matters, specific combinations of diseases might be even more important (29). The evidence is more homogeneous for specific diseases, such as **diabetes** (16), **Parkinson's**

disease (16), **osteoporosis** (30), **stroke** (16), **arthritis** (17)**, heart disease** (31), and **rheumatic diseases** (16), which have all proven to increase the risk of falls. These results indicate that many chronic diseases do not have an impact on the functions needed to restore a low risk profile for falls, while others affect the systems that are important, for example; cognitive domains, the nervous system and physical functions. Other health disorders such as **hypotension** (23, 31) and **incontinence** (16, 17) have also shown an association to an increased risk of falling.

Depression and **depressive symptoms** are associated with a higher risk of falls (17, 32, 33), even after controlling for the use of antidepressants (34, 35).

Impairment in physical function, such as impaired **balance**, **muscle-strength,** and **gait speed**, is strongly associated with falls (17, 23). Impaired balance assessed by the one-leg stand test has been shown to be independently associated with a higher risk of falls (36, 37). To rise from a chair without using the arms demands balance, but mainly muscle strength in the lower extremities. The 5 times chair stand test has been found to be associated with an increased risk of falling (38). Slow gait is associated with a higher risk of falls (39, 40), although the relationship between gait speed and falls has been suggested to be U-shaped in some studies (41); with both exceptional fast walkers and slow walkers having an increased risk of falls. Walking is a complex task that involves both physical and cognitive domains, thus having a slower walking speed is associated to both a physical and a cognitive decline (42, 43).

Dependency in activities of daily living, both instrumental and basic **(IADL** and **ADL),** are associated with a higher risk of falls (16, 17, 23, 44).

Impaired global **cognitive function** is also associated with falls (16, 17, 23, 45). Individuals with dementia are at a higher risk of experiencing a fall, and are also more likely to get hospitalized due to a fall than cognitively intact individuals (46). In addition, interventions to avoid falls among older people have been found to be less effective among individuals with dementia (47). Even small changes in specific cognitive areas among non-demented older persons has been shown to be associated to a higher fall risk (45, 48, 49).

<u>Behavioral risk factors</u>**. Physical activity** level has been shown to be associated with falling. Having a low physical activity level may increase the risk of experiencing a fall (50), although being very physically active may also increase the risk, as seen in some studies (51). This relationship is similar to the one suggested for walking speed. Those considered very active might have an increased risk due to being more prone to taking part in risky behaviors, rather than for biological reasons (52, 53). **Smoking** is associated with a higher risk of falls, as for most other adverse health outcomes (54). In addition, smoking is related to osteoporosis, and in turn to a higher risk of fractures (55). Having a high consumption of **alcohol**

may also increase the risk of falls (56). Although, when distinguishing moderate drinkers from those who are abstainers, a moderate alcohol consumption has been found to be associated to a reduced risk (54). This might be explained by the fact that people with worse health often abstain from drinking alcohol and that moderate drinking is associated with other factors associated with good health, such as being married (57).

Polypharmacy and in particular specific medications may increase the risk of falls (23, 58). In this thesis, Fall Risk Increasing Drugs (**FRID**s) were defined according to the Swedish National Board of Health and Welfare, and includes the following Anatomical Therapeutic Chemical (ATC) classification codes: C01D, C02, C03, C07, C08, C09, G04CA, N04B, N02A, N05A, N05B, N05C, and N06A (59).

Previous falls are known to be the main risk factor for future falls, (17, 23, 30), suggesting that we may be able to reduce the number of falls by delaying or even preventing the first fall.

1.3 Multifactorial aspect

Many of the risk factors listed above are associated to each other, and are therefore likely to co-exist. For example, lifestyle factors, sociodemographic factors, and many diseases are strongly interrelated (60), and so is the decline in physical and cognitive functions (61). A combination of two risk factors can increase the risk of falling exponentially, or just give an additive effect. Still, we know very little about interaction effects between known risk factors. Because of this, it might be problematic to deal with risk factors for falls one by one. To get a more complete picture, we need to study falls from a multifactorial perspective (23, 62, 63). In addition, different risk factors may affect fall risk differently. Thus, we need to weigh different risk factors against each other, to emphasize each risk factor's importance. In this thesis, the focus is mainly on individuals with a high risk of falling, in contrast to examining risk factors individually.

1.4 Screening tools

Current guidelines for fall risk prevention in community-living older people recommend three sequential stages: screening to identify people at increased risk of falls, multifactorial fall risk assessment for those identified as at risk, and implementation of tailored interventions (64). There are many assessment tools to detect people at risk of falls. Tools for injurious falls are very scarce, despite injurious falls having the most detrimental impact on individuals and the society. The literature about predicting injurious falls focuses mainly on single-item physical tests (36, 37, 65). Therefore, the following section is about the assessment tools for fall risk in general.

Most tools have been developed to be used within a hospital or nursing home setting, among those are also tools for specific patient groups, such as stroke inpatients. Assessment tools profiled for primary care or for community-dwelling older individuals are scarcer. Use of disease-centered inpatient scores are in most cases not suitable for a healthier community-dwelling population that is visiting primary care centers, the probable outcome would be to only find those at the absolute highest risk or previous fallers. This might be an issue if we want to be able to prevent falls and decrease the number of fallers. Traditionally, different physical tests have been used to detect people at risk, e.g.; Timed-Up-And-Go (66) or a simple balance test (67). There are also generic batteries of different physical tests that have been used to find people at risk of falls, e.g., Short Physical Performance Battery (SPPB) (68) (**Table 1**).

Table 1. Generic screening tools for physical function that are validated for screening of falls in a community-settings/for primary care.

Name of the tool	Type of tool	Target population	Study design	Predictive value for falls	Outcome assessment
SPPB (68, 69)	Generic lower extremity test, 3–6 items	Community	Longitudinal	OR 3.46/3.82 (Highest score vs. lowest score)	Self-reported recurrent falls + medical records
PPA (70)	Physical test battery, 16 items	All settings	Longitudinal	PPV: 79%, 75%	Multiple falls, 12 months
Quickscreen (71)	Brief physical test battery, 8 items	Primary Care	Longitudinal	AUC 0.72	Multiple falls, 12 months

Since the cause of falls is likely multifactorial, assessment tools that include risk factors from several different domains might give a more complete picture of an individual's fall risk. Several different multifactorial tools have been developed; either as a part of a more comprehensive fall assessment program or as shorter screening tools that aim to quickly screen for fall risk (**Table 2**). Limitations of most existing tools are that they were constructed based on cross-sectional data and self-reported falls, which increases the risk of reverse causality and recall bias. Furthermore, the few studies that constructed assessment tools using longitudinal data have a follow-up time of maximum 12 months. Finally, these multifactorial assessment tools typically include information about previous falls, thus focusing on recurrent fallers. Considering the rather low predictive value of existing assessment tools, it might be more effective to focus on reliable screening tools that can detect individuals at elevated risk, with a subsequent assessment with a person-centered approach.

Table 2. Multifactorial screening tools developed or validated to predict falls in community-settings or for primary care.

Name of the tool	Type of tool	Target population	Study design	Predictive value for falls	Outcome assessment
STEADI (CDC Injury Center) (72, 73)	Fall risk assessment in several steps, flow chart	Community	Reviews, qualitative	-	Built on reviews, AGS/BGS guidelines and clinical experience
FROP-com (74)	Assessment tool after fall, 26 items	Community/ after ED visit	Longitudinal	AUC 0.68	Recurrent falls, 12 months (patients discharged from ED due to a fall)
FROP-com screening (75)	Screening, 3-item version of FROP-Com	Community/ after ED visit	Longitudinal	Sensitivity 67.1%, Specificity 66.7%	Recurrent falls, 12 months (patients discharged from ED due to a fall)
FRAT (76)	Screening (5 item) + guide	Primary Care	Longitudinal	0.57 (3/5 factors)	Any fall within 6 months
FRAT-up (77, 78)	Assessment tool, 28 items	Community	Meta-analysis (validated longitudinal)	AUC 0.65	Built on meta-analysis (16) (validated 12 months)
Thai-FRAT (79)	Risk assessment, 6 items	Community	Cross-sectional (validated longitudinal)	Sensitivity 0.92, Specificity 0.83	Multiple falls (validated: 6 months)
Bongue et al (80)	Screening, 6 items	Community	Longitudinal	AUC 0.7	Any fall within 12 months
Covinsky et al (81)	Risk Index, 3 items	Community	Longitudinal	C statistics 0.71	Any fall within 12 months
Pluijm et al, LASA fall risk profile (62, 82)	Fall risk profile, 9 items	Community	Longitudinal	AUC 0.65	Recurrent falls (2 times within 6 months during a 3-year period)
Renfro et al, FRAST (83)	Screening, 15 items (including 3 separate scores)	Community/ Primary Care	Literature review	-	Based on literature review
Stalenhoef et al (84)	Risk model, 4 items + different scoring for males/females	Community	Longitudinal	Sensitivity 52%, Specificity 90%	Recurrent falls, 36 weeks
Tromp et al (85)	Screening, 4 items, different for any or recurrent falls	Community	Longitudinal	AUC 0.65, 0.71	Any fall + recurrent falls, 12 months

1.5 Sex differences

Women fall more frequently than men, and are at higher risk of an injurious fall (17, 86, 87), while men are more at risk of receiving fatal injuries as a consequence of a fall (1). Despite the numerous studies on risk factors of falls in older adults, studies examining sex differences are relatively rare (27, 88–90). These studies show differences in risk factors for falls between men and women. The results are quite diverse, and due to the heterogeneity of the study methods, it is difficult to compare the results. In addition, these studies are either cross-sectional in their design or study single risk factors. There is, however, a need to clarify the extent to which risk factors are sex-specific, and if there are, explore the extent of these differences. These variations are typically not considered in screening tools, despite recent findings suggesting that sex should be considered when designing fall-preventing strategies (90, 91). So far, no other screening tool has considered the differences in fall risk factors between women and men.

1.6 Course of disability after an injurious fall

Previous studies have examined the course of disability and physical function after a fall or a fall-related injury (92–95). These have all shown that fallers have higher levels of disability and poorer physical function than non-fallers, both in short- and long-term. Remaining independent and mobile while aging is the most prioritized health aspect for older adults themselves, and should therefore also be prioritized by policy makers and the health care system. A few previous studies have shown that the magnitude and/or trajectories of these adverse outcomes after a fall seem to differ between individuals (96, 97). As examples, sociodemographic factors such as cohabitation status and sex have been suggested to play a role (96), while the role of health-related factors such as activity level and health perceptions before the falls are yet to be explored. In order to help the health care system find the most vulnerable fallers, who are at the highest risk of adverse outcomes, we need to know more about which factors or characteristics predict these trajectories.

