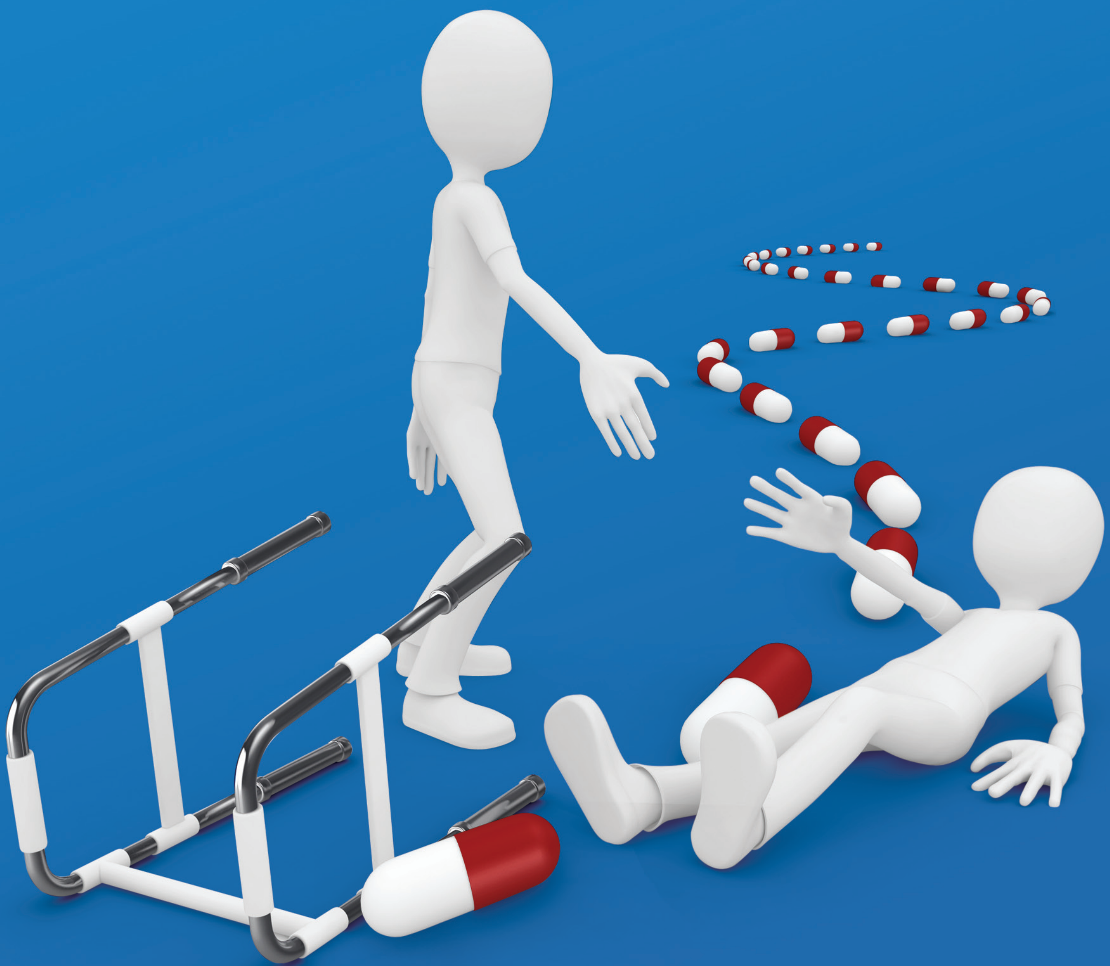
Falls and drugs in the older population

medical and societal consequences



K.A. Hartholt

Falls and Drugs in the Older Population: medical and societal consequences

Klaas Albert Hartholt

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dr. T.J.M. van der Cammen
dr. E.F. van Beeck

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Chapter 1

General introduction

Chapter 1.1

Falls in the older population: not that simple

Falls: current scope and trends

Fall incidents among the older population represent a major public health problem worldwide.[1-4] The majority of nonfatal injuries in adults aged 65 year and older who were treated in Emergency Departments in the United States in 2001 were caused by falls.[1] Approximately a third of all persons aged 65 years and older fall annually; a sixth of this age-group falls recurrently; for institutionalized persons this percentage is even higher.[4-9] The incidence of falls is age-related; the highest incidence of falls is seen in the oldest old. The Netherlands, a country with 16.5 million inhabitants, has 2.4 million persons aged 65 years and older.[10] Annually, an estimated total number of 800,000 falls occur in this age-group in The Netherlands. Falls often go without clinical attention for a variety of reasons: the patient does not mention the incident to a healthcare professional; there is no direct injury resulting from the trauma; the healthcare provider does not ask the patient about the history of falls; finally, either the healthcare professional or the patient erroneously believe that falls are the inevitable consequence of ageing. Furthermore, treatment of injuries resulting from a fall often does not include an assessment of the possible underlying cause(s) of the fall. However, almost 60% of patients with a positive falls history will have a subsequent fall.[6]

The majority of falls result in minor injuries, such as bruises and superficial injuries, which require no medical attention or are fully treated in the primary healthcare setting. In approximately a tenth of all falls medical treatment in an Emergency Department is required.[11] Most common injuries diagnosed at the Emergency Department after a fall are fractures, head injuries and bleedings.[12, 13] Falls do not only represent a serious public health problem due to the high healthcare demand and related healthcare costs,[14-19] but also have a major impact on the individual patient. Fall-related injuries require a long-term recovery and may lead to a reduced quality of life due to a reduction in the ability of self care and dependency on social care.[20] Older persons frequently report 'fear of falling' and a decreased functional activity after a fall,[21] both of which may result in social isolation. The outcome of falls has been described in several international papers for the United States and Scandinavian countries in mainly cross-sectional studies.[12, 14, 22-24] However, it is unclear whether the situation in The Netherlands is comparable with those of other western societies. This thesis highlights the fall-related healthcare demand in The Netherlands. Because hospital admissions in The Netherlands are recorded in a unique database with national coverage over an extensive period of time, the number of hospitalizations, the diagnoses and incidence rates can be determined, and changes in time trends can be detected. Furthermore, the availability of these data makes it possible to analyze secular trends on an injury specific level, such as falls and drugs, as well as mortality in older persons over a period of nearly 30 years. The results of these secular trend analyses are useful for clinicians and policymakers to determine changes over time, and adjust healthcare policies for the near future.

Falls: the role of multiple drug use and the potential of medication withdrawal

The issue of age-related problems, including falls, is expected to rise in the coming decades due to ageing societies worldwide,[25] as well as in The Netherlands. In 2008, 15% of the Dutch population was aged 65 years and over. Due to the “double ageing”, based on an increasing number of the oldest old and an increasing life expectancy,[26] the absolute number of elderly is rising rapidly. The absolute number of older persons will double to over 4.6 million in The Netherlands in 2050, representing a quarter of the total Dutch population at that time.[10] As a result of the demographic changes, the burden of age-related diseases and healthcare demand are expected to increase.[26, 27]

Ageing itself is associated with functional changes of the human body. Normal changes include among others; neurologic changes, reduced vision, reduction of muscle mass, and reduced mobility. The pattern of walking changes with ageing. Compared to younger persons, older adults have a slower gait, decreased stride length and arm swing, forward flexion at head and torso, increased flexion at shoulders and knees, and an increased lateral sway. Neurologic changes include and increased reaction time, slower gait and a decreased propriocepsis.

Age-related diseases are frequently treated with pharmacotherapy. The majority of all prescribed drugs are delivered to the age-group of 65 years and over,[28] which is closely related with the fact that age-related diseases develop with ageing. Changes in pharmacokinetics and pharmacodynamics make older persons more prone to adverse drug reactions.[29, 30] Because of these changes, an adverse drug reaction can occur without any recent changes in the drug regimen. In this thesis the number of hospitalizations in older adults due to an adverse drug reaction in The Netherlands has been studied to gain insight in severe adverse drug reactions over time. A lack of knowledge of drugs, such as the dosage or frequency of administration could contribute to improper drug use. Therefore, the drug knowledge of older adults has been studied.

Falls in the older population have been the topic of numerous studies over the last decades, and multiple risk factors have been identified. By now, over twenty risk factors have been identified and often there are multiple causes for falls in a given patient.[2, 4, 11, 20, 31] Risk factors can be divided in intrinsic and extrinsic factors. Risk factors for falls vary from direct causal ones, such as impaired mobility, to indirect ones, such as age. Intrinsic factors include medical conditions, impaired vision, and hearing. Extrinsic factors include *e.g.* medications, improper use of assistive devices and, the environment.

Recently several reviews have provided evidence that there is an increased fall-risk due to the use of drugs and falls in older persons.[32, 33] Especially the use of sedatives and hypnotics, antidepressants, and benzodiazepines has been shown to be significantly associated with falls in elderly individuals.[34-36] Not only psychotropic drugs have been associated with an increased fall-risk, this association has also been demonstrated for cardiovascular drugs and for polypharmacy (the use of three or more prescribed drugs).[35] Polypharmacy in itself, however, is not a risk factor unless it includes at least one fall-risk increasing drug.[37] In order to counteract for the expected increase in fall-related injuries and healthcare use, falls prevention is needed. Intrinsic risk factors for falls are nearly impossible to change, such as age and gender. Extrinsic risk factors are more suitable to adjust, and lower the fall risk in older adults. Several interventional studies have been conducted, including educational programs, interventions to improve strength or balance, optimize drug use, and modify environmental factors in homes or institutions.[38-40] Some interventions have targeted on a single risk factor, while others have attempted to address multiple factors in one study with different success rates.[41-48] Due to the multiple interventions design of those studies it is difficult to confirm which measurements or interventions are effective to prevent falls, and which are not. A promising intervention could be withdrawal of fall-risk increasing drugs.[34, 36, 40] In a prospective cohort study of geriatric outpatients, withdrawal of fall-risk-increasing-drugs reduced falls incidence by 50% in a 3 month follow-up period.[38, 40, 47] A review by Iyer *et al.* on the safety of drug-withdrawal in older patients showed that withdrawal of cardiovascular and psychotropic medications can be done safely in the majority, and that psychotropic drug withdrawal was associated with a reduction in falls and improved cognition.[34] In short, there is evidence that specific fall risk increasing drugs can be reduced without side effects and that this intervention lowers the risk for a future fall. However, this conclusion is based on observational studies only, which is not the highest level in medical evidence. To answer this question, a randomized controlled trial should confirm whether withdrawal of fall-risk increasing drugs contributes significantly to a reduction in fall risk of older fallers and if this intervention can be done safely. Therefore, a study protocol for a randomized controlled trial of medication withdrawal and fall-risk will be presented in this thesis in order to determine the effectiveness of this intervention.

In this thesis

The aim of this thesis is to gain knowledge concerning the magnitude of falls in the older population in The Netherlands. The main focus will be on the healthcare burden due to falls in older adults. In **Chapter 2**, the healthcare demand due to falls in The Netherlands is quantified. Fall-related health care demand includes the number of hospitalizations, Emergency Department visits, as well as the type of injury and related health care costs. That the findings are comparable with other countries will be presented by a combined study of fall-related hospitalizations in the United States. Falls are one of the main causes of hip fractures, head injuries, and vertebral body fractures in the older population. Trend analyses for these specific injury groups are presented in **Chapter 3** from the early 1980s until now, and reveal the healthcare usage as well as the duration of hospital admission. The most severe outcome of a fall incident is mortality. Therefore, fall-related mortality rates have been quantified in **Chapter 4** in the older population. Due to one of the oldest and best official mortality statistics in the world, it was possible to retrieve data from 1969 onwards on a nationwide level. In order to manage for the large and increasing burden of fall-related injuries effective falls prevention studies are needed. A protocol for a single intervention study on medication withdrawal and fall risk will be discussed in

Chapter 5, as well as drug knowledge and hospitalizations by older patients due to Adverse Drug Reactions in The Netherlands. In **Chapter 6** there is a reflection of the findings in this study, and a speculation on the impact of the results as presented in this thesis.

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Chapter 2

The societal consequences of falls

Chapter 2.1

The societal consequences of falls in the older population: injuries, healthcare costs and long term reduced quality of life

K.A. Hartholt, E.F. van Beeck, S. Polinder, N. van der Velde, E.M.M. van Lieshout, M.J.M. Panneman, T.J.M. van der Cammen, P. Patka

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Abstract

Background
Fall incidents are a major cause of morbidity and mortality in older adults. The aim of this cohort study was to determine the incidence, costs, and quality of life for fall-related injuries in the older Dutch population presenting at the emergency department.

Methods
Data on fall-related injuries in persons 65 years or older were retrieved from the Dutch Injury Surveillance System, which records injuries treated at the emergency department, and a patient follow-up survey conducted between 2003 and 2007. Injury incidence, discharge rates, healthcare costs, and quality of life measures were calculated.

Results
Fall-related injuries were to the upper or lower limb in 70% of cases and consisted mainly of fractures (60%), superficial injuries (21%), and open wounds (8%). Falls led to a total healthcare cost of €474.4 million, which represents 21% of total healthcare expenses due to injuries. Both admitted and nonadmitted patients reported a reduced quality of life up to 9 months after the injury.

Conclusions
Fall-related injuries in older adults are age and gender related, leading to high healthcare consumption, costs, and long-term reduced quality of life. Further implementation of falls prevention strategies is needed to control the burden of fall-related injuries in the aging population.

Introduction

Fall incidents represent a major public health problem, because approximately one-third of all community-dwelling people aged 65 years or older fall once a year, and this goes up to 50% in persons aged 80 years or older.[1] Older persons are at an increased risk of serious injuries, even after a relatively minor trauma such as a fall, because of to the number and severity of comorbidities, including osteoporosis.[2] In 22 to 60% of cases, medical treatment is required after a fall incident.[1] Therefore, falls are the leading cause of emergency department (ED) visits and hospitalisations due to an injury in those aged 65 years and older and result in a high healthcare demand worldwide.[3] Fall-related injuries are also accompanied by short- and long-term functional impairment and consequent reduction of quality of life among the elderly.[4] With the predicted aging of societies[5] and increasing trends in fall-related injuries in older adults,[6, 7] falls are expected to increase to one of the major public health problems for communities worldwide.[6, 8] Consequently, this will lead to expanding healthcare expenses.[9, 10] For prioritizing limited resources, for monitoring the impact of injury prevention strategies, and for optimal allocation of the restricted healthcare budget, the integrated measurement of fall-related morbidity and costs is essential.

Previous studies focused on injuries or costs alone.[9, 10] However, comprehensive studies on the societal impact of falls in older people focusing on both economic costs and quality of life are lacking. The aim of this study was to overview the societal consequences of falls among the older Dutch population in terms of injuries, healthcare costs and reduced quality of life.

Methods

Injury incidence and healthcare costs

In this study, we used the Dutch Burden of Injury model,[11] *i.e.*, a previously developed incidence-based model, to measure and describe healthcare use and costs resulting from injuries occurring during a specified period.[9, 12] Annual incidence rates of ED visits are extracted from the Dutch Injury Surveillance System (LIS). The LIS database is a continuous monitoring system in which injury diagnoses and injury mechanisms are registered by using the International Classification of Diseases of the World Health Organization (ICD 10th revision). LIS is based on 13 geographically distributed EDs in The Netherlands, resulting in a representative 12% sample of injury-related ED visits that can be extrapolated to national estimates. Per injury group, the number, healthcare consumption, and related costs are calculated based on the registered data in the LIS database, National Hospital Discharge Registry, and a patient survey. Healthcare consumption is split up in multiple categories, in which all healthcare consumptions are used; before, during, and after ED attendance. Costs and healthcare consumption are injury, gender, and age dependent. In this model, incidence rates, healthcare consumption, and costs can be selected for all injury mechanisms and age groups.

In this study, the model was applied to all unintended falls among persons aged 65 years or older between 2003 and 2007. An unintended fall was defined by using International Classification of Diseases, 10th revision, code for external causes of injuries (W00-W19).

Injury groups were based on a consensus of European expert groups (EUROCOST, APOLLO and INTEGRIS) and have been used in previous international publications.[3, 13] Based upon the 39 EUROCOST injury groups, an aggregation into 37 groups was used in this study.[13] Injuries by a fall were selected based upon the registered primary diagnosis. In case of multiple injuries, the primary injury in LIS was determined by application of an algorithm giving priority to spinal cord injury, skull/brain injury, and lower extremity injury above injuries in other body parts, and fractures above other types of injury to determine the most serious injury. Incidence rates were expressed per 1,000 person-years.

Direct medical costs were estimated using the Dutch Burden of Injury Model.[11] The age- and injury-specific costs are based on the estimated healthcare supplied to the individual injury patients. Healthcare costs of injuries were calculated by multiplication of incidence, healthcare volumes (*e.g.* length of stay in hospital or institution, number of outpatients visits, General Practitioner visits, home care hours, and physical therapy treatments), and unit costs (*e.g.* costs per day in hospital or institution, per visit, per hour, and per treatment). Healthcare volumes were estimated with national registration data and a patient follow-up survey. All unit costs were estimated according to national guidelines for healthcare costing.[14]

Reduced Quality of Life

A random sample of patients recorded in LIS (n=668 patients aged 65 years or older) had received an invitation to complete questionnaires on their quality of life at 2 months, 5 months, and 9 months after the fall incident.[15] Quality of life was measured with the EuroQuality of life-5D (EQ-5D). The EQ-5D classification system describes the respondents' health in three levels of severity on the health domains: "mobility", "self-care", "usual activities", "pain/discomfort", and "anxiety/depression". In our questionnaire "cognition" was added as a sixth dimension. In addition, a scoring algorithm based on empiric valuations from the Dutch general population and subsequent statistical modeling was used to express the separate five dimensions of the EQ-5D into a summary score.[16] This summary score is named the EQ-5D utility score. It ranges from 1 for full health to 0 for death, and can be interpreted as a judgment on the relative desirability of a health status compared with perfect health. The EQ-5D utility score of the patients was compared with the general population norm of older persons (age 65 years or older) at 2 months, 5 months, and 9 months after a fall-related injury.

Results

Between 2003 and 2007, a national annual estimated number of 67,300 Dutch persons aged 65 years or older (*i.e.*, 2.9% of the older population) visited the ED because of a fall incident, which resulted in 22,170 (32.9%) hospital admissions annually. Patients had a mean age of 78.8 years, and three-quarters of the patients were women (Table 1).

Table 1. Patient characteristics, annual numbers, and incidence rates of fall-related Emergency Department visits of older persons (aged 65 years or older) with admission characteristics and discharge locations (The Netherlands, 2003-2007)

Characteristic	Overall ≥65 yr	65-74 yr	75-84 yr	85-94 yr	≥95 yr
Population (x 1,000 persons)	2,273	1,247	787	224	18
Annual number of ED visits (η)	67,300	22,100	27,850	15,770	1,470
Incidence (per 1,000 persons)	29.1	17.7	35.4	70.4	105.0
Female gender (%)	76	71	76	81	86
Hospital admissions (η)	22,170	4,940	9,540	6,970	720
- Admitted (%)	32.9	22.4	34.2	44.0	44.6
- Median length of stay (d)†	10 (4-17)	7 (3-12)	10 (5-18)	11 (6-20)	11 (5-19)
Discharge after hospitalisation (%)					
- Home	68.5	83.1	68.3	59.5	60.2
- Transfer	19.0	10.6	19.8	23.8	18.1
- Long-term care	6.6	3.8	6.6	8.6	8.4
- Deceased	5.9	2.6	5.3	8.1	13.3

Transfer, transferred to another hospital; Long term care, nursing facility and rehabilitation facility; Deceased, died during hospital admission. †25th to 75th percentile; total numbers are different from the total count in the table because the counts have been rounded.

The overall incidence rate of fall-related ED attendance was 29.1 per 1,000 person-years in all patients aged 65 years or older. The incidence rate increased with age, from 17.7 for persons aged 65 to 74 years to 105.0 in persons aged 95 years or older. Admission rates and discharge destination were also age related. With a higher age, we found increasing proportions of patients who were admitted (22.4% in patients 65-74 years to 44.6% in patients aged ≥95 years), discharged to a long-term facility (3.8% in patients 65 years to 74 years to 8.4% in patients aged 95 years or older), or deceased during admission (2.6% in patients aged 65 years to 74 years to 13.3% in patients aged 95 years or older).

Four types of injury diagnosis groups represented 91.9% (61,790 injuries) of all fall-related injuries in older persons. Falls mainly caused fractures (59.6%), superficial injuries (20.9%), and head injuries (8.7% head wounds and skull-brain injuries). A more detailed analysis revealed that fractures of the hip (27.5%), wrist (19.8%), upper arm (7.2%), and clavicle (7.0%) represent the most frequently diagnosed fractures.

The five most frequently occurring injuries for men and women, specified by age group, are shown in Table 2. In both men and women, the majority of falls resulted in superficial injuries and hip fractures in all age groups. However, after a fall, men presented more often with open wounds and skull/brain injuries, whereas women presented more frequently with wrist and upper arm fractures. The proportion of hip fractures for fall-related injuries increased with age from 7% in persons aged 65 years to 74 years up to ~30% in patients aged 85 years or older. Approximately 40% of all hip fractures and upper arm fractures were due to slipping or stumbling. In only 3% to 6%, hip fractures or upper arm

Table 2. Top 5 injuries due to falls in older persons (aged 65 years or older) presented at the Emergency Department, specified for gender and age group (The Netherlands, 2003-2007)

	Description	%	Description	%	Description	%
Males	65-74 yr (η=5,970)		75-84 yr (η=6,120)		≥85 yr (η=3,019)	
	Superficial wounds	26.8	Superficial wounds	26.1	Hip fracture	28.5
	Wound head/face	9.0	Hip fracture	18.0	Superficial wounds	24.8
	Skull/brain injury	7.5	Wound head/face	8.5	Wound head/face	8.5
	Hip fracture	7.0	Skull/brain injury	7.2	Skull/brain injury	5.4
	Wrist fracture	5.9	Wrist fracture	4.9	Wrist fracture	4.0
Females	65-74 yr (η=15,650)		75-84 yr (η=21,280)		≥85 yr (η=14,060)	
	Superficial wounds	19.8	Superficial wounds	19.3	Hip fracture	25.5
	Wrist fracture	16.6	Hip fracture	16.4	Superficial wounds	21.3
	Hip fracture	7.0	Wrist fracture	15.0	Wrist fracture	9.2
	Ankle fracture	5.3	Upper arm fracture	5.2	Upper arm fracture	4.1
	Elbow fracture	5.0	Clavicle/Scapula fracture	4.7	Femur shaft fracture	4.0

fractures were caused by a fall from steps or stairs. However, skull/brain injuries were frequent (21%) due to a fall from a stairs or steps, fall from height (9%), and only in 15% due to slipping or stumbling.

Numbers and incidences of the 15 most common fall-related injuries are shown in Table 3. Serious injuries, such as hip and femur fractures, were accompanied with a high admission rate. Table 3 shows that fall-related injuries among older persons put a high demand on healthcare services and lead to considerable cost amounts. Fall-related injuries among older adults in The Netherlands led to an estimated total annual cost of €474.4 million (€98.2 million for men and €376.2 million for women). This is 20.8% of the national healthcare budget spent on injuries and poisoning for all ages. The 15 most frequently occurring fall-related injuries among older persons account for 90.1% of the costs, with a major share for hip fractures (42.3%) because of a high incidence rate combined with high costs per case. Other costly injuries are skull-brain injury (7.7%), femur shaft fractures (6.8%; also because of high costs per case), and superficial injuries (6.5%; because to high incidence rates). Healthcare costs increased with age. Persons aged 75 years and older accounted for half of all older persons with fall-related injuries, but were responsible for three-quarters (€355 million) of the total fall-related healthcare costs in those aged 65 years or older. The mean costs per case were €7,058. The most expensive injuries per case were femur shaft fractures (€19,000) and hip fractures (€18,223), which were both characterized by a very high proportion of admitted patients and long admission duration.

All fall-related injuries together had a substantial impact on the quality of life. Compared to norms of the general older population, both admitted and nonadmitted patients reported a reduced quality of life score, even at 9 months after the incident (a reduced utility score of 0.19 and 0.03, respectively). For all older fallers treated at the ED, the overall utility score was reduced by 0.09 at long term (Figure 1). Admitted patients overall reported more problems on the five dimensions of the EQ-5D, compared with the Dutch population norm of persons aged 65 years or older.

Although there is a slight improvement in the quality of life over time, problems at 9

Table 3. Annual numbers, incidence rates, admission characteristics optimization, and healthcare costs of fall-related injuries in older persons (aged 65 and older; The Netherlands, 2003-2007)

	ED visits		Admissions		Healthcare costs		
Diagnostic group	Number	Incidence†	Percent	LOS‡	Total (x 1,000)	Per case	Costs (%)
Superficial injury, incl. contusions	14,000	6.1	10.9	6 (2-11)	€31,064	€2,219	6.5
Hip fracture	11,000	4.6	94.6	12 (8-20)	€200,450	€18,223	42.3
Wrist fracture	7,900	3.4	6.1	2 (2-4)	€21,303	€2,697	4.5
Wound head/face	3,300	1.4	23.5	2 (1-4)	€13,448	€4,075	2.8
Upper arm fracture	2,900	1.3	17.4	6 (3-12)	€16,128	€5,561	3.4
Clavicle/scapula fracture	2,800	1.2	13.7	4 (2-9)	€14,924	€5,330	3.1
Skull/brain injury	2,550	1.1	64.5	3 (2-10)	€36,418	€14,281	7.7
Hand/fingers fracture	2,200	0.9	1.7	1 (1-2)	€4,991	€2,269	1.1
Elbow/forearm fracture	2,100	0.9	19.0	3 (2-7)	€9,890	€4,710	2.1
Ankle fracture	2,000	0.9	29.8	8 (4-15)	€11,110	€5,555	2.3
Open wounds	1,800	0.8	7.7	8 (3-17)	€3,128	€1,738	0.7
Femur shaft fracture	1,700	0.7	93.4	14 (9-23)	€32,300	€19,000	6.8
Pelvis fracture	1,500	0.6	56.1	11 (6-18)	€16,170	€10,780	3.4
Foot/toes fracture	1,500	0.6	4.4	5 (2-10)	€2,960	€1,973	0.6
Fracture knee/lower leg	1,400	0.6	47.7	12 (6-20)	€13,013	€9,295	2.7
Subtotal	58,650	25.3	33.9	10 (3-17)	€427,297	€7,180	90.1
Other	8,650	3.9	27.5	8 (4-16)	€47,064	€6,154	9.9
Total overall	67,300	29.1	32.9	10 (4-17)	€474,361	€7,048	100.0

†Incidence rate per 1,000 person years. ‡LOS: Length of hospital stay in days, median length of stay (25th -75th percentile). Injuries to internal organs, complex soft tissue injuries, eye injuries, and injuries to the spinal cord were rare and therefore not shown in the table.

months after the fall incident were still reported for "mobility" (70%), "self-care" (41%), "usual activities" (64%), and "anxiety/depression" (28%) in admitted patients. Nonadmitted patients reported problems at 9 months after the fall mainly on "self-care" (22%) and "usual activities" (41%).

Table 4 shows the prevalence of limitations at 9 months follow-up on the five health dimensions of EQ-5D and cognition for hip fractures, arm fractures, and skull-brain injuries. Compared to the general older population, all three injury types are accompanied by large increases in reported problems with self-care and usual activities. In addition, specific increases in functional problems by type of injury were found, such as long-term mobility problems occurring in 90% of the hip fracture cases.

Figure 1. Quality of Life up to 9 months after presentation at the Emergency Department in persons aged 65 years or older due to a fall incident in The Netherlands between 2003 and 2007

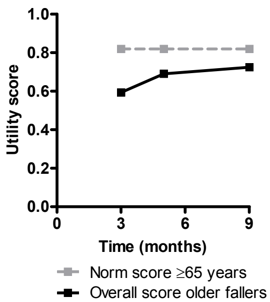

Table 4. Prevalence of functional problems on the five dimensions of the EQ-5D and cognition at 9 months after a fall-related injury in patients aged 65 year or older in The Netherlands

Injury-group	Mobility (%)	Self-care (%)	Usual activities (%)	Pain/Discomfort (%)	Anxiety/Depression (%)	Cognition (%)
Population norm	37.9	8.3	21.9	41.4	12.1	11.4
Hip fracture	90.0	54.4	73.3	69.1	26.9	37.7
Upper arm fracture	32.2	30.3	52.7	61.0	13.7	9.5
Skull/brain injury	44.8	21.7	31.0	40.8	24.8	32.2

Discussion

For this study a representative sample of ED visits between 2003 and 2007 was used to estimate national incidence rates, quality of life measures, and healthcare costs because of fall incidents among older adults in The Netherlands. Fall incidents led to high numbers of injuries and resulted in a major public health problem in older adults with large financial consequences. Injury patterns due to falls were gender and age related and resulted mainly in fractures, superficial injuries, and open wounds. A substantial loss in the quality of life was found after a fall-related injury in admitted and nonadmitted patients. Injuries resulting in a long-term reduction of the quality of life were accompanied by high healthcare costs (*e.g.*, hip fractures) and by large increases in problems with self-care and usual activities compared with the general older population.

Of the Dutch population aged 65 years or older, women compromise 60% of the population. Especially, women and the oldest old are at risk for fall-related injuries.[10, 17] This is not surprising because age, female gender, and medication use are well-known risk factors for fall incidents. Also, the type of injuries is changing with an increasing age to a higher severity level, because the oldest old presented with a higher incidence rate of hip and pelvic fractures.[18] There is most likely an association with fall techniques and comorbidity.[19] "Younger" adults are trying to reduce the impact of a fall in a moment of time by stretching their arms, which endures high pressure on impact. This mechanism leads to fractures of the upper extremity. As the oldest old fail to do so, because of less muscle mass, muscle strength, and reflexes reaction time, they cannot reduce the impact of their fall as younger adults can do. Also, underlying diseases as osteoporosis is more pronounced in females and the oldest old and could potentially explain the higher numbers of hip and wrist fractures in these groups compared with males and younger persons.[2, 20]

Fall-related injuries are leading to a reduced quality of life even at 9 months after a fall incident, suggesting that patients are still suffering from the consequences of their injuries. Problems with "self-care" and "usual activities" were most frequently reported in both patients with major and minor injuries. At population level, not only "major" but also "minor" injuries have a serious impact on the quality of life, because of the very high frequency of fall incidents leading to minor injuries. Apparently, there is room for treatment improvement for the full severity spectrum of older fallers presented at the ED. Observed differences in quality of life for admitted and nonadmitted patients can possible be explained by the severity of injuries. Admitted patients often required surgery and rehabilitation. The proportion of admitted patients increased with age, and besides the high proportion of hip fractures, also frailty could influence the risk of falling and severity of injuries. Older adults who sustained an injurious fall often complain of loss of independence, confidence, and functional activity, and of fear to fall again.[21, 22] Disabilities resulting from injuries are reflected in the increased number of older adults reporting problems of "self-care" and "usual activities". This could be the difference between independent living and the need for social care. Therefore, the social impact exceeds the medical and economical consequences of falls as described in our study. Further research is needed to determine the cause for the observed reduced quality of life in the fall-related injuries and to suggest injury-specific treatment adaptations to optimize the quality of life.