1.7 Interventions

Multifactorial tailored interventions are the most effective to decrease the number of fall injuries (98–101). These interventions can be conducted by multidisciplinary teams and are tailored to each individual's profile. An example could be a combination of physical training, medication reviews, and preventive actions in the home environment. Multifactorial interventions can be carried out as a primary intervention for people who have not fallen, but who have an increased risk, or as a secondary prevention for those who have experienced a fall. Only exercise interventions can also be effective, for example balance training

programs (100, 102). The current approach in falls prevention tend to focus on preventive strategies among individuals who have received health care for a fall injury, thus mainly secondary prevention. Since falls are causing a great deal of suffering for the individual and a high cost for the society, implementing primary prevention for falls has the capability of both reducing suffering and to be more cost effective than secondary prevention. Screening tools need to be utilized in order to identify people at risk of a fall, and to implement both primary and secondary intervention strategies.

1.8 Knowledge gap

- Despite the detrimental effect an injurious fall can have on the individual, there is a lack of literature studying injurious falls as opposed to any falls.
- A major part of existing literature focuses on risk factors in isolation, ignoring possible interactions and additive effects the different risk factors can have on each other
- A few recent studies have indicated there might be a sex difference in risk factors for falls. More longitudinal studies on this issue are needed.
- Multifactorial screening tools developed to find older individuals at risk of falling all include previous falls, targeting recurrent fallers. There is a need for a tool that can detect those at risk for first time falls.
- Although, it is well known that injurious falls often led to disabilities, more knowledge is needed to distinguish which individuals are at risk of worse functional outcomes than others are after a fall.

1.9 Theoretical framework

The WHO has chosen to base their strategic work with healthy aging and falls prevention on a redefinition of the Active Aging approach. Healthy Aging is the combination of intrinsic capacity, environmental characteristics and the interaction between them (1, 103). The Healthy Aging strategies builds on the Life-course Approach, developed and added on by Kalache et al (104) and Kuh et al (105). In this thesis, the view of fall risk is derived from the Life-Course Approach, although with a focus on the later life. The emphasis is on the threshold for disability and dependency (possibly crossed as a consequence of a fall) and the increasing heterogeneity in aging. I focus on what might cause the steeper decline that results in earlier disability and/or dependency and also on how we can find individuals at risk before they cross that threshold, to be able to intervene successfully (**Figure 1**). Thus, the falls and fall-related injuries are considered a symptom of an aging phenotype with a steeper general decline. With this point of view, also fall-related injuries can be looked at and prevented with the same tools that are used in the Active Ageing framework.

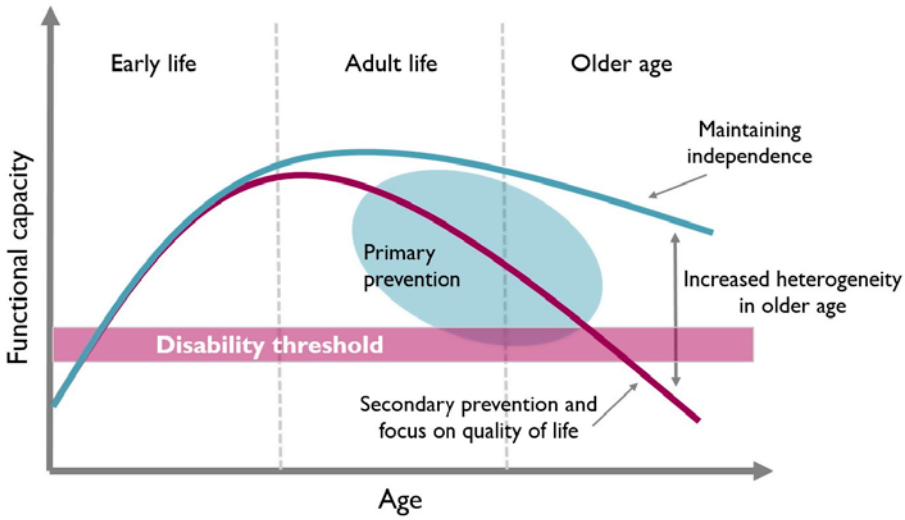

Figure 1. Life-course approach for disability. *Modified from World Health Organization, 2002* (106).

2 AIMS

2.1 Overall Aim

The overall aims of this thesis are to enable early detection of older women and men at different levels of risk for injurious falls, and examine the long-term consequences of fall injuries on functional status. The specific aims and research questions are as follows:

2.2 Specific aims

Study I. To identify specific clusters of older people with similar health- and lifestyle-related risk factors for falls, and assess the association between those clusters and the risk of injurious falls. Research questions:

a) Which are the specific risk profiles for injurious falls among older adults?

b) To what extent are the different clusters related to the risk of future injurious falls?

Study II. To examine differences in fall risk factors between women and men, and to determine the most important risk factors for fall-related injuries for men and women over the short- and long-term

Research questions:

a) How do fall risk factors for injurious falls differ between women and men?

b) Which are the most important risk factors for injurious falls, for women and men over a shorter versus a longer follow-up time?

Study III. To construct a multifactorial sex-specific index for the prediction of injurious falls, to enable early detection of fall-prone older persons who can be targets for primary interventions. Research questions:

a) Which individual factors are independently associated with an increased risk for first time fall-related injuries?

b) Which combination of risk factors can best discriminate between older adults who will suffer fall-related injuries from those who will not?

Study IV. To examine the long-term course of disability after an injurious fall.

Research questions:

a) How does the course of disability differ between those who suffer an injurious fall and those who do not during a 12-year period?

b) How do sociodemographic- and health-related factors affect the course of disability among fallers and non-fallers?

3 MATERIALS AND METHODS

3.1 Data

3.1.1 Study sample

We used data from the Swedish National study on Aging and Care in Kungsholmen (SNAC-K) (107). The population in Kungsholmen, a central area of Stockholm, were first stratified by age and then randomly sampled from each of the 11 age cohorts (60, 66, 72, 78, 81, 84, 87, 90, 93, 96 and 99+ years). At the baseline survey (year 2001–2004), 5111 persons were initially invited to participate in the SNAC-K study, of those 200 died before the start of the study, 262 were not able to be contacted, four were deaf, 23 did not speak Swedish, and 32 had moved. Of the remaining 4590 persons, 3363 (73.3%) were examined at baseline. The younger cohorts (60–72) are followed-up every sixth year and the older cohorts (78+) every third year. The data collection for the SNAC-K study is ongoing. SNAC-K is linked to the National Patient Register and to the Swedish Cause of Death Registry. **Figure 2** shows which waves of SNAC-K that are used for the four individual studies.

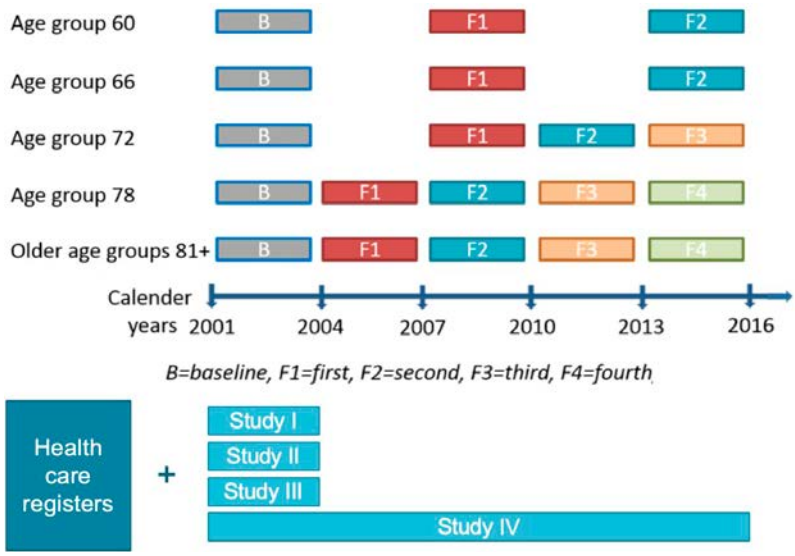

Figure 2. Waves of the Swedish National study on Aging and Care in Kungsholmen and data used for each individual study included in the thesis.

3.1.2 Risk factors and covariates

Nurses and physicians collected data through interviews, clinical examinations, and physical function tests. Education, smoking, alcohol consumption (108), physical activity level (109), activities of daily living (ADL/IADL) (110), vision (24), and incontinence were assessed by interview while self-rated health was assessed by a questionnaire. Depressive symptoms were assessed by the Montgomery-Åsberg Depression Rating Scale (MADRS) and cognitive impairment was assessed with the Mini-Mental State Examination (MMSE), which are both validated for an older population (111, 112). Diseases were diagnosed based on a combination of medical records, clinical examination, and patient history. A disease was defined as chronic if it was of prolonged duration, left residual disability, worsened quality of life, or required a long period of care, treatment, or rehabilitation (28). Blood pressure was measured twice in a sitting position on the left arm using a mercury sphygmomanometer; a mean of the two measures was used. Hypotension was defined as systolic blood pressure <130 mmHg (113). Fall Risk Increasing Drugs (FRIDs) included the following Anatomical Therapeutic Chemical (ATC) classification codes: C01D, C02, C03, C07, C08, C09, G04CA, N04B, N02A, N05A, N05B, N05C, and N06A (59). The assessment of physical performance included tests of balance, walking speed, and 5-time chair stands. One-leg balance stand was defined as the time in seconds that the participants could stand on either leg with their eyes open up to 60 seconds, the longest time of standing in two attempts was used (114). Walking speed was assessed by asking the participant to walk at a normal pace either for 6 or 2.44 meters, depending on the location of the test and capability of the participant (115). For the 5-time chair stand, the participant was asked to sit and rise from a chair 5 times as quickly as possible, without using their arms (115).

3.1.3 Injurious falls

The outcome of injurious falls was assessed by health care registers. An injurious fall was defined as a receipt of inpatient or outpatient care because of a fall. Discharge diagnoses from the International Classification of Diseases, Tenth Revision (ICD-10), were used to identify falls from the date of the baseline examination until the last available date (December 2011). These included the external cause codes W00, W01, W05-W10, and W17-W19, which represent falls on the same level (W00, W01, W18), falls including furniture, wheelchair etc. (W05-W09), falls from one level to another, e.g. from stairs (W10, W17), and unspecified falls (W19). These codes were chosen to represent a low energy trauma fall without involvement of a second person. This information was retrieved from the National Patient Register, which includes data from inpatient care and specialized outpatient care, and from the Local Outpatient Register, which includes

data from primary care in the Stockholm County Council area (116). Outcome status was determined by linking each participant's personal identification number (PIN) to the registers. Because of the PIN linkage the loss of follow-up data is minimal (117). The Swedish health care registers have been shown to be highly reliable (116). Data on previous falls included injurious falls within three years of the baseline examination.

3.2 Statistical analyses

Study I: Clusters of individuals were identified using Ward's linkage. Ward's linkage clustering is a hierarchical agglomerative clustering method that builds on the ANOVA sum of squares, where the sum of squares within-cluster is minimized (118). This clustering procedure is characterized by the tree-like structure, and the clusters are generated according to the characteristics of the subjects and not according to the single variables. In the first step, each subject represents an individual cluster. These clusters are then sequentially merged according to their similarity. First, the two most similar clusters (those with the smallest distance between them) are merged to form a new cluster at the bottom of the hierarchy. In the next step, another pair of clusters is merged and linked to a higher level of the hierarchy, and so on. The number of clusters was chosen based on the balance between intra-cluster similarity and inter-cluster variance, and a combination of studying tree diagrams and proportions of each.