Reduced quality of life may lead to more healthcare consumption and related healthcare expenses. For example, patients with a hip fracture often require hospitalization, surgical treatment, and long-term rehabilitation. This explains the higher costs of injuries with an intensive treatment and a reduced quality of life compared with patients with minor injuries who are not admitted. Costs of falls in older adults have been analyzed in a small number of previous studies. It have estimated that falls lead to high healthcare costs in other countries,[3, 10] comparable to in The Netherlands. Because the population worldwide is ageing,[5] the population at risk for falls is increasing. To control for healthcare cost, prevention of falls and more healthcare efficiency are needed.

Although a representative sample of the Dutch population was used, numbers of fall-related injuries observed could be an underestimation of the real situation. A possible underestimation might have occurred because not all fall-related injuries were recognized as fall related in the discharge letters and coded accordingly. In addition, fall incidents resulting in direct death before reaching the hospital and patients with minor injuries who presented only to their General Practitioner were not recorded in this database and consequently not analyzed in this study. Therefore, this study represents the incidence rate, costs, and functional consequences of mild and serious fall-related injuries resulting in ED attendance. In case of multiple injuries, the primary injury in LIS was determined by application of an algorithm giving priority to spinal cord injury, skull/brain injury, lower extremity injury above injuries in other body parts, and to fractures above other types of injury to determine the most serious injury. Injuries to specific body parts (*e.g.*, internal injuries) or injuries noted at a tertiary survey (*e.g.*, spinal cord injuries) could be underestimated. In this study, functional problems were estimated with a generic quality of life measure and compared to norm scores of the general older population. For this aim, we used the EQ-5D, which is internationally recommended to assess quality of life in older fallers. However, a problem in making comparisons with general population norms is the potential difference in the "pre-injury health status" between this general population and a population of older fallers. On one hand, falling could be the result of a more active lifestyle reflecting a better than average pre-injury health status but on the other hand, it could be associated with frailty.

Valid data on pre-injury health status are difficult to obtain and were not available for our study. Therefore, we may have overestimated or underestimated the impact of fall-related injuries on quality of life. Only a few studies have measured a pre-injury health state so far in quality of life after injury studies, showing a better than average health status among injured populations in Australia[23] and the United Kingdom.[24] These studies support our conclusion of a reduced quality of life after fall-related injuries, because they indicate an underestimation of this effect in our study.

Multiple effective falls programs have been developed in the past years with promising results.[25] These programs should be further implemented and focused on the high-risk groups, such as in women and the oldest old. Also, the use of proven effective bone quality improving drugs can be used to reduce the number of serious injuries due to falls according to the guidelines for osteoporosis treatment. Furthermore, optimization of medical treatment and social support to maintain independence living in older adults should be further developed.

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Chapter 2.2

Costs of falls in an aging population: a nationwide study from The Netherlands (2007-2009)

K.A. Hartholt, S. Polinder, T.J.M. van der Cammen, M.J.M. Panneman, N. van der Velde, E.M.M. van Lieshout, P. Patka, E.F. van Beeck

Submitted

Abstract

Objective

Falls are a common mechanism of injury in the older population, putting an increasing demand on scarce healthcare resources. The objective of this study was to determine healthcare costs due to falls in the older population.

Methods

An incidence-based cost model was used to estimate the annual healthcare costs and costs per case spent on fall-related injuries in patients ≥65 years, The Netherlands (2007-2009). Costs were subdivided by age, gender, nature of injury, and type of resource use.

Findings

In the period 2007-2009, each year 3% of all persons aged ≥65 years visited the Emergency Department due to a fall incident. Related medical costs were estimated at €675.4 million annually (€281 per inhabitant in The Netherlands). Fractures led to 76% (€540 million) of the fall-related healthcare costs. The mean costs per fall were €9,370, and were higher for women (€9,990) than men (€7,510) and increased with age (from €3,900 at ages 65-69 year to €14,600 at ages ≥85 year). Persons ≥80 year accounted for 47% of all fall-related Emergency Department visits, and 66% of total costs. The costs of long-term care at home and in nursing homes showed the largest age-related increases and accounted together for 54% of the fall-related costs in older people.

Conclusion

Fall-related injuries are leading to a high healthcare consumption and related healthcare costs, which increases with age. Programs to prevent falls and fractures should be further implemented in order to reduce costs due to falls in the older population and to avoid that healthcare systems become overburdened.

Introduction

Falls and fall-related injuries are a major public health issue among older adults worldwide.[1-3] Approximately one third of people aged 65 years and older fall at least once each year, and one sixth fall recurrently.[4] Many factors have been associated with an increased risk of falls, such as medication, co-morbidity, decreased mobility, female gender, and age.[4-6]

Older persons are at an increased risk for serious injuries even after a minimal trauma, such as a fall, due to underlying medical conditions like osteoporosis. Approximately a third of older fallers sustain fall-related injuries, which require medical treatment.[7] Due to the large burden of injurious falls, fall incidents put a high[7-10] and increasing demand on healthcare resources.

Populations worldwide are aging.[11] The Netherlands, a country with 16.5 million people, is facing the challenge of an aging population as well. The population of persons aged ≥65 years is expected to increase from 15% (2.4 million persons) in 2008 to 25% (4.5 million persons) around 2040.[12] With an increasing population of older people, it might be expected that falls and the related healthcare consumption will grow accordingly. This could lead to an overburdening of the healthcare system due to scarcity of resources. In order to optimize healthcare policy and allocation in ageing populations, data on healthcare use and related costs are needed. The Netherlands is an ideal country to collect such data due to compulsory national health insurance and the availability of administrative databases with wide coverage.

The aim of this study was to determine healthcare use and costs due to falls in the older Dutch population. Costs were specified for gender, age, nature of injury, and type of resource use.

Methods

A previously developed incidence based model, the Dutch Burden of Injury Model, was used to describe healthcare consumption and costs resulting due to injuries occurring during a specified period.[13] In this model, patient numbers, healthcare consumption, and related costs are calculated, specified by location and nature of injury.[14] Healthcare consumption is split up in multiple categories, in which all types of healthcare resources (before, during, and after Emergency Department attendance) are taken into account. The model uses data from the Dutch Injury Surveillance System (LIS), the National Hospital Discharge Registry, and a patient follow-up survey conducted in 2007.[13, 15-17]

The LIS database is a continuous monitoring system at the Emergency Department in which injury diagnoses and injury mechanisms are registered by using the International Classification of Diseases of the World Health Organization (ICD 10th revision). An unintended fall was defined using the codes for external causes of injuries (ICD 10th revision W00-W19). The LIS database is based upon 13 geographically distributed Emergency Departments, and provides a representative 12% sample of injury-related Emergency Department treatments in The Netherlands. An extrapolation factor was calculated by the Consumer and Safety Institute, by comparing the adherence population of the participating hospitals with the total population in The Netherlands to generate national estimates. A full description of the model has been published by the Consumer and Safety Institute previously.[13]

Data on hospitalizations, in-hospital care and outpatient care were obtained from the National Hospital Discharge Registry, which has a nearly complete (≥95% coverage) national coverage. Healthcare costs of injuries were calculated by multiplication of incidence, healthcare volumes (*e.g.*, length of stay in hospital or institution, number of outpatients visits, General Practitioner visits, home care hours, and physical therapy treatments), and unit costs (*e.g.*, costs per day in hospital, per visit, hour, or per treatment). Healthcare volumes were estimated with national registration data and a patient-follow-up survey. All unit costs were estimated according to national guidelines for healthcare costing.[18] The proportions of patients who incurred emergency services and General Practitioner services preceding Emergency Department treatment were calculated with data from LIS. For each type of healthcare service the costs per volume unit that reflects the real resource was used (Table 1). For this study it has been assumed that healthcare fees were representative of real resource use for General Practitioner consultations, inpatient medical procedures, home care, and rehabilitative treatment.
Unit costs of emergency and ordered transport, inpatient hospital days (excluding medical procedures), out patient visits, nursing home days, other rehabilitation services, physical therapy, pharmaceuticals, aids, and appliances were calculated from national production and financial statistics. For Emergency Department visits the full cost price was calculated consisting of detailed measurement of investments in manpower by injury group.

Table 1. Unit Costs

Unit Costs	€
General Practitioner	
Visit	40
Consultation by telephone	20
Home visit	79
Ambulance	
Emergency journey	514
Scheduled journey	197
Hospital	
Admission (University Medical Center), per day	600
Admission, per day	439
Intensive Care Unit, per day	1,672
Day care, per day	620
Outpatient visit, per visit	170
Emergency Department visit	
Costs per visit	288
Long term care	
Admission in nursing home, per day	253
Day care, per day	133
Physical therapy, per visit	28
Home care	
Household assistance, per hour	29
Nursing care, per hour	65

The Dutch Burden of Injury Model was applied to all persons aged 65 years and over who presented to the Emergency Department of a participating LIS hospital due to an unintended fall between the January 1, 2007 and December 31, 2009. Fall-related injuries were selected based upon the registered primary diagnosis. Incidence rates were expressed per 1,000 person years. All costs are expressed in 2009 Euros (NB: as at 19 March 2009 €1.00 = US $1.31).

Results

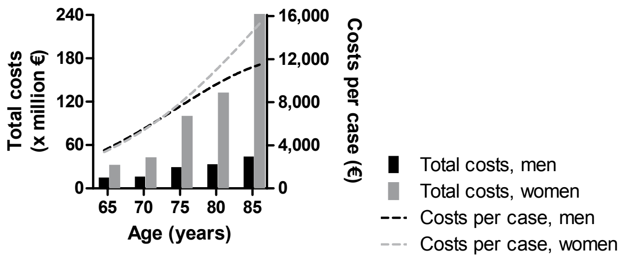
In the period 2007-2009, approximately 72,000 persons aged 65 years and over visited the Emergency Department annually with injuries due to an unintended fall. The costs of falls in The Netherlands were estimated to be €674.5 million per year (€281 per older person), of which 85% (€574 million) occurred in the population aged over 75 years. The overall incidence rate of Emergency Department visits in older persons due to a fall was 30.0 per 1,000 person years, for 17.4 men and 39.4 women, respectively. For persons aged 80 years and older the incidence was at least three times the rate of those aged 65-69 years (65-69 years 16.0; ≥85 years 72.5 per 1,000 person years (Table 2)). Approximately a sixth of the patients were treated and released after Emergency Department attendance. Half of all patients were referred to an outpatient clinic or their own General Practitioner, and a third of the patients were admitted to hospital after Emergency Department attendance.

Table 2. Annual number of registered, national estimated cases, incidence and costs of fall-related injuries in the older (≥65 years) Dutch population (2007-2009)

Age-group, year	Cases†	Estimated cases‡	Incidence§	Costs per case#	Total costs*
≥65	13,504	71,958	30.0	9,370	674.5
65-69	2,163	11,525	16.0	3,880	44.7
70-74	2,260	12,050	20.4	4,660	56.1
75-79	2,612	13,906	29.1	9,130	127.0
80-84	2,827	15,046	44.0	10,830	163.0
≥85	3,642	19,430	72.5	14,600	283.7
Gender					
Males	3,365	17,916	17.4	7,510	134.6
Females	10,139	54,042	39.4	9,990	539.9
Injury group					
Fracture	7,797	41,557	17.3	13,000	540.2
Concussion/Contusion	3,146	16,758	7.0	4,130	69.3
Laceration	1,196	6,358	2.6	3,020	19.2
Internal injury	38	201	0.1	9,450	1.9
Strain / Sprain	826	4,401	1.8	4,770	21.0
Other	409	2,192	0.9	7,800	17.1
Unknown	92	491	0.2	11,810	5.8

ED, Emergency Department; †Mean number of registered cases in the LIS database per study year; ‡National estimated cases; §Incidence rate per 1,000 person years; #costs per case are rounded at 10 Euro; *Healthcare expenses in million Euro's 2009

Figure 1. Total healthcare costs of injury and costs per patient by age and sex due to falls among the older population in The Netherlands (2007-2009)



Overall, the mean costs per fall were €9,370, and were higher for women (€9,990) than for men (€7,510) as shown in Table 2. Furthermore, the costs per fall increased with age (Figure 1). In women, the costs per fall increased from €3,830 in individuals aged 65-69 years old to over €13,000 per case in females aged 85 years and older. For men, the mean costs per case increased from €3,990 (65-69 year) to €11,470 (aged ≥85 years).

Injury groups representing the majority of fall-related healthcare costs are shown in Table 3. Hip and femoral fractures were most expensive (approximately €22,000 per case) followed by pelvic fractures (€14,000) and skull/brain injuries (€6,600). However, other injuries such as superficial injuries also resulted in high healthcare costs due to their frequent occurrence. Fractures accounted for 76% (€540 million) of the total fall-related expenses. Hip fractures made the largest contribution (€292 million) to fall-related healthcare costs, because of the high incidence rate combined with high costs per case.

Healthcare costs are skewly distributed, with admitted patients in hospital and nursing homes accounting for approximately two-third of costs in all age groups. Nursing home care accounted for 33.8% of total costs, followed by in-hospital treatment (31.6%) and long term care at home (20.2%). However, a shift in healthcare costs was seen for the different age-groups (Table 4). The costs of long term care at home and in nursing homes showed the largest age-related increases and together accounted for 54% of the fall-related costs in older people. Direct treatment costs, such as Emergency Department visits and ambulance journey costs were relatively higher in the younger age-groups, compared with the oldest old. In the oldest old, the costs of nursing home care were most substantial. For example, the average costs of fall-related injuries in admitted women aged 80 year and older were €21,000 per case, with €11,130 per case resulting from 43 days on average spent in a nursing home after injury.

Table 3. Fall-related annual incidence, costs per case and total costs by injury diagnosis for men and women (≥65 years), 2007-2009

	Men				Women			
	Number	Incidence†	Costs per case‡	Total costs+	Number	Incidence†	Costs per case‡	Total costs+
Superficial Injury	4,143	3.9	2,380	10.3	10,697	7.6	3,680	41.4
Hip fractures	2,607	2.4	19,730	60.1	8,565	6.1	23,280	232.1
Wrist fractures	827	0.8	2,670	2.4	7,292	5.2	4,170	32.9
Wound head/face	1,371	1.3	2,030	2.8	1,914	1.4	2,690	5.2
Upper arm fracture	470	0.4	5,320	3.0	2,665	1.9	7,130	22.5
Clavicle/Scapula fracture	683	0.6	4,880	3.7	2,257	1.6	6,930	17.4
Skull/brain injury	1,508	1.4	6,690	11.1	2,266	1.6	7,470	18.4
Fracture hand/fingers	590	0.6	2,220	1.4	1,778	1.3	3,170	5.8
Elbow/forearm fracture	283	0.3	4,230	1.4	1,857	1.3	6,040	12.8
Ankle fracture	480	0.4	5,440	3.1	1,777	1.3	9,080	19.5
Open wounds	649	0.6	1,720	1.1	1,251	0.9	3,030	3.9
Femur shaft fracture	406	0.4	21,250	9.8	1,316	0.9	23,730	36.0
Pelvic fracture	251	0.2	14,180	3.8	1,527	1.1	14,410	23.4
Knee/lower leg fracture	317	0.3	7,380	2.5	1,181	0.8	12,710	16.7
Subtotal	14,585	13.6		116.5	46,343	32.9		488.0
Other	3,330	3.1	5,090	18.1	7,697	5.5	6,330	52.1
Total	17,915	17.4	7,510	134.6	54,040	39.4	9,110	540.1

†Incidence rate is expressed per 1,000 person years; ‡Costs per case are rounded at 10 Euro; +Total costs in million Euro.

Table 4. Mean fall-related healthcare costs and care volumes by type of resource use in the Dutch population aged ≥65 years (2007-2009)

	Men						Women					
	Costs†	Care Volume	Costs†	Care Volume	Costs†	Care Volume	Costs†	Care Volume	Costs†	Care Volume	Costs†	Care Volume
Healthcare resource	≥65	≥65	65-79	65-79	≥80	≥80	≥65	≥65	65-79	65-79	≥80	≥80
Ambulance Journey, *r*	220	0.5	180	0.4	270	0.6	220	0.5	160	0.4	270	0.6
ED visit, *v*	280	1	270	1	290	1	290	1	280	1	300	1
Hospital inpatient, *d*§	5,280	10	4,690	9	5,9230	11	5,500	10	4,840	10	5,900	10
Outpatient attendance, *v*	270	1.6	290	2	240	1	300	2	330	2	280	2
GP consultations, *v*	100	2.3	90	2	110	3	110	3	100	2	120	3
Nursing care at home, *hr*	820	18	530	12	1,230	27	1,950	48	1,190	31	2,680	66
Nursing home, *d*§	6,870	27	5,150	20	8,770	34	9,410	34	6,570	25	11,130	43
Physiotherapy, *v*	200	7.3	200	7	210	8	300	11	290	10	310	11

§Mean cost and length of hospital and/or nursing home stay calculated for admitted patients only; *r*, ride; *v*, visit; *d*, days; *hr*, hours; †costs per case are rounded at 10 Euro

Discussion

During the study period, 3% of the Dutch population aged 65 years and older attended at the Emergency Department due to an unintended fall per year (2007-2009). The total healthcare expenses, including medical treatment, hospitalization and long term care, exceeded €674.5 million per year (€281 per older person). The mean costs per fall were €9,370, and were higher for females than males and increased with age. Fractures alone accounted for more than three quarters of all costs of falls. Persons aged ≥80 year accounted for about half of all fall-related Emergency Department visits, but two-thirds of all costs. More than half of the fall-related healthcare expenses were due to long term care at home and in nursing homes.

A major strength of the present study is that it presents comprehensive estimates of healthcare costs, including all relevant healthcare sectors for all fall-related injuries. Because a uniform coding method has been used to estimate the costs, it was possible to compare the healthcare use and related healthcare costs of all types of fall-related injuries. Registries with national coverage were used to analyze the healthcare resources that are most important for injuries, such as hospital inpatient care, medical procedures, rehabilitation clinics, and care in nursing homes and long-term care at home.[13]

A possible limitation is that only patients were included who presented at an Emergency Department. The total number of fall-related injuries will be higher, due to the fact that patients who were fully treated by their General Practitioner were not included in this study. Furthermore, in case of multiple injuries, the primary injury in LIS was determined by application of an algorithm giving priority to spinal cord injury, skull/brain injury, lower extremity injury above injuries in other body parts, and to fractures above other types of injury to determine the most serious injury. However, this may only have caused a slight underestimation of the total fall-related costs, since the majority of healthcare costs were related to in-hospital care, admission to nursing homes and long term care at home. For fall-related injuries such as permanent brain injury, spinal cord injury, and injuries involving joint damage this is relevant. However, the majority of injury related healthcare use and needs has been shown to occur in the first year post-injury.[19]

Falls in older adults contributed to a significant amount of injury-related healthcare expenses, which is seen in other western countries as well.[20] From an economic perspective falls are a more serious public health problem in older adults than other common diseases. For example, in another Dutch study the national budget spent on falls exceeded those of diabetes or heart failure for persons aged ≥65 years.[15] Studies from the United Kingdom[9], United States[10], and Australia[21] underline the economic impact of falls and related healthcare demand. The results of our study, €281 per older inhabitant, are within the range of previous findings from those countries. Costs of falls among older adults in the United Kingdom have been estimated at 1 billion GBP (12.1 million persons ≥60 year, €133 per older inhabitant) in 1999, in the United States at $19 billion (35 million persons ≥65 year, €372 per older inhabitant) in 2000, and in Western Australia Australian $18 million (200,000 persons ≥65 year, €256 per older inhabitant), respectively.[9, 10, 21]

The current study shows the breakdown of fall-related healthcare costs by age, gender, and type of healthcare resources. The high incidence rate of injurious falls combined with the high costs per fall resulted in an overrepresentation in the fall-related healthcare expenses of persons aged 80 and over, and women in this age group in particular. The higher healthcare costs in older women might potentially be explained by two mechanisms. First, the higher costs per fall-related injury could be due to differences in injury patterns between men and women.[1, 3, 22, 23] Females present more often with a hip fracture than males, and consequently a larger proportion of hip fractures in women contributes to higher average costs per fall.[1, 22] Furthermore, due to differences in life expectancy, many older women live alone after surviving their partner. As a consequence, they are often dependent on rehabilitation care in nursing homes and long term home care, even in cases of less severe injury.

Over the last decades the number of fall-related hospitalizations is increasing rapidly, based upon an increasing number of older adults, as well as an increasing life expectancy.[12, 24] Therefore, it might be expected that the number of falls, related injuries and related healthcare costs will largely increase in the future. The results of the current study show that fall-related healthcare costs result in a substantial part of total healthcare costs, which is not only based on costs of acute medical care, but also on long term healthcare costs. Implementation of programs to prevent falls and/or fractures are needed, not only in order to limit the number of falls and fractures, but also to reduce the required healthcare demand and related costs, and to improve the quality of life for the individual patient. Multiple strategies for prevention have been developed and several prevention programs have already been shown to be effective.[25] Implementation of some of those effective interventions has the potential to contribute to a reduction of fall-related healthcare consumption in the near future.

In conclusion, the success of aging of populations is accompanied by the presence of age-related consequences such as an increased fall- and fracture-risk, and the use of required healthcare resources. In order to control for the economic burden of fall-related healthcare costs the number of falls and related injuries should be reduced. Multiple prevention strategies have been developed over the last decades and time for implementation has arrived.

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Chapter 2.3

Trends in fall-related hospital admissions in older persons in The Netherlands

K.A. Hartholt, N. van der Velde, C.W.N. Looman, E.M.M. van Lieshout, M.J.M. Panneman, E.F. van Beeck, P. Patka, T.J.M. van der Cammen

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Abstract

Background
Fall-related injuries, hospitalizations, and mortality among older persons represent a major public health problem. Owing to aging societies worldwide, a major impact on fall-related health care demand can be expected. We determined time trends in numbers and incidence of fall-related hospital admissions and in admission duration in older adults.

Methods
Secular trend analysis of fall-related hospital admissions in the older Dutch population from 1981 through 2008, using the National Hospital Discharge Registry. All fall-related hospital admissions in persons 65 years or older were extracted from this database. Outcome measures were the numbers, and the age-specific and age-adjusted incidence rates (per 10,000 persons) of fall-related hospital admissions in each year of the study.

Results
From 1981 through 2008, fall-related hospital admissions increased by 137%. The annual age-adjusted incidence growth was 1.3% for men vs 0.7% for women ($P<.001$). The overall incidence rate increased from 87.7 to 141.2 per 10,000 persons (an increase of 61%). Age specific incidence increased in all age groups, in both men and women, especially in the oldest old (>75 years). Although the incidence of fall-related hospital admissions increased, the total number of fall-related hospital days was reduced by 20% owing to a reduction in admission duration.

Conclusions
In The Netherlands, numbers of fall-related hospital admissions among older persons increased drastically from 1981 through 2008. The increasing fall related health care demand has been compensated for by a reduced admission duration. These figures demonstrate the need for implementation of falls prevention programs to control for increases of fall-related health care consumption.

Introduction

Approximately one third of all people aged 65 years or older fall each year, and half of those fall repeatedly.[1, 2] Even a low-energy trauma, such as a fall incident, causes physical injuries. Around 10% of all fall incidents result in serious injuries and require a hospital admission. Fall-related hospital admissions in older patients are generally due to hip fractures (50%), fractures of the arm (13%), and head injuries (10%).[3, 4] Falls do not only lead to physical injuries, but may also have a large impact on the quality of life of the old[2, 3, 5-10] and on health care costs.[11-13]

The cause of a fall incident in the older age groups is often multifactorial. Risk factors associated with fall incidents include a higher age, female sex, the use of fall-risk-increasing medication, and certain co-morbidities. Many older patients visit their general practitioner or the emergency department after a fall.[7] Treatment is usually restricted to management of the direct fall-related injuries. Because the cause of the fall is often not investigated, the patient may remain at risk for future falls, which calls for the implementation of preventive services.[5]

In The Netherlands, the proportion of people aged 65 years and older is expected to increase to compromise up to 25% of the population in 2040 (the proportion was 15% in 2008).[14] These figures are comparable to worldwide trends,[15] and it can be expected that this will have an enormous impact on the fall-related health care consumption.
Therefore, we aimed to quantify time trends of fall-related hospitalization and in-hospital length of stay (LOS) in older patients over the past decades.

Methods

For this study, all accidental fall-related hospital admissions during the period 1981 through 2008 were collected. Throughout the study period, an accidental fall was defined using the International Classification of Diseases, Ninth Revision, codes E880 to E888 (Table 1), for external causes of injury. Older persons were defined as persons 65 years or older. The age-specific fall-related clinical incidence rates were calculated in 5-year age groups. Data were retrieved from the Statistics Netherlands,[16] which combines information of the National Medical Registration (Landelijke Medische registratie [hereinafter, LMR]) with the National Hospital Discharge Registry. The LMR collects hospital data of all hospitals in The Netherlands.

Table 1. International Classification of Diseases 9th Revision (ICD-9), codes for falls by external cause

ICD-9 code	Description
E880	Accidental fall on or from stairs or steps
E881	Accidental fall on or from ladders or scaffolding
E882	Accidental fall from or out of building or other structure
E883	Accidental fall into hole or other opening in surface
E884	Other accidental falls from one level to another
E885	Accidental fall on same level from slipping, tripping, or stumbling
E886	Accidental fall on same level from collision, pushing, or shoving by or with other person
E887	Fracture cause unspecified
E888	Other and unspecified fall

Data regarding hospital admissions, admission diagnosis, LOS in days, sex, age, causes of external injuries, main diagnosis (such as fractures), and mortality are stored in this database. Data on hospital admissions, mortality, and population numbers were verified with the Dutch Birth Registry. The LMR uses a uniform classification and coding system for all hospitals and has an almost complete national coverage (missing values are <5%).[17] These figures were extrapolated to full national coverage for each year. An extrapolation factor was estimated by comparing the adherence population of the participating hospitals with the total Dutch population in each year. Specific data on admission duration, fall mechanisms and main injuries were not fully available in the first years of the study owing to data aggregation in the past. The medical ethical review board of the Erasmus University Medical Center, Rotterdam, approved the study.

Numbers of fall-related hospital admissions, main injuries, and LOS were specified for age and sex in 1981, 1986, 1991, 1996, 2001, 2006, and 2008. The age-specific incidence was calculated using the number of the fall-related hospital admissions in that specific age group, divided by the number of total population within that specific age group for male and female patients, and was expressed per 10,000 persons in that age group. Overall growth in the number of hospital admissions was calculated for 2008 in percentages relative to the year 1981. The population numbers as of January 1 were used in each year of the study.

To model the trend in hospital admissions, a linear regression model with Poisson error and log link was built with log (population size as of January 1 of each year of the study) as the offset factor. A linear spline model, with age, year, sex and population size, was built to assess whether the annual growth changed over the study period for both sexes. The parameter for calendar year, corrected for sex and age group, was transformed into Percentage Annual Change (PAC). Our spline function accommodated 2 piecewise linear fits, connected with one another at the knot.[18] The knot was placed in the middle of the study period (January 1, 1995). The analysis including splines yielded estimates of annual changes in admission rates within each 14-year period (1981-1994 and 1995-2008). Comparison of these 2 periods enabled us to detect and quantify changes in the secular trend in admission rates such as a stagnation or an increase of admission rates. A likelihood ratio test was performed to assess the significance of the spline over a single trend for the study period. Interactions of the spline vs sex and age were added and tested to investigate differences in increase for sex and age. All statistical analyses were performed using SPSS software (version 16.1.1; SPSS Inc, Chicago, Illinois). *P*-value <.05 was considered statistically significant.