We used flexible parametric survival models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between the different clusters and injurious falls. Participants were considered at risk from the date of the baseline examination. Risk of injurious falls was analyzed, censoring the observation time at three different points in time: 3, 5, and 10 years after baseline or at the date of death. The Population Attributable Risk (PAR) of injurious falls was calculated by using the formula for survival studies to estimate the proportion of injurious falls averted in the hypothetical scenario that we would be able to eliminate the specific cluster of risk factors. To explore possible age and sex differences for the risk of injurious falls between the clusters, we also ran the analyses stratifying by sex and age. An additional analysis was conducted excluding individuals living in a nursing home. Finally, the effect of missing values was evaluated by performing imputations of 15 imputed datasets using multiple imputations chained equations (MICE) (119). We pooled the estimates using Rubin's rule to obtain valid statistical inferences. All the relevant variables included in the main analysis, including the outcome, were used in the multiple imputation models.

Study II: Baseline characteristics were compared by sex using the chi-square test. Cox proportional hazards models were initially stratified by sex and adjusted for age and education and performed to identify the potential risk factors most strongly associated with injurious falls. The follow-up time was divided into two intervals (0–3 years and 4–10 years after baseline examination). Participants were censored at the date of the first injurious fall, death, or the end of the follow-up period, whichever came first. The aim of the study was to detect the most common risk factors, because of this, we excluded risk factors that had a prevalence lower than 10% from the multivariate models. Second, risk factors showing an association with injurious falls of $p<0.05$ were included in multivariate Cox proportional hazard models. Last, a backward stepwise elimination was conducted, stopping at a model where all factors included were significant at a 95% level. Since the data was stratified for both sex and follow-up time, it resulted in four separate models.

Study III: Baseline characteristics were compared by sex using the chi-square test. To achieve the screening tools, each potential risk factor was first analyzed using Cox proportional hazards models adjusting for sex, age, and education. Participants were censored at the date of the first injurious fall, death, or the end of the follow-up period (5 years from baseline), whichever came first. Second, risk factors showing an association with injurious falls of $p<0.01$ were included in multivariate Cox proportional hazards models. Risk factors were selected using a backward stepwise procedure. For each variable excluded, we compared the C-statistic and Akaike Information Criterion between the different models. Third, when reaching the final optimal combination of risk factors, we stratified by sex, to retrieve values adapted for possible sex differences. Fourth, on the basis of the final Cox hazards models, risk scores were assigned for each risk factor with the respective β coefficients. To make the scores approach an integer and be intuitive for the user, all β coefficients were standardized by multiplying the β value by a constant and rounding to the nearest integer, which means that those factors with the lowest risk were assigned a value of 1. The two screening tools (separate for women and men) were then obtained by summing the scores for each of the risk factors. Harrell's C statistics were calculated from the specificity and sensitivity of the scores ability to predict injurious falls. Last, to enhance interpretation of the tools, the scores were categorized according to increase in HR value, indicating low risk, medium risk, and high risk. Finally, Cox proportional hazards models were conducted to examine the HR for injurious falls by the level of risk on the screening tools.

Study IV: Each binary predictor including sex, cohabitation status, physical activity level, and self-rated health was combined with injurious falls (falls/no falls) to create four different indicator variables with four mutually exclusive categories each. Linear mixed-effects models with random effects for intercept and slope were used to examine the association between the indicator variables and the changes in disability score over time, resulting in four separate models. To measure the effect of the exposures on the average annual change in the number of disabilities, the interaction term between follow-up time (in years) and each of the four indicator variables was included as a fixed effect. Each of the four models were adjusted for all other exposures, as well as age, education level, multimorbidity, and MMSE. Initially, survival was also included in the models but was omitted due to collinearity with other covariates. Non-linearity of follow-up time was tested but was not significant. In order to verify that recurrent falls or severity of the injury did not drive the results, we performed the following sensitivity analyses: a) excluding individuals with an injurious fall within three years of baseline, and b) considering only fractures in the definition of injurious falls. Finally, to take into accunt the missing data, MICE was performed to obtain five imputed datasets. All the variables included in the main analyses were used in the multiple imputation models.

Statistical analyses were performed with version 14 or 15 of Stata software (StataCorp, TX, USA).

Table 3 summarizes the methods used in the four individual studies.

Table 3. Overview of the methods used in the four studies.

Study	Outcome	Exposures	Covariates	Analytical sample	Follow-up time	Statistical analyses
Study I	Injurious falls	Age, sex, education, cohabitation status, BMI, smoking, alcohol intake, physical activity level, vision, pain, depressive symptoms, MMSE, multimorbidity, FRIDs, ADL, IADL, walking speed, balance, 5-time chair stand, previous falls	-	Exclusion criteria: missing data in any risk factor N=2,566	3, 5 and 10 years	Ward's linkage cluster analysis Flexible parametric survival analysis Population attributable risk analysis
Study II	Injurious Falls	Cohabitation status, BMI, smoking, alcohol intake, physical activity level, vision, pain, depressive symptoms, MMSE, multimorbidity, stroke, Parkinson disease, heart disease, diabetes, rheumatic disease, arthritis, hypotension, incontinence, FRIDs, ADL, IADL, walking speed, balance, 5-time chair stand, previous falls	Age, education Stratified by sex	Exclusion criteria: living in institution N=3,112	0-3 and 4-10 years	Cox proportional hazards
Study III	Injurious falls	Cohabitation status, BMI, smoking, alcohol intake, physical activity level, vision, pain, depressive symptoms, MMSE, multimorbidity, stroke, Parkinson disease, heart disease, diabetes, rheumatic disease, arthritis, hypotension, incontinence, FRIDs, ADL, IADL, walking speed, balance, 5-time chair stand, previous falls	Age, sex, education	Exclusion criteria: living in institution, previous fallers N=2,808	5 years	Cox proportional hazards
Study IV	Disability	Injurious falls in combination with; sex, living alone, physical activity level and self-rated health, respectively	Age, education, multimorbidity, MMSE, survival (and other exposures)	Exclusion criteria: living in institution, experiencing a fall after the exposure period (0-3 years), missing data on outcome, exposures or covariates at baseline on baseline, data from less than two time points N=1,426	12 years	Linear mixed models

3.3 Ethical considerations

As a population-based cohort study, the primary ethical issues SNAC-K deals with is anonymity and informed consent.

When entering the study each participant is given a personal identification number, upon which name and PIN is then removed from all data to ensure anonymity. The original forms and questionnaires that contain both PIN and identification number are stored in locked safety cabins.

Written informed consent was obtained from all participants. If a person could not answer, a proxy (usually a close family member) was also asked. All participants were informed about the purpose and content of the study. The participants were also made aware that they could chose to drop out at any point, without giving a reason.

Apart from informed consent and anonymity, safety during the testing is also an important ethical issue. Participants are asked if they can, or want to, perform the different physical tests before testing. Nurses and physicians working with the data collection also evaluate if they think it is safe to conduct the physical tests before starting. If the participant deems it as unsafe or does not dare to try, or if the test leader evaluates it as unsafe the test is not performed. The test leader is always standing close to be able to help if the participant slips or loses their balance.

A last issue that might arise from participants undergoing thorough medical testing is the possibility to discover unknown medical issues or diseases. In most cases people want to know about diseases but there might be exceptions. The participants get a letter with their test results sent home to them, after the testing. In this letter, the staff also recommend them to see their family doctor if anything unknown turned out that needs medical attention. This could for example be high blood pressure or early signs of dementia. The obvious benefits of discovering medical issues sooner would outweigh possible unwanted sensitive information.

The SNAC-K project was approved by the Regional Ethical Review Board in Stockholm, Sweden (01-114, 04-929/3, 26-2007, 2010/447-31/2, 2013/828-31/3, 2009/595-32). The SNAC-K study is designed in agreement with the Declaration of Helsinki. In addition, all researchers are respecting and following the ethical guidelines of the Swedish Council for Research in the Humanities and Social Sciences.

4 MAIN RESULTS

4.1 Fall risk profiles

Study I

The analytical sample (n=2566) had a mean age of 72.1 (SD 9.86) and 61.2% were women. The cluster analysis identified five major clusters of risk profiles for falls with distinctively different characteristics. The first cluster was termed "**Healthy**" because they represented a relatively healthy subpopulation, while the second cluster was very similar to the first with the addition of a high rate of "**Multimorbidity**". The third cluster, in its turn, was similar to cluster 2 but had a high rate of FRID consumption and had the highest rate of depressive symptoms of all clusters, thus termed the "**Medication and depressive symptoms**" cluster. The fourth cluster had a high rate of combined "**Physical and cognitive impairment**", and also differed in other characteristics from the previous clusters. The fifth and last cluster consisted of individuals who were the worst off with an accumulation of most of the risk factors, and the major part of the individuals had an ADL or IADL "**Disability**". The main characteristics, and proportion of individuals of each cluster is presented in **Figure 3a**.

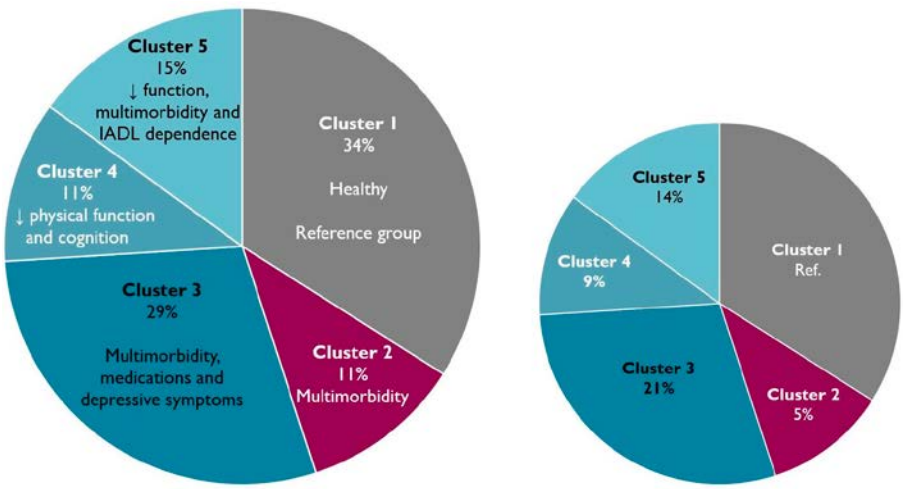

Figure 3. A) Main characteristics and proportion of individuals in the five clusters. B) The population attributable risk for each cluster, in percentage.

From baseline up to 3 years, 180 individuals endured an injurious fall, 327 over 5 years, and 599 over a 10-year period. Over 3 years of follow-up the risk doubled in each cluster (using cluster 1 as a reference). This trend was similar for clusters 2 and 3 but decreased slightly for cluster 4 and 5 over the longer follow-up periods. Results from the survival analysis are shown in **Figure 4.**

The population attributable risk analysis (PAR) showed that the combination of the risk factors in each cluster respectively contributed to 5%, 21%, 9%, and 14% of the injurious falls. When adding up the numbers, it showed that about 50% of all falls could had been avoided if the individuals in clusters 2–5 had shared characteristics with the reference cluster 1 (shown in **Figure 3b**).

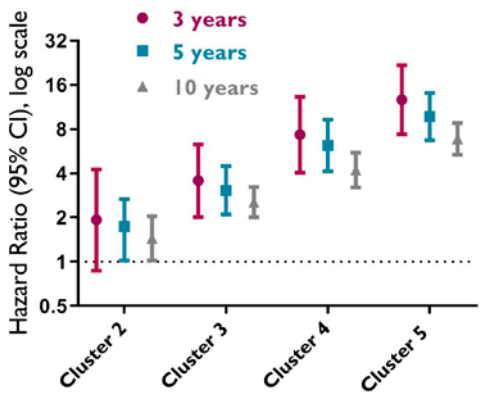

Figure 4. Hazard ratio for cluster 2–5 with cluster 1 as reference, over 3, 5 and 10 years.

4.2 Sex differences in risk factors for injurious falls

Study II

The 3112 participants in the study sample had a mean age of 75.2 (SD 11.0) and 1981 (63.5%) were women. During the shorter follow-up of 0 to 3 years, 229 (11.6%) of the women and 70 (6.2%) of the men endured an injurious fall, whereas for the longer follow-up (4–10 years) it was 369 (21.1%) and 140 (13.2%) for women and men, respectively. **Figure 5** shows the association between included risk factors and injurious falls for men and women during the two time periods (0–3 years and 4–10 years after baseline examination), adjusted for age and education.

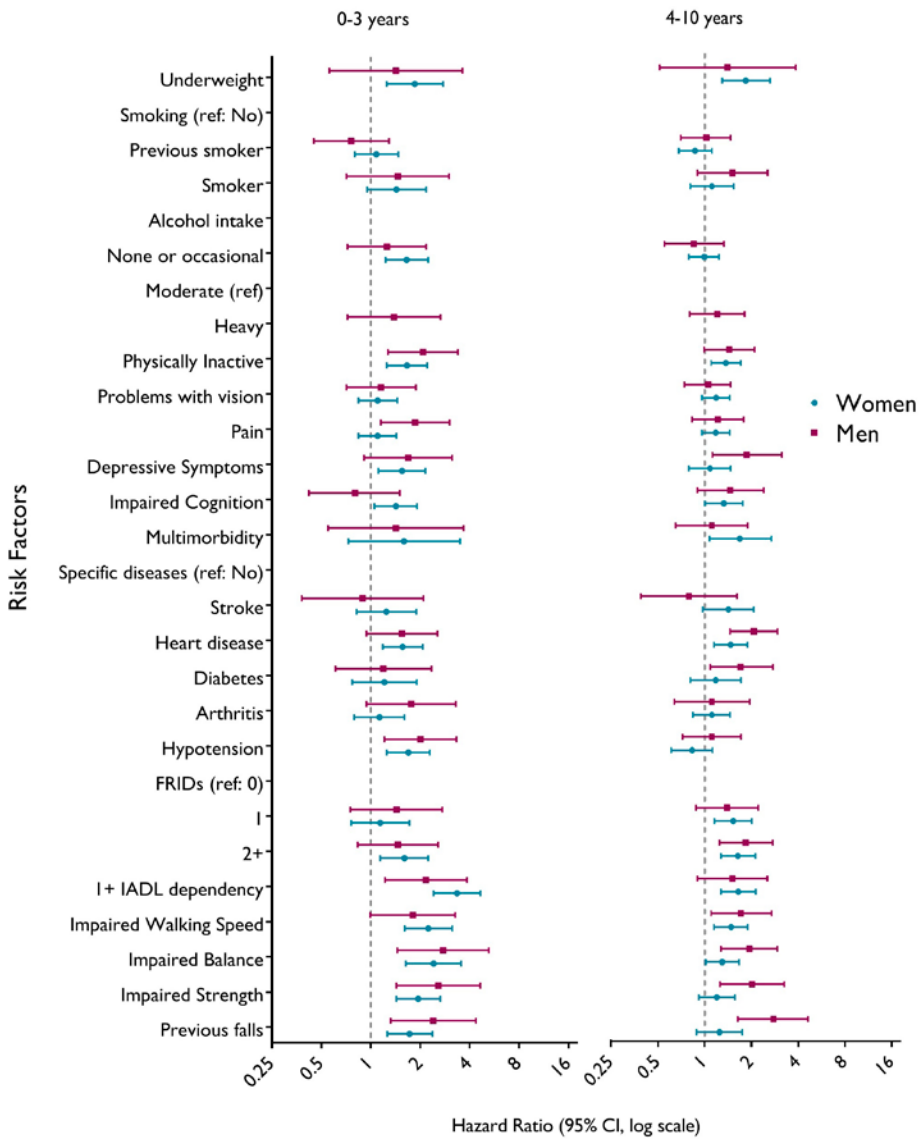

Figure 5. Hazard ratios and 95% confidence intervals (CIs) of individual risk factors for first injurious fall up to 5 years after baseline. Controlled for age and education.

For women, during the short-term follow-up period, living alone, any IADL dependency, and previous falls were the most prominent risk factors in the final fall risk profile. During the long follow-up being underweight, having cognitive impairment, taking one or more FRIDs, and IADL dependency were the chief risk factors. For men, low blood pressure, impaired strength, and previous falls formed the final risk profile over the shorter follow-up time, while being a smoker, having a heart disease, impaired balance, and a previous fall were the most important risk factors over the long follow-up period. Hazard ratios and confidence intervals are shown in **Table 4**. In the interaction analysis, only the risk associated to previous falls at the longer follow-up was significantly different between men and women.

Table 4. Hazard ratios and 95% confidence intervals (CIs) from multivariate analyses for injurious falls in men and women at 0–3 years and 4–10 years after baseline*.

	Hazard Ratio (CI)			
	0–3 years		4–10 years	
	Women	Men	Women	Men
Living alone	1.83 (1.13–2.96)	-	-	-
Underweight	-	-	2.03 (1.4–2.95)	-
Current smoker	-	-	-	1.71 (1.03–2.84)
Cognitive impairment	-	-	1.49 (1.08–2.06)	-
Heart disease	-	-	-	2.2 (1.5–3.24)
Low SBP	-	1.96 (1.04–3.71)	-	-
FRIDs				
0			ref	
1	-	-	1.5 (1.11–2.03)	-
2+	-	-	1.67 (1.27–2.2)	-
IADL	2.59 (1.73–3.87)	-	1.58 (1.19–2.11)	-
Impaired balance	-	-	-	1.68 (1.08–2.62)
Impaired strength	-	3.0 (1.52–5.93)	-	-
Previous falls	1.71 (1.08–2.72)	2.81 (1.32–5.97)	-	3.61 (1.98–6.61)

* Final multivariate models from backward elimination with a 0.05 significance limit. Controlled for age and education in all elimination steps.

Abbreviations and cutoffs used: underweight = body mass index <20; cognitive impairment = <28 points on MMSE; heart disease = arrhythmia, bradycardia and conduction disease, atrial fibrillation, ischemic heart disease, and heart failure; low SBP = systolic blood pressure <130 mmHg; IADL = instrumental activities of daily living (managing finances, using telephone, grocery shopping, using public transportation, preparing meals, cleaning, and doing laundry); impaired balance = <5 seconds one leg balance; impaired strength = unable to perform 5 consecutive chair stands without using arms; previous falls = any injurious fall during the 3 years prior to baseline.

4.3 The development of a fall risk screening tool

Study III

The study sample consisted of 2808 individuals with a mean age of 71 years (SD 9.6), and 1750 (62%) were women. Two hundred ninety-seven (17%) women and 96 (9%) men experienced a first injurious fall from baseline up to 5 years. Risk factors associated to an injurious fall with a p-value less than 0.01 (adjusted for age, sex, and education) were: an increase in age by ten years, living alone, underweight, physically inactive, cognitively impaired, and having depressive symptoms, heart disease, hypotension, IADL dependency, impaired walking speed, impaired balance, and impaired strength (all risk factors studied are presented in **Appendix Figure 1**). The final risk factors derived from the backward stepwise elimination from the multivariate regression were older age, living alone, IADL dependency, and impaired balance.

The weighted- and sex-specific values derived from the β-coefficient of each risk factor included in the final score are presented in **Table 5**. Women had a maximum score of eight points, whereas men had a maximum score of seven. The predictive capacity of the scores was measured with Harrell's C statistics, showing 0.75 and 0.77 for women and men, respectively.

Table 5. Hazard ratios and 95% confidence intervals (CIs) for first injurious fall in women and men up to 5 years after baseline in relation to age, living alone, IADL dependency, and impaired balance (final multivariate models after backward elimination and the weights for the different factors included in the score).

	Hazard ratio (CI)	p-value	Coefficient		
Women				x 2.63	≈
70–79*	1.63 (1.09–2.44)	0.017	0.49	1.29	1
80–89*	2.52 (1.61–3.95)	<0.001	0.93	2.45	2
90+*	4.18 (2.54–6.88)	<0.001	1.43	3.76	4
Living alone	1.46 (1.05–2.04)	0.026	0.38	1.00	1
IADL dependency	2.24 (1.67–3.02)	<0.001	0.81	2.13	2
Impaired balance	1.60 (1.16–2.19)	0.004	0.47	1.24	1
					= max 8
Men				x 1.92	≈
70–79*	2.64 (1.41–4.97)	0.002	0.97	1.86	2
80–89*	4.00 (1.97–8.12)	<0.001	1.39	2.67	3
90+*	9.64 (4.14–22.41)	<0.001	2.27	4.36	4
Living alone	1.69 (1.08–2.64)	0.022	0.52	1.00	1
IADL dependency	1.92 (1.09–3.39)	0.024	0.65	1.25	1
Impaired balance	1.93 (1.13–3.28)	0.015	0.66	1.27	1
					= max 7

* Age 60–66 as the reference

Abbreviations and cutoffs used: IADL = instrumental activities of daily living (managing finances, using telephone, grocery shopping, using public transportation, preparing meals, cleaning, and doing laundry); impaired balance = <5 seconds one leg stand test.

We aimed for the screening tool to be flexible and possible to utilize in different settings and for different populations. Nevertheless, for the clinical usability, we developed two different possible ways to categorize the scores:

1) To obtain three different risk levels (low, medium, high), a first cutoff (between low and medium) was set where the risk was significantly associated to an injurious fall. The second cutoff (between medium and high) was set where the risk doubled from one value to the next. This resulted in a low risk for women being 0 and 0–2 for men, a medium risk being 1–3 for women and 3–4 for men, while a high risk was set at values above four and five, for women and men respectively. The sex specific HRs for an injurious fall for the different levels of risk are presented in **Table 6**, HRs for the whole scores are presented in **Appendix Table 1**. We also conducted a survival analysis for the categories, the results are shown in **Figure 6.**
2) To get only one cutoff, we used the Youden index. It was defined as a score value of three for both men and women. For women at this cutoff, the sensitivity was 0.69, the specificity 0.70, and the percentage of fallers that were correctly classified at this cutoff were 70%. For men, the sensitivity, specificity, and percentage of correct classified fallers were 0.72, 0.71, and 72%, respectively. Sensitivity and specificity of the scores are presented in **Appendix Table 2**.