Results

In The Netherlands, the number of fall-related hospital admissions in older persons grew from 14,398 in 1981 to 34,091 in 2008 (a 137% increase). This reflects an annual growth of 778 fall-related hospital admissions during the study period. In particular, the number of persons 80 years or older showed a strong increase (from 6,535 in 1981 to 20,253 in 2008,

Table 2. Patient characteristics of hospital admissions due to falls, length of stay (LOS), main injury diagnosis, and external cause in older adults, 1981 through 2008, in The Netherlands

Characteristic	1981	1986	1991	1996	2001	2006	2008
Population (x 1,000 persons)	1,642	1,769	1,934	2,061	2,175	2,330	2,415
Population, sex (%) female	59.0	59.9	60.2	59.8	58.9	57.6	57.0
Hospital admissions, No.	14,398	18,872	21,879	26,281	25,490	30,368	34,091
Men, No.	3,440	4,415	4,974	6,134	6,059	7,705	8,830
Women, No.	10,958	14,457	16,905	20,147	19,431	22,663	25,261
LOS, mean (SD), *d*	33.8 (NA)	29.5 (NA)	26.3 (33.3)	21.1 (24.3)	20.5 (27.9)	12.9 (13.7)	11.1 (12.4)
Incidence, per 10,000 persons	87.7	106.7	113.1	127.5	117.2	130.3	141.2
Patient age, mean, *y*	NA	79.3	79.8	79.9	80.5	80.7	81.0
Main injuries: No. (%)							
Hip fractures	NA	9,059 (48.0)	11,200 (51.2)	13,110 (49.9)	13,478 (52.9)	13,884 (45.7)	14,258 (41.8)
Wrist fractures	NA	591 (3.1)	639 (2.9)	843 (3.2)	889 (3.5)	1,444 (4.8)	1,760 (5.2)
Upper arm fractures	NA	356 (1.9)	484 (2.2)	769 (2.9)	764 (3.0)	1,284 (4.2)	1,440 (4.2)
Skull brain injury	NA	840 (4.5)	888 (4.1)	1,131 (4.3)	1,056 (4.1)	2,081 (6.9)	2,798 (8.2)
Superficial injuries	NA	776 (4.1)	716 (3.3)	1,073 (4.1)	837 (3.3)	1,573 (5.2)	2,097 (6.2)
Accidental fall, external cause, No. (%)							
On or from stairs or steps	NA	5,151 (27.3)	5,630 (25.7)	5,923 (22.5)	5,608 (22.0)	7,285 (24.0)	7,651 (22.4)
On or from ladders or scaffolding	NA	267 (1.4)	277 (1.3)	383 (1.5)	481 (1.9)	702 (2.3)	664 (1.9)
From or out of building or other structure	NA	156 (0.8)	134 (0.6)	140 (0.5)	140 (0.6)	165 (0.5)	182 (0.5)
On or from chair or bed		3,670 (19.4)	4,180 (19.1)	4,569 (17.4)	4,020 (15.8)	4,844 (16.0)	5,233 (15.3)
On same level from slipping tripping or stumbling	NA	9,407 (49.8)	11,329 (51.8)	14,937 (56.8)	14,923 (58.5)	17,074 (56.2)	19,990 (58.6)
On same level from collision pushing or shoving by or with other person	NA	197 (1.0)	294 (1.3)	276 (1.0)	249 (1.0)	234 (0.8)	330 (1.0)
Other and unspecified	NA	23 (0.1)	35 (0.2)	54 (0.2)	68 (0.3)	64 (0.2)	41 (0.1)

Abbreviation: NA, not available; SD, Standard Deviation; *d*, day; *y*, year.

an increase of 210%). The mean age of the patients increased from 79.3 years in 1986 to 81.0 years in 2008, and three-quarters of the patients were female (Table 2). Fall incidents resulted mainly in hip, wrist and upper arm fractures as well as skull and brain injuries and superficial injuries (Table 2).

Numbers of the main injuries all increased, but the proportion of hip fractures slightly decreased (from 48.0% in 1986 to 41.8% in 2008). The incidence rate of hospital admissions due to a fall with a hip fracture in older Dutch adults increased from 51.2 per 10,000 older adults in 1986 to 63.6 in 1996, while in the period 1997 through 2008 the incidence rate of hospital admissions for hip fractures caused by a fall decreased to 59.0 per 10,000 older adults. The proportion of wrist and upper arm fractures together with superficial and head injuries increased from 13.6% (2,563) in 1986 to 23.8% (8,095) in 2008. Mechanisms of fall incidents hardly changed over time. Most fall incidents happened on the stairs, or near bed or chair; were due to slipping, tripping or stumbling; and remained stable at 96% throughout the study period.

The annual growth of fall-related hospital admissions for men and women differed ($P<.001$) and was 1.3% for men vs 0.7 % for women, respectively, throughout the study period, corrected for age and population at risk. The annual growth, however, was not constant during the whole period. The linear spline model revealed an annual growth of 1.62% (95% confidence interval [CI], 1.47%-1.78%) in men and 1.10% (95% CI, 1.01%-1.18%) in women in the period 1981 through 1994. The growth decreased to 1.07% (95% CI, 0.94%-1.20%) in men and 0.37% (95% CI, 0.30%-0.44%) in women in the period 1995 to 2008. The age-specific annual change is shown in Table 3 and was highest in men 80 years or older.

Table 3. Annual change in fall-related hospital admissions, corrected for population size in men and women in The Netherlands, 1981 through1994 and 1995 through 2008

	Change in men, % (95% CI)[a]		Change in women, % (95% CI)[a]	
Age group, y	**1981-1994**	**1995-2008**	**1981-1994**	**1995-2008**
65-70 years	0.49 (0.11-0.87)	1.19 (0.85-1.52)	0.02 (-0.24-0.27)[b]	0.31 (0.07-0.55)
70-75 years	0.75 (0.40-1.11)	1.04 (0.73-1.36)	1.08 (0.86-1.30)	-0.36 (-0.56- -0.16)
75-80 years	1.65 (1.32-1.99)	0.38 (0.10-0.66)	1.33 (1.14-1.52)	0.31 (0.14-0.48)
80-85 years	2.42 (2.07-2.77)	1.01 (0.73-1.28)	1.40 (1.22-1.58)	0.42 (0.27-0.57)
85-90 years	2.49 (2.08-2.90)	1.47 (1.14-1.79)	1.15 (0.95-1.34)	0.76 (0.60-0.92)
90-95 years	2.28 (1.69-2.88)	1.95 (1.47-2.44)	1.28 (0.99-1.57)	0.35 (0.13-0.57)
≥95 years	3.27 (2.09-4.47)	1.41 (0.43-2.40)	1.92 (1.31-2.53)	0.73 (0.30-1.16)
Overall	1.62 (1.47-1.78)	1.07 (0.94-1.20)	1.10 (1.01-1.18)	0.37 (0.30-0.44)

Abbreviations: CI 95%, 95% Confidence Interval.
[a] $P<.05$ for all, except where indicated.
[b] $P<.05$ was observed in all cases, except this one, for which $P=0.89$.

For all age-specific groups, the incidence of admissions in the female population exceeded the incidence in men. A 5- to 10-year shift was noticed in the age-specific incidence between men and women. For example, in 2008 the admission rate for men aged 85 to 90 years was 280.4 per 10,000 compared to 277.0 per 10,000 women aged 80 to 85 years. The incidence rate was consistently higher for women than for men (Table 4).

Sex- and age-specific incidence rates of fall-related hospital admissions increased in all age-groups, both for men and women (Table 4). The overall incidence rate increased from 87.7 in 1981 per 10,000 older adults to 141.2 per 10,000 in 2008 (an increase of 61%). Regarding the age-specific incidence in women, the largest absolute and relative increase was seen in patients aged 95 years or older (57.0%; 95% CI, 33.8%-84.3%). For men, the largest absolute and relative increase was also seen in patients aged 95 years or older (157.7%; 95% CI, 87.2%-254.6%).

Table 4. Incidence rate of fall-related hospital admissions per 10,000 persons in older adults in The Netherlands, 1981 through 2008 (continued)

	Age range, y							
	65-69		70-74		75-79		80-84	
Year	Men	Women	Men	Women	Men	Women	Men	Women
1981	27.9	49.5	34.4	73.8	57.4	117.0	92.0	198.0
1986	29.8	51.7	45.9	81.9	67.7	135.9	109.1	227.4
1991	28.3	51.5	41.6	84.7	70.1	145.3	126.5	228.5
1996	33.1	55.7	48.6	94.3	83.2	155.1	145.5	260.8
2001	29.2	46.6	42.3	79.4	74.1	143.1	130.1	238.3
2006	33.7	53.2	45.8	87.5	78.5	155.1	146.3	252.8
2008	34.7	60.9	53.9	89.0	82.5	157.0	154.0	277.0
Absolute change[a] (95% CI)	6.7 (3.7-10.2)	11.4 (7.6-15.6)	19.5 (14.8-24.7)	15.3 (10.2-20.6)	25.0 (18.2-32.5)	40.0 (32.3-48.0)	62.0 (48.9-76.3)	79.0 (66.4-92.3)
Percent change[a] (95% CI)	24.2 (13.1-36.4)	23.1 (15.2-31.4)	56.7 (42.9-71.9)	20.7 (13.9-27.9)	43.6 (31.7-56.6)	34.1 (27.6-41.0)	67.4 (53.1-82.9)	39.9 (33.5-46.6)

	Age range, y					
	85-89		90-94		≥95	
Year	Men	Women	Men	Women	Men	Women
1981	137.8	304.7	237.2	382.9	217.1	459.6
1986	182.1	360.2	275.4	465.4	330.7	492.3
1991	211.9	359.9	310.6	521.9	411.7	533.2
1996	230.6	392.2	334.2	536.1	408.2	576.5
2001	216.0	370.0	337.2	483.2	464.4	545.3
2006	263.4	406.9	392.9	537.2	560.0	605.4
2008	280.4	450.4	451.4	565.5	558.6	721.5
Absolute change[a] (95% CI)	142.6 (114.6-173.6)	145.7 (122.7-169.9)	213.9 (152.4-285.1)	182.6 (138.1-231.0)	342.3 (189.4-552.7)	261.8 (155.3-387.7)
Percent change[a] (95% CI)	103.4 (83.2-126.0)	47.8 (40.3-55.7)	90.2 (64.3-120.2)	47.7 (36.0-60.3)	157.7 (87.2-254.6)	57.0 (33.8-84.3)

Abbreviation: 95% CI, 95% Confidence Interval; [a]Change is 2008 compared with 1981.

The LOS for fall-related hospital admissions was age related and peaked in patients of 85 to 90 years old. However, the LOS of a fall-related hospital admission in older persons decreased over the past 25 years for all age-specific groups. Overall, the mean (SD) LOS was reduced from 26.3 (33.3) days in 1991 to 11.1 (12.4) days in 2008. The mean LOS in days is shown in Table 5.

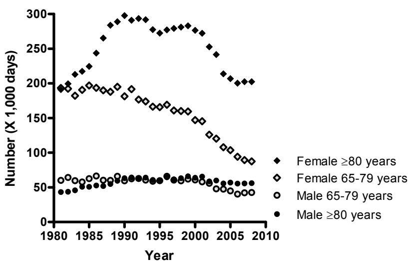
The change in LOS affected the total number of hospital bed-days. The total number of fall-related hospital bed-days decreased from 487,769 days in 1981 to 388,650 days in 2008. The overall number of hospital bed-days remained stable for male patients 65 years or older (approximately 103,000 days) between 1981 and 2008. For women between 65 and 80 years old, the number of hospital bed-days decreased gradually from 192,360 days in 1981 to 87,475 days in 2008 (a 54% reduction). In women 80 years or older, however, the number of hospital bed-days increased from 191,077 in 1981 to 297,825 in 1993 days and decreased to 202,343 days in 2008 (Figure 1).

Table 5. Mean hospital length of stay (LOS) due to falls in the older Dutch population, 1981 through 2008

	LOS, Mean (SEM), d						
Age range, y	**1981[a]**	**1986[a]**	**1991**	**1996**	**2001**	**2006**	**2008**
Men							
65-69	26.9	21.6	17.8 (0.6)	15.7 (0.7)	12.5 (0.8)	8.2 (0.3)	8.0 (0.3)
70-74	27.3	26.7	21.4 (1.0)	19.0 (0.7)	15.9 (0.7)	10.0 (0.3)	9.1 (0.3)
75-79	33.0	28.3	24.7 (0.9)	21.5 (0.7)	20.4 (0.8)	12.3 (0.3)	11.4 (0.3)
80-84	32.1	29.0	27.6 (1.1)	22.0 (0.6)	21.8 (0.8)	14.6 (0.4)	12.6 (0.3)
85-89	32.6	30.0	28.3 (1.4)	25.2 (1.0)	25.0 (1.1)	14.7 (0.4)	12.5 (0.3)
90-94	28.6	26.9	24.3 (1.3)	22.0 (1.2)	22.1 (1.2)	14.6 (0.5)	13.7 (0.5)
≥95	21.1	21.8	21.1 (2.2)	18.3 (1.6)	20.9 (3.4)	12.5 (1.0)	11.4 (0.9)
Women							
65-69	29.3	25.4	19.6 (0.5)	14.5 (0.3)	12.1 (0.4)	8.2 (0.2)	7.3 (0.2)
70-74	33.9	27.8	22.3 (0.5)	18.1 (0.4)	16.6 (0.5)	10.4 (0.2)	8.8 (0.2)
75-79	36.0	30.1	26.0 (0.5)	21.0 (0.4)	20.2 (0.5)	11.9 (0.2)	10.6 (0.2)
80-84	37.3	31.5	29.8 (0.6)	22.5 (0.3)	22.8 (0.4)	14.0 (0.2)	12.1 (0.2)
85-89	36.8	32.8	30.7 (0.7)	24.4 (0.4)	23.8 (0.5)	14.7 (0.2)	13.1 (0.2)
90-94	35.2	31.7	29.9 (1.0)	23.2 (0.6)	23.3 (0.6)	14.9 (0.3)	13.3 (0.3)
≥95	33.0	31.7	26.3 (1.5)	22.7 (1.1)	21.9 (1.2)	14.8 (0.6)	13.0 (0.4)

[a]The standard error of the mean was not available until 1991.

Figure 1. Total number of fall-related hospital admission days in the older Dutch population (1981-2008)



Discussion

To gain insight into the absolute numbers, incidences, and trends of fall-related hospital admissions in older patients, registration data of all persons 65 year or older in The Netherlands were studied between 1981 and 2008. Both the absolute numbers and the incidences of fall-related hospital admissions in older people had strongly increased over time. This increase was more pronounced in male patients than in female patients, although the total incidence rate remained consistently higher for female patients in all age groups. The main injuries at admission were hip, wrist, and upper arm fractures, and, together with superficial and skull or brain injuries, these accounted for two-thirds of all injuries. Because the LOS was reduced over time, the increased numbers of fall-related hospital admissions did not lead to an increased overall number of admission days until now.

A major strength of this study is the availability of population-based in-hospital data for an extensive period of 28 years (recording started in 1981). Since that year, absolute numbers of fall-related hospital admissions and hospital bed-days in all hospitals in The Netherlands have been recorded in a highly accurate electronic database with an almost complete national coverage. A possible limitation of this study is that the data describe a national situation for one country, which may not directly translate to other countries because demographics and health care system characteristics may differ. Nevertheless, because falls data in older populations in western societies are comparable with the data of The Netherlands,[19] we have no reason to assume that the prevalence of fall-related hospital admissions is different.[20] However, additional studies are required to confirm if these trends in fall-related injuries and hospital admissions are comparable with those in other populations. Furthermore, patients who were not admitted to the hospital were not registered in the National Hospital Discharge Registry databases and, consequently, were not included in this study. Therefore, this study mainly reflects trends regarding the incidence rates of serious fall-related injury and excludes isolated minor fall-related injuries. The actual societal impact of all fall-related injuries, both major and minor, is most likely to exceed the burden as described in this study.

A limitation of the use of this link administrative database is that it does not contain data regarding underlying diagnosis, comorbidities, treatments, injury severity, lifestyle, or medication use of the patients. This hampers the interpretation of causal mechanisms behind the observed trends. Readmissions in one calendar year were not excluded and could potentially lead to some “double registration”. However, readmissions most likely did not influence our results because readmissions constitute only 2.6% (at the maximum) in The Netherlands, as was found in a study by Polinder *et al*.[21]

Trends in hospital admission rates and LOS as observed in this study are important for two reasons: first, the population at risk is increasing worldwide,[15] and second, the age-specific incidence of fall-related hospital admissions is increasing. Multiple studies, focusing on fall-related injuries, such as hip fractures, proximal humeral fractures, and severe head injuries in elderly in individuals, have shown a comparable trend over time.[20, 22-26]

Throughout the study period, no major policy changes that might have affected the increase in admission rates were introduced. The Dutch health care system was, and continuous to be, characterized by full health insurance coverage and full accessibility for the whole population during the study period. As in other countries, clinical practice has changed during the study period (*e.g.*, introduction of geriatric medicine, improved anesthetical care and surgical techniques for older adults), but this probably only marginally affected the admission policies because of the low general admissions threshold in The Netherlands. However, rapidly increasing rates of admissions for wrist and upper arm fractures may be partly explained by improved surgical procedures and techniques in the oldest old and an associated drop in admission threshold.

Another potential cause for the observed increase in fall-related hospital admission rates might be "the aging society". Because life expectancy is increasing in The Netherlands[27] and older persons are living longer with multiple medical problems, the risk of falls and fall-related injuries can be expected to increase. Nevertheless, population health analyses in The Netherlands have shown that these patients are reporting fewer problems of mobility,[28, 29] which may be explained by improved medical care and the use of walking aids and other equipment (*i.e.*, electric mobility scooters). The consequence of sustained walking abilities among older persons with multiple morbidities is that these patients remain at risk for fall incidents. This trend of improved mobility in older adults is seen in other countries as well.[30, 31] Another cause for the observed increased incidence of fall-related injuries might be an increasingly active lifestyle (*i.e.*, cycling, jogging, walking). All these factors do have an influence on fall risk and outcomes and may (partly) explain the observed rise in incidence rate of fall-related hospital admissions. Besides a more active life style, other fall mechanisms, a lower surgical intervention threshold, and improved anesthetical care for older adults may have also contributed slightly to the changed distribution of main injuries.

The deceleration of growth in admission rates in the most recent period might partly be explained by a reduction in hip fracture rates, as observed in our study and other studies worldwide.[22, 32-34] The possibility of a birth cohort effect resulting in a healthier aging population with improved functional abilities and a reduced level of injurious falls has been suggested.[22] Our findings raise the question of which other factors could be associated with a more favorable trend in fall-related admission rates in recent years. We have no clear answers to this specific question.

The total number of hospital bed-days due to falls has decreased between from 1981 through 2008. This can be explained partly by the larger decline in trend in the number of hospital admissions in females compared to males, which has been shown previously in fall-related injury studies outside The Netherlands.[25, 32-34] An additional explanation for the phenomenon may be that during the last decade, multiple medications with proven positive effects on bone quality have become available, and clinical practice guidelines, focusing primarily on older women, have been introduced.[35, 36] Additional research is needed to determine the causes behind the observed differences between trends in men and women. In addition, lifestyle interventions and falls prevention programs have been implemented following the recent introduction of falls prevention guidelines.[37] This might be one of the reasons for the decline in age-specific incidence rates in fall-related hospital admissions in older women in the most recent period. However, the total burden is still increasing owing to an increased population of older women.

Despite the fact that the society is aging and comorbidities are increasing in number, the total number of hospital-bed-days decreased because the mean LOS decreased in all age groups. This reduction may, at least partly, be explained by improvement in surgical techniques (*e.g.*, minimally invasive procedures), the development of clinical guidelines (*e.g.*, hip fracture guidelines), and more efficient treatment strategies.[36-39] With respect to the LOS, in The Netherlands, specific and readily available rehabilitation facilities for older patients with hip fractures, supported by multidisciplinary teamwork, have been instituted in nursing homes. However, the oldest old seem to need more time in hospital, most probably owing to more comorbidities and reduced functional reserves.

In summary, our data highlight the importance of monitoring hospitalization trends over time across age groups and sex in order to visualize possible changes in health care needs and usage. Insight into fall-related hospital admission numbers can contribute to optimization of planning, resource allocation, and staff distribution in the future. Improved implementation of falls prevention programs in older populations and specialized in-hospital tracks for older fallers seems required to control for possible further increases in fall-related morbidity and health care consumption.

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Chapter 2.4

Increase of fall-related hospitalizations in the United States, 2001-2008

K.A. Hartholt, J.A. Stevens, S. Polinder, T.J.M. van der Cammen, P. Patka

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Abstract

Background
The objective was to determine secular trends in unintentional fall-related hospitalizations in people aged 65 and older in the United States.

Materials and Methods
Data were obtained from a nationally representative sample of emergency department visits from January 1, 2001 to December 31, 2008, available through the National Electronic Injury Surveillance System-All Injury Program (NEISS-AIP). These data were weighted to estimate the number, incidence rates and the annual percent change of fall-related hospitalizations.

Results
From 2001 to 2008, the estimated number of fall-related hospitalizations in older adults increased 50%, from 373,128 to 559,355 cases. During the same time period, the age-adjusted incidence rate, expressed per 100,000 population, increased from 1,046 to 1,368. Rates were higher in women compared to men throughout the study period. The age-adjusted incidence rate showed an average annual increase of 3.3% (95% CI: 1.66-4.95).

Discussion
Both the number and rate of fall-related hospitalizations in the United States increased significantly over the 8-year study period. Unless preventive action is taken, rising hospitalization rates in combination with the aging US population over the next decades will exacerbate the already stressed healthcare system, and may result in poorer health outcomes for older adults in the future. Further research is needed to determine the underlying causes for this rising trend.

Introduction

Older adults experience falls frequently; approximately one-third of people aged 65 years and older fall at least once a year.[1, 2] Falls are the leading cause of injuries in older adults in the United States and worldwide. Approximately 30% of falls require medical treatment,[3] often resulting in emergency department (ED) visits and subsequent hospitalizations, increasing the demand for healthcare services and raising associated healthcare costs.[4-6] Because the risk of falling increases with age[2], fall injuries would be expected to increase in the coming decades as the population ages.[7] We have investigated the impact of an aging society on the demand for fall-related healthcare in the United States by quantifying hospitalizations following ED visits for fall-related injuries in older adults from 2001 to 2008.

Materials and Methods

This study analyzed ED data from January 1, 2001 to December 31, 2008 that was obtained from the National Electronic Injury Surveillance System-All Injury Program (NEISS-AIP). NEISS-AIP is a collaborative effort by the National Center for Injury Prevention and Control and the Consumer Product Safety Commission and is an expansion of the NEISS. NEISS collects data from 100 hospitals that are a stratified probability sample of all US hospitals (including US territories) that have at least six beds and provide 24-hour emergency services.NEISS-AIP data are collected from about 60 of the 100 NEISS hospitals (the number varies from 60 to 66, depending on year). The program collects data on initial visits for all types of injuries treated in EDs. From this sample, the total number of injuries treated in hospital emergency rooms nationwide can be estimated. Information is abstracted from the medical record and includes data on gender, age, intent of injury (*i.e.*, unintentional, intentional, assault, self harm, and legal intervention), injury mechanism (in general the one most severe injury) and primary diagnosis. Mechanisms of injury were classified by trained coders into major external cause-of-injury groupings using definitions consistent with International Classification of Diseases of the World Health Organization, 9th Revision, Clinical Modifications (ICD-9-CM) external cause coding guidelines.

This study analyzed a sample of 53,009 fall-related injury cases among persons aged 65 years and older who were hospitalized after ED attendance. National estimates were obtained using sample weights assigned to NEISS-AIP cases. Each case initially was assigned a sample weight based on the inverse probability of selection into the NEISS-AIP sample. The inverse of the probability of selection was computed within each of five hospital stratum - four based on size (number of annual ED visits) of the NEISS sample hospital (very large, large, medium and small) and one stratum for children's hospitals. Initial sample weights were then adjusted for non-response and post-stratified to weight up to the total number of hospitals with EDs in the year of treatment. Sample weights were post stratified to adjust for changes in the number of US hospital EDs across time. These final sample weights were summed to produce national estimates of fall-related injuries for persons initially treated in a US hospital ED and then hospitalized. A full description of the survey design and weighting methodology has been published by Schroeder and Ault.

Age-specific incidence rates for 5-year age groups (65-69, 70-74,…, ≥85 year) were expressed per 100,000 population, for both men and women. An age-adjusted incidence rate for the overall population aged 65 year and older was calculated by direct standardization to the 2000 US Census Bureau population estimates, to control for changes in the age distribution among the age 65 and older population during the study period. The adjusted incidence rate allowed us to compare the overall incidence rate throughout the study period. The age-adjusted incidence rate was calculated by applying the observed age-class specific incidence rates, for each 5-year subgroup, for both men and women, to the standard population of 2000, and was expressed per 100,000 population. To model the trend in Percent Annual Change (PAC), logarithms of the hospitalization rates were analyzed using a weighted linear regression model with "1/variance (rate)" as the weight. A *p*-value of <0.05 was considered as statistically significant.

Results

The absolute number of fall-related hospitalizations in older adults increased 50% during the study period, from 373,128 in 2001 to 559,355 in 2008. The distribution of hospitalizations between the different age groups is shown in Figure 1. The majority of fall-related admissions occurred in females aged 75 years and over throughout the study period. Both age-specific and age-adjusted incidence rates (per 100,000 population) increased rapidly between 2001 and 2008 (Table 1). The incidence rates were age-related, and increased with age (Figure 2).

Figure 1. Number of fall-related hospitalizations in the older US population (≥65 year) for age group and gender, 2001-2008

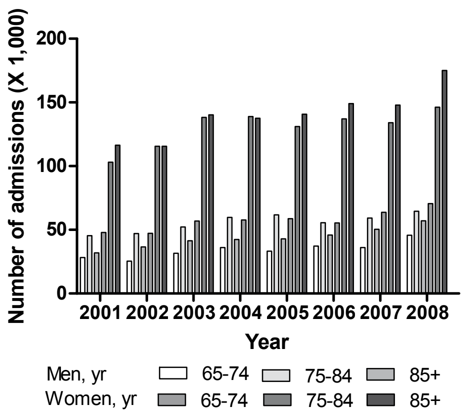
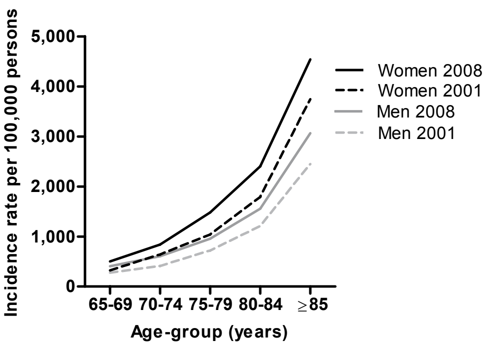


Figure 2. Age-specific incidence rates of fall-related hospitalizations in persons ≥65 years, United States, 2001 and 2008



Age-adjusted incidence rates in males increased from 803.7 (95% CI: 626.1-981.3) to 1,063.5 (95% CI: 847.1-1,280.0) and in females from 1,182.5 (95% CI: 885.3-1,479.8) to 1,558.8 (95% CI: 1,200.2-1,917.3). This reflects a PAC of 3.5% (95% CI: 2.15-4.89) in males and 3.3% (95% CI: 1.57-5.14) in females. For both males and females, the PAC was higher among the younger age groups (65-69 years) compared to the older age groups. The proportion of cases hospitalized after ED treatment increased slightly, from 23% in 2001 to 26% in 2008. In 2008, the most frequent primary diagnoses among persons hospitalized for fall-related injuries were fractures (63%) and contusions or abrasions (13%), followed by lacerations (5%), strain or sprain (2%), internal injury (12%) and other injuries (5%).

Discussion

Epidemiologic information about fall-related injuries is essential for allocating healthcare resources, determining healthcare expenses, and planning for future healthcare needs. This study shows a substantial increase of the number of hospitalized fall-related injuries of 50% over the last eight years. The age-adjusted incidence rates of fall-related hospitalizations in the United States rose 31%. These increases were seen in both men and women and cannot be explained solely by the growing number of older adults. Similar increasing trends for both fall-related injuries and injury rates have been observed in other western countries such as The Netherlands and Finland.[5, 8]

There are several possible explanations for the observed increase in fall-related hospitalizations. The life expectancy in the United States is increasing[7] and older age is an independent risk factor for falls.[2] Older adults are living longer with multiple health problems. This would result in an increasing number of frail elderly who are at a high risk for falls, and may explain the increase in age-specific hospitalization rates. Furthermore, older adults are maintaining an active life style and experiencing fewer functional limitations than in the past.[9] By remaining mobile, older adults actually may be increasing their fall risk.

Table 1. Numbers and rates[a] of fall-related hospitalizations among people aged 65 and older treated in Emergency Departments, by gender and age-group, United States, 2001-2008

	Year								Annual percentage change[c]
	2001	2002	2003	2004	2005	2006	2007	2008	
Age-adjusted incidence rate	1,045.6 (803.3-1,287.9)	1,066.9 (863.2-1,270.6)	1,243.6 (975.6-1,511.6)	1,256.6 (972.9-1,540.2)	1,221.8 (944.7-1,498.9)	1,223.5 (935.2-1,511.8)	1,229.4 (935.8-1,523.0)	1,368.1 (1,067.8-1,668.4)	3.3% (1.66-4.95)
Gender & age-group				Rate (95% CI)[b]					
Men									
65-69	278.2 (206.6-349.8)	261.4 (182.6-340.2)	278.4 (213.2-343.7)	332.6 (259.1-406.2)	348.7 (257.1-440.4)	325.2 (247.8-402.6)	335.7 (254.4-416.9)	408.8 (318.6-499.0)	5.3% (2.92-7.64)
70-74	412.4 (311.3-513.5)	359.0 (281.1-437.0)	493.6 (376.2-611.0)	542.9 (423.4-662.3)	441.3 (326.7-555.8)	561.0 (417.3-704.6)	494.7 (367.0-622.3)	606.1 (468.4-743.7)	6.2% (1.97-10.61)
75-79	720.5 (569.6-871.4)	706.5 (514.4-898.7)	791.2 (5843-998.1)	913.6 (673.6-1,153.6)	894.7 (657.0-1,132.4)	802.6 (575.2-1,030.0)	850.9 (626.9-1,075.0)	958.8 (747.7-1,170.0)	3.8% (1.81-5.74)
80-84	1,207.3 (897.0-1,517.6)	1,263.3 (985.4-1,541.1)	1,342.9 (988.3-1,697.7)	1,484.0 (1,053.0-1,914.9)	1,569.6 (1,123.7-2,015.5)	1,394.0 (1,034.3-1,753.7)	1,481.3 (1,074.7-1,887.9)	1,556.0 (1,166.8-1,945.1)	3.5% (1.95-5.03)
≥85	2,446.9 (1,731.0-3,162.8)	2,681.9 (1,955.2-3,408.6)	2,877.5 (2,170.6-3,584.4)	2,824.5 (2,059.3-3,589.7)	2,710.3 (2,010.4-3,410.1)	2,735.0 (1,948.3-3,521.8)	2,836.2 (1,983.2-3,689.1)	3,063.2 (2,308.0-3,818.3)	2.0% (0.57-3.54)
Women									
65-69	323.2 (220.1-426.3)	345.4 (270.4-420.4)	452.9 (335.5-570.3)	467.4 (365.2-570.3)	473.6 (327.7-619.6)	428.9 (333.6-524.2)	425.8 (304.7-546.8)	501.3 (358.5-644.2)	5.4% (1.83-9.04)
70-74	640.7 (474.7-806.8)	609.6 (493.9-725.3)	695.9 (523.2-868.5)	696.2 (525.3-867.1)	706.2 (559.3-867.1)	670.9 (482.3-859.5)	831.0 (620.3-1,041.7)	838.2 (640.1-1,036.2)	4.2% (2.23-6.10)
75-79	1,038.0 (775.4-1,300.5)	1,116.4 (892.2-1,340.5)	1,362.0 (1,056.3-1,667.7)	1,285.5 (992.4-1,578.6)	1,264.1 (976.1-1,552.1)	1,281.4 (983.1-1,579.6)	1,292.5 (953.3-1,631.6)	1,480.2 (1,157.6-1,802.8)	4.0% (1.81-6.16)
80-84	1,790.8 (1,335.4-2,246.3)	2,024.1 (1,629.4-2,418.8)	2,345.1 (1,804.5-2,885.7)	2,423.3 (1,804.5-2,885.7)	2,208.5 (1,612.0-2,804.9)	2,357.6 (1,731.7-2,983.5)	2,269.6 (1,718.1-2,821.2)	2,402.0 (1,838.9-2,965.1)	3.4% (1.13-5.81)
≥85	3,743.1 (2,771.9-4,714.2)	3,635.7 (2,956.6-4,314.7)	4,283.0 (3,330.6-5,235.3)	4,108.3 (3,119.1-5,097.5)	4,056.6 (3,058.1-5,055.1)	4,139.0 (3,061.4-5,216.5)	3,955.1 (2,992.5-4,917.6)	4,538.2 (3,428.7-5,647.7)	2.2% (0.37-4.01)

[a]Per 100,000 population
[b]95% confidence interval
[c]The average annual rate of change over the 8-year time period. P-value for trend was <0.001 for all age groups

Higher hospital admission rates may reflect changes in hospital policies that encourage admission following ED treatment as well as the utilization of surgical techniques to improve survival and optimize older adults' functional outcomes.[10] For example, head injuries in older adults are frequently caused by a fall.[11] Since the introduction in 2000 of revised guidelines for the diagnosis and management of head injuries, the number of head injury admissions has increased in the United States.[12] However, the overall admission rate after ED presentation due to fall-related injuries remained between 24-26% during the study period.