Table 6. Hazard ratios and 95% confidence intervals (CIs) for first injurious fall in women and men up to 5 years after baseline in relation to categories of the score.

	n	cases	Score cutoff	Hazard ratio (CI)	p-value
Women (n=1607)					
Low risk	317	12	0	ref	
Medium risk	889	98	1–3	3.12 (1.71–5.68)	<0.001
High risk	401	143	≥4	14.18 (7.86–25.58)	<0.001
Men (n=998)					
Low risk	677	23	0–2	ref	
Medium risk	221	30	3–4	4.66 (2.71–8.02)	<0.001
High risk	100	30	≥5	14.66 (8.48–25.35)	<0.001

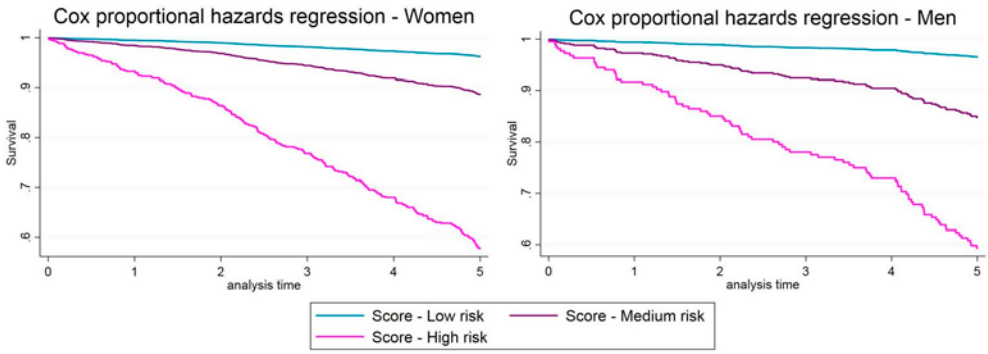

Figure 6. Survival plots showing time to an injurious fall for the different score categories, for women and men. (Number of participants at risk for women: low=317, medium=887, high=401; for men: low=677, medium=221, high=100.)

4.4 Sociodemographic and health related factors to modifies the course of disability after an injurious fall

Study IV

The study sample of 1426 individuals had a mean age of 69.3 (SD 8.5) and 867 (60.8%) were women. Seventynine of those individuals (5.5%) endured an injurious fall between baseline and the 3-year follow-up assessment. Due to the methodological design of the study we had the possibility to compare fallers and non-fallers' status of the sociodemographic and health-related factors before the exposure period of an injurious fall and then to follow the evolvment of disability of up to 9 years after the exposure period. The results showed that women had more disabilities than men at baseline, independent of a future fall, but that there were no sex differences in the trajectories of disability. Comparing those living with someone to those living alone, we found no difference at baseline but that the number of disabilities increased faster for all fallers and especially for those living alone. Inactive individuals had a higher number of disabilities already at the baseline assessment, and the increase in disabilites over time for inactive fallers was the fastest. Independent of future falls, individuals with poor self-rated health had more disabilities at baseline compared to those who rated their health as good. The highest increase in disbailities was for the fallers with poor self-rated health. Non-fallers with poor health had a very similar increase in disabilities to fallers with good health. All results are shown in **Table 7** and **Figure 7**. The interaction term between the exposures and falls on disability were all significant ($p<0.05$) except for sex.

Table 7. β coefficient and 95% confidence intervals (CI) for the relation of injurious falls in combination with sex, cohabitation, physical activity level, and self-rated health and changes in disability over 12 years.

	n	Baseline, β	(95% CI)	p-value	Annual change, β	95% CI	p-value
Sex							
Man, no fall	541	Ref.			Ref.		
Woman, no fall	806	0.105	0.000 to 0.209	**0.048**	0.014	-0.017 to 0.047	0.365
Man, fall	18	0.109	-0.318 to 0.536	0.616	0.341	0.200 to 0.482	**<0.001**
Woman, fall	61	0.310	0.066 to 0.554	**0.013**	0.324	0.246 to 0.402	**<0.001**
Cohabitation							
Cohabiting, no fall	759	Ref.			Ref.		
Alone, no fall	588	-0.068	-0.172 to 0.037	0.203	0.059	0.027 to 0.090	**<0.001**
Cohabiting, fall	24	-0.062	-0.434 to 0.310	0.742	0.203	0.086 to 0.320	**<0.001**
Alone, fall	55	0.229	-0.023 to 0.480	0.075	0.408	0.328 to 0.489	**<0.001**
Physical activity							
Active, no fall	1,113	Ref.			Ref.		
Inactive, no fall	234	0.187	0.058 to 0.316	**0.005**	0.112	0.071 to 0.152	**<0.001**
Active, fall	58	-0.082	-0.319 to 0.154	0.495	0.250	0.174 to 0.326	**<0.001**
Inactive, fall	21	1.123	0.731 to 1.517	**<0.001**	0.587	0.458 to 0.717	**<0.001**
Self-rated health							
Good, no fall	1,083	Ref.			Ref.		
Poor, no fall	264	0.194	0.067 to 0.321	**0.003**	0.153	0.115 to 0.192	**<0.001**
Good, fall	41	-0.034	-0.314 to 0.245	0.811	0.120	0.112 to 0.288	**<0.001**
Poor, fall	38	0.663	0.358 to 0.959	**<0.001**	0.514	0.420 to 0.609	**<0.001**

Controlled for age, education, multimorbidity, MMSE, and the other exposure variables (sex, living alone, physical activity level, and self-reported health). Significant p-values on a 95% confidence interval level in **bold**.

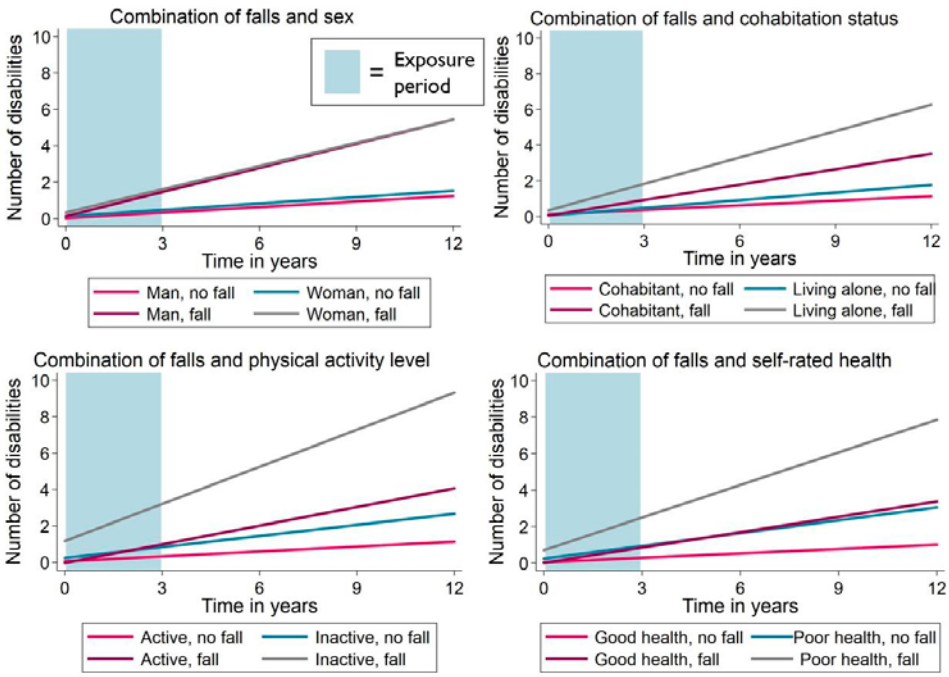

Figure 7. Graph for the relation of injurious falls in combination with sex, cohabitation, physical activity level, and self-rated health and changes in disability over 12 years, exposure period for falls between baseline and 3 years.

4.5 Falls and survival

While the dropout rate from the SNAC-K study was similar between fallers and non-fallers (21.5% vs 21.2%), the rate of mortality at the end of the 12 years follow-up was significantly higher for those who had endured a fall anytime during the period. Among the fallers 53.4% died, compared to 35.4% among non-fallers. An overview plot of status (participated/no fall, participated/fall, dropout, died) at baseline, 6 years follow-up, and 12 years follow- up is presented in **Figure 8**.

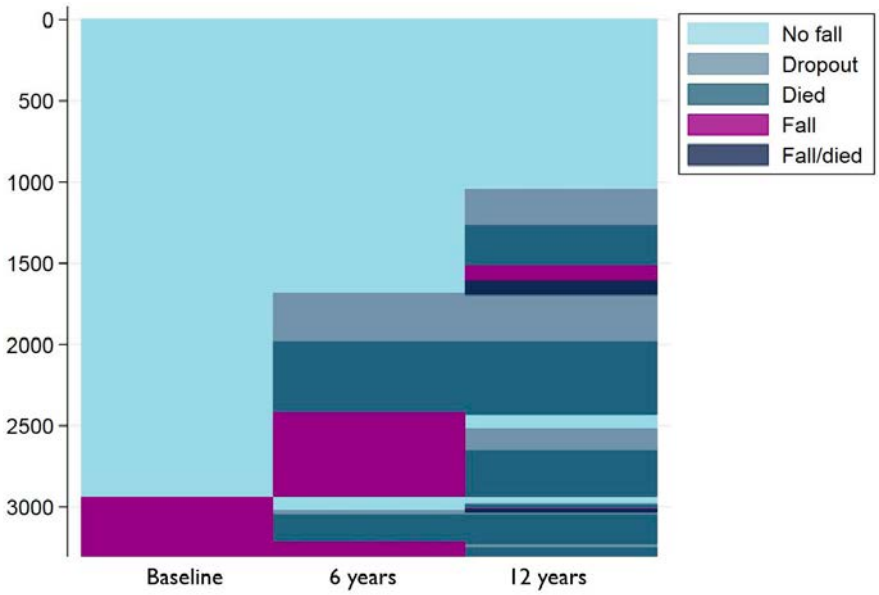

Figure 8. Status at baseline, 6 years, and 12 years of follow-up in the SNAC-K study. The fallers at baseline are those experiencing an injurious fall within 3 years from baseline. The Fall/died category are those who fell and then died between 6 to 12 years of follow-up.

Table 8 describes the health status at baseline, and number of deaths and droouts at 12-year follow-up, stratified by falls in combination with sex, cohabitation status, physical activity level, and self-rated health status of the participants included in Study IV.