Higher incidence rates for fall-related hospitalizations were seen for women in all age groups. This finding is not unexpected and could be partially explained by women's higher prevalence of osteoporosis and increased risk of fractures, compared to men.[13] In addition, women are more likely to live alone because they have a greater life expectancy. We hypothesize that older women who live alone are more likely to be hospitalized. However, this hypothesis would need to be investigated further.

A limitation of this study is that NEISS-AIP includes only injuries treated in the ED, so only the fall-related injuries that were treated in the ED and subsequently hospitalized were included in our analysis. Although injuries treated in the ED represent the majority of serious fall-related injuries, patients who were admitted directly to the hospital, such as those with hip fracture, were not included in this study. Therefore, the true burden fall-related hospitalizations which would include patients who did not survive treatment in the ED or were directly admitted, likely exceeds the numbers presented in this study.

It has been estimated that the number of persons age 65 years and older in the United States will double in next 30 years, eventually exceeding 80 million persons.[7] An increasing life expectancy has made people more than age 85 years the fastest growing segment of the population. An important, and increasing segment of this population will be hospitalized for a fall.[14, 15] Unless preventive action is taken, increasing hospitalization rates, combined with the aging of the US population over the next decade, will exacerbate the already stressed healthcare system and may result in poorer health outcomes for older adults in the future. The oldest old (aged 85 years and older) are at greatest risk and are 10 times more likely to be hospitalized after a fall compared to persons aged 65-69 years. Therefore, falls prevention programs should pay special attention to this population.

Effective falls prevention interventions have been developed. These include clinical assessment and treatment of fall risk factors; exercise programs that focus on balance and strength training; and multifaceted interventions that include exercise, medication management, vision checking and improvement, and home hazard assessment.[16, 17] However, these interventions have not been widely applied. A variety of effective interventions need to be implemented in the coming years to counteract the expected increase in fall-related injuries in older adults and to limit the associated healthcare costs.[6]

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Chapter 3

Time trends in fall-related injuries

Chapter 3.1

The epidemic of hip fractures, are we on the right track?

K.A. Hartholt, C. Oudshoorn, S.M. Zielinski, P.T.P.W. Burgers, M.J.M. Panneman, E.F. van Beeck, P. Patka, T.J.M. van der Cammen

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Abstract

Background
Hip fractures are a public health problem, leading to hospitalization, long-term rehabilitation, reduced quality of life, large healthcare expenses, and a high 1-year mortality. Especially older adults are at greater risk of fractures than the general population, due to the combination of an increased fall risk and osteoporosis. The aim was to determine time trends in numbers and incidence rates of hip fracture-related hospitalizations and admission duration in the older Dutch Population.

Methods and Findings
Secular trend analysis of all hospitalizations in the older Dutch population (≥65 years) from 1981 throughout 2008, using the National Hospital Discharge Registry. Numbers, age-specific and age-adjusted incidence rates (per 10,000 persons) of hospital admissions and hospital days due to a hip fracture were used as outcome measures in each year of the study. Between 1981 and 2008, the absolute number of hip fractures doubled among the older Dutch population. Incidence rates of hip fracture-related hospital admissions increased with age, and were higher in women than in men. The age-adjusted incidence rate increased from 52.0 to 67.6 per 10,000 older persons. However, since 1994 the incidence rate decreased (percentage annual change -0.5%, 95% CI: -0.7; -0.3), compared with the period 1981-1993 (percentage annual change 2.3%, 95% CI: 2.0; 2.7). The total number of hospital days was reduced by a fifth, due to a reduced admission duration in all age groups. A possible limitation was that data were obtained from a linked administrative database, which did not include information on medication use or co-morbid diseases.

Conclusions
A trend break in the incidence rates of hip fracture-related hospitalizations was observed in The Netherlands around 1994, possibly as a first result of efforts of preventing falls and fractures. However, the true cause of the observation is unknown.

Introduction

Fall incidents and fall-related injuries among older people are a major public health problem in the ageing societies worldwide.[1-3] Of people aged ≥65 years approximately one third fall each year.[4-7] Especially older individuals are at an increased risk of sustaining fractures after a low energetic trauma, *e.g.* a fall incident, due to underlying medical conditions, especially osteoporosis.[8]

Osteoporosis, a highly prevalent condition in the older population, is characterized by low bone mass and micro-architectural deterioration of bone tissue. Osteoporosis results in an increased bone fragility and increased susceptibility to fractures.[8] Typical sites of osteoporotic fractures include those of the hip, wrist, vertebrae, and upper arm.[9] Approximately 85% of all hip fractures occur in individuals aged ≥65 years.[10] Hip fractures are, more than any other type of fracture, associated with a loss of independence,[11] morbidity,[12] and mortality.[13]

Besides the health impact on the individual patient, the socioeconomic impact of osteoporosis and of hip fractures in particular is very substantial.[14] Hip fractures are currently leading to nearly half (46%) of all injury related healthcare costs in older adults in The Netherlands.[15, 16] In a global perspective, the annual estimated worldwide direct and indirect costs of hip fractures amounted to US $34.8 billion in 1990, and are expected to rise to an estimated US $131 billion by 2050.[17] With the expected continuing ageing of populations worldwide,[18] it might be expected that the number of hip fractures will increase accordingly, making it necessary to prepare our healthcare systems for this burden.

In order to optimize healthcare use and healthcare planning in an ageing society, accurate numbers in hip fracture incidence are mandatory. The aim of this study was to provide secular trends of age- and gender specific numbers, incidence rates and length of hospital stay (LOS) of hip fractures in the older Dutch population.

Materials and Methods

For this study all hospital admissions due to a hip fracture in persons aged ≥65 years were collected from 1981 throughout 2008 in The Netherlands. The data were retrieved from Statistics Netherlands (CBS, The Hague, The Netherlands), which combines information of the National Medical Registration (LMR)[19] and the National Hospital Discharge Registry. Data regarding hospital admissions, admission diagnosis, LOS in days, age, and gender are stored in this database. The LMR database has a high nationwide coverage and nearly all admissions are stored in this database (less than five percent missing). Hospital admissions data and population numbers were verified with the national Birth-Registry.[19] The Birth-Registry is used to identify individual patients in the National Medical Registration. Data were corrected for missing values by the Statistics Netherlands, and extrapolated to full national coverage.[20] A uniform classification and coding system is used by the LMR for all hospitals and did not change during the study period. Official coding clerks register the diagnosis and injury mechanism of all hospital admissions, based on data obtained from medical records. Throughout the study period, a hip fracture was defined by using the International Classification for Diseases, 9^{th} revision of the World Health Organization, code 820. Older persons were defined as persons aged 65 years and older. Demographic numbers were retrieved from the Statistics Netherlands. In this study the mid-year population was used. The medical ethical review board of the Erasmus MC, University Medical Center, Rotterdam, approved the study (MEC-2010-402) and provided a waiver for "informed consent", because the data were retrieved from a large public freely accessible database, containing anonymous data on admissions, which cannot be traced to individuals.

Numbers of hospitalizations due to hip fracture were specified for age and gender. The age-specific incidence rates were calculated in 5-year age groups using the number of hip fractures in that specific age group, divided by the population size within that specific age-group for male and female patients, and was expressed per 10,000 persons in that age-group. Age-adjusted incidence rates allowed us to compare the incidence rate for a standardized population during the study period, and were performed by "Direct Standardization" to correct for demographic changes throughout the study period. Growth in the numbers of hospital admissions and LOS were calculated in percentages compared to 1981.

Data were analyzed using a Poisson regression analysis for annual growth in overall hospital admissions for older persons, corrected for population size and age composition. In order to model the trend in hospital admissions, a linear regression model with Poisson error and log link was built with log (mid year population size of each year of the study) as offset factor. To assess if the annual growth changed during the study period for both genders, the Joinpoint Regression Program, Version 3.4.3. (Statistical Research and Applications Branch, National Cancer Institute, USA) was used. This program showed the necessity for assuming a spline instead of a simple linear model, for men and women separately, and determines where to place the knot. The spline function accommodated two piecewise linear fits, connected with one another at the knot. Comparison of these two periods enabled us to detect and quantify changes in the secular trend in admission rates such as stagnation or an increase in admission rates. The best knot was found to be January 1, 1994. The parameter for calendar year, corrected for gender and age-group was transformed into Percentage Annual Change (PAC). The analysis including splines yielded estimates of annual changes in admission rates within each period (1981-1993 and 1994-2008). All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 16.1.1). A p-value <0.05 was considered statistically significant.

Results

During the study period from 1981 throughout 2008, 355,320 patients aged ≥65 years were admitted due to a hip fracture in The Netherlands. The annual number of hip fracture-related hospitalizations doubled in both men and women, from 7,614 cases in 1981 to 16,049 cases in 2008 (Table 1). The male:female ratio remained 1:3 throughout the study period. The overall crude incidence rate increased, from 46.4 per 10,000 older adults in 1981 to 66.5 per 10,000 in 2008 (increase 43.3% compared to 1981), and peaked in 1995 (70.4 per 10,000 older adults). For older men the crude incidence rate increased from 27.6 to 39.5 (increase 43.3%) and for older women from 59.5 to 86.8 (increase 46.0%) in 1981 and 2008 respectively.

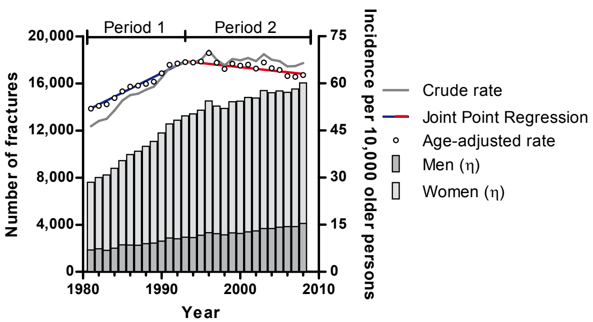
Table 1. Population characteristics of persons aged ≥65 years, number, incidence and mean admission duration of hip fracture-related hospitalizations in persons aged ≥65 years (The Netherlands, 1981-2008)

Characteristic	1981	1986	1991	1996	2001	2006	2008
Population ≥65 year (x 1,000)	1,642	1,769	1,934	2,061	2,175	2,330	2,415
Female (%)	59.0%	61.2%	60.2%	59.8%	58.9%	57.6%	57.0%
Admissions overall (η)	7,614	9,958	12,565	14,508	14,810	15,249	16,049
- men (η)	1,857	2,281	2,879	3,326	3,385	3,845	4,105
- women (η)	5,757	7,677	9,686	11,182	11,425	11,404	11,944
Incidence rate†	46.4	56.3	65.0	70.4	68.1	65.4	66.5
Mean admission duration, day	37.0	32.1	30.0	23.8	23.1	15.4	14.0

†Crude incidence rate, expressed per 10,000 older adults.

Gender and age-specific incidence rates of hip fracture-related hospital admissions are shown in Table 2. For men and women aged 65-74 years the age-specific incidence rates of hip fractures did not change significantly if 2008 was compared to 1981. However, a strong increase (>50%) in the incidence rate of hospital admissions due to hip fracture was seen in men aged ≥80 years since 1981, up to an increase of 127% in men aged ≥95 years (from 156.3 per 10,000 in 1981 to 354.7 per 10,000 in 2008). Age-specific incidence rates for women of ≥75 years showed a growth of one sixth to a quart.

Figure 1. Absolute numbers, crude and age-xpecific incidence rates of hip fracture-related hospitalizations in the Dutch population ≥65 years (1981-2008)



Period 1 (blue line): 1981-1993, percentual annual change 2.30%, (95% CI: 2.00; 2.59)
Period 2 (red line): 1994-2008, percentual annual change -0.50% (95% CI: -0.70; -0.30)

Table 2. Incidence rates of hip fracture-related hospital admissions per 10,000 persons in the older Dutch population (1981-2008)

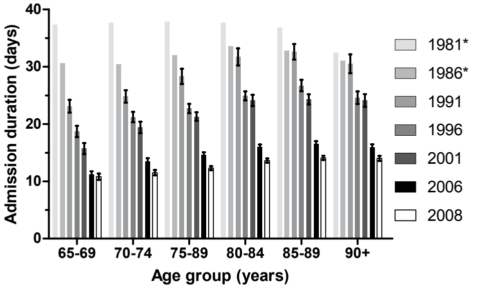
	Age range													
	65-69		70-74		75-79		80-84		85-89		90-94		≥95	
Year	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
1981	10.2	16.6	16.6	29.5	31.9	58.8	57.7	113.1	89.7	209.8	156.2	272.4	156.3	319.4
1986	11.0	19.6	20.3	34.6	34.8	66.9	65.1	128.6	107.3	229.7	190.0	303.5	233.7	349.2
1991	12.2	21.7	20.7	40.0	41.9	78.9	77.9	134.0	141.1	235.5	220.4	369.9	296.4	379.3
1996	12.2	21.8	24.4	45.5	45.6	82.0	86.3	147.2	148.1	240.0	211.0	363.5	269.0	410.9
2001	9.1	18.0	18.4	38.3	45.1	81.5	80.9	144.6	148.3	241.4	237.3	338.1	345.1	369.3
2006	9.8	15.8	16.9	32.5	38.2	72.1	85.3	138.2	159.6	229.7	265.5	326.1	372.3	385.1
2008	9.1	16.8	18.1	32.2	38.9	70.1	81.1	139.3	161.6	237.5	275.7	325.5	354.7	388.2
Change† (95% CI)	-11% (-24; 5)	1% (-10; 14)	9% (-5; 26)	9% (-1; 20)	22% (8; 37)	19% (11; 28)	41% (25; 58)	23% (16; 31)	80% (58; 106)	13% (6; 21)	77% (47; 112)	19% (8; 32)	127% (55; 233)	22% (0; 48)

† Change is 2008 compared to 1981; 95% CI:, 95% Confidence Interval

The overall age-adjusted incidence rate of hip fractures increased (Figure 1) from 52.0 per 10,000 older adults in 1981 to 62.7 in 2008 (increase 20.6%). Throughout the study period, the age-adjusted incidence rate for women (68.6 per 10,000 older women in 1981 and 79.9 in 2008) remained twice as high compared with men (27.9 per 10,000 older men in 1981 and 37.8 in 2008).
The PAC, change per year, of the age-adjusted incidence rate was 1.13% (CI 95%: 0.80; 1.45) for men versus 0.52% (CI 95%: 0.24; 0.81) for women over the whole study period. A joint-point regression analysis showed that the change in age-adjusted incidence rates was not constant over time and could be divided into two phases: first, the incidence of hospital admissions due to a hip fracture in older patients increased between 1981 and 1993, and second, decreased between 1994 and 2008 (Figure 1). The annual growth in men was 2.46% (CI 95%: 1.98; 2.94) and in women 2.16% (CI 95%: 1.89; 2.43) in the period 1981-1993. The PAC decreased in the period 1994-2008 to a negative annual growth of -0.34% (CI 95%: -0.86; 0.19) in men and -0.64% (CI 95%: -0.83; -0.46) in women.

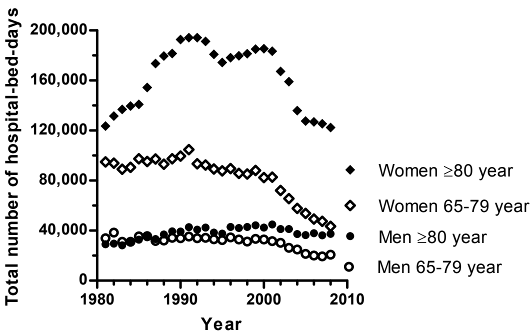
Also the mean LOS decreased throughout the study period in both men and women, from 37.0 days in 1981 to 14.0 days in 2008 (Figure 2). The admission duration decreased in male and female patients of 65-79 years with over 60%. Reduction in LOS became smaller in the older patient groups. In patients ≥80 years the LOS per admission was reduced by a third. In general, the LOS was age-related: the higher the age, the longer the admission duration (Figure 2). Although the total number of hip fracture-related hospital admissions increased, the total number of hospital-bed-days decreased due to a reduced LOS per admission. The total numbers of hospital-bed-days are shown in Figure 3 and decreased from 281,396 days in 1981 to 224,002 days in 2008 (decrease of 20%). For all men aged ≥65 years, the total number of hospital days decreased with 8% (62,980 days in 1981 to 58,146 days in 2008). In women aged 65-79 years, a reduction of 54% in hospital days was seen (94,903 days in 1981 to 43,474 days in 2008). In women ≥80 years the number of hospital days increased until 1991 to 194,264 days and from there on started to decrease, with the total number of hospital days in 2008 (122,382 days) just below (-1%) the total number of hospital days in 1981 (123,513 days).

Figure 2. Mean hospital admission duration in persons aged ≥65 years due to a hip fracture in The Netherlands between 1981-2008



* No SD data were available before 1991.

Figure 3. Total number of hip fracture-related hospital-bed-days in persons of ≥65 years in The Netherlands between 1981-2008



Discussion

In order to determine trends in hip fractures in the older Dutch population, all hip fracture-related hospitalizations were analyzed from 1981 throughout 2008. The age-adjusted incidence rates of hip fractures increased until the end of 1993 in the population ≥65 years. After that year, a trend break was observed and the incidence rates started to decrease. Although an encouraging decrease in the age-adjusted incidence rates was observed, the absolute number of hip fractures continued to increase due to a rising number of older persons in the population.

Similar trends of decreasing incidence rates for hip fracture-related hospitalizations since the mid-nineties have been reported in other countries such as the United States,[21] Canada,[22] and Finland.[23] However, not all findings across western countries are consistent. A recent study from Germany failed to demonstrate a decline in hip fracture incidence rates.[24] The decreasing incidence rates that have been reported in several countries now raise the question, which factors might have contributed to this trend break. There is no simple answer to this question, because risk factors for hip fractures are multifactorial, as mentioned by Leslie *et al.*[22] Important developments over the last two decades include: the increasing awareness of falls,[25, 26] the implementation of guidelines for the diagnosis and treatment of osteoporosis,[27, 28] increasing availability and use of bisphosphonates,[29] and an improvement of calcium intake and vitamin D status, although the latter is argued by some.[22] Other nationwide changes, such as the prevention and improved treatment of cardiovascular diseases in the general population may also have contributed to the observed trend break. A large Finnish twin-study recently demonstrated that cardiovascular diseases are associated with the development of hip fractures.[30] However, the exact mechanism behind this association is not clear yet.[30] Another suggestion might be that general health[31] and bone quality[32] have improved since smoking has been discouraged. The proportion of smokers is decreasing rapidly in The Netherlands[31, 33] as well as in other countries.[34, 35] Furthermore, the Statistics Netherlands (CBS) reported that the mean body weight increased in the whole Dutch population.[33] An increasing Body Mass Index is associated with a lower fracture risk.[36]

A remarkable difference was observed between the younger and older age-groups. Where incidence rates decreased in persons <80 years, the incidence rate stabilized in females aged ≥80 years, and continued to increase in males ≥80 years. This finding is worrisome because the population of 80 years and over is the fastest growing segment in the ageing population[37] and because mortality and morbidity associated with hip fractures are greater for the oldest old, and are higher in men than in women in the first year after sustaining a hip fracture.[38, 39] A possible explanation for this observation might be that life expectancy increased more rapidly in men compared to women over the last decades, resulting in a smaller gap in life expectancy between men and women.[40] Consequently, men become more vulnerable for age-related (co)morbidities, such as osteoporosis and hip fractures, which were previously frequently seen in older women. This assumption is supported by a previous report on a more rapid increase in fall-related injures, hospitalizations, and mortality in older men than in older women in The Netherlands over the last decades.[1, 41] Another possible explanation might be that osteoporosis in men is frequently underdiagnosed and undertreated.[42]

The number of hospital bed-days per admission is considered to be one of the most important determinants of total costs of a hip fracture in an individual patient.[43] Therefore, a reduced LOS is mandatory in order to reduce hospital care demands and to limit related healthcare costs. During the study period the LOS decreased by two-thirds. Several factors might have contributed to this impressive reduction: the rapid improvement of surgical and anesthetical care over the last decades, resulting in less invasive surgical procedures; the introduction of new hip prostheses, and implants; protocols for early timed surgery after a hip fracture; better pain management and better post-operative care with early mobilization; early discharge designated rehabilitation places in skilled nursing homes; and the implementation of hip fracture treatment guidelines.[44-46] In addition, during the final years of the study period a change in the financing structure of Dutch hospitals, which was introduced in 2004, may have led to a further decline in LOS.

A strength of the present study is the availability of population-based in-hospital data, covering a period of 28 years. The Dutch healthcare system is characterized by full health insurance coverage and full accessibility for the whole population during the study period. Since 1981 absolute numbers of hip fracture related hospital admissions and hospital-bed-days in all hospitals in The Netherlands have been recorded with almost complete national coverage in a highly accurate electronic database. Throughout the study period, the coding system of the National Medical Registration did not change during the study period and no major policy changes were introduced in The Netherlands which might have affected the increase in admission rates. However, this study has some limitations. A possible limitation of this study is that these data describe the situation for one country, which may not directly translate to other western countries, because of differences in healthcare system characteristics and demographics. Nevertheless, since hip fracture trends[21, 22, 47] in other western populations are comparable with the trends in The Netherlands, there is no reason to assume that hip fractures trends will be substantially different in other countries. This study is based on a linked administrative database, which does not contain clinical data regarding underlying diagnosis, co-morbidity, injury severity, lifestyle, or medication use of the patients. This limits the interpretation of the causal mechanisms behind the observed trends. Furthermore, readmissions in one calendar year were not excluded and could potentially lead to some "double registration". However, it is unlikely that readmissions influenced our results, since readmissions for injuries constitute only 2.6% (at the maximum) in The Netherlands, as was found in a study by Polinder *et al.*[48]

In summary, the increase in hip fracture incidence rates slowed down, and the incidence rates started to decrease over the last 12 years. However, incidence rates nowadays remain higher than in 1981, suggesting that there is still room for improvement. Furthermore, the continuing increasing incidence rates in the oldest men is a worrying trend that deserves specific attention, since the group of persons aged 80 years and older are the fastest growing segment of aging societies. With the expected ageing of societies worldwide, continued attention is needed in order to cope with the demand of hip fracture related care in the near future.

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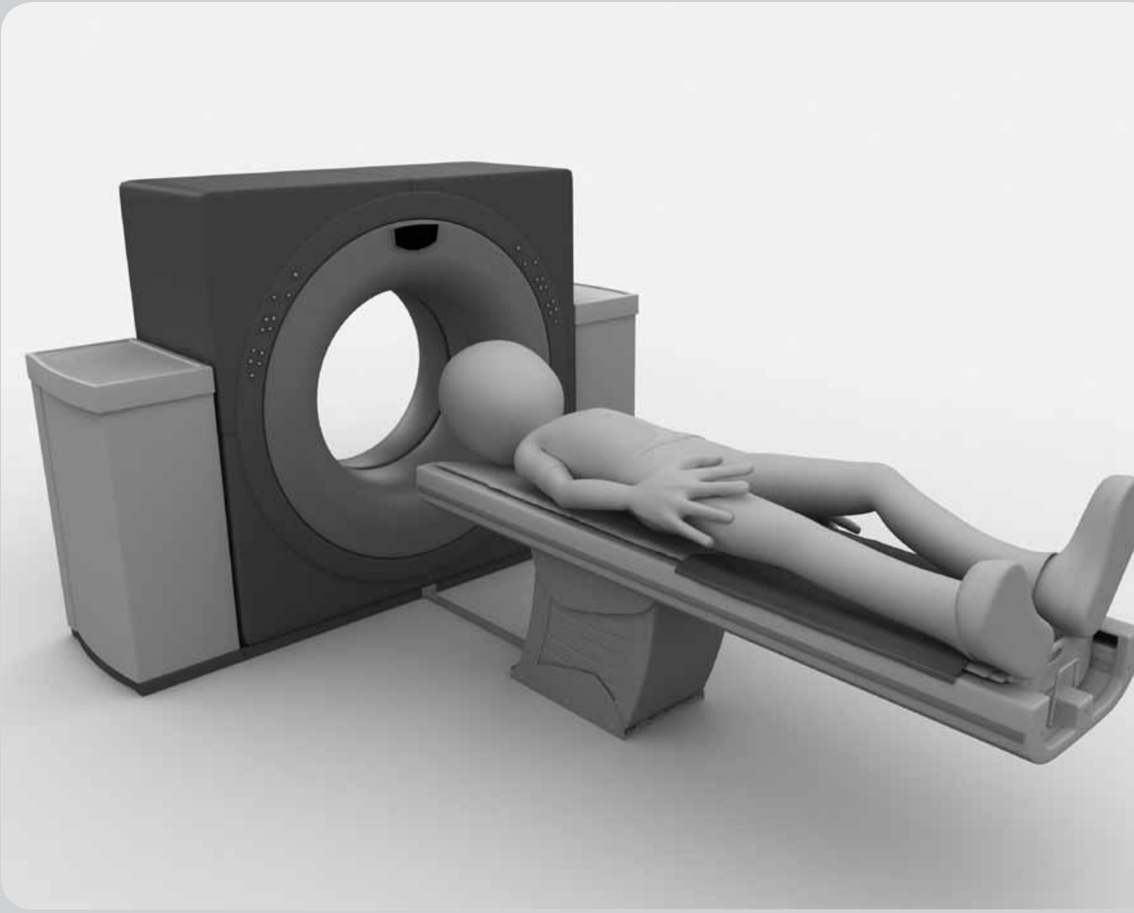
Chapter 3.2



Rapid increase in hospitalizations due to fall-related head injury in older adults in The Netherlands 1986-2008

K.A. Hartholt, E.M.M. van Lieshout, S. Polinder, M.J.M. Panneman, T.J.M. van der Cammen, P. Patka

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Abstract

Falls occur frequently in older adults. With ageing populations worldwide, an increase in fall-related traumatic head injuries can be expected. The aim of our study was to determine trends in traumatic head injury-related hospitalizations among older adults. Therefore, a secular trend analysis of fall-related traumatic head injuries in the older Dutch population between 1986 and 2008 was performed, using the National Hospital Discharge Registry. All significant fall-related traumatic head injury hospitalizations in persons aged ≥65 years were extracted from this database. During the study period, traumatic head injury-related hospitalizations increased by 213% to 3,010 in 2008. The incidence rate increased annually by 1.2% (95%CI: 0.6; 1.9) between 1986 and 2000. Since 2001 the increase accelerated up to 11.6% (95%CI: 9.5; 13.8) per year. Overall, the age-adjusted incidence rate increased from 53.1 in 1986 to 119.1 per 100,000 older persons in 2008. Age-specific incidence rates increased in all age groups, especially in persons aged ≥85 years. Despite an overall reduction in the length of hospital stay per admission, the total number of hospital-bed-days increased with 31.5% to 20,250 between 1991 and 2008. In conclusion, numbers and incidence rates of significant traumatic head injury related hospitalization after a fall are increasing rapidly in the older Dutch population, especially in the oldest old, resulting in an increased health care demand. The recent increase might be explained by the ageing population, but also other factors may have contributed to the increase, such as an increased awareness of traumatic head injuries, the implementation of renewed guidelines for traumatic head injuries, and improved radiographic tools.

Introduction

Falls occur frequently among older adults and falls are the main injury mechanism among the older population. The high number of falls, mainly resulting in fractures, traumatic head injuries and wounds[1-3], leads to a large burden of health care consumption, including Emergency Department visits[4] and hospital admissions.[1, 5, 6] Approximately a sixth to a quarter of all fall-related injuries are located to the head and face[3] and are the leading cause of traumatic head injuries in older adults.[7] Incomplete recovery from their head injury could lead to a loss of functional activity and a reduction in the quality of life.[8] Outcome may range from death or dependency on social care services to full independent living.

A recent study in the older Finnish population aged ≥80 years showed an increase of 200% in the incidence rate of severe traumatic head injuries in females between 1970 and 2004.[9] Also an increase in the number and age-specific incidence rates of injurious falls and concomitant health care consumption was shown for the older Dutch population.[5] The increased awareness of the likelihood of structural brain damage and traumatic head injuries over the last decades, has resulted in new national and international guidelines for the diagnosis and management of traumatic head injuries.[10, 11] In 2001 a renewed national guideline with diagnostic and therapeutic algorithm for traumatic head injuries has been implemented in The Netherlands[12], *e.g.*, when to make a CT-scan[13] or hospitalize a patient. Furthermore, the quality and availability of diagnostic tools such as the CT scanner, has improved rapidly.

For health care services and health care economics it is essential to gain insight into the epidemiology, trends, and forecast for the future. The aim of this study was to quantify secular trends of fall-related hospitalizations due to head injuries in older adults in The Netherlands.

Methods

For this study, all significant head injury related hospitalizations caused by a fall incident between 1986 and 2008 were collected. Throughout the study period a significant traumatic head injury was defined using the International Classification of Diseases, 9th revision (ICD9) codes for head injuries: more specific code (skull fracture) 800-804.X, (contusion and concussion) 850-851.X, (bleeding) 852-853.X, and (other) 854.X (Table 1). A fall was defined by the ICD9 codes for external cause of injuries code E880-E889 and E929.9.

Table 1. International Classification of Diseases of the World Health Organization codes, 9th Revision, for head Injuries

Group	Code	Description
Fracture	800	Fracture of vault of skull
	801	Fracture of base of skull
	803	Fracture of face bones
	804	Multiple fractures involving skull or face with other bones
Concussion/ contusion	850	Concussion
	851	Cerebral laceration and contusion
Bleeding	852	Subarachnoid subdural and extradural haemorrhage following injury
	853	Other and unspecified intracranial haemorrhage following injury
Other	854	Intracranial injury of other and unspecified nature

Older persons were defined as persons aged ≥65 years. Data were retrieved from the National Medical Registration (LMR). The LMR collects hospital data in The Netherlands with a uniform classification system with a high national coverage (missing values <5%, except in 2007, when they were 12%).[14] These figures were extrapolated by the Consumer and Safety Institute to full national coverage for each year. An extrapolation factor was estimated by comparing the adherence population of the participating hospitals with the total Dutch population in each year.[14] Data regarding hospital admissions, admission diagnosis, length of hospital stay (days), gender, age, and causes for external injuries are stored in this database. For each individual patient only one injury code, the primary diagnosis, was used. The primary diagnosis is based upon the medical records completed by the physicians treating the patient, has been used as main diagnosis at discharge (in general the most severe injury).

Numbers of significant traumatic head injury-related hospital admissions and admission duration were specified for age and gender in 1986, 1991, 1996, 2001, 2006 and 2008. The age-specific incidences were calculated in 5-year age groups using the number of fall-related hospital admissions resulting from a traumatic head injury in that specific age group, divided by the midyear population size within that specific age group for male and female patients, and was expressed per 100,000 persons in that age group. Age-adjustment was done by "Direct Standardization". Overall growth in the number of hospital admissions was calculated for 2008 in percents relative to the year 1986. The midyear population was used in each year of the study.[15]

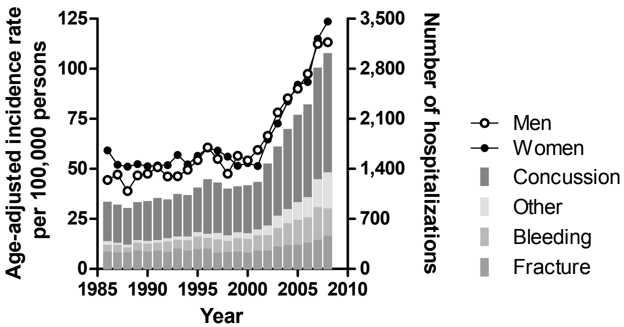
In order to model the trend in hospital admissions, a linear regression model with Poisson error and log link was built with log (mid year population size of each year of the study) as offset factor. A linear spline model,[16] with age, year, gender, and population size, was built to assess whether the annual growth changed over the study period for both genders. The parameter for calendar year, corrected for gender and age group, was transformed into Percentage Annual Change (PAC). The spline function accommodated two piecewise linear fits, connected with one another at the knot. The best knot was estimated using the "Joinpoint Regression Program", Version 3.3.1. (Statistical Research and Applications Branch, National Cancer Institute, USA), and found to be January 1, 2001. The analysis including splines yielded estimates of annual changes in admission rates within each period (1986-2000 and 2001-2008). Comparison of these two periods enabled us to detect and quantify changes in the secular trend in admission rates, such as a stagnation or and increase of admission rates. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 16.1.1). A *p*-value <0.05 was considered statistically significant.

Results

During the study period from 1986 throughout 2008, a total number of 32,133 patients in The Netherlands aged ≥65 years, who had a significant traumatic head injury required hospitalization after a fall incident. The annual number of older persons admitted with a significant traumatic head injury increased from 932 in 1986 to 3,010 (223% increase) in 2008 (Figure 1). In the same period, the population of adults aged ≥65 years increased from 1.8 million in 1986 to 2.4 million (33% increase) in 2008 in The Netherlands.

The overall age-adjusted incidence rate of hospitalization of head trauma patients increased from 53.1 per 100,000 persons in 1986 to 119.3 per 100,000 persons in 2008. In men, the age-adjusted incidence rate increased from 44.4 per 100,000 persons in 1986 to 113.3 per 100,000 persons in 2008. In women it increased from 59.2 to 123.6 (Figure 1).

Figure 1. Numbers and type of head injury and age adjusted incidence for traumatic fall-related head injuries, requiring hospitalization in persons ≥65 years in The Netherlands, 1986-2008



Using a joint point analysis, the study period could be divided in two periods (1986-2000 and 2001-2008). The incidence rate increased annually by 1.2% (95%CI: 0.6; 1.9) between 1986 and 2000. From 2001 onwards, the increase accelerated up to 11.6% (95%CI: 9.5; 13.8) per year. The PAC of hospitalizations resulting from significant fall-related traumatic head injuries was different for men and women throughout the study period. Between 1986 and 2000 inclusively, the PAC for men was 1.8% (95%CI: 0.8; 2.9) and increased to 9.9% (95%CI: 7.4; 12.4) since from 2001 onwards. For women a comparable pattern was observed. The PAC increased from 0.6% (95%CI: -0.1; 1.3) between 1986 until 2000 to 12.3% (95%CI: 10.1; 14.5) from 2001 onwards.

Table 2. Age specific incidence rates, per 100,000 persons, of traumatic head injuries requiring hospitalization in The Netherlands 1986-2008

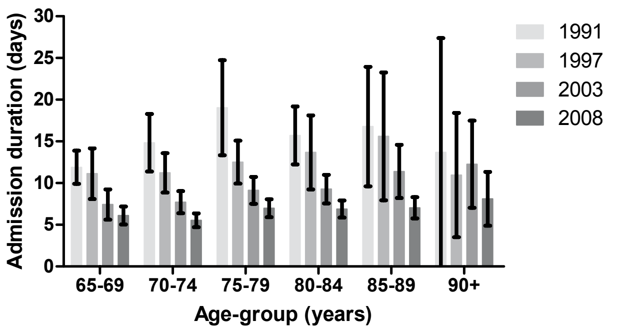
	Age rage, y											
	65-69		70-74		75-79		80-84		85-89		≥90	
Year	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
1986	33.3	27.7	40.2	48.0	51.3	65.4	53.3	89.8	70.2	110.2	127.3	88.0
1991	36.0	23.2	45.5	36.8	54.2	61.8	77.7	78.6	91.6	98.9	102.8	86.2
1996	43.0	28.8	40.4	43.3	74.7	60.5	101.1	100.8	115.6	120.6	163.6	102.3
2001	41.2	17.2	52.0	33.8	62.2	61.0	99.5	89.7	112.1	95.4	100.1	107.4
2006	57.9	36.5	78.0	54.1	96.3	95.1	177.5	144.3	246.4	225.3	265.9	242.9
2008	63.9	50.8	94.4	67.5	125.1	109.3	185.2	216.0	270.6	281.8	357.1	352.9
Percent change† (95%CI)	92% (49-145)	84% (41- 135)	135% (85-206)	41% (14- 75)	144% (88-219)	67% (36-102)	247% (151-384)	140% (96-186)	285% (155-502)	156% (103-225)	180% (64-376)	301% (164-478)

†Change is 2008 compared with 1986; 95% CI:, 95% Confidence Interval

The age-specific hospitalization rates increased throughout the study period for both genders and in all age groups (Table 2). The age-specific incidences increased with age and were highest among persons aged ≥85 years. The largest increase in incidence rate was seen in persons aged ≥90 years, in both men (180% increase to 357.1 per 100,000 persons) and women (301% increase to 352.9 per 100,000 persons) (Table 2).

The majority of hospitalizations due to a traumatic head injury were because of a concussion or contusion (57.3%). Fractures, bleeding, and other/unspecified injuries were seen less frequently (Table 3). Increases in incidence rates were mostly attributed to an increase in concussions/contusions and bleedings. The number of patients admitted because of a fall-related concussions/contusions increased from 552 admissions in 1986 to 1,666 in 2008. Fall-related bleedings in the head increased from 96 in 1986 to 382 in 2008 (Table 3).

Figure 2. Mean admission duration for traumatic fall-related head injuries per age group in persons ≥65 years in The Netherlands, 1991-2008



Error bars indicate the 95% confidence interval.

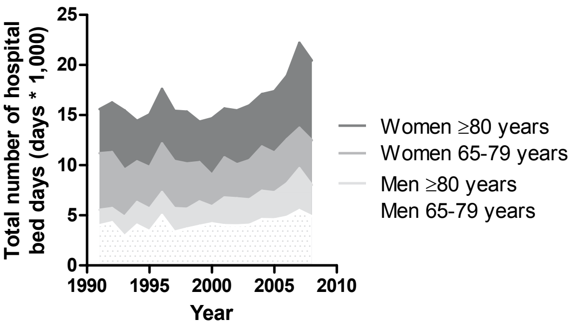
Table 3. Causes and localization of traumatic head injuries leading to hospitalization between 1986 and 2008 in older adults ≥65 years of age in The Netherlands

	Men		Women		Overall	
Type of injury	η	%	η	%	η	%
Fracture	2,646	20.5	3,625	18.9	6,270	19.5
Concussion & Contusion	6,940	53.7	11,485	59.8	18,425	57.3
Bleeding	2,272	17.6	2,312	12.0	4,583	14.3
Other	1,067	8.3	1,787	9.3	2,854	8.9
Total	12,924	100.0	19,208	100.0	32,133	100.0

The mean admission duration in older adults decreased over the last 17 years for all age-specific groups, from 16.5 days in 1991 to 6.7 days in 2008 (Figure 2). Length of hospital stay for fall-related traumatic head injuries increased with age and peaked in patients of 85-89 years of age.

Despite a decreased admission duration per admission, the total number of hospital-bed-days increased by a third, from 15,402 days in 1991 to 20,250 days in 2008, because of a rising number of admissions. For both men and women the overall number of hospital-bed-days increased gradually. In older men from it increased from 5,346 days in 1991 to 7,822 in 2008 (46% increase). In all women aged ≥65 years the number of hospital-bed-days increased from 10,056 in 1991 to 12,428 days in 2008 (24% increase; Figure 3).

Figure 3. Total number of hospital bed days due to fall-related traumatic head injuries in persons ≥65 years in The Netherlands, 1991-2008



Discussion

In this study, the number of significant fall-related traumatic head injuries in all persons aged ≥65 years in The Netherlands was quantified, in order to gain insight into time trends in admissions related to these injuries in older adults from 1986 throughout 2008. The incidence rates and numbers of hospitalizations increased in both men and women throughout the study period, especially among the oldest old.

In the first period (1986-2000) of this study, the overall age-adjusted incidence changed only marginally. This is comparable data from the United States, where the incidence of traumatic brain-injury-related hospitalizations in persons ≥65 years hardly changed between 1980-1981 and 1994-1995.[17] However, Kannus *et al.* reported an increasing incidence rate between 1970 and 2004 in fall-related traumatic head injuries among Finnish men and women aged ≥80 years of age.[9] In the current study, a similar increasing trend from 1986 was noted for the oldest old. The increase between 1986 and 2000 might have several causes. It could, at least partly, be explained by "the aging society" in The Netherlands.[15] As life expectancy is increasing, older persons live longer, but with multiple medical problems. This may lead to increased risk of falls and fall-related injuries, such as traumatic head injuries.[18] Although the age-adjusted incidence rates for men and women were similar, the absolute number of hospitalizations in women was higher than for men because of a female preponderance in the older Dutch population.[15] Second, population-based health analyses in The Netherlands have shown that older adults are reporting fewer problems with their mobility,[19] which may partly be explained by improved medical care and the wide spread introduction and use of walking and transportation mobility aids. As a result of improved mobility, patients may be at higher risk for falls. A similar trend of improved mobility in older adults has been reported for the United States.[20] The observed increased incidence rate of significant traumatic head injuries might also be the result of a more active lifestyle, such as walking, cycling and sporting.[21]

Hospitalization rates resulting from falls among the older population in general increased by 137% over the last decades.[5] Hospitalization rates resulting from fall-related traumatic head injuries increased more rapidly. A clear explanation for this finding is not known yet. Possible factors that may have contributed might be that head injuries have been topic of research and preventive medicine over the last decades. This could have led to an increased awareness of the likelihood of structural brain damage in the elderly among health care professionals, and, consequently, to increased use of CT scanning and recognition of injuries. Moreover, the availability and quality of CT scanners has improved over the last decades, which also might have led to increased detection of minimal clinical symptomatology.

In 2001, a guideline for traumatic head injuries was introduced in The Netherlands.[12] This guideline instructs, for example, that patients with specific risk factors such as anticoagulant drug intake, should be screened radiographically. In 2000 and 2002, similar guidelines were introduced in the Scandinavian countries[22] and the United States,[7,23] respectively. A recent report of the Center for Disease Control and Prevention of the United States on Traumatic Head Injuries was published. During the period 2002-2006 the incidence rate of hospitalizations increased from 67.6 in 2002 to 90.7 in 2006 per 100,000 older adults in the United States.[7] This increase is similar to our results (increase from 65.4 in 2002 to 95.0 in 2006 per 100,000 older adults). Although no data are available to confirm a causal relation, the increased awareness in scientific literature and the implementation of the guideline, and consequently an increased use of radiographic imaging could have contributed, at least partly, to the increased detection of traumatic head injuries that require observation and hospitalization.

The recent development of admissions in significant fall-related traumatic head injuries has broad consequences for the required number of hospital beds and the related health care expenses. Although the length of hospital stay decreased between 1991 and 2008, it was not enough to compensate for the increased number of admissions. The decrease in length of hospital stay is in line with the general trend of reduced admission duration for injuries in our previous study.[5] The length of hospital stay was age-related and increased with age. However, the oldest old (persons aged ≥90 years) had a shorter admission duration, which might be explained by a higher number in this age group who are already living in a nursing home and consequently can be discharged from the hospital more rapidly.

A strength of this study is the availability of a highly accurate, electronic national population-based in-hospital database for an extensive period of 22 years (1986-2008) with the same coding system. But this study has also some limitations. In The Netherlands there is full national health care insurance, therefore the study results may not be directly translated to other countries. Further studies should confirm similar trends in other countries. Also some "double registration" could have occurred, as readmissions were not excluded. However, it is unlikely that readmissions influenced our results, because readmissions because of a trauma constitute in general only 2.6% of admissions in The Netherlands.[24] Another limitation of this link administrative database is that it does not contain data regarding underlying diagnoses, co-morbidities, treatments, injury severity, life style, or medication use of the patients. This hampers the interpretation of causal mechanisms behind the observed trends.

In conclusion traumatic head injuries are frequently observed after a fall, and the number is increasing rapidly. As falls are the leading cause of head injuries and other types of injury in older adults,[25] preventative strategies should focus on the prevention of falls. Known effective strategies[26-28] should be further implemented to slow down the rising incidence of traumatic head injuries and their related therapies and morbidities, and to optimize the quality of life and functional outcome in elderly patients.

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Chapter 3.3

Emergency department visits due to vertebral fractures in The Netherlands, 1986-2008: Steep increase in the oldest old, strong association with falls

C. Oudshoorn, K.A. Hartholt, M.C. Zillikens, M.J.M. Panneman, N. van der Velde, E.M. Colin, P. Patka, T.J.M. van der Cammen

Submitted

Abstract

Background
Vertebral fractures are a common consequence of osteoporosis in older persons. With the ageing of the population, numbers are expected to rise.

Objective
To determine trends in health care demand due to vertebral fracture related Emergency Department (ED) visits and hospitalizations in the older Dutch population.

Design and setting
Secular trend analysis of vertebral fracture related ED visits between 1986 and 2008, using the Dutch Injury Surveillance System. All ED visits with a primary diagnosis of a vertebral fracture in persons aged ≥65 years were extracted from this database.

Main outcome measure
Numbers, age-specific and age-adjusted incidence rates (per 100,000 population) of ED visits and hospitalization rates due to vertebral fractures in the older Dutch population were calculated for each year of the study.

Results
The total number of ED visits due to a vertebral fracture increased from 913 in 1986 to 2,502 in 2008 (174% increase). The majority of fractures were caused by a low-energetic fall incident (83%). The overall age-adjusted incidence rate increased from 51.6 per 100,000 population in 1986 to 103.6 in 2008. Incidence rates increased with age and were higher in females than in males. The hospitalization rate remained stable at about 50-55%, in both females and males.

Conclusion
Vertebral fracture related ED visits and hospitalizations are increasing rapidly in the older Dutch population, especially in the oldest-old. Most vertebral fractures were associated with falls. These findings indicate that a pro-active approach in the diagnosis and treatment of osteoporosis and in the prevention of falls in both men and women is warranted.

Introduction

Osteoporosis is a growing public health concern in developed countries worldwide.[1] It is a skeletal disease, characterized by low bone mass and micro-architectural deterioration, which results in an increased bone fragility and fracture risk.[2] Vertebral fractures are one of the most common osteoporotic fractures. Approximately 90% of vertebral fractures are associated with osteoporosis.[18] Vertebral fractures lead to functional impairment, impaired quality of life and increased mortality.[8, 13, 22] A previous vertebral fracture is associated with an increased risk of further vertebral fractures and hip fractures.[3]

It was estimated that in the year 2000, nine million osteoporotic fractures occurred worldwide, and of these approximately 1.4 million (15%) were clinical vertebral fractures.[4] The majority of vertebral fractures however are morphometric, *i.e.* clinically silent. The prevalence of radiographically identified vertebral deformities has been estimated to be 5% between the age of 50-54 years, and rises to 50% at age 80-84 years.[19]

The number of patients with a vertebral fracture is expected to increase because of the increasing life expectancy and the increasing number of osteoporotic individuals in the population.[16, 23] However, there is few data on time trends of healthcare demand due to clinical vertebral fractures. The aim of this study was to analyze time-trends in clinical vertebral fractures by analyzing trends in Emergency Department (ED) visits and hospitalization rates after ED visit.

Methods

Data on ED visits due to a vertebral fracture in the Dutch population aged 65 years and over was extracted from the Dutch Injury Surveillance System (LIS). The LIS database is a continuous monitoring system in which injury diagnoses and injury mechanisms are registered by using the International Classification of Diseases of the World Health Organization (ICD 10th revision).[5] LIS is based on 13 geographically distributed EDs in The Netherlands, resulting in a representative 12% sample of injury-related ED visits. Numbers were extrapolated to national estimates. An extrapolation factor was calculated by the Consumer and Safety Institute (Amsterdam, The Netherlands) based on the adherent population of the participating hospitals and Dutch population numbers in each year of the study. The database makes it possible to measure and describe healthcare use during a specific period. The full-model description has been published by the Consumer and Safety Institute, Amsterdam and has been used previously.[6, 9, 17]

The model was applied to all persons aged 65 years and older who attended an ED between 1986 and 2008. A vertebral fracture was defined using the ICD 10th revision.[5] Vertebral fractures were selected based upon the registered primary diagnosis in the LIS. In case of multiple injuries, the primary injury in LIS was determined by application of an algorithm giving priority to spinal cord injury, skull and brain injury, and lower extremity injury above injuries in other body parts, and to fractures above other types of injury to determine the most serious injury. Numbers of ED visits due to vertebral fractures were specified for age and gender. Furthermore, discharge was registered as treated-and-released or treated-and-admitted to calculate the admission rate. Age-specific rates were calculated in 5-year age groups. The overall age-adjusted incidence rate for the population aged 65 years and older was calculated by using "Direct Standardization" to correct for changes in demographics. Incidence rates were expressed per 100,000 person years. A linear regression analysis was used to analyse the age-adjusted incidence rate of vertebral fracture related ED visits over time. The statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 16.1.1). A p-value <.05 was considered statistically significant.

Results

From 1986 throughout 2008, the population aged ≥65 years increased from 1.6 million to 2.4 million persons in The Netherlands. During that same period, a total number of 31,650 patients were seen and diagnosed in the ED with a vertebral fracture. The annual number of vertebral fractures requiring ED visits increased with 174% (from 913 in 1986 to 2,502 in 2008), Table 1. The majority (83%) of vertebral fractures was related to falls in both males and females; this remained unchanged throughout the study period (Table 2).

Table 1. Population characteristics of persons aged ≥65 years, number, incidence, and admissions due to a vertebral fracture (The Netherlands, from 1986 throughout 2008)

Characteristic	1986	1991	1996	2001	2006	2008
Population ≥65 yr (x 1,000)	1,769	1,934	2,061	2,175	2,330	2,415
Population female, %	61.2	60.2	59.8	58.9	57.6	57.0
ED incidence rate†	51.6	56.6	65.9	60.3	83.1	103.6
ED visits, No.	913	1,095	1,358	1,311	1,938	2,502
- Female, No. (%)	634 (69)	789 (72)	981 (72)	816 (62)	1,328 (69)	1,643 (66)
Hospitalization rate†	NA	32.6	36.0	30.0	42.2	57.5
Hospitalized, No. (%)	NA	631 (58)	741 (55)	643 (49)	984 (51)	1,389 (55)
- Females, No. (%)	NA	445 (71)	510 (69)	392 (61)	622 (63)	905 (65)

†Crude incidence rate, expressed per 100,000 older adults; NA, not available

Table 2. Causes of vertebral fractures requiring Emergency Department attendance in older adults aged 65 years and older in The Netherlands between 1986-2008

	Men		Women		Overall	
Trauma mechanism	**η**	**%**	**η**	**%**	**η**	**%**
Fall	7,736	78.7	18,390	84.3	26,126	82.5
MVA	1,481	15.1	1,835	8.4	3,316	10.5
Other	610	6.2	1,598	7.3	2,208	7.0
Total	9,826	100.0	21,823	100.0	31,650	100.0

Abbreviation: MVA, motor vehicle accident

Table 3. Age-specific incidence rates for vertebral fractures related Emergency Department visits in persons ≥65 years, per 100,000 older Persons (The Netherlands, from 1986 throughout 2008)

	Age range, y									
	65-69		70-74		75-79		80-84		≥85	
Period	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
1986-1990	33.4	38.8	18.9	60.0	58.6	90.7	53.1	95.3	89.5	88.9
1991-1995	17.2	29.8	25.0	40.0	37.1	62.6	48.3	75.3	123.0	124.4
1996-2000	29.8	54.6	33.5	60.0	47.4	69.5	89.2	125.6	151.8	123.1
2001-2005	35.4	37.1	40.2	58.3	59.7	82.3	73.3	94.9	106.1	140.7
2006-2008	51.5	58.4	61.3	70.8	77.9	112.2	113.8	141.0	216.8	222.8

Gender and age-specific incidence rates are shown in Table 3. Incidence rates increased with ageing and were higher in women than in men for all age groups. The crude incidence rate for men increased from 39.3 per 100,000 older adults in 1986 to 82.7 in 2008 (110% increase). The crude incidence rates for women increased from 59.9 per 100,000 older adults in 1986 to 119.4 in 2008 (99% increase). Figure 1 shows the age-specific incidence rate of vertebral fractures according to 5 year age groups for the periods 1986-1988 and 2006-2008, respectively. The strongest increase in incidence rate occurred in women ≥85 years, from 88.9 per 100,000 during the period 1986-1990 to 222.8 per 100,000 during the period 2006-2008 (150% increase).

Figure 1. Incidence rate (expressed per 100,000 population) of vertebral facture related emergency department visits in The Netherlands; 1986-1988 and 2006-2008.

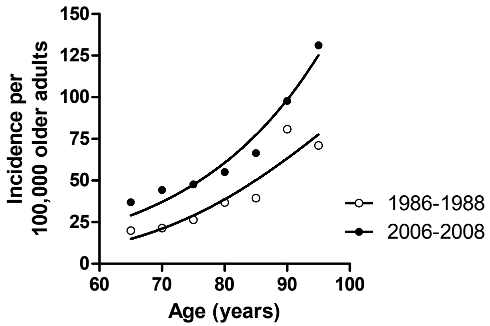
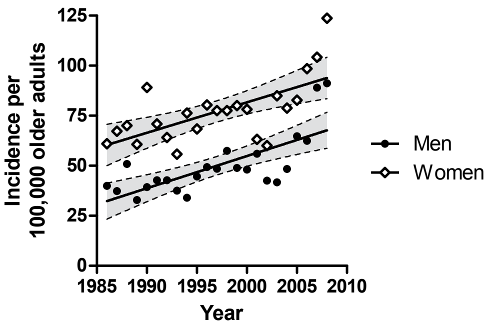


Figure 2. Age-adjusted incidence rate (expressed per 100,000 older persons) of vertebral fracture related emergency department visits in persons 65 years and older, The Netherlands, 1986 throughout 2008



The line indicates the age-adjusted incidence rate of ED visits due to a vertebral fracture and the gray area the 95% confidence interval of the linear regression analysis (Trend is significantly different as zero, *p*<.001 for both lines)

The overall age-adjusted incidence rate for ED visits due to vertebral fractures in older adults increased from 51.9 to 102.3 per 100,000 persons (increase 97%) throughout the study period. The age-adjusted incidence rate in women increased from 59.9 per 100,000 population in 1986 to 116.3 in 2008. For men the age-adjusted incidence rate increased from 39.7 in 1986 to 81.2 per 100,000 population in 2008 (Figure 2).

During the period 1991-2008 14,658 patients were admitted to the hospital after being diagnosed with a vertebral fracture at the ED. The absolute number of hospital admissions increased from 631 in 1991 to 1,389 in 2008 (120% increase). The overall percentage of patients admitted from the ED during the whole period was 56%. The percentage of hospital admissions did not change over time and remained between 50-55% for both men and women during the study period (Table 1).

The adjusted incidence rate of hospital admission after an ED visit for a vertebral fracture increased from 32.6 per 100,000 population in 1991 to 57.1 in 2008. The incidence rate increased most in the age group 85-89 years, from 46.2 per 100,000 population in 1991 to 152.0 in 2008 (229% increase).

Discussion

The aim of this study was to gain insight into secular trends of health care demand due to vertebral fracture related ED visits in the older Dutch population. From 1986 throughout 2008 the absolute number of vertebral fractures requiring an ED visit increased by 174% to over 2,500 ED visits per year. The age-adjusted incidence rate for ED visits nearly doubled (97% increase) over the last two decades. Especially a strong increase in vertebral fracture related ED visits was seen in individuals aged 80 years and over. The hospital admission rate for people diagnosed with a vertebral fracture at the ED remained fairly constant during the study period at about 55% for both men and women. In over 80% of the cases, the vertebral fracture was related to a fall incident.

Data on clinical-epidemiological characteristics of vertebral fractures are scarce and, as far as we are aware, this is the first study to report on national data regarding vertebral fracture related ED visits and hospital admissions with a study period of over two decades. Some studies with a shorter follow-up have examined incidence rates of vertebral fracture related hospital admissions.[2, 14] Vertebral fractures in Spain led to a hospitalization rate of 27.6 per 100,000 population for individuals aged ≥30 years in the year 2002, with a peak of 108.2 per 100,000 population among individuals aged 80 years and over.[2] The Spanish study showed that vertebral fractures affected predominantly women with a female:male ratio of 1.5:1, which is in line with our data. A second study from the United States reported on vertebral fracture related hospital admissions from 1993 throughout 2004. In this study the admission rate increased from 160.9 per 100,000 United States population in 1993 to 180.9 in 2004.[6] In addition, several studies examined the incidence rate of radiographical vertebral fractures in older individuals. In the Rotterdam Study, an ongoing cohort study in over 7,000 older individuals, the incidence of a radiographically diagnosed vertebral fracture in men aged 65-75 years was 5.1 per 1,000 person years. In men aged 75 years and over, the incidence rose to 9.3 per 1,000 person years. In women, the incidence was 17.0 in those aged 65-75 years and 19.6 per 1,000 person years in those aged 75 years and over.[7]

In the current study, numbers of fall-related and non-fall related vertebral fractures increased equally as strong. The observed increase in both fall- and non-fall related vertebral fractures might have several causes. An important cause for the observed increase in number of vertebral fractures might be the ageing of the population.[8] Nowadays people live longer, often with multiple medical problems.[9] Ageing and frailty are both risk factors for an increased fall risk and for osteoporosis, and could thus contribute to an increase in vertebral fracture incidence. In the present study, about 80% of the vertebral fractures diagnosed at the ED were fall related. In the literature it has been estimated that about 75% of all vertebral fractures that come to clinical attention are precipitated by routine daily activities such as bending, making beds or lifting (light) objects, and that only 25% of all vertebral fractures in older people is the result of a fall-incident.[10] It can be postulated that fall-related vertebral fractures are over-represented because the ED was taken as intake point in our study. Given the fact that a substantial proportion of the acute hospital care for vertebral fractures is fall-related, it seems plausible that in order to reduce the burden of vertebral fracture related acute admissions, the focus should not only be on the treatment of osteoporosis, but also on the reduction of falls in older persons.

While vertebral fractures are the most common osteoporotic fracture, hip fractures are the second most common osteoporotic fracture, and data on time trends of hip fracture is more readily available. Recent data on secular trends of incidence rates for hip fractures reported a trend break in incidence rates of hip fracture in the United States.[11] Since 1995, incidence rates of hip fracture started to decline in the American population aged ≥65 years, and similar results are reported in a Canadian study.[12] A similar trend break for vertebral fractures was not found in the current study.