Table 8. Distribution of baseline health status, number of deaths and dropouts during a 12-year follow-up, by the different groups of combinations of injurious falls with sex, cohabitation status, physical activity level, and self-rated health. Percentages in parentheses.

	n	Baseline multimorbidity	Baseline cognitive impairment	Previous falls	Number of deaths at 12-year follow-up	Number of dropouts at 12-year follow-up
Sex						
Man, no fall	541	425 (78.6)	40 (7.4)	12 (2.2)	111 (20.5)	61 (11.3)
Woman, no fall	806	660 (81.9)	44 (5.5)	41 (5.1)	127 (15.8)	114 (14.2)
Man, fall	18	16 (88.9)	2 (11.1)	3 (16.7)	9 (50.0)	1 (5.6)
Woman, fall	61	56 (91.8)	8 (13.1)	10 (16.4)	19 (31.2)	8 (13.1)
Cohabitation						
Cohabiting, no fall	759	589 (77.6)	36 (4.7)	24 (3.2)	104 (13.7)	95 (12.5)
Alone, no fall	588	496 (84.4)	48 (8.2)	29 (4.9)	134 (22.8)	80 (13.6)
Cohabiting, fall	24	22 (91.7)	1 (4.2)	2 (8.3)	7 (29.2)	2 (8.3)
Alone, fall	55	50 (90.9)	9 (16.4)	11 (20.0)	21 (38.2)	7 (12.7)
Physical activity						
Active, no fall	1,113	895 (80.4)	66 (5.9)	41 (3.7)	192 (17.3)	136 (12.2)
Inactive, no fall	234	190 (81.2)	18 (7.7)	12 (3.1)	46 (19.8)	39 (16.8)
Active, fall	58	51 (87.9)	7 (12.1)	7 (12.1)	16 (27.6)	7 (12.1)
Inactive, fall	21	21 (100.0)	3 (14.3)	6 (28.6)	12 (57.1)	2 (9.5)
Self-rated health						
Good, no fall	1,083	832 (76.8)	61 (5.6)	40 (3.7)	153 (14.1)	141 (13.0)
Poor, no fall	264	253 (95.8)	23 (8.7)	13 (4.9)	85 (32.3)	34 (12.9)
Good, fall	41	36 (87.8)	7 (17.1)	7 (17.1)	9 (22.0)	5 (12.2)
Poor, fall	38	36 (94.7)	3 (7.9)	6 (15.8)	19 (50.0)	4 (10.5)

5 DISCUSSION

5.1 Main findings

The main purpose behind this thesis is to investigate injurious falls among older adults using a holistic approach, moving away from specific risk factors. It was also to challenge some of the traditional methodology within the research field, by focusing on objectively measured injurious falls, first time fallers, and exploring different follow-up times. This, with the aim to enable more precise early prediction to ultimately lay a foundation for future clinical work that includes primary prevention for falls. The main findings can be summarized, very briefly, as follows:

- Risk factors seem to cluster within individuals, suggesting that both clinical and research focus should be more on fall risk profiles than on individual risk factors. (Study I)
- Women and men share most risk factors for injurious falls. However, there is diversity in the importance of some risk factors, resulting in sex-specific risk profiles. (Study II)
- Fall risk profiles over the short-term (0–3 years), differ from long term (4–10 years) profiles. The short-term risk factors can be interpreted as direct risk factors that can lead to an acute fall event, while the long-term risk factors may have a more general health impact and can be seen as indirect risk factors that can subsequently impact acute risk factors over several years. (Study II)
- We developed a concise and user-friendly screening tool for first time falls, and its predictive abilities are promising. The screening tool might fill the gap for a general primary care tool that is not targeting recurrent fallers, thus giving the opportunity to target community-dwelling older individuals at risk, for primary prevention. (Study III)
- An individual's sociodemographic- and health-related characteristics can modify the course of disability after a fall. Older individuals that are living alone, being physically inactive, and rate their health as poor are more vulnerable for the physical consequences of an injurious fall. (Study IV)

The results from all four studies in this thesis can help policy makers and health care staff to target and prioritize older individuals at the highest risk of injurious falls and the consequences of it. Thus aiding in both primary and secondary prevention.

5.2 Risk profiles and levels of risk

Study I, II, III

The results from study I confirmed our hypothesis that specific risk factors tend to cluster within individuals, forming risk profiles for falls. To investigate possible clusters of risk factors (or risk profiles) further, we stratified the analytical sample by both sex and follow-up time in study II. We found that people with unhealthy lifestyles and several chronic diseases (as in cluster 2), had an increased risk of falling over a longer period of follow-up, despite having good physical and cognitive function, which is in line with previous research (120). Verbrugge et al. suggested that chronic diseases might be the first phase of a process leading to disability (121). The results from study II support this finding, that cardiovascular risk factors, such as heart disease and smoking, were associated with a long-term risk for falls, but not in the short-term. These factors might not directly affect the fall risk in the short-term but they can lead to further decline in health and thus directly increase the risk of a fall, for example impaired physical function. Previous research has shown that cardiovascular risk factors (for example smoking) can increase the risk of physical impairment (122, 123). These results strengthen the conclusion made by two meta-analyses suggesting that generic primary prevention, for example physical activity, may prevent falls in a long-term perspective (124, 125).

The time aspect is one way of looking at levels of risk acute or long-term. Another, more common, way to look at levels of risk is to grade the risk into low and high, or even into low, medium, or high. This is apparent between the clusters in study I. For each cluster, the hazard to experience an injurious fall doubled, despite the clusters being determined according to clustering analysis without taking the injurious falls into the analysis. The individuals in clusters 3–5 might represent those who need to be targeted for fall prevention, while the individuals in cluster 2 could be targets for general health promotion strategies. In study III, we tried to identify these individuals in a quick and feasible way by developing the screening tool for first time falls. By changing the cutoffs and number of levels we can adapt the screening tool for different areas of use and subgroups. For example, in a primary care setting (where a screening test would lead to further assessment) one might want to use a cutoff with a quite high sensitivity, to be sure to find all at high risk. Another example would be a public health intervention where a higher specificity could be more ideal, to be sure to target those at highest risk, for the best return of money and time spent.

Last, with a three-level risk gradient one has the possibility to adapt the intervention according to the level of risk. Those at medium risk might receive less time-consuming oral information about how to decrease fall risk while those at high risk can be offered tailored multifactorial interventions.

5.3 Sex differences

Study II, III, IV

The incidence of falls among older adults seem to be more common among women. Although the ratio differs between studies and samples, most studies show a double risk for women to fall compared to men (17, 86, 87). In SNAC-K, 74% of the injurious falls occurred among women. This ratio remained stable even after excluding nursing home residence (as was done in study II–IV). The difference between previous results and ours might be that most other studies have used self-reported falls as an outcome. Thus it is possible that men in the SNAC-K study experienced more "non-injurious" falls than women, and therefore did not need health care and were not registered. Another reason might be the mean age difference between the men and women in SNAC-K, which is four years, already at baseline, and fall incidence is known to increase by age (8). Last, as shown in **Table 8**, it is more common for men to die during the follow-up period than women, among fallers and non-fallers. Although that probably does not differ substantially from other studies, the competing risk of mortality seems higher among men than among women.

In Study II, we found only small differences between women and men in a stratified univariate analysis for each risk factor, in general (see **Figure 5**). Exceptions were for example impaired cognition for women and pain for men. While pain has previously shown to be a more important risk factor for men than women (126), the finding that impaired cognition was only significant for women has not been shown before. One possibility could be biological differences in the body-mind connection. This finding needs further study, in order to understand the mechanisms behind it. Despite the minor differences between women and men in the univariate analysis, when analyzing all significant risk factors in one model and performing a backward selection, the risk profiles emerging were quite different between women and men. This finding confirms our hypothesis and finding from Study I that risk factors might be more relevant to study in terms of risk profiles, rather than in isolation. Potential reasons for differences we see between men and women are:

1) Biological differences. The aging process differs between men and women (127). These differences might influence different aspects of functions that are needed to avoid adverse outcomes, such as falls. As an example, Tian et al. recently showed that the speed of decline in muscle function is affected by specific cognitive domains in women but not in men (128).
2) Behavioral differences. The behavioral aspect can include both health-related behaviors but also behavior according to the surroundings. It is for example shown by Duckham et al. that women more often fall indoors while doing chores, whereas for men it is more common to fall outdoors (129). These differences might affect which factors are key for women and men.

We also have to consider the imbalance of both number of individuals and number of falls between men and women, our results might be biased by different levels of power for men and women in the statistical analysis.

When developing the screening tool in Study III we wanted to take the sex differences into account, yet create a feasible and user-friendly tool. The solution was to start with non-stratified analyses, to end up with risk factors that were important for both men and women. In the end, these factors received a value in the score based on their sex-specific importance. Indeed the results demonstrated that the value of some of the factors differed between the sexes.

Also consequences of falls have shown to differ between sexes, but the results are somewhat conflicting. Results from our fourth study agrees with the report from the WHO, that the rate of mortality after a fall is higher for men than for women (1). In terms of disability and physical function, previous results are inconsistent, with studies showing better physical function for men (130), and also a better recovery for women (131). The results from our study IV are consistent with those from Beaupre et al. (132) showing that there is no significant difference in the trajectory of function after an injurious fall for men and women. The incoherent results can be due to differences in study design and follow-up time. In addition, in our study, we controlled for a number of health-related factors that are known to differ between men and women (in terms of incidence and progression in old age), for example cognition and multimorbidity (133, 134). In the basic model (only controlling for age and education) there was a significant difference between men and women, showing that women had a steeper increase in number of disabilities than men. After adding the covariates one by one in the model, mainly physical activity level and self-rated health turned the difference between men and women to non-significant. The possible mediating effect of these factors needs further investigation.

Our results strengthen the few previous studies about sex differences in risk factors for falls. More studies are needed to disentangle the mechanisms and importance of these differences, nevertheless, these differences need to be considered in primary and secondary prevention of fall injuries.

5.4 Predicting a fall

Study I, III

The PAR analysis in study I showed that about 50% of the injurious falls were a consequence of the risk factors present in clusters 2–5. Considering that the risk of falls may also depend on environmental and unpredictable factors, this proportion is encouraging and suggests that tailored person-centered interventions could be effective to prevent falls. To be able to target the right individuals for these interventions there is a need for tools that can find those at elevated risk.

When reviewing the literature for screening tools for primary care or public health use it became obvious that all multi-item tools included questions or information about previous falls (62, 72, 75–77, 79–81). Previous literature has clearly shown that previous falls are one of the most important, if not the most important, risk factor for falls. This makes existing fall risk tools rather screening tools for recurrent falls than falls in general. While secondary prevention for fallers is essential, we believe that detecting older individuals at a higher risk for falling *before* they start falling can make the biggest difference in terms of effectiveness of interventions. We also believe this would decrease the number of injurious falls, lower the big costs for the health care systems, and most important, lead to less suffering for the individual. In addition, there is also an ethical aspect – shall we wait to intervene until something already has happened if we have the possibility to do something to prevent it from happening?

In study III we developed a screening tool for primary care or public health interventions. The aim was to make it unspecific for patient groups or diseases and sensitive enough for seemingly healthy community-dwelling older individuals. While starting with a variety of established risk factors and narrowing it down to only four items, we essentially did not lose that much predictive value. We hypothesize that the few final items are able to serve as proxies for many other risk factors that are absent in the tool. Examples of this could be IADL dependency that could embody elements of specific diseases, social network, and cognitive status (135, 136). Despite excluding previous fallers in the study sample we reached a quite high predictive value for our tool, especially considering that we are using predictive analyses created for diagnostic tools, for a screening tool. Although, it is important to keep in mind that our predictive results are from the same sample that we developed the tool in, and we are therefore examining the external validity of it in other samples (ongoing).