The strength of the present study is the availability of continuous ED monitoring system for an extensive period of 22 years. Throughout the study period, no major policy changes that might have affected the increase in admission rates were introduced in The Netherlands. The Dutch health care system was, and continues to be, characterized by full health insurance coverage and full accessibility for the whole population. Furthermore, the coding system of the LIS did not change during the study period and takes place by official trained coding clerks. A limitation of the use of this linked administrative database is that it does not contain data regarding underlying diagnosis, co-morbidity, treatments or medication use. This hampers the interpretation of causal mechanisms behind the observed trends. Furthermore, readmissions in one calendar year were not excluded and could potentially have led to some “double registrations”. However, readmissions have been shown to contribute to only 2.6% of all injury related hospitalizations in The Netherlands.[21]

The true burden of vertebral fractures in the older Dutch population will probably exceed the numbers as presented in our study, since only a third of all vertebral fractures are currently diagnosed in clinical practice.[13] This low percentage is partly due to under-diagnosis, especially in the oldest old, and to the atypical presentation of patients with a vertebral fracture.[4]

In conclusion, the incidence rate of ED visits in The Netherlands due to a vertebral fracture in persons aged 65 years and over, doubled in the period from 1986 throughout 2008. The increase was most pronounced in the oldest old. A fall was the most frequent cause. This should be a further imperative to a pro-active approach in the diagnosis and treatment of osteoporosis and the prevention of falls in both men and women.

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Chapter 4

Fall-related mortality

Chapter 4.1

End of the spectacular decrease in fall-related mortality rate: men are catching up

K.A. Hartholt, S. Polinder, E.F. van Beeck, N. van der Velde, E.M.M. van Lieshout, P. Patka, T.J.M. van der Cammen

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Abstract

Objective
Determine time trends in numbers and rates of fall-related mortality in an aging population, for men and women.

Methods
Secular trend analysis of fall-related deaths in the older Dutch population (persons aged 65 years or older) from 1969 throughout 2008, using the national Official-Cause-of-Death-Statistics.

Results
Between 1969 and 2008, the age-adjusted fall-related mortality rate decreased from 202.1 to 66.7 per 100,000 older persons (decrease 67%). However, the annual percentage change (change per year) in mortality rates was not constant, and could be divided in three phases. First, a rapid decrease until the mid-eighties [men -4.1% (95%CI: -4.9; -3.2), women -6.5% (95%CI: -7.1; -5.9)]. Second, flattening of the decrease until the mid nineties [men -1.4% (95%CI: -2.4; -0.4), women -2.0% (95%CI: -3.4; -0.6)]. Third, stable mortality rates for women 0.0% (95%CI: -1.2; 1.3) and rising rates for men 1.9% (95%CI: 0.6; 3.2) over the last decade.

Conclusion
The spectacular decrease in fall-related mortality has ended, and is currently rising in older men to similar rates as seen in women. Due to the ageing society, absolute numbers in fall-related deaths are increasing rapidly.

Introduction

Unintended falls present a major public health problem worldwide.[1-3] The World Health Organization has estimated that approximately 392,000 people worldwide died due to an unintended fall in 2004.[4] According to the Centers for Disease Control and Prevention in the United States, unintended falls are the leading cause of fatal injuries among older adults.[5]

Falls in older adults mainly occur in or around the home and their cause is often multifactorial.[6] Risk factors associated with fall incidents include a higher age, female gender, use of fall-risk-increasing medication, and co-morbidities.[7] Approximately a third of all community-dwelling persons aged ≥65 years fall annually [7, 8] which leads to a high healthcare demand, morbidity and mortality.[2, 9-13] The incidence rate of falls is age- and gender dependent. The majority of falls and related injuries occur in older females (≥75 year).[9, 14, 15] Furthermore, the incidence rates of fall-related injuries among older adults increased over the past 30 years.[3] New guidelines and preventive strategies have been developed in order to reduce falls among older adults.[16]

Absolute numbers of fall-related deaths are rising due to ageing societies worldwide.[17] In The Netherlands, the absolute number of persons aged ≥65 years is expected to double, up to 25% of the population in 2040 (15% in 2008).[18] The figures of aging societies are comparable to worldwide trends.[19] Due to the expanding older population, based on an increasing life expectancy, an increase in absolute numbers of fall-related deaths might be expected in the near future. In order to investigate how fall-related mortality in persons aged ≥65 years developed over time in The Netherlands, absolute numbers of fall-related deaths and adjusted mortality rates corrected for demographic changes were quantified from 1969 throughout 2008. In the older population, significant health differences between both genders have been demonstrated[20] and it is known that temporal trends in disease mortality may show large gender differences as well.[21, 22] Therefore, separate analyses for males and females were conducted, which were further specified by age-group.

Methods

Mortality data were obtained from the public accessible electronic database[23] of the Statistics Netherlands (CBS), including the Official-Cause-of-Death-Statistics (OCDS), in which the data is stored in 5-year age-groups for both genders during the study period. Data on unintended fall-related deaths of persons aged ≥65 years were collected between 1969 and 2008. An unintentional fall was defined using the International Classification of Diseases of the World Health Organization (8^{th} revision, code E880-E887; 9^{th} revision, code E880-E888; 10^{th} revision W00-W19, X59.0), *i.e.*, slipping, tripping and stumbling.

The Statistics Netherlands collects mortality data with a uniform classification system and has almost complete national coverage (99.7% in 2008). The OCDS is based upon the registration of the cause of death, by an official death certificate, which is required in all cases of death.[24] A death certificate may only be completed by the consulting physician who declares the patient dead or by a coroner. The death certificate includes data on age, gender, location, cause of death and co-morbidities that contributed to the death. Completeness and acceptability of the death certificates is verified with the national birth registry. In cases of uncertainty, the physician who completed the death certificate is contacted to provide additional information. In case of a non-natural death (*e.g.*, traffic accident, fall, or suicide) the coroner can perform an official autopsy to determine the official cause of death.

Numbers of fall-related deaths were specified for age and gender. The age-specific mortality rates were calculated in 5-year age groups using the number of the fall-related deaths in that specific age group, divided by the population size within that specific age-group for male and female patients, and was expressed per 100,000 persons in that age-group. Age-adjusted incidence rates allowed us to compare the incidence rate for a standardized population during the study period, and were performed by "Direct Standardization" to correct for demographic changes throughout the study. The age-adjusted incidence rate is therefore the outcome of interest. The mid-year population was used for each year of the study. Data on demographics were obtained from the Statistics Netherlands. Mortality data were absolute numbers covering the whole Dutch population.

Statistical analysis

In order to model the trend in fall-related mortality, a regression model with Poisson error and log link was built with log mid-year population size of each year of the study as offset factor. This model gives evidence of increasing linear trends, stable trends over time, or decreasing trends. To assess whether the trend was stable, or changed during the study period, a Joint-Point regression analysis was used. This analysis identifies points where a statistically significant change over time occurred in the linear slope of the trends in fall-related mortality rates (Join-Point Regression Program, Version 3.4.3. Statistical Research and Applications Branch, National Cancer Institute, USA). The Joint-Point function accommodates piecewise linear fits, connected with one another at the best Joint-Point[25], and showed the necessity for assuming a spline instead of a simple linear model. In Joint-Point analysis, the best-fitting points correspond to where the rate changes significantly (*i.e.*, increases or decreases). The analysis starts with the minimum number of joint points and tests whether one or more joint points are statistically significant in the model and should be added. In the final model, each joint point indicates a statistically significant change in trend, and an annual percentage change is computed for each of those segments by means of generalized linear models assuming a Poisson distribution. The best joint points were used for the analysis, and divided the study in three periods (1969-1983; 1984-1996; 1997-2008). The parameter for calendar year, corrected for gender and age-group was transformed into Percentage Annual Change (PAC). Interactions of the spline for gender were added and tested in order to investigate differences in trends for genders. Statistical analyses were performed using SPSS software (version 16.1.1). A p-value <0.05 was considered as statistically significant.

Table 1. Absolute number of fall-related mortality in the Dutch population, 1969-2008

	<65 year		65-69 year		70-74 year		75-79 year		80-84 year		≥85 year		Total
Period	**η**	**%**	**η**	**%**	**η**	**%**	**η**	**%**	**η**	**%**	**η**	**%**	**η**
1969-1974	1,322	10.7	525	4.2	960	7.8	1,906	15.4	3,087	24.9	4,577	37.0	12,377
1975-1979	831	9.0	355	3.8	632	6.8	1,267	13.7	2,178	23.5	3,989	43.1	9,252
1980-1984	774	9.6	257	3.2	490	6.1	1,027	12.8	1,700	21.1	3,804	47.2	8,052
1985-1989	729	9.6	207	2.7	375	5.0	864	11.4	1,505	19.9	3,879	51.3	7,559
1990-1994	704	8.9	189	2.4	369	4.7	807	10.3	1,480	18.8	4,320	54.9	7,869
1995-1999	846	10.6	231	2.9	417	5.2	844	10.6	1,451	18.2	4,176	52.4	7,965
2000-2004	1,068	11.4	269	2.9	476	5.1	1,052	11.2	1,726	18.4	4,794	51.1	9,385
2005-2008	813	10.0	257	3.2	430	5.3	846	10.5	1,583	19.6	4,162	51.4	8,091
Total	7,087	10.0	2,290	3.2	4,149	5.9	8,613	12.2	14,710	20.9	33,701	47.8	70,550

Table 2. Age-specific incidence rates of fall-related mortality in the older Dutch population per 100,000 persons, 1969-2008

	≥65 year	65-69 year		70-74 year		75-79 year		80-84 year		85-89 year		90-94 year		≥95 year	
Period	**Overall**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**
1969-1974	129.5	18.3	17.5	38.9	45.2	94.6	140.7	242.7	414.8	504.7	867.4	1,062.7	1,617.0	1,727.9	2,713.3
1975-1979	110.0	15.5	11.9	30.3	29.2	73.0	93.8	193.0	279.6	409.0	681.2	862.5	1,268.5	1,565.9	2,223.0
1980-1984	87.0	11.3	8.0	23.7	20.0	59.5	62.0	149.9	174.9	338.1	449.9	721.9	915.4	1,311.1	1,702.7
1985-1989	75.0	9.2	5.4	18.3	14.1	53.7	43.3	129.5	126.1	311.4	327.1	733.7	753.1	1,457.0	1,319.2
1990-1994	72.7	7.7	4.7	16.7	12.7	47.7	38.4	123.6	109.2	298.3	305.1	670.4	717.5	1,323.9	1,330.3
1995-1999	67.9	9.4	5.4	17.6	13.3	46.5	36.2	108.8	103.6	274.2	251.8	596.1	580.3	1,294.5	1,202.4
2000-2004	75.2	10.4	6.2	20.4	13.8	51.1	42.8	124.5	106.5	294.7	264.7	659.1	603.4	1,405.0	1,162.6
2005-2008	76.7	11.2	7.0	24.0	13.5	54.0	37.5	132.4	107.7	292.8	248.7	784.6	548.7	1,357.8	1,048.4

Results

General information

The population aged ≥65 years increased from 1.3 million in 1969 to 2.4 million in 2008, representing 10.0% and 14.7% of the Dutch population, respectively. Approximately 90% (63,463) of all fall-related deaths in The Netherlands during that time-span occurred in the population aged ≥65 years (Table 1).

Absolute numbers

The absolute number of fall-related deaths in persons aged ≥65 years annually decreased from 1,927 in 1969 to 1,312 deaths in 1985, but since the mid 1980's the number of deaths has shown a persistent increase to 1,892 in 2008 for men and women together (Figure 1). The majority of fall-related deaths occurred in the population aged ≥85 years, which represented an increasing share in the proportion of fall-related mortality among older persons, from 37% in 1969 to over 50% since 1985 (Table 1).

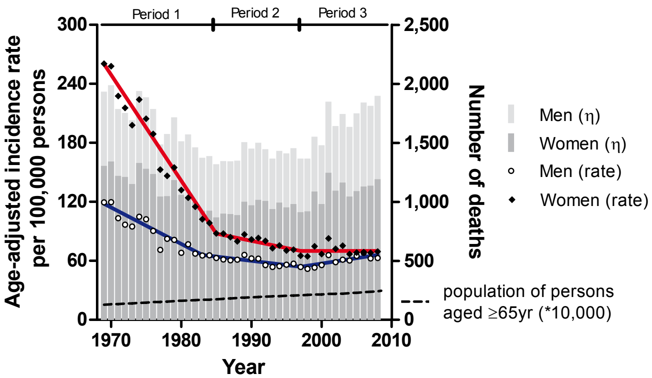
Gender and age-specific mortality rates

Gender and age-specific fall-related mortality rates in persons aged ≥65 years decreased in all age-groups, both for men and women throughout the study period. However, age-specific rates of fall-related mortality increased with age, and continued to be highest among adults over 95 years for both men and women (Table 2).

Trends in age-adjusted mortality rates for males and females

During the whole study period (1969-2008) the PAC for the age-adjusted fall-related mortality rate decreased with -1.54% (95% CI: -1.66; -1.43, $p<0.001$) per year in older men and by -3.61% (95% CI: -3.69; -3.53, $p<0.001$) per year in older women. The Joint-Point regression analysis revealed that the PAC in mortality rate was not stable over time and can be divided in three phases (see Figure 1)

Figure 1. Absolute number of fall-related deaths and age-adjusted fall-related mortality rates in persons ≥65 years in The Netherlands 1969-2008



The Percentual Annual Change (95% CI) was:
Period 1: rapid decrease, men [1969-1983] -4.1% (-4.9; -3.2), and women [1969-1985] -6.5% (-7.1; -5.9);
Period 2: flattening decrease, men [1984-1996] -1.4% (-2.4; -0.4), and women [1986-1996] -2.0% (-3.4; -0.6);
Period 3: slight increase men [1997-2008] 1.9% (0.6-3.2), stabilized rate women [1997-2008] 0.0% (-1.2; 1.3)

Until the mid-eighties the PAC in mortality rates due to a fall decreased strongly in both men (-4.1%, 95% CI: -4.9; -3.2, p<0.001) and women (-6.5%, 95% CI: -7.1; -5.9, p<0.001). Subsequently, after that period until the mid-nineties the decrease leveled off in both men (-1.4%, 95% CI: -2.4; -0.4, p<0.001) and women (-2.0%, 95% CI: -3.4; -0.6, p<0.001). Finally, over the last decade, the age-adjusted mortality rate remained stable among older women (0.0%, 95% CI: -1.2; 1.3, p=0.97) and started to rise again in older men (1.9%, 95% CI 0.6; 3.2, p=0.005).

In 1969, the age-adjusted mortality rate for women (260.4 per 100,000 persons) was twice as high as for men (119.4 per 100,000 persons). However, the rates for men are catching up with those of women. In 2008 the age-adjusted mortality rates were 69.8 per 100,000 older women and 62.8 per 100,000 older men (Figure 1).

Discussion

This observational study was based upon the OCDS of the Statistics Netherlands. The aim was to determine secular trends in fall-related mortality in persons ≥65 years. The spectacular reduction in the age-specific and age-adjusted fall-related mortality rate in the seventies and eighties of the previous century has ended in the mid-nineties. Moreover, since then, mortality rates due to falls are rising among older men to similar rates as seen for women.

A strength of this study is the accurate OCDS monitoring of nearly all deaths in The Netherlands (99.7% in 2008), which allowed us to assess long-term trends over an extensive period of 40 years, covering the whole Dutch population. Since the database is verified with the national birth registry,[24] the mortality rates and numbers presented are real figures rather than estimates of the entire older Dutch population.

Petridou *et al.* found decreasing trends in unintended fall related mortality rates in persons aged 65 years and older for most European countries, but this study did not go beyond 2002 and may have been conducted too early to pick up unfavorable trends within the first decade of the 21st century.[26] Similar trends in fall-related mortality as observed in our study were seen in Finland, with a recent increasing trend for men and a stable rate for women.[27] The observed change in the trend in fall-related mortality rates in the final period of our study might be explained by an increasing life expectancy, which is accompanied by a prolonged period of co-morbidities and disabilities.[28] Our hypothesis is that the fall-related mortality mainly occurs among older adults who are frail, resulting in an increased fall-risk and less functional reserve to cope with the consequences of falls. It is not likely that migration has significantly affected the observed mortality trends to a large extent, since the proportion of migrants is only 4% of the older Dutch population and no significant differences in fall-related mortality by ethnic background exist in The Netherlands.[29]

Although the age-specific mortality rates remained highest among women, the mortality rates of men are catching up to the mortality rate of women. A possible explanation for this finding could be that the life expectancy in men increased more rapidly than in women over the last decades, resulting in a smaller gap in the life expectancy between men and women.[28] Consequently, men become more vulnerable for age-related (co)morbidities over a prolonged period of life. This assumption is supported by our previous report on a more rapid increase in fall-related hospitalizations in older men than in older women in The Netherlands.[3, 30] Since age itself is an independent risk factor for falls,[31] the number of falls will grow with an increasing life expectancy.

The shift in mortality rates could also be based upon gender-specific injury patterns that have been demonstrated for men and women.[9] Fractures are the main fall-related injuries in women. Fracture treatment, especially for hip fractures, has improved rapidly over the last decades, and might have contributed to the decreasing fall-related mortality rates. Men however, present more often with severe skull-brain injuries,[1] with fewer therapeutic options. These gender-specific injury patterns, together with the differential increase in life expectancy, may have contributed to the (near) closure of the gap between the fall-related mortality rates between men and women.

A limitation of the current study is that the numbers and incidence rates of fall-related mortality among older Dutch adults might not be directly generalizable to other populations. However, absolute numbers and rates of fall-related mortality also increased in the USA[32] and Finland[2] over recent years, which shows that our findings are not unique and could possibly indicate a universal phenomenon for western countries. Further studies are required to show similar trends for other countries.

In addition, during the study period, new versions (9^{th} and 10^{th} revision) of the ICD classification system were published and implemented in the OCDS, which may have led to changes in the coding of subgroups of falls. The code for "falls" in the ICD 8^{th} and 9^{th} revision included a category "Fractures unspecified". In the ICD 10^{th} revision, this code has been replaced by code X59.0 (*i.e.*, fracture, cause unspecified). Analysis of coroner reports by Statistics Netherlands has shown that nearly all fractures contributing to the mortality cases in older adults are caused by a fall. Because of these findings, after introduction of ICD10, Statistics Netherlands decided to include all cases with the code X59.0 within the category of falls. In our study we followed this decision and included all codes X59.0 in the analysis to avoid artificial trend interruptions in our time series analyses due to changes in registration practice and/or coding. However, the WHO and Euroipn analytical databases do not include X59.0 in the category of falls, which must be considered and comparing our findings with studies using these databases.

For comparative purposes, a sensitivity analysis of trends in fall-related deaths was conducted from the introduction year of ICD10 (1996) onwards under different assumptions concerning the cause of fractures, cause not specified (X59.0). The sensitivity analysis showed that the addition of the code X59.0 did not inflate our time trend figures, but has instead produced a conservative estimate of unfavorable developments in the most recent period of our study (1997 – 2008).
Mortality rates are a combination of injury incidence and case-fatality rates.[33] In a

recent study we have shown that the incidence of severe fall-related injuries requiring hospitalization increased with 61% to over 30,000 annually in The Netherlands between 1981 and 2008.[3] The decreasing rate of fall-related mortality makes it therefore likely that the case-fatality rate of fall incidents has dropped. The decrease might be explained by several factors. During the study period new diagnostic tools like Computed Tomography and Magnetic Resonance Imaging have been introduced. Also standardized protocols for treatment of trauma patients at the Emergency Department have been introduced, such as the Advanced Trauma and Life Support.[34] Furthermore, new and better treatment possibilities were developed during the study period, *e.g.*, osteosynthesis material and Intensive Care Units. The possible effects of all these factors cannot be specified, but it is unlikely that the introduction of falls prevention guidelines had a strong effect on fall-related mortality, since the guidelines were only introduced in The Netherlands after the year 2000.[35] Fall-risk and hence fall-related mortality in general, may be rising because of increased mobility of frail elderly, due to the use of walking aids and other equipment (*i.e.* electric mobility scooters), which is seen in among others The Netherlands and the United States.[36, 37] As a result of sustained walking abilities, these older persons remain at risk for fall incidents. Another potential cause that has been shown to contribute to an increased fall-risk in older adults, is a more active lifestyle (*e.g.*, sports participation).[38]

In conclusion, the spectacular decrease in fall-related mortality since 1969 has ended around the mid-nineties. Currently the mortality rates in women are stable and they are increasing in older men. Falls are expected to become an even more serious cause of death in the near future due to aging societies worldwide. In recent years, the health care system has not been able to compensate fully for the ageing society and for rising numbers of fall-related injuries. These findings indicate the need for further research identifying factors which can be used to reduce fall-related mortality among older adults and to control for the recent unfavorable trend.

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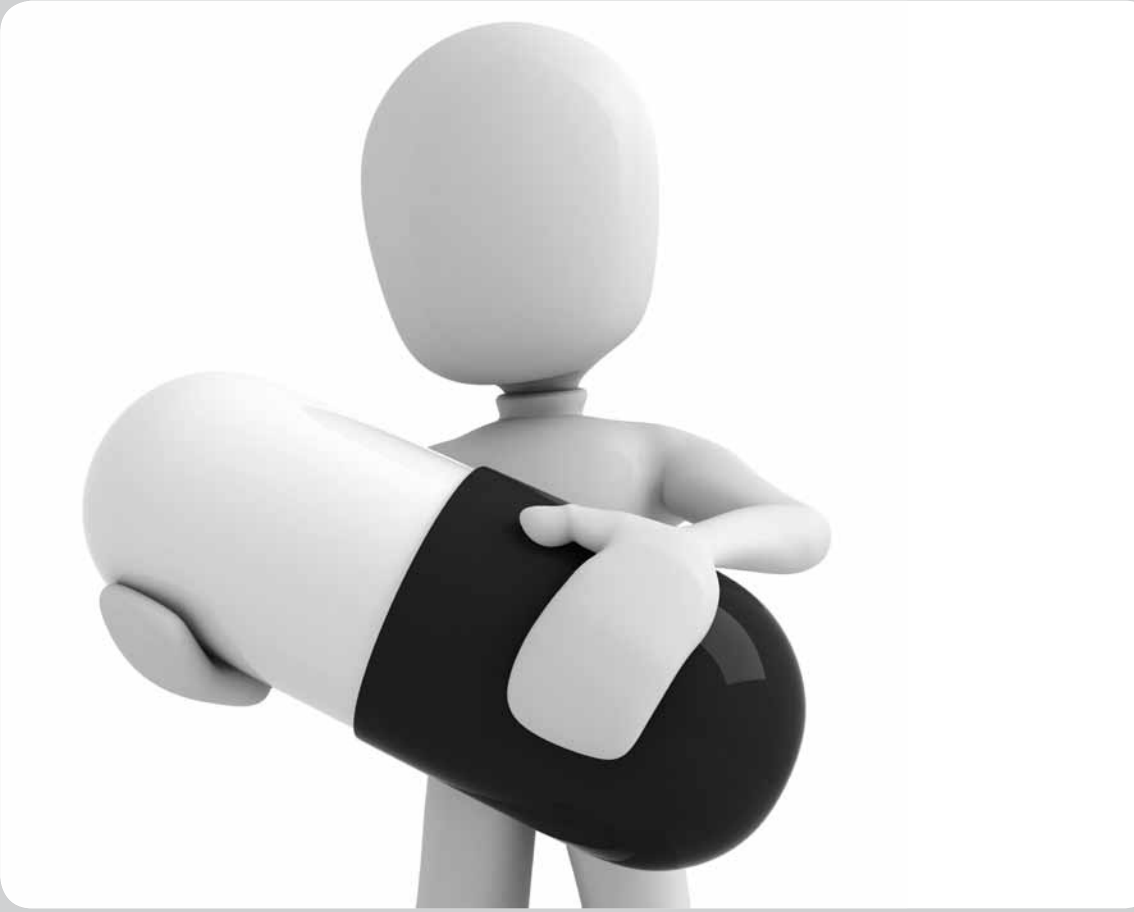
Chapter 5

Drugs and falls

Chapter 5.1



[Cost]effectiveness of withdrawal of fall-risk increasing drugs versus conservative treatment in older fallers: design of a multicenter randomized controlled trial (IMPROveFALL-study)

K.A. Hartholt, N. van der Velde, E.M.M. van Lieshout, S. Polinder, O.J. deVries, N.D.A. Boyé, A.J.H. Kerver, G. Ziere, M.M.M. Bruijninckx, M.R. de Vries, F.U.S. Mattace-Raso, A.G. Uitterlinden, E.F. van Beeck, P. Lips, P. Patka,T.J.M. van der Cammen

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Abstract

Background
Fall incidents represent an increasing public health problem in aging societies worldwide. A major risk factor for falls is the use of fall-risk increasing drugs. The primary aim of the study is to compare the effect of a structured medication assessment including the withdrawal of fall-risk increasing drugs on the number of new falls versus "care as usual" in older adults presenting at the Emergency Department after a fall.

Methods/Design
A prospective, multi-center, randomized controlled trial will be conducted in hospitals in The Netherlands. Persons aged ≥65 years who visit the Emergency Department due to a fall are invited to participate in this trial. All patients receive a full geriatric assessment at the research outpatient clinic. Patients are randomized between a structured medication assessment including withdrawal of fall-risk increasing drugs and "care as usual". A 3-monthly falls calendar is used for assessing the number of falls, fallers and associated injuries over a one-year follow-up period. Measurements will be at three, six, nine, and twelve months and include functional outcome, healthcare consumption, socio-demographic characteristics, and clinical information. After twelve months a second visit to the research outpatient clinic will be performed, and adherence to the new medication regimen in the intervention group will be measured. The primary outcome will be the incidence of new falls. Secondary outcome measurements are possible health effects of medication withdrawal, health-related quality of life (Short Form-12 and EuroQol-5D), costs, and cost-effectiveness of the intervention. Data will be analyzed using an intention-to-treat analysis.

Conclusions
The successful completion of this trial will provide evidence on the effectiveness of withdrawal of fall-risk increasing drugs in older patients as a method for falls reduction.

Background

Falls constitute one of the most common and serious public health problems in older populations. Fall incidents are associated with considerable morbidity and mortality.[1-3] Even a low energetic trauma, such as an unintended fall, can lead to major injuries in older adults with long-term consequences.[4, 5] The incidence of falls and the severity of fall-related complications rises steeply beyond the age of 65 years.[1, 2, 4-6.] Approximately 72,000 older adults visit an Emergency Department in The Netherlands each year due to a fall. Over 30,000 are hospitalized, and nearly 1,600 elderly die due to a fall per year.[7, 8] The large burden of fall-related healthcare consumption is leading to high healthcare costs in western societies.[5, 9, 10] Over the past decades several risk factors for falls have been identified. Major risk factors include one or more previous falls, mobility impairments, high age, and the use of fall-risk increasing drugs.[11, 12] The majority (73%) of older persons use one or more drugs.[13] In 2008, nearly half of all drug prescriptions in The Netherlands were delivered to persons aged 65 years and older who constituted only 15% of the Dutch population in that year.[14] Adverse Drug Reactions are frequently seen in older adults.[15] A meta-analysis of observational studies showed an increased fall risk with certain drug groups, *i.e.*, psychotropic.[16] and cardiovascular drugs.[17] Approximately three-quarters of the community dwelling elderly used at least one prescribed drug, and about a third used at least one fall-risk increasing drug.[13]

There is evidence that withdrawal, reduction, or substitution of fall-risk increasing drugs can reduce fall risk in older adults. Only one small, randomized controlled trial on drug withdrawal has been performed.[18] Campbell *et al.* found that withdrawal of psychotropic medication significantly reduced the risk of falling, but permanent withdrawal proved very difficult to achieve. Therefore the authors made recommendations for a larger randomized controlled trial (RCT) to study the single effect of drugs assessment and drugs modification on fall risk. A recent prospective cohort study with a two-month follow-up period showed that the withdrawal of fall-risk increasing drugs was associated with a reduction in falls.[19]

Furthermore, an increased susceptibility to certain adverse drug reactions may partly be due to genetic polymorphisms that alter responses of individual persons to various drugs. A possible cause might be the pathway of hepatic drug metabolization by the cytochrome P-450 family of biotransformation enzymes.[20] Consequently, poor, extensive and ultra-rapid metabolizers for certain cytochrome pathways and membrane bound transporters can be distinguished,[21] which influence the pharmacodynamics and pharmacokinetics. The majority of fall-risk increasing drugs are metabolized by a small number of enzymes, the major ones being CYP450 2D6, 2C9, 2C19 and 3A4/5.[22] Due to polypharmacy among older adults, the risk of a CYP 450 interaction increases.

A systematic fall-related drugs assessment combined with medication changes and a one-year follow-up assessment among older fallers may contribute to a reduction in the incidence of new falls and related consequences.[19] At this moment a structured medication assessments are not part of standard care of older fallers presenting at the Emergency

Department. In The Netherlands, the current care of fall-related injuries consists of treatment of the injuries of the fall. However, before a systemic fall-related medication assessment can be incorporated in the routine work-up of older persons presenting with a fall, further evidence is required. The aim of this randomized controlled trial is to compare the effect of withdrawal of fall-risk increasing drugs versus "care as usual" on future falls. The primary outcome of this study is be the number of new falls and fallers. Secondary outcome measurements are possible health effects of medication withdrawal, health-related quality of life, costs, and cost-effectiveness of the intervention.