5.5 Predicting trajectories of disability after a fall

Study IV

In study IV we examined sociodemographic- and health-related factors that can predict the trajectory of disabilities after a fall. To be able to compare the predictors' impact on fallers and non-fallers, side by side, we chose to create indicator variables. By this study design we did not expect to disentangle any causation but rather to compare the levels of disability for the different combinations, since disability is expected to increase over time on a population level.

Our results indicated that disability level did not differ that much between those living alone and those who were cohabitants, before the exposure period, but that it mattered after a fall. Those who were living alone developed more disabilities over time. This is in line with previous research (96), and could both reflect a physical aspect (to be forced to take care of everything at home by one self), but also a social aspect, including a lack of social support and maybe even loneliness (137). The results showed that physically inactive individuals had more disabilities before a possible fall and also that the increase in disabilities over time was much faster for inactive fallers than for both active fallers and inactive non-fallers. The important role of physical activity both as fall prevention but also after a fall, as well as for quality of life in aging in general, is already well established (124, 138, 139). Our results emphasize yet another health issue for older adults that can be improved and even prevented by general physical activity interventions (50). Self-rated health followed the same pattern as for physical inactivity, those with poor self-rated health who endured an injurious fall developing more disabilities over time. Noticeable, fallers with good health had as many disabilities as non-fallers with poor health. Since we were controlling for other health related factors that would affect an individual's view of their health (sex, age, education, cognitive status, multimorbidity, living alone, and physical activity level), it seems like subjective health might reflect something more than the objective health. This is in line with previous research conducted by Brenowitz et al. reporting that low self-rated health predicted a decline in physical function (140). According to Bailis et al, self-rated health is a comprehensive concept that measures not only a persons subjective health but also individual health goals (141). It seems like subjective health can predict adverse health outcomes beyond objective health measures, possibly by adding the dimension of an individuals health perceptions and expectations. As an example, Aylan et al. have shown that satisfaction with aging can be protective against falls (142).

There are two ways of looking at the results from study IV: 1) as a mean to target the vulnerable profiles that emerge, such as fallers living alone, being physically inactive and with a negative view on their health, which should be monitored extra after a fall because they are at higher risk to lose their independence after

the fall; or 2) for those who have people around them, are physically active, and consider their health as good seem to manage adverse acute events better than their peers. This is in line with previous research about physical resilience (143). In fact, studying trajectories after an injurious fall and comparing characteristics of different trajectories could be an opportunity to test the physical resilience concept.

5.6 Methodological considerations

All studies have methodological limitations. The text below describes a few of the most important issues in epidemiological cohort studies in general, in SNAC-K particularly, and specifically in the studies included in this thesis:

5.6.1 Internal validity:

Random error. Random errors occur in all studies and are by definition unknown and unpredictable, in other words, error "by chance". Random error can appear both in the sampling and in the measuring. A way to minimize the effect of random error is by using large sample sizes, to increase power and narrow confidence intervals of the measured effect. SNAC-K is a large cohort study with 3363 individuals measured at baseline, although depending on exclusion criteria and rare outcomes, the sample size should be big enough to dilute possible effects from random error.

Systematic error. In this thesis we have chosen to study only objectively measured falls leading to any type of health care visit. The strengths of this approach are several. We do not have to rely on the participants subjective perception of what a fall is, which has been shown to differ quite a lot between individuals and subgroups (1). Another issue related to this is that people tend to forget, this is of course especially common among older adults (144). By using objective measures we avoid **recall bias** that is commonly present in studies about self-reported falls.

Like in all population-based studies, despite being randomly sampled, SNAC-K risks to end up with a healthier, younger, and more educated sample than the population it is sampled from. To avoid some of this attrition, the SNAC-K data collection staff offer home visits if a participant has difficulties getting to the testing center. Thus, the participation rate is very high (73.3% at baseline). Nevertheless, the **selection bias** remains and needs to be noticed whenever data are presented. There is also a potential selection bias for the outcome of injurious falls. Since we only know about the falls that are severe enough to require medical attention, one could hypothesize that different subgroups tend to seek health care for less severe injuries, while others do not. To deal with this, in this thesis, we have chosen to exclude those living in nursing homes (because

we know they have different health care seeking patterns, e.g. minor injuries can be taken care of at the facilities), and we have also conducted sensitivity analyses including only severe injuries. Another way of looking at the selection of injurious falls, compared to all falls, is that we target those who will have the worst consequences of the fall, and therefore are most important to prevent.

In Studies I–III, the attrition due to dropout is not an issue since the outcome data is received from health care registers, thus it does not depend on the participant to come back for the follow-up measurements. In Study IV, this was a bigger issue, and to clarify this we chose to show the attrition due to death and dropout in an appendix table. The possible selection bias that could arise from exclusion criteria have been tested using multivariate imputation by chained equations (MICE) (119), the results have been similar to the original analysis . This indicates that there were no significant effects of selection bias.

A **misclassification** might appear if a test or a question does not test or answer what it was intended to. If this **information bias** is equal for all individuals, or randomly spread, the bias is non-differential. If the information bias is more common among a specific subgroup, the bias is differential. If a differential information bias is related to the studied outcome, it might affect the associations. Examples to avoid this issue in SNAC-K are: 1) the use of validated questionnaires and tests whenever possible (for example the MMSE and the MADRS score (111, 112)); 2) several attempts on tests, such as balance tests and blood pressure, to get a "best of" or a mean value; and 3) training and regular meetings about data collection for the SNAC-K staff. Also, the turnover among the data collection staff is very low, the long experience among the staff helps to minimize the information bias.

The use of categorical variables and cutoffs can introduce misclassification, if the cutoff is not suitable for the population studied. In this thesis, we have tried to avoid this by carefully choosing scales and cutoffs that have been tested for similar populations, examples of this is a high cutoff for impaired cognition on the MMSE for highly educated individuals and well-studied cutoffs for an older population on the physical tests (111, 115).

A **confounder** is a factor that effects both the dependent and the independent variable, and thus can alter the association between them. This could either show a false association or hide a true one. In the studies in this thesis, we have controlled for likely and possible confounders. The confounders are chosen based on prior knowledge from the literature. Nevertheless, it is impossible to control for all possible confounders, resulting in **residual confounding**. Likely residual confounding in this thesis are the environmental factors that are associated to an injurious fall, for example slippery floors. Due to the study design of

SNAC-K, or any other quantitative cohort study, it is not possible to fully control for environmental and other circumstantial factors.

When making a **causal inference** we assume a time order in a chain of events, or that one thing is causing another thing to happen. In studies with a cross-sectional design, this assumption is difficult to test. The use of longitudinal data aims to control for **reversed causality**, so is also excluding individuals with the outcome at baseline. As an example, in Study III, we aimed to target first time fallers and therefore excluded previous fallers at baseline, making sure that we only had "incident fallers" in our analysis sample.

5.6.2 External validity:

Generalizability. SNAC-K consists of older individuals living on an island in the inner city of Stockholm. The quite wealthy, urban population is likely to differ from the general older population in Sweden, and even more so from a worldwide older population. This difference is mainly regarding education level but also a general socioeconomic level and healthy lifestyle. Because of this, the SNAC-K sample can be assumed to be healthier compared to other older population-based samples. When studying health outcomes this might not be a big issue, considering the effect size of adverse health outcomes would likely be attenuated in the SNAC-K sample compared to other samples. While studying incidence and prevalence, it might lead to underestimations of the magnitude of a health issue in the population. To test the generalizability of the screening tool developed in Study III, an external validation study is being conducted.

5.6.3 The concept of injurious falls

In the research of falls, there are two main focuses: falls in general and fractures. While falls are usually self-reported and defined as "unintentionally coming to the ground", the data on fractures are more often derived from health care registers. An important difference is that the research area on fractures is often conducted within the field of osteoporosis while the "general fall" is a broader geriatric concept. Fewer studies are looking into injurious falls. While we know that our registered injurious falls are not only fractures (see **Table 9**), one could hypothesize that the injurious falls end up somewhere in the middle of falls and fractures, shown in **Figure 9**. An injurious fall can be both a fracture but also a fall without a fracture, while never being a fracture without a fall. An issue with this mix-up of concepts can be that forming a research hypothesis based on previous research might prove difficult. The literature about injurious falls is rather scarce, at least in comparison to the magnitude of research about self-reported falls or fractures. Even if the risk factors for self-reported falls and fractures are quite similar, there is the osteoporosis aspect of fractures that have an impact

on the type of risk factors that might be important. In this thesis, reference literature consists of research about injurious falls when available, otherwise falls in general are referred to and occasionally fractures. There is a need for more research based on injurious fall data, to be able to investigate possible differences between the concepts.

Figure 9. Conceptual hypothesis on how existing literature about fractures, injurious falls, and general falls tangentially relate to each other.

Table 9. Type of injuries after a fall in the SNAC-K study.

Type of injury	All, n (%)	Women, n (%)	Men, n (%)
Superficial injury or wound	230 (27.3)	169 (27.0)	61 (28.4)
Fracture	438 (52.0)	338 (53.9)	100 (46.5)
Dislocation	29 (3.4)	23 (3.7)	6 (2.8)
Intracranial injury	67 (8.0)	42 (6.7)	25 (11.2)
Other severe injury (e.g. injury to nerve or tendon)	11 (1.3)	5 (0.8)	6 (2.8)
Unspecified	67 (8.0)	50 (8.0)	17 (7.9)
All (n)	842	627	215

6 RELEVANCE AND CLINICAL IMPLICATIONS

The three pillars of the WHO Falls Prevention Model (1) are:

1. **Building awareness of the importance of falls prevention**

   By focusing a whole research line on falls among older adults at the Aging Research Center at Karolinska Institutet in Stockholm, we wish and hope that we contribute to the increased awareness about the importance of fall prevention. The continuing work is also widening the focus towards clinical implementation, building on knowledge within both clinical prevention and rehabilitation and epidemiology. Our aim is to build a bridge between epidemiology of falls and clinical work with screening and intervention.

2. **Improving the identification and assessment of risk factors and determinants of falls**

   The major part of this thesis is focusing on identification of those at risk and making screening for fall risk quick and feasible, yet as accurate as possible (studies I–III). With our screening tool we hope to contribute to the "improvement of identification and assessment" of older individuals at risk of enduring an injurious fall.

3. **Identifying and implementing realistic and effective interventions**

   Several studies have shown that there are effective preventive methods (98–101, 145), but the third pillar depends on the other two pillars, in order for implementation to be possible.

7 CONCLUSIONS AND FUTURE DIRECTIONS

The results from our study suggest that it can be more appropriate to study **fall risk profiles**, rather than risk factors in isolation. This allows for a more comprehensive and truer picture of who is at risk of injurious falls, and to enable a more precise prediction of fall risk among older adults. In addition to that, we found that it is possible to detect fall risk among individuals up to ten years in advance, and that **risk factors may differ between shorter and longer follow-up** times.