Methods

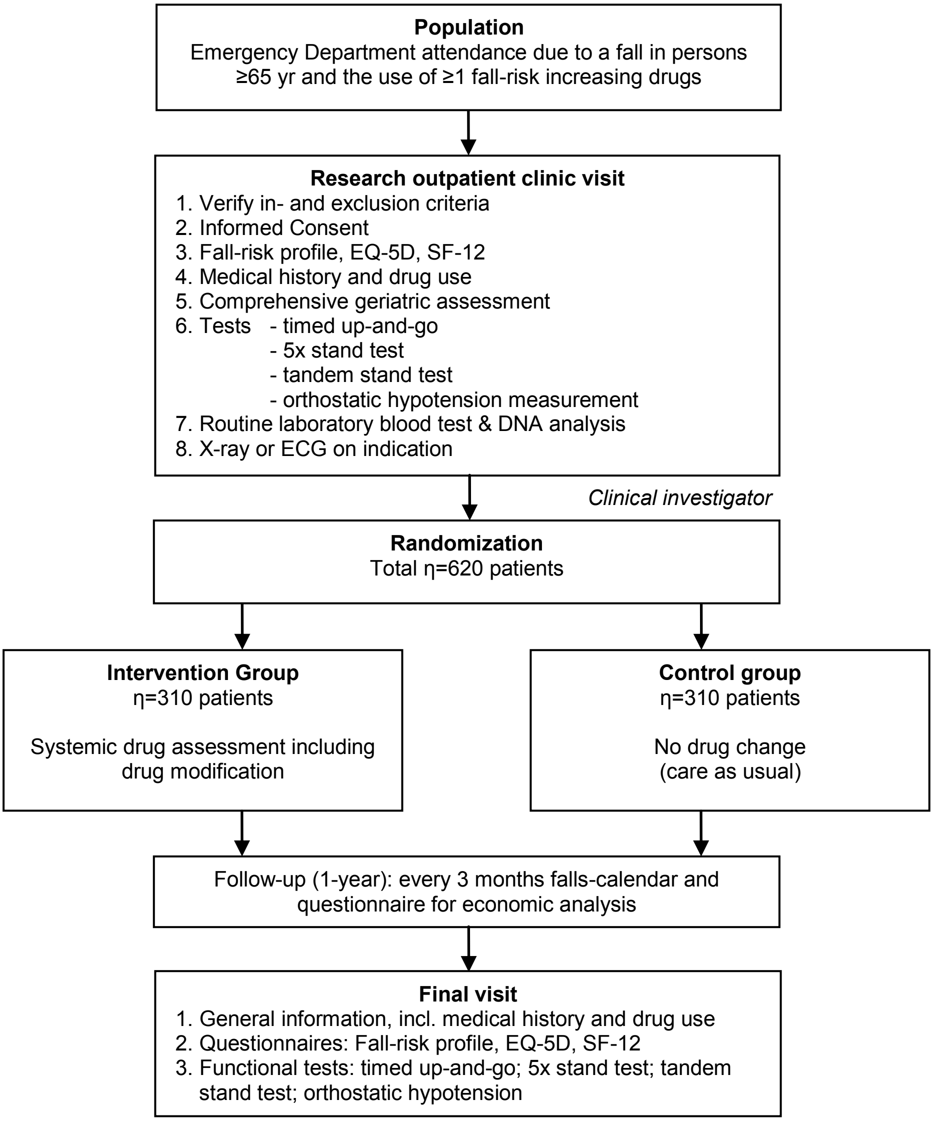
The study is designed as a multicenter RCT with a one-year follow-up period in The Netherlands. The Medical Ethics review board of the Erasmus MC, University Medical Center, approved the study protocol. The study started in October 2008.

Study population
Patients aged 65 years and over, who visit the Emergency Department of a participating hospital due to a fall, are eligible for inclusion. A fall is defined as coming to rest unintentionally on the ground or a lower level with or without losing consciousness, but not induced by acute medical conditions, *e.g.*, stroke, or exogenous factors such as a traffic accident.[23]

Patients meeting the following inclusion criteria are eligible for enrollment:
1. Aged 65 years or older (no upper age limit)
2. Attended the Emergency Department due to a fall incident
3. Taking one or more fall-risk increasing drugs for at least two weeks prior to the fall
4. Mini-Mental State Examination score of 21/30 points or over
5. Able to walk independently
6. Community dwelling
7. Provision of informed consent by patient

If any of the following criteria applies, patients will be excluded:
1. Patient participation in another trial
2. Fall not meeting criteria of specified definition
3. Likely problems, in the judgment of the investigators, with maintaining follow-up (*e.g.*, patients with no fixed address)
4. Not willing to complete the research protocol (such as attending at a follow-up visit)

Figure 1. Flow Chart



Procedure

All persons visiting the Emergency Department due to a fall receive care as usual for their injuries. Within two weeks following the Emergency Department attendance, patients are contacted by telephone with information about the study (Figure 1).

All eligible study participants will receive written information about the study and all interested patients will receive an appointment for the research outpatient clinic. The visits to the outpatient clinic take place within two months after Emergency Department attendance. If the patient meets all eligibility criteria and no exclusion criteria are present at the research outpatient clinic, the patient will be asked to sign the Informed Consent Form before the study procedures take place. Patients who do not meet the inclusion criteria will be excluded. During the outpatient clinic visit a record is made of the Falls Risk Profile (FRP), falls history, Health-Related Quality of Life (HRQoL) and physical performance are measured of all study participants. Furthermore, a geriatric assessment and a standardized medication assessment will take place. Eligible patients will be randomized to one of the treatment arms, the intervention group versus "care as usual". The aim in the intervention group will be to reduce fall-risk increasing drugs, and in the "care as usual" group no (medication) change will be made. All included participants receive a Falls Calendar for reporting falls during a one-year follow-up period as well as a cost-evaluation form at three, six, nine and twelve months after the first research outpatient clinic visit. One year after the first visit, the study participants are invited for a final visit to the research outpatient clinic in order to reassess the FRP, falls history, HRQoL, and physical performance. Adherence to their medication is also evaluated. After the final visit to the outpatient clinic a brief letter concerning the study start and completion will be sent to the patient's General Practitioner. Table 1 shows the chart of events of this study.

Table 1. Schedule of events

	Screening	1st visit	3 months	6 months	9 months	12 months
Telephone call	X					
Information package	X					
Informed Consent		X				
Randomization		X				
Baseline data		X				
EQ-5D		X				X
SF-12		X				X
FRP		X				X
Orthostatic hypotension test		X				X
Complications			X	X	X	X
Falls calendar			X	X	X	X
Healthcare consumption			X	X	X	X
ADL		X				X
Physical functioning (VAS)		X				X

EQ-5D, EuroQol 5-D questionnaire; SF-12, Short Form-12; FRP, Fall Risk Profile; ADL, Activities of Daily living; VAS, Visual Analogue Scale.

Randomization

Participants will be allocated to one of two treatment arms using a web-based randomization program that will be available 24 hours a day. Variable block randomization will be accomplished via a trial website. Allocation will be random. It is not possible to blind the geriatrician and patients for the allocation of the study group.

Intervention

The single intervention will consist of a systematic fall-related medication assessment combined with drug withdrawal or modification, if safely possible. Fall-risk increasing drugs, as defined in the literature,[16, 17, 19, 24] will be stopped, reduced or substituted with potentially safer drugs in the intervention group. A complete list of fall-risk increasing drugs, based on current literature, is shown in Table 2.

Table 2. Drugs classified as fall-risk increasing drugs in the IMPROveFALL-study

Category	Drug type
Central nervous system	Anxiolytics/hypnotics (benzodiazepines and others); antidepressants (tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors and monoamine oxidase inhibitors), neuroleptics (dopamine D2-receptor agonists and serotonin dopamine receptor antagonists)
Cardiovascular	Antihypertensives (diuretics, beta-adrenoceptor blockers, alpha-adrenoceptor blockers, centrally acting antihypertensives, calcium channel blockers, angiotensin converting enzyme inhibitors and angiotensin receptor blockers); Anti-arrhythmic drugs (Antiarrhythmics, nitrates, digoxin, vasodilators)
Anti-inflammation	NSAIDs
Gastro-Intestinal	Antacids (H-2 receptor antagonists)
Analgesics	Opioids
Pulmonary	Sympathomimetics, anti-histaminics
Diuretics	Thiazide diuretics, loop diuretics

For each drug, the clinical investigator will assess whether the initial indication still exists. Proposed changes in medication will be discussed with a senior geriatrician and the participant's General Practitioner and with the prescribing doctor if other than the General Practitioner. If consensus is obtained, fall-risk increasing drugs will be discontinued when considered redundant, reduced in dose over a one-month period, if safely possible, or substituted for potentially safer drugs if necessarily and available. For each drug modification, the clinical investigator will follow the standardized instructions of the Dutch National Formulary,[25] and a clinical pharmacologist will be available for advice when needed. A research nurse will offer counseling and evaluate possible negative effects by weekly telephone calls over a period of 1 month, and discuss any problems with the clinical investigator and the geriatrician (project leader).

Outcome measures

The primary outcome measure will be the incidence of new falls, fallers, based on the Falls Calendar. Secondary outcome measures will be fall-related injuries, generic health-related HRQoL, compliance, Quality Adjusted Life Years (QALY), genetic polymorphisms associated with increased adverse drug reactions, and positive or negative health effects, cost, and cost-effectiveness.

Measurements

Medication use

Medication use will be assessed by registering the drug names directly from the medication packaging. For each drug, both prescription and over-the-counter (OTC), the name, intake frequency, dosage, start and stop dates, and whether the drug was prescribed before or after the fall will be registered. The information will be verified and compared with data retrieved from the patients' General Practitioner and local pharmacist.

Quality of life

The level of independency of the Activities of Daily Living (ADL) will be examined using the Barthel Index (ranging from zero for full independency to 20 for full dependency.[26] Quality of life will be measured using the Dutch version of the SF-12 and EQ-5D (EuroQol) questionnaire. The EQ-5D has been designed by the Euro-HRQoL Group to assess the experienced general quality of life in large populations in order to provide a simple, generic measure of health for clinical and economic appraisal [27]. The EQ-5D questionnaire covers five health domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a Visual Analogue Scale (VAS) to record the current experienced health status. The EuroQol (EQ-5D) is a validated and extensively used general health questionnaire to measure quality of life.[28, 29] It is recommended for the assessment of HRQoL in trauma patients, especially for economic assessments.[30] The SF-12 contains 12 questions and has been designed and validated to assess the quality of life in large population studies.[31, 32] Fall-risk will be assessed using a validated FRP.[33] The FRP contains five questions, two measurements (handgrip strength and body weight), and two interacting items. Hand grip strength will be measured using a digital strain-gauged dynamometer (Takei TKK 5401, Takei Scientific Instruments Co, Ltd., Tokyo, Japan). Body weight will be measured with a calibrated beam scale. For each item points are scored and summed (range 0-30), where zero represents a low risk of recurrent falling and 11 and over indicates a high risk of recurrent falling (2 or more falls in the next 12 months).[33]

Physical performance

In order to assess the physical activity, three tests will be conducted. First, the chair stand test, which is a standardized test in which the participant stands up and sits down five consecutive times. The patient is not permitted to use the chair's arms supports during standing up or sitting down.[34] The Timed Up-and-Go test (TUG-test) will be conducted, in which the participant has to stand up from sitting position and walks three meters along a line, perform a 180 degree turn and walk back to the chair and sit down.[34] A tandem stand test will be used in order to assess balance. The test will be performed in standing position, in which the patient has to stand fully independently for 10 seconds with both feet in front of each other, and is scored as correct or failed. All three mobility tests are conducted twice, and the best time (where appropriate) will be used.

Orthostatic hypotension will be measured by using a calibrated sphygmomanometer, in supine position followed by five minutes standing straight up. The blood pressure will be measured in supine position and after one, two, three, four, and five minutes standing. The blood pressure is registered in millimetres of mercury (mmHg), heart rate in beats per minute. Orthostatic hypotension is defined as a decrease of 20 mmHg systolic or a decrease of 10 mmHg diastolic in standing position.[35]

Costs

The total direct and indirect costs of both fall-risk increasing drugs withdrawal and "care as usual" will be measured. All analysis will be performed in accordance with Dutch guidelines for economic evaluations.[36] Direct healthcare costs include the additional costs of the systematic fall-related drugs assessment and modification, drug consumption (including the costs for substitution drugs), and fall-related and non-fall-related healthcare consumption during one year of follow-up (*e.g.* General Practitioner, outpatient visits, and hospital admissions).

Real medical costs are calculated by multiplying the volumes of health care use with the corresponding unit prices. For the intervention (systematic fall-related drugs assessment) the full cost price will be calculated and for the other health care costs standard cost prices will be used as published by Oostenbrink.[36] The full cost price of patient identification at the Emergency Department and the systematic fall-related drugs assessment will be determined based upon time measurements and employment of personnel. Costs of medication use will be recorded in the study, and unit costs will be determined with information from the National Dutch Formulary.[25]

Healthcare consumption, both fall and non-fall related, and patient costs will be recorded from the Hospital Information System for hospital care, and three-monthly questionnaires for other healthcare and patient costs. These will be supplemented with data on healthcare costs of injury from previous research.[9] The number of injuries prevented will be calculated with data recorded in the study, supplemented with epidemiological data on falls and injury risks.

Cost-effectiveness will be assessed by calculating the incremental cost-effectiveness ratio, defined here as the difference in average costs between medication assessments including withdrawal of fall-risk increasing drugs and "care as usual" and by the difference in prevented fall-related injury. Secondary, a cost-utility analysis will be performed, *i.e.*, as cost per QALY. Policy makers and health economists have proposed that costs varying from €25,000 up to €75,000 per QALY may be considered as acceptable.[37, 38]

The QALY combines mortality and morbidity into a single number. The morbidity component is referred to as HRQoL and is based on a descriptive health-state measure. Because of a long track record in health economic analyses, the EQ-5D measure will be used for this purpose.[28] Furthermore, the lifetime health effects (cardiovascular events such as myocardial infarction, stroke, and mortality) due to possible increased cardiovascular risks (*i.e.*, cardiac failure, rebound hypertension) will be calculated with existing models for cardiovascular disease risk management. In accordance with guidelines for differential discounting, effects will be discounted at a rate of 1.5% and costs at 4% per year.[39]

Full blood for DNA isolation will be drawn during the first visit (5 mL). The blood will be stored at -80 degrees Celsius, until DNA-isolation will take place. After DNA isolation, polymorphisms (CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1 en CYP3A4) will be analyzed using the TaqMan allelic discrimination assays on the ABI Prism 9700 HT sequence detection system. If needed, other polymorphisms will be added to the analysis.

Follow-up

Patients will be followed for one year. After the first visit to the research outpatient clinic patients receive a Falls Calendar.[33] During a one-year follow-up period, the participant will be asked to record every week whether they have experienced a fall that week. The 3-monthly calendar sheet will be returned once per 3-months by mail. Cost-effectiveness will be measured using a cost-evaluation questionnaire. Participant can register the number of visits to physicians, therapists, day care centers, hospitalizations, adaptations of the living area, and the current living location (*e.g.*, home or nursing home). The cost-evaluation questionnaire will be returned with the falls calendar at three, six, nine, and twelve months after the first visit to the research outpatient clinic. In case no calendar sheet or questionnaire is received, or when it is completed incorrectly, the calendar sheet or questionnaire will be completed by telephone.

During the last visit to the outpatient clinic, one year after the first visit, all physical performance tests are conducted, as well as questionnaires regarding medical history, drug use, quality of life, and fall risk profile. Adherence to the drug-use recommendations (complete withdrawal, lowering of dosage, or substitution) will be evaluated by reassessment of drug use as described above. Information of the participants regarding medical history and drug use will be verified by the General Practitioner and local pharmacist.

Sample size calculation

A total number of 620 patients will be included in the study, 310 in the control group and 310 in the intervention group. Calculation of the required sample size is based on the assumption that the annual cumulative incidence of further falling is 50% without intervention,[40] a 15% drop-out (including death), drug withdrawal being possible in 50% of the participants in the intervention group and a 50% decrease of further falls among participants with successful withdrawal. A single-sided test with an alpha level of 0.05 and a beta of 0.2 indicates that 310 patients in both groups is sufficient in order to detect a 25% decrease of respondents reporting further falls in the intervention group.

Statistical analysis

Data will be primarily analyzed according to the intention-to-treat principle. Patients with protocol violations will be followed up, and data will be recorded. Data will be analyzed with and without inclusion of patients with protocol violation. At baseline, differences in baseline characteristics will be compared between the intervention and control group in order to assess comparability between the two groups. Student's T-test (parametric numeric data), Mann-Whitney U-test (nonparametric numeric data) or Chi-square test (categorical data). Data will be presented as mean ±SD (parametric data) or medians and percentiles (non-parametric data).

The hazard ratio for falling will be calculated using a Cox-regression model. Herein, the time between the intervention (*i.e.*, drug assessment/change or not) and the first and/or second fall will serve as the primary outcome measure. Fallers will be defined as those who will fall once or more during the one-year follow-up. Differences in cumulative incidence of falls will be analyzed using log-linear or Poisson regression, adjusted for over dispersion because of interdependence among the dependent variable (falls). Differences in adverse health effects between both trial arms will be assessed using Chi^2 testing. Several subgroups will be distinguished in order to examine whether the effect of the intervention depends upon sex, age, race and risk of future falls. Since healthcare costs per patient are typically highly skewed, non-parametric techniques will be used to derive a 95% confidence interval for the differences in distributions of the costs. In a sensitivity analysis the impact on cost-effectiveness of statistical uncertainty on the main study outcomes will be determined (uni- and multi-variable).

The association between genetic polymorphisms and falls history will be evaluated using a multivariate logistic regression analysis. A p-value of <0.05 will be used as threshold for statistical significance.

Ethical considerations

The study will be conducted according to the principles of the Declaration of Helsinki (59^{th} World Medical Association General Assembly, Seoul, October 2008)[41] and in accordance with the Medical Research Involving Human Subjects Act (WMO). The Medical Ethics review board of the Erasmus MC acts as central ethics committee for this trial (reference number MEC-2008-254; NTR1593). In addition approval has been obtained from the local Medical Ethics review boards in all participating hospitals. An information letter regarding the patients' participation and severe abnormal findings will be sent to their general practitioners, unless a patient does not agree with this.

Liability insurance has been obtained, which is in accordance with the legal requirements in The Netherlands (Article 7 WMO and the Measure regarding Compulsory Insurance for Clinical Research in Humans of 23^{th} 2003). This insurance provides cover in case of damage to research subjects through injury or death caused by the study.

Discussion

The strength of this study is that a single intervention, the withdrawal of fall-risk increasing drugs, will be studied versus "usual care" using a randomized controlled approach. The study results will provide valuable knowledge for clinicians and healthcare policymakers on the necessity of withdrawal of fall-risk increasing drugs in falls prevention strategies in the older population. If proven effective and cost-effective, fall-risk increasing drugs withdrawal in persons with a high risk of recurrent falling, might lower the risk of future falls and consequently contribute to reductions in fall-related injuries, related healthcare consumption, and costs. As far as we are aware, up till now no large RCT's have been published reporting the effects of withdrawal, dose reduction or substitution of fall-risk increasing drugs after a fall. The inclusion of patients started October 2008 and is expected to be complete by July 2011. Because of the one-year follow-up period, presentation of data can be expected in the second half of 2012.

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Chapter 5.2

Drug-induced falls in older persons: is there a role for therapeutic drug monitoring?

K.A. Hartholt, M. Becker, T.J.M. van der Cammen

Submitted

Abstract

Background
Falls are the leading cause of injuries among older persons. Because of ageing societies world wide, falls are expected to become a prominent public health problem. The usage of several types of drugs has been associated with an increased fall- and fracture risk. In order to reduce future falls, preventative measure are needed. Therapeutic drug monitoring may help to identify persons who are at risk for falls due to drug use. The aim was to demonstrate how drugs can contribute to falls and the role of therapeutic drug monitoring.

Methods
Descriptive case series of 4 patients.

Results
All patients were referred to the Geriatric Outpatient Clinic of a University Medical Center. The presented cases contained different underlying mechanisms contributing to an increased fall-risk in older adults, including renal failure, genetic variation, overdose and ageing.

Conclusion
Older adults are more prone to the side effects of drug use, including falls. Therapeutic drug monitoring may be useful to identify the patients who have an increased drug-related fall-risk, and to prevent future falls by individualizing the drug regime.

Introduction

Falls in older persons are associated with a high morbidity and mortality,[1] and result in high numbers of emergency department visits and hospital admissions.[2] In the United States 559,000 persons aged ≥65 years are admitted due to a fall annually.[2] Because of ageing societies world wide, falls are expected to become a more prominent public health problem. Over the past decades over 20 risk factors for falls have been identified, including drug use.[3, 4] A number of commonly used drugs has been associated with an increased fall- and fracture-risk.[4-7] The use of sedatives, hypnotics, antidepressants, and benzodiazepines have been established as a significant risk factor for falls in elderly individuals.[4] Other drug classes associated with an increased fall-risk are antihypertensives, diuretics, NSAIDs and ß-blockers.[4-6]

The number of falls caused by drugs and/or drug intoxications is not known, because falls are not officially recognized as an adverse drug reaction. A decrease in fall risk has been demonstrated after reduction or cessation of fall-risk-increasing-drugs.[8-10] The mechanisms by which drugs contribute to fall risk, as well as the role of therapeutic drug monitoring (TDM) are not well-established. In this paper, four cases will be discussed with drug-induced falls, and the possible role of TDM.

Patient A

A 57-year old woman presented with frequent falls since 2 years. Because of apathy after a cerebrovascular accident, the psychiatrist had started her on amantadine, without effect. Furthermore, she was on dipyridamol b.i.d. 200 mg., candesartan s.i.d. 16 mg., lisinopril s.i.d. 20 mg., carbasalatecalcium s.i.d. 100 mg., amantadine t.i.d. 100 mg., and simvastatine s.i.d. 40 mg. On examination she had orthostatic hypotension (OH); blood pressure (BP) supine of 110/70 mmHg, 97/56 mmHg on 3 minutes standing, and a regular heart rate of 74/min.. Serum sodium was 142 mmol/l., potassium 4.9 mmol/l., ureum 12.2 mmol/l., creatinine 159 umol/l, estimated GFR 29 ml/min.. Because of the impaired renal function amantadine was stopped immediately after her first visit to the Geriatric outpatient clinic (OPC). A serum level of amantadine was in the toxic range, 2.8mg/l (toxic >1.0 mg/l). After discontinuing the amantadine, her orthostatic hypotension disappeared and she had no further falls (follow-up two years).

Patient B

A 74-year old female presented with numerous falls occurring after rising from chair or bed. The GP had started betahistine t.i.d. 16 mg., without effect. In addition, she was on bromazepam t.i.d. 3 mg., and citalopram s.i.d. 30 mg. On examination, BP was 140/80 mmHg, with no OH. The serum citalopram level was in the therapeutic range and the bromazepam level was in the toxic range 0.55 mg/l (therapeutic 0.05-0.2 mg/l; toxic level >0.3 mg/l). Bromazepam was reduced to t.i.d. 1.5 mg, at three months follow-up she had had no further falls. However, because she felt unwell, she resumed the original dosage of bromazepam, and started to fall once more.

Patient C
A 70-year old male was referred to the Geriatric OPC, because of 1-2 falls a week. He had a medical history of alcohol-abuses and behavioural problems and had become psychotic during diazepam-withdrawal in the past. His psychiatrist had achieved a stable situation with the current drug-regimen. Patient C used diazepam t.i.d. 5 mg., olanzapine s.i.d. 7.5 mg., and venlafaxine s.i.d. 150 mg. plus s.i.d. 75 mg. On examination, he was depressed and nervous with a BP of 145/85 mmHg, and no OH. Gamma-GT was 70 U/l and ALAT 39 U/l. Because olanzapine, diazepam, and venlafaxine can contribute to falls and dizziness, a serum level of all three drugs was obtained. Olanzapine was in the therapeutic range. Level of desmethyldiazepam, the active metabolite of diazepam, was 1702 mcg/l (therapeutic range 200-600 mcg/l), levels of venlafaxine and the active metabolite O-desmethylvenlafaxine were 1180 mcg/l (toxic >1000 mcg/l) and 29 mcg/l (therapeutic 150-500 mcg/l). Because of his previous psychotic episode on diazepam-withdrawal the psychiatrist preferred not to reduce the diazepam- and venlafaxine-dosages, despite the problem of falls in this patient.

Patient D
An 80-year old woman was referred to the Geriatric OPC because of falls twice a month. She used nortriptyline s.i.d. 50 mg., nifedipine s.i.d. 30 mg., labetalol b.i.d. 200 mg., bromazepam s.i.d. 1.5 mg., and omeprazol s.i.d. 20 mg. She had OH, BP 153/70 mmHg supine, 130/60 mmHg after 3 minutes standing. Her serum-level of nortriptyline was 196 mcg/l (therapeutic range 75-250 mcg/l). Because nortriptyline can induce OH, the dosage was reduced to s.i.d. 25 mg.. At follow-up three months later, she had not had any further falls, and the serum level of nortriptylin had decreased to 65 mcg/l.

Discussion

The four patients presented in this case series all suffered from drug-induced falls. It was already known that the use of certain drugs is associated with an increased fall risk. As our four cases illustrate, the attention for the patient's drugs as a potential cause of the falls can reverse the situation. Older patients are more susceptible to adverse drug reactions such as falls than younger patients,[11] due to increased drug use, reduced physiological functions, and altered pharmacokinetics and pharmacodynamics.[12]

Patient A was treated with amantadine 100 mg t.i.d.. Amantadine is primarily excreted unchanged in the urine by glomerular filtration and tubular secretion. In patients with a GFR of 29 ml/min a dose of 100 mg once every three days is recommended. In patient A, the dose of 100 mg t.i.d. resulted in a toxic plasma level of 2.8 mg/l, resulting in OH and falls.

Patient B used bromazepam, and could not discontinue this drug due to her panic disorder. Bromazepam is metabolized to 3-hydroxybromazepam by cytochrome P450 (CYP) 1A2.[13] Benzodiazepines are widely prescribed among the elderly, and increases the risk of falls with 60%.[14] A daily dose of nine milligrams is the maximum dose, although in severe cases higher doses can be prescribed. In older patients a dose reduction is recommended. In this patient, the plasma level of bromazepam was in the toxic range, and was the result of a decreased hepatic elimination. Since was no indication of liver dysfunction, the decreased hepatic elimination may be the result of aging.

Patient C received subtherapeutic to therapeutic doses of three psychotropic drugs; diazepam, olanzapine, and venlafaxine. The plasma levels of venlafaxine and desmethyldiazepam, an active metabolite of diazepam, were respectively two and three times the upper limit of the therapeutic range. Venlafaxine is metabolized to the active metabolite O-desmethylvenlafaxine by the CYP2D6 enzyme and O-desmethylvenlafaxine is conjugated to an inactive metabolite. Both metabolites are excreted renally. In this patient a high venlafaxine level and a low O-desmethylvenlafaxine level was measured, suggesting a poor functioning of the CYP2D6 enzyme. The patient did not use medication that inhibited the CYP2D6 enzyme, and therefore we suspected a genotype coding for a poorly functioning CYP2D6 enzyme. The patient's genotype was indeed CYP2D6 *4/*4 coding for two non-functioning CYP2D6 enzymes. In a Caucasian population approximately 5-10 percent of the population has no functioning CYP2D6 enzymes.[15] Diazepam undergoes demethylation by the CYP2C19 enzyme to desmethyldiazepam and hydroxylation by the CYP3A4 enzyme to temazepam and oxazepam. The levels of diazepam were in the therapeutic range, while the levels of desmethyldiazepam were above the therapeutic range. This may indicate that in patient C the functioning of the CYP2C19 enzyme was much better than the functioning of the CYP3A4 enzyme. Genetic variation resulting in a poor functioning CYP3A4 enzyme is rare. With aging and decreased hepatic functioning, the cytochrome enzymes are affected differently. It has been suggested that the CYP3A4 enzymes are more prone than the CYP2C19 enzymes, which is in line with the higher desmethyldiazepam levels.[13] The fragile balance between inappropriate behavior and psychosis on diazepam-withdrawal in this case demonstrates the difficulty of pharmacotherapy in some patients, and that some side effects should be accepted in order to prevent a new psychosis.

Patient D was using a therapeutic dosage of nortriptyline, and her plasma levels were within the therapeutic range. Nonetheless, she experienced falls induced by nortriptyline (OH as an anticholinergic side effect). Reducing the dosage stopped the falls and the orthostatic hypotension. This case illustrates that plasma levels within the therapeutic range do not exclude drug-induced falls.

In conclusion, the four patients in this case-series all presented with drug-induced falls,[3] (A, B, C) had a drug intoxication, but the underlying mechanism varied. Patient A had decreased renal functioning, and was prescribed a renally excreted drug without dose adjustment. Patient B and C had decreased hepatic metabolism, likely related to aging; in addition patient C had an inherited absence of the CYP2D6 enzyme. The prescribed drug regimens resulted in toxic plasma levels in these patients. Patient D had serum-levels within the therapeutic range, but had falls due to the anticholinergic side effects of nortriptyline. Lowering the dose stopped the falls. Most likely, this patient had a higher sensitivity due to pharmacodynamic changes. Drug-related falls are potentially preventable, and TDM can help in identifying patients with drug-induced falls and confirm clinical suspicion. However, plasma levels within the therapeutic range do not exclude the diagnosis of drug-induced falls.

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Chapter 5.3

Adverse Drug Reactions related hospital admissions in persons aged 60 years and over, The Netherlands, 1981 - 2007: less rapid increase, different drugs

K.A. Hartholt, N. van der Velde, C.W.N. Looman, M.J.M. Panneman, E.F. van Beeck, P. Patka, T.J.M. van der Cammen

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Abstract

Background

Epidemiologic information on time trends of Adverse Drug Reactions (ADR) and ADR-related hospitalizations is scarce. Over time, pharmacotherapy has become increasingly complex. Because of raised awareness of ADR, a decrease in ADR might be expected. The aim of this study was to determine trends in ADR-related hospitalizations in the older Dutch population.

Methodology and Principal Findings

Population based, secular trend analysis of ADR-related hospital admissions in patients ≥60 years between 1981 and 2007, using the National Hospital Discharge Registry of The Netherlands. Numbers, age-specific and age-adjusted incidence rates (per 10,000 persons) of ADR-related hospital admissions were used as outcome measures in each year of the study. Between 1981 and 2007, ADR-related hospital admissions in persons ≥60 years increased by 143%. The overall standardized incidence rate increased from 23.3 to 38.3 per 10,000 older persons. The increase was larger in males than in females. Since 1997 the increase in incidence rates of ADR-related hospitalizations flattened (percentage annual change 0.65%), compared to the period 1981-1996 (percentage annual change 2.56%).

Conclusion/Significance

ADR-related hospital admissions in older persons have shown a rapidly increasing trend in The Netherlands over the last three decades with a temporization since 1997. Although an encouraging flattening in the increasing trend of ADR-related admissions was found around 1997, the incidence is still rising, which warrants sustained attention to this problem.