We also found that risk factor profiles for falls differ between women and men. This indicates that **sex differences** need to be considered both when studying and working with the prevention of injurious falls, although further investigation is warranted.

Within the frames of this thesis, we developed a **screening test**, targeting community-dwelling first time fallers. The test is quick and easy to administer and showed high predictive values. In addition, it is the first screening test that does not rely on previous falls to detect individuals at risk and it is also the first tool to consider sex differences. Enabling **primary prevention** for those who are at risk but have not yet endured an injurious fall, alongside with secondary prevention for recurrent fallers, this screening test would presumably decrease the number of fall injuries in a more effective way.

Last, the results from this thesis show that sociodemographic and health related factors may help to **identify extra vulnerable fallers**, who might need extra rehabilitation and attention after an injurious fall, to **maintain independence**.

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10 APPENDIX

Dissertations from the Aging Research Center and Stockholm Gerontology Research Center, 1991–2019

1991

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

1992

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

1993

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

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

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

1994

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

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

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

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

Forsell Yvonne. Depression and dementia in the elderly.

1995

Mattiasson Anne-Cathrine. Autonomy in nursing home settings.

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

1996

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

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

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

1997

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

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

1998

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

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

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

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

1999

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

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

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

2000

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

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

2001

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

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

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

2002

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

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

2003

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

2004

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

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

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

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

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

2005

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

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

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

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

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

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

2006

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

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

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

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

2007

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

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

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

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

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

2008

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

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

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

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

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

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

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

2009

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

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

Paillard-Borg Stéphanie. Leisure activities at old age and their influence on dementia development.

Livner Åsa. Prospective and retrospective memory in normal and pathological aging.

Atti Anna-Rita. The effect of somatic disorders on brain aging and dementia: Findings from population-based studies.

2010

Fors Stefan. Blood on the tracks. Life-course perspectives on health inequalities in later life.

Keller Lina. Genetics in dementia. Impact in sequence variations for families and populations.

2011

Schön Pär. Gender matter. Differences and changes in disability and health among our oldest women and men.

Caracciolo Barbara. Cognitive impairment in the nondemented elderly: Occurrence, risk factors, progression.

Rieckmann Anna. Human aging, dopamine, and cognition. Molecular and functional imaging of executive functions and implicit learning.

2012

Haasum Ylva. Drug use in institutionalized and home-dwelling elderly persons.

Mangialasche Francesca. Exploring the role of vitamin E in Alzheimer's disease. An epidemiological and clinical perspective.

Lovén Johanna. Mechanism of women's own-gender bias and sex differences in memory for faces.

2013

Hooshmand Babak. The impact of homocysteine and B vitamins on Alzheimer's disease, cognitive performance and structural brain changes.

Rizzuto Debora. Living longer than expected: protective and risk factors related to human longevity.

2014

Sjölund Britt-Marie. Physical functioning in old age: Temporal trends and geographical variation in Sweden.

Wastesson Jonas. Unequal drug treatment: age and educational differences among older adults.

2015

Sköldunger Anders. Dementia and use of drugs: Economic modelling and population-based studies.

Craftman Åsa Gransjön. Medicine management in municipal home care; delegating, administrating and receiving.

Svärd Joakim. Emotional facial processing in younger and older adults.

Wang Rui. Cardiovascular risk factors, brain structure, and cognitive decline in old age.

Pantzar Alexandra. Cognitive performance in old-age depression.

2016

Kelfve Susanne. Gotta survey somebody: methodological challenges in population surveys of older people.

Heap Josephine. Living conditions in old age: Coexisting disadvantages across life domains.

Håkansson Krister. The role of socio-emotional factors for cognitive health in later life.

Shakersain Behnaz. Impact of nutritional status and diet on cognitive decline and survival.

Bellander Martin. Plasticity of memory functioning: genetic predictors and brain changes.

2017

Ferencz Beata. Genetic and lifestyle influences on memory, brain structure, and dementia.

Köhncke Ylva. Lifestyle, cognitive aging, and brain correlates.

Santoni Giola. How well are we aging? Capturing the complexity of health trajectories of older adults.

Becker Nina. Inter-individual differences in associative memory: Structural and functional brain correlates and genetic modulators.

2018

Nilsen Charlotta. Do psychosocial working conditions contribute to healthy and active aging? Studies of mortality, late-life health, and leisure.

Darin-Mattsson Alexander. Set for life? Socioeconomic conditions, occupational complexity, and later life health.

Marseglia Anna. The Impact of diabetes on cognitive aging and dementia.

Heiland Emerald. Cardiovascular risk factor profiles in the development and progression of physical limitation in old age: A population-based study.

Sjöberg Linnea. Using a life-course approach to better understand depression in older age.

Samrani George. Interference control in working memory: neurobehavioral properties and age differences.

2019

Seblova Dominika. Causal effects of education on cognition – How do we generate evidence.

Berggren Rasmus. Cognitive development and educational attainment across the life span.

Vetrano Davide Liborio. Impact of cardiovascular and neuropsychiatric multimorbidity on older adults' health.

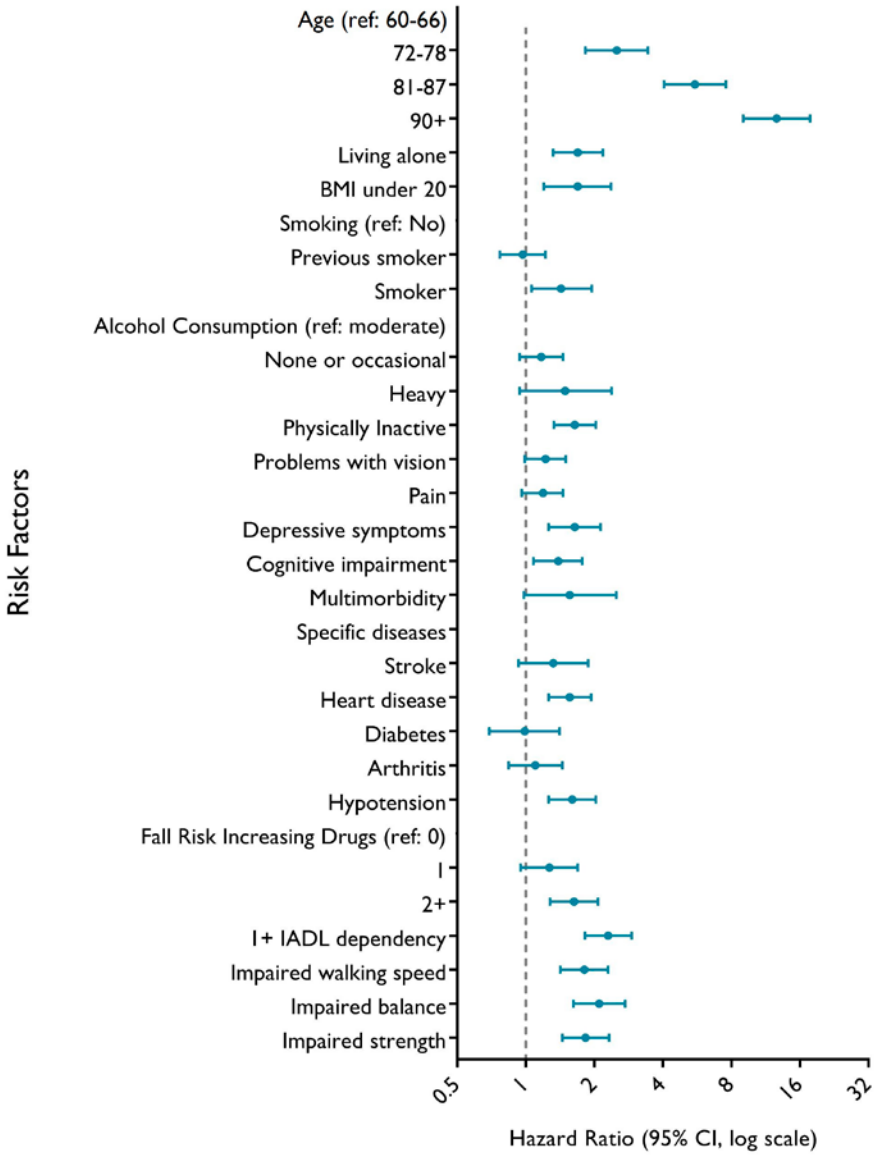
Rehnberg Johan. Inequalities in life and death: income and mortality in an aging population.

Pan Kuan-Yu. Impact of psychosocial working conditions on health in older age.

Avelar Pereira Bárbara. Multimodal imaging: Functional, structural, and molecular brain correlates of cognitive aging

Lucas Morin. Too much, too late? Drug prescribing for older people near the end of life.

Lieke de Boer. Dopamine, decision-making, and aging: Neural and behavioral correlates.



Appendix Figure 1. Hazard ratio and 95% confidence intervals (CIs) of individual risk factors for injurious falls up to 5 years after baseline. Controlled for sex, age and education.

Appendix Table 1. Hazard Ratios for all values in the scores for women and men.

Women Score			Men Score		
Value	**Hazard Ratio (CI 95%)**	**p-value**	**Value**	**Hazard Ratio (CI 95%)**	**p-value**
1	2.23 (1.16–4.32)	0.017	1	1.43 (0.53–3.85)	0.48
2	3.29 (1.70–6.36)	<0.001	2	1.56 (0.58–4.18)	0.38
3	5.06 (2.60–9.86)	<0.001	3	5.06 (2.26–11.36)	<0.001
4	9.19 (4.76–17.76)	<0.001	4	7.36 (3.15–17.24)	<0.001
5	8.74 (4.17–18.31)	<0.001	5	12.07 (5.15–28.27)	<0.001
6	17.18 (9.08–32.51)	<0.001	6	27.31 (11.43–65.25)	<0.001
7	18.24 (5.88–56.58)	<0.001	7	52.49 (17.22–160.03)	<0.001
8	28.19 (14.83–53.56)	<0.001			

Appendix Table 2. Sensitivity, specificity and percentage of correctly classified first injurious falls up to five years after baseline for each value of the score, in women and men.

Women Score	Sensitivity	Specificity	Correctly classified
0	100.0%	0.0%	15.7%
1	95.3%	22.5%	34.0%
2	81.8%	51.0%	55.8%
3	68.8%	69.7%	69.5%
4	56.5%	81.0%	77.1%
5	43.1%	87.9%	80.8%
6	36.4%	91.5%	82.8%
7	18.6%	96.1%	83.9%
8	17.0%	96.6%	84.1%
Men Score	**Sensitivity**	**Specificity**	**Correctly classified**
0	100.0%	0.0%	8.3%
1	89.2%	34.3%	38.9%
2	80.7%	53.4%	55.7%
3	72.3%	71.5%	71.5%
4	51.8%	85.0%	82.3%
5	36.1%	92.4%	87.7%
6	20.5%	97.2%	90.8%
7	6.0%	99.2%	91.5%

Karolinska Institutet

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