Introduction

Medication use among older persons has grown over the last decades.[1] Pharmacotherapy has become increasingly complex[2] due to growing knowledge about disease pathophysiology, discovery of new drug therapies over time, and secondary preventive therapies, usually laid down in guidelines or protocols.[3] In 2007, persons aged ≥65 years constituted 14.4% of the Dutch population, whereas 44% of all drug prescriptions was for this age-group.[4] This is not surprising, as older persons in general have the highest prevalence of chronic and multiple (co-morbid) diseases. However, benefits of medication use are always accompanied by potential harm. Even when medication is prescribed in the recommended doses according to the guidelines,[3] Adverse Drug Reactions (ADR) can occur. The frequency of ADR increases with increasing age.[5-9] Older adults are at increased risk of developing an ADR[10] due to their social setting[11, 12], polypharmacy[3, 11-15], co-morbidity[16], cognitive impairment[12, 15], and physiological changes affecting the pharmacokinetics and pharmacodynamics of many drugs.[2, 11, 17, 18]

Recent studies have shown that ADR-related hospital admissions are increasing,[8, 19] and account for approximately 5-12% of all hospital admissions in older patients[6, 7, 9, 11, 14, 20, 21] with a high in-hospital mortality rate of 8-10%.[9] Furthermore, ADR-related hospital admissions appear to be preventable in two fifth of cases.[11, 13, 20] All in all, ADR in the older population form a large public healthcare problem, resulting in significant morbidity, healthcare consumption and high costs. Because of ageing societies[22] and an increasing life expectancy[23], ADR might be expected to become even a more serious public health problem.

Since multiple studies on ADR-related hospital admissions in older persons and their possible preventability have been performed, awareness on ADR has increased.[24, 25] We were interested in time trends of ADR-related hospitalizations, and especially whether the increased awareness about ADR has led to an actual decline of ADR-related hospitalizations. However, there is a paucity of data on time trends in healthcare use due to ADR.[26] Therefore, the aim of this study was to provide accurate data on trends in ADR-related hospitalization in older patients over the last decades.

Methods

Data on ADR-related hospital admissions were retrieved from Statistics Netherlands (CBS, The Hague, The Netherlands), which combines information of the National Medical Registration (LMR) and the National Hospital Discharge Registry.[27] The LMR collects hospital data of nearly all hospitals in The Netherlands. Data regarding hospital admissions, primary admission diagnosis (*i.e.*, the most dominant reason for admission), gender and age are stored in this database. Data on hospital admissions, mortality, and population composition were verified with the official Birth-registry. The Birth-registry is used to identify individual patients in the National Medical Registration. Based on specific personal characteristics, such as date of birth, gender, and address it is possible to determine individual patients. A uniform classification and coding system by the LMR is used for all hospitals and has a high coverage (less than 5% missing between 1981-2005, 12.0% in 2007). The coding system did not change during the study period. Extrapolation to full national coverage for each year was done by Statistics Netherlands. An extrapolation factor was estimated by comparing the adherence population of the participating hospitals with the total Dutch population in each year of the study.[28] Demographic data were also collected from Statistics Netherlands. The mid-year population number was used as denominator in this study.

ADR were defined as: "Medicinal and Biological substances causing adverse effects in therapeutic use", using the International Classification for Diseases, 9th revision (ICD-9), code E930 – E949 (Table 1) throughout the study period.

Table 1. International Codes of Diseases of the World Health Organization, 9th revision, for Adverse Drug Reactions

Code	Description
E930	Antibiotics causing adverse effects in therapeutic use
E931	Other anti-infectives, causing adverse effects in therapeutic use
E932	Hormones and synthetic substitutes causing adverse effects in therapeutic use (including a.o. cortical steroids, androgens, ovarian hormones, insulins, and thyroid derivates)
E933	Primarily systemic agents causing adverse effects in therapeutic use (including a.o. anti-neoplastic, immunosuppressive drugs, bisphosphonates, vitamins and enzymes)
E934	Agents primarily affecting blood constituents causing adverse effects in therapeutic use (including a.o. anti-coagulants, anti-coagulant antagonists, anti-anemic agents, iron)
E935	Analgesics antipyretics and anti-rheumatics causing adverse effects in therapeutic use
E936	Anticonvulsants and anti-parkinsonism drugs causing adverse effects in therapeutic use
E937	Sedatives and hypnotics causing adverse effects in therapeutic use
E938	Other central nervous system depressants and anesthetics causing adverse effects in therapeutic use
E939	Psychotropic agents causing adverse effects in therapeutic use
E940	Central nervous system stimulants causing adverse effects in therapeutic use
E941	Drugs primarily affecting the autonomic nervous system causing adverse effects in therapeutic use
E942	Agents primarily affecting the cardiovascular system causing adverse effects in therapeutic use
E943	Agents primarily affecting gastrointestinal system causing adverse effects in therapeutic use
E944	Water mineral and uric acid metabolism drugs causing adverse effects in therapeutic use
E945	Agents primarily acting on the smooth and skeletal muscles and respiratory system causing adverse effects in therapeutic use
E946	Agents primarily affecting skin and mucous membrane ophthalmological otorhinolaryngological and dental drugs causing adverse effects in therapeutic use
E947	Other and unspecified drugs and medicinal substances causing adverse effects in therapeutic use
E948	Bacterial vaccines causing adverse effects in therapeutic use
E949	Other vaccines and biological substances causing adverse effects in therapeutic use

The E-codes of the ICD-9 classification are used to describe the external cause of injuries. Drug-classes used in this study were based on the ICD-9 codes (E930-E949). Official coding clerks register the diagnosis and injury mechanism of all hospital admissions, based on data obtained from medical records. For this study, hospital admissions in older patients with ADR as the primary admission diagnosis were collected over the period 1981-2007. Older persons were defined as persons aged ≥60 years. Numbers of ADR-related hospital admissions were specified for age and gender. Age-specific incidence rates, in 5-year age-groups, were calculated using the number of the ADR-related hospital admissions in that specific age-group, divided by the total mid-year population number within that specific age-group. The age-specific incidence rates were separated for both genders, and expressed per 10,000 persons of that specific age-group. Direct standardization, based on

Table 2. Overall numbers of Adverse Drug Reactions related hospital admissions in The Netherlands (1981-2007)

	0-59 years		60-69 years		70-79 years		80-89 years		≥90 years		Total	Female : Male ratio
Period	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	
1981-1985	17,913	36.2%	9,867	20.0%	13,239	26.8%	7,685	15.5%	742	1.5%	49,446	1 : 0.69
1986-1990	17,524	32.5%	10,998	20.4%	14,969	27.8%	9,235	17.2%	1,122	2.1%	53,848	1 : 0.74
1991-1995	19,400	30.8%	12,406	19.7%	18,064	28.6%	11,761	18.6%	1,434	2.3%	63,065	1 : 0.78
1996-2000	23,095	30.2%	14,064	18.4%	22,321	29.2%	14,960	19.6%	2,050	2.7%	76,490	1 : 0.72
2001-2005	25,278	30.8%	14,909	18.1%	22,641	27.5%	16,889	20.5%	2,473	3.0%	82,190	1 : 0.75
2006-2007	10,912	29.7%	7,255	19.8%	9,771	26.6%	7,595	20.7%	1,188	3.2%	36,721	1 : 0.75
Total	114,122	31.5%	69,499	19.2%	101,005	27.9%	68,125	18.8%	9,009	2.5%	361,760	1 : 0.74

the mean population size per 5-year age-group throughout the study period, was used to calculate the overall age-adjusted incidence in males and females. Growth in the number of hospital admissions was calculated in percentual increases compared to the year 1981. This model has been used in a previous study.[29]

Statistical analysis

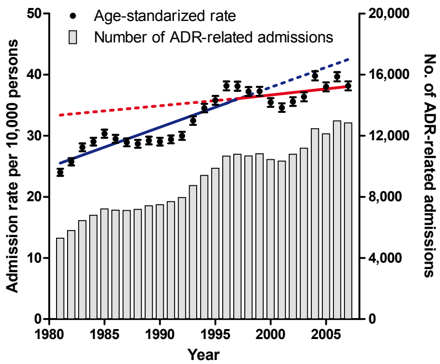
To model the trend in hospital admissions, a regression model with Poisson error and log link was built with log mid-year population size (per 5-year age-groups) of each year of the study as offset factor. A linear spline model, with age, year, gender, and population size was built to assess whether the annual growth changed over the study period for both genders. The parameter for calendar year, corrected for gender and age-group was transformed into Percentage Annual Change (PAC). Our spline function accommodated two piecewise linear fits, connected with one another at the best knot[30], which was estimated with "Joinpoint Regression Program", Version 3.3.1. (Statistical Research and Applications Branch, National Cancer Institute, USA). This program decided where to place the knot and showed the necessity for assuming a spline instead of a simple linear model. The best knot, for males and females together, was found to be January 1, 1997. Therefore this knot was used for the analysis in both males and females. The analysis including splines yielded estimates of annual changes in admission rates within each period (1981-1996 and 1997-2007 respectively). Comparison of these two periods enabled us to detect and quantify changes in the secular trend in overall admission rates. A likelihood ratio test was performed to assess the significance of the spline over a single trend for the study period. Interactions of the spline for gender were added and tested to investigate differences in trends for genders. A Chi^2-test was used to detect changes in drug-classes and admission diagnosis. Statistical analyses were performed using SPSS software (version 16.1.1). A *p*-value <0.05 was considered as statistically significant.

Results

During the 26 years of observation a total of 361,760 ADR-related hospitalizations were identified in The Netherlands (Table 2).

Over two-thirds of the admissions (247,638) occurred in persons ≥60 years, which constituted only 17.6% on average of the Dutch population over 1981-2007. The total number of ADR-related hospital admissions in the Dutch population aged ≥60 years increased from 5,291 admissions in 1981 to 12,836 in 2007 (Figure 1). ADR-related hospitalizations increased by 175% in males aged ≥60 years (from 2,056 in 1981 to 5,651 in 2007) and by 112% in females aged ≥60 years (from 3,235 in 1981 to 7,185 in 2007). The overall standardized incidence rate (per 10,000 persons) of ADR-related hospital admissions in persons aged 60 years and over was 23.3 in 1981 and 38.3 in 2007 (Figure 1). The overall incidence rates (per 10,000 persons) increased in males from 21.3 in 1981 to 37.5 in 2007 and in females from 24.8 in 1981 to 39.0 in 2007.

Figure 1. Adverse Drug Reactions, annual numbers and age-standardized rates per 10,000 persons aged ≥60 years in The Netherlands, 1981-2007



Separate regression lines are fitted to the period 1981-1996 (blue) and the period 1997-2007 (red). Solid lines indicate regression lines fitted to data points for the corresponding time period; dashed lines indicate the regression lines extrapolated for the remaining time period. Error bars indicate the 95% confidence interval.

The overall annual growth in the Dutch population over 60 years, corrected for age and population size was 1.78% (95% CI: 1.70-1.86) for males versus 1.47% (95% CI: 1.40-1.54) for females throughout the study period. A more detailed examination of the incidence curve of ADR (joint point regression analysis) revealed that the incidence growth has changed over time and can be divided in two phases: the incidence of hospital admissions due to an ADR increased strongly between 1981-1996 (2.56%, CI 95%: 2.46-2.67) and the percentage annual change slowed down between 1997-2007 (0.65%; CI 95%, 0.52-0.78). This flattening of the growth rate remained significant after correction for age and population size for both genders. Comparing 1986-1996 and 1997-2007, the annual growth rate decreased from 2.80% (95% CI: 2.63-2.96) to 0.38% (95% CI: 0.18-0.59) in males and from 1.86% (95% CI: 1.73-2.00) to 0.90% (95% CI: 0.72-1.08) in females respectively (*p*<0.001 for differences in slopes in both males and females).

Table 3. Age-specific incidence rates of Adverse Drug Reactions related admissions per 10,000 persons in The Netherlands

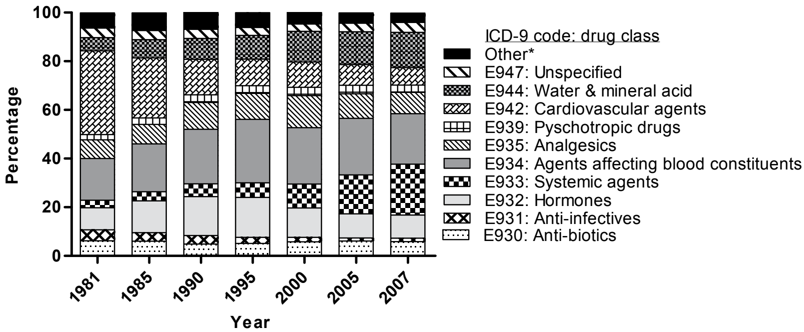
	Age range, y													
	60-64		65-69		70-74		75-79		80-84		85-89		≥90	
Period	**Males**	**Females**	**Males**	**Females**	**Males**	**Females**	**Males**	**Females**	**Males**	**Females**	**Males**	**Females**	**Males**	**Females**
1981	12.8	11.3	17.9	16.8	24.3	24.4	30.3	35.8	34.8	48.1	38.1	49.2	26.8	33.4
1985	15.5	13.1	25.8	20.4	32.6	30.2	45.2	41.6	44.5	56.8	52.2	61.6	39.2	42.9
1990	15.4	12.2	23.4	19.7	34.0	29.0	46.0	38.6	47.2	49.2	54.5	54.5	39.1	45.1
1995	16.5	15.1	28.1	23.3	40.9	32.8	55.5	50.5	65.0	66.2	66.0	71.5	53.1	53.2
2000	15.9	15.5	26.7	23.4	40.6	31.9	55.9	48.4	69.7	62.4	69.8	71.7	48.9	62.2
2005	17.6	17.9	28.2	24.2	41.0	35.1	57.5	51.2	71.2	66.4	83.5	77.5	79.9	69.7
2007	17.7	19.9	27.0	26.8	42.7	33.4	62.5	48.3	71.0	64.8	72.0	78.7	70.2	70.6
Absolute Change† (95% CI)	5.0 (2.9-7.3)	8.6 (6.4-11.2)	9.1 (6.2-12.4)	9.9 (7.2-12.9)	18.4 (14.0-23.2)	9.0 (5.9 - 12.5)	32.3 (25.6-39.8)	12.5 (8.3-17.1)	36.2 (26.9-47.0)	16.7 (10.8-23.1)	33.9 (20.7-49.9)	29.5 (20.0-40.2)	43.4 (21.3-75.8)	37.2 (22.1-55.5)
Relative Change† (95% CI)	39% (23-57)	77% (57-99)	51% (35-69)	59% (43-77)	75% (58-96)	37% (24-51)	107% (85-132)	35% (23-48)	104% (77-135)	35% (22-48)	89% (54-131)	60% (41-82)	162% (80-283)	112% (66-169)

Abbreviation 95% CI, 95% Confidence Interval; †Change is 2007 compared to 1981

Gender and age-specific incidence rates of ADR-related hospital admissions increased in all age-groups, both for males and females throughout the study period. All age-specific groups for both genders showed an increase in incidence of ADR-related hospital admissions when 2007 was compared to 1981. Among males (Table 3), the largest (relative and absolute) increase in incidence rates was seen in patients aged ≥90 years (162%, 95% CI: 80-283), the absolute increase in incidence rate was 43.3 per 10,000 persons (95% CI: 21.3-75.8). For females (Table 3), the largest increase was also seen in patients aged ≥90 years (112%, 95% CI: 66-169), the absolute increase was 37.2 per 10,000 persons (95% CI: 22.1-55.5). The distribution of medication groups causing ADR changed significantly ($p<0.001$) throughout the study period (Figure 2). The contribution of cardiovascular agents (ICD-9: E942) to ADR-related hospitalizations decreased from 36.0% in 1981 to 8.3% in 2007. Drugs affecting water, mineral and uric acid metabolism increased (ICD-9: E944) from 5.4% to 15.4%, primarily systemic agents (ICD-9: E933) increased from 3.2% to 24.4%, and agents affecting blood constituents (ICD-9: E934) increased from 17.9% to 24.2% between 1981 and 2007.

Approximately 45% of all ADR-related admissions were caused by six diagnostic groups (bleeding, gastrointestinal symptoms, anemia, cardiac symptoms, pulmonary symptoms, other) between 1991 and 2007 (Table 4). The distribution of admission diagnoses shifted during the study period ($p<0.001$).

Figure 2. The composition of drug groups causing adverse drug reactions related hospital admissions in persons aged ≥65 years in The Netherlands (1981-2007)



The ICD-9 codes for Adverse Drug Reactions are shown. The main drug groups causing ADR-related admissions are shown separately in this figure. *"Other" drug groups were less frequently seen (<2% per group) and includes ICD-9 codes: E936-E338, E940, E941, E943, E945, E946, E948 and E949. The distribution changed during the study (p<0.001, Chi^2-test).

Table 4. Primary admission diagnosis for Adverse Drug Reactions related hospital admissions in patients ≥60 years in The Netherlands (1991-2007)

	1991	1994	1997	2000	2003	2006	2007
Bleeding	640	857	1,006	920	917	1,013	853
Gastrointestinal symptoms	349	442	446	491	527	549	513
Anemia	243	353	419	389	432	398	352
Cardiac system	398	513	564	452	433	435	377
Pulmonary system	123	191	290	329	390	474	486
Other	1,379	1,686	1,794	2,113	2,169	2,514	2,516
Hypoglycemic coma	617	692	456	384	399	359	332
Dehydration/ Electrolyte Disturbance	183	239	381	497	637	791	721
Urinary Tract Infection	109	136	168	133	170	239	283
Bone/Cartilage disease	70	94	115	313	214	201	202
Agranulocytosis	58	97	142	191	198	317	364
Obstipation	174	232	306	355	355	394	433
Pulmonary embolism	168	196	226	240	196	213	181

Data on primary admission diagnoses were available since 1991. Chi^2-test for change in distribution of primary admission diagnosis was p<0.001.

Discussion

This study shows that both the absolute numbers and the incidence rates of ADR-related hospitalizations in persons aged ≥60 years in The Netherlands increased strongly between 1981 and 2007. Although a slow down of the curve occurred in 1997, the incidence rates since then are still increasing, albeit at a less rapid rate. Of all ADR-related admissions, two-thirds were in the age-group of ≥60 years. The increase occurred in both males and females, although it was more pronounced in males and in the higher age-groups. Drugs classes leading to ADR-related hospitalizations shifted throughout the study period.

Our data represent an important first step in secular trend analysis of ADR-related admissions in developed countries. As far as we are aware from the literature, this study is the first to show a deceleration in the increasing incidence rates of ADR-related hospital admissions. Several factors may have contributed to this finding. The deceleration in growth of ADR-related hospital admissions started in the mid-nineties, after the introduction and widespread use of personal computers and software, with prescribing applications for doctors and pharmacists, which warns for possible drug interactions and errors.[31-33] Furthermore, due to professional publications and increasing media coverage, since the mid-nineties awareness about ADR among both professionals and the general public may have increased.[24, 25] Also standardized protocols and prescribing guidelines may have contributed to this trend.[3] Other studies did not show the decline in ADR-related hospitalizations, maybe due to their shorter study period[8] or ending in 2002, before flattening of the incidence rates of ADR-related hospital admissions had taken its full effect.[19] Theoretically the slowdown in ADR-related hospitalizations might also be (partly) caused by changes in admission policy at the Emergency Departments. However, a survey among Emergency Departments in The Netherlands[34] showed that the proportion of patients presenting with an ADR, followed by subsequent hospital admission, remained stable at 72% in The Netherlands between 1998 and 2008.

A major strength of this study was the availability of very accurate in-hospital data over an extensive period of 26 years (1981-2007) with almost complete national coverage. Absolute numbers of ADR-related hospital admissions in The Netherlands were recorded in a computerized database, with the same coding system (ICD-9) throughout the study period. This allowed us to gather reliable population-based data for our trend analysis. However, the data are only accurate within the limitations of the coding system, which is likely to be dependent on the accuracy of the data in the medical records and the recognition of ADR in the first instance by the patient's physician writing the record.

A number of limitations may have affected the interpretation of our findings. First of all, diagnosis codes were taken from a linked administrative database, which may be prone to coding errors and variation.[35] However, a recent quality survey showed a high accuracy of coded injury data (correctly coded in 91% of cases and in 9% incomplete).[36] This provides support for the validity of our data on ADR-related hospital admissions as extracted from the LMR database, and is comparable to the registration in New Zealand (period 1996-1998).[37]

A second but unsolved limitation, however, is that the database does not contain information regarding specific drug(s), medication compliance, number of medications, co-morbidities, and clinical details of the ADR. Therefore, it was not possible in this study to draw conclusions regarding ADR details for specific drugs and certain high risk groups, for example patients with polypharmacy. Also, the database does not contain definitions of the ADR according to the Naranjo[38] or other algorithms, so a distinction between definite, probable, or possible ADR can not be made.

Third, we should take into account that underregistration of ADR might have occurred, since ADR recognition is very complex, especially in older adults, therefore ADR are not always noticed by medical personnel.[39, 40] For example, in older persons, falls and delirium caused by drug-use are still under-recognized as an ADR in current medical practice. For this reason, it is likely that the actual societal impact of all ADR-related morbidity, both mild and serious, exceeds the burden described in our study.[7]

Fourth, this study is based on the national situation in The Netherlands, with a full healthcare insurance coverage system and may be not representative for other countries. However, comparable increasing time trends were found in England[8] and Australia[19]. It therefore seems likely that the incidence of hospital admissions due to ADR will progress similarly in other developed countries.

In summary, drug prescription is a fundamental part of the care of older persons. Adverse drug reactions are a known drawback of medication use and represent an increasing public health problem, especially among older persons.[10] Changes in demographics alone cannot explain the increasing frequency of ADR and ADR-related healthcare demand in an ageing society. Although we found an encouraging deceleration in the increasing trend of ADR-related hospitalizations around 1997, the incidence rates continued to increase from 1997 onwards, therefore our attention to this problem remains needed. Since ADR-related admissions have been shown to be preventable in two-fifth of the cases,[11,13, 20] much is to be gained by further increasing the awareness among healthcare professionals that symptoms in older patients may be related to their drug use and by improving the ADR detection by the use of an ADR Risk score in daily practice.[41]

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Chapter 5.4

Better drugs knowledge with fewer drugs, both in the young and the old

K.A. Hartholt, J.J. Val, C.W.N. Looman, M. Petrovic, A. Schakel, T.J.M. van der Cammen

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Abstract

Little is known about drug knowledge of patients, which is relevant for both the compliance and quality of pharmacotherapy. Drug knowledge was quantified in 160 patients in the outpatient clinics of the departments of Internal and Geriatric Medicine. Medication knowledge was generally poor, especially among older patients. Better knowledge was associated with the use of fewer drugs. Caregivers of dementia patients performed as well as younger patients, indicating that older people can perform well, if well-instructed.

List of frequently used abbreviations

GO	Geriatric outpatients without dementia
caregivers of GO patients	Main caregivers of geriatric outpatients with dementia
older IM	Older (≥65 years) internal medicine outpatients
younger IM	Younger (18-65 years) internal medicine outpatients

Introduction

Populations worldwide are ageing,[1] due to an increasing life expectancy. Age-related diseases and co-morbidities increase with age.[2, 3] The presence of multiple co-morbidities can lead to polypharmacy, *i.e.* the use of ≥3 drugs.[4] Over the last decades, the number of complex drug prescriptions has increased considerably.[5] In 2008 in The Netherlands, 44% of drugs were prescribed to the age-group of persons aged ≥65 years,[6] which constituted 15% of the Dutch population in 2008.[7]

In addition to the high drug use among older adults, this age-group is also frequently seen in acute situations, such as a hospital admission due to an acute illness or trauma.[8, 9] In acute situations, patients may not have their medication with them. Therefore doctors and other medical personnel have to rely on the knowledge provided by the patients about their own drugs.

Multiple previous studies have demonstrated that better drug knowledge improves patients' compliance and is associated with a better result of pharmacotherapy on the target disease.[10-13] In order to achieve better drug knowledge in patients, attention must be paid to patient information and provision of adequate instructions.[14-16]

In The Netherlands there is a paucity of data on patients' drug knowledge, especially in older patients. Therefore, the aim of this study was to investigate the knowledge of outpatients regarding the name (generic and/or commercial), indication, dosage, and administration frequency of their drugs; and to compare younger and older patients.

Methods

This cross-sectional observational study was performed among community-dwelling patients in the outpatient clinics of the departments of Internal Medicine and Geriatric Medicine at the Erasmus MC, a University Medical Center (hereafter Erasmus MC) in Rotterdam, The Netherlands, between March 1st and May 31st, 2005. The study protocol was approved by the Medical Ethics Committee of the Erasmus MC (number MEC-2005-102).

To assess drug knowledge, a standardized interview was performed in all participants by a research fellow (AS) before they visited the physician in the outpatient clinic. The interviewed persons were asked to provide the information about their drugs by heart, because in an acute setting the patient is our first information source. For patients with a diagnosis of dementia, the main caregiver was interviewed, and included in the analysis.

Patients, both new and controls, were eligible for inclusion if they were aged 18 years or older, used one or more drugs for at least two weeks prior to the outpatient visit, and signed the consent form before the interview. Persons were excluded if they did not use medication in the last two weeks prior to the visit, or if there was a language barrier resulting in the inability to complete the interview. Patients were allowed to participate only once in the study.

Participants were divided into four groups, depending on which outpatient clinic they visited: (1) older (≥65 years) Internal Medicine (IM) outpatients, (2) younger (<65 years) IM outpatients, (3) GO: geriatric (≥65 years) outpatients without dementia, and (4) caregivers of GO patients: main caregivers of geriatric outpatients with dementia.

Data were collected on: age, gender, number of drugs, years of education, and the presence of a diagnosis of dementia before the visit. Four items concerning medication knowledge were noted: drug name (commercial and/or generic), indication, dosage, and administration frequency. Answers were scored dichotomous: correct or incorrect. Patients were asked to give their answer by speaking. For each drug, answers were considered as correct, if the patient was able to recall the generic or commercial drug name. Names that sounded phonetically the same were considered as correct. Data on drug name, dosage, and frequency retrieved from the interview were compared with medication data from the patient's own pharmacist.

All data were stored in an electronic database Statistical Package for the Social Sciences (SPSS) version 16.0.1.1. A multilevel analysis was used in order to estimate probabilities on the level of the patient and on the level of the drug of a patient, because the probability of drug knowledge depends not only on the drug itself or the number of drugs, but also on the patient. If a patient, who uses multiple drugs, knows the first drug, the probability that he will know the second drug as well will increase. Therefore, for every patient an individual probability of knowledge about drugs was estimated. The multilevel analysis showed that there was dependency of the knowledge of drugs: the probability of a correct answer depended on the respondent. All prevalences, relations, and *p*-values were obtained in this way. Statistical analyses were performed with "The R Foundation for Statistical Computing" (R 2.7.1, 2008). A *p*-value <.05 was considered as statistically significant.

Results

One hundred-and-sixty consecutive patients who presented at the participating outpatient clinics were asked to participate. There were no refusals to participate and the groups consisted of: 40 (25%) in the older IM group, 40 (25%) in the younger IM group, 43 (27%) in the GO group, and 37 (23%) in the caregivers of GO patients group. The caregivers of GO patients group were the patient's partner in 32/37 cases, in 5/37 cases the patient

Table 1. Patient characteristics per group for gender, age, number of drugs and years of education of the study population

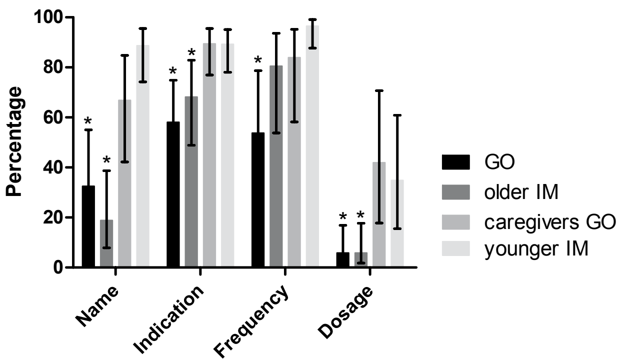
Characteristic	Overall	Geriatric outpatients without dementia	Geriatric outpatients with dementia†	Internal Medicine outpatients ≥65 years	Internal Medicine outpatients <65 years
Number	160	43	37	40	40
Men (%)	49%	47%	76%	40%	37%
Age (± SD)	69.2 ± 16.8	80.8 ± 6.0	79.9 ± 5.4	71.7 ± 5.0	44.2 ± 12.6
Number of drugs (± SD)	5.9 ± 3.5	6.8 ± 3.9	5.3 ± 3.2	7.0 ± 3.7	4.5 ± 2.7
Years of education (± SD)	10.6 ± 4.1	9.3 ± 3.4	10.1 ± 3.2	9.0 ± 3.3	14.1 ± 4.2

†Data is of the dementia patients, and not of the caregivers; SD, Standard Deviation

was accompanied by a daughter or son. Characteristics of the patients are shown in Table 1. The mean age was 69.1 years (±16.8 SD) and 51% of the patients were female. All patients together used a total number of 946 drugs, with a mean of 5.9 (±3.5 SD) drugs per patient. The mean number of years of education was 10.6 (±4.1 SD). Polypharmacy, the use of 3 or more drugs, occurred in 87% of the patients.

For dementia patients (η=37) we interviewed the main caregiver. For the other three groups (η=123) we interviewed the patients. Differences between the four groups regarding the knowledge of their drugs are shown in Figure 1. Knowledge of the drug name was best in the younger IM group (89%), followed by the caregivers of the GO patients (67%), GO patients (33%), and the older IM group (19%). In 89% the younger IM group knew the indication, compared to 58% of the GO group. The dosage was best-known in the caregivers of the GO patients group (42%) and least-known (6%) of the older IM group. Knowledge of the caregivers of the GO patients group was comparable with that of the younger IM group.

Figure 1. Medication knowledge per group for name, Indication, administration frequency and dosage



Older IM: Older (≥65 years) internal medicine outpatients (η=40); younger IM: Younger (<65 years) internal medicine outpatients (η=40); GO: Geriatric outpatients without dementia (η=43); caregivers GO: Main caregivers of geriatric outpatients with dementia (η=37). The error bars indicate the 95% Confidence Interval. (*) indicates a significant difference p<.05 compared to the reference group: younger IM patients.

In order to compare the medication knowledge of younger patients versus older patients, the older IM and GO were aggregated and compared with the younger IM group (Table 2). The younger IM outpatients had a statistically significant better drug knowledge compared to the group aged 65 years and over.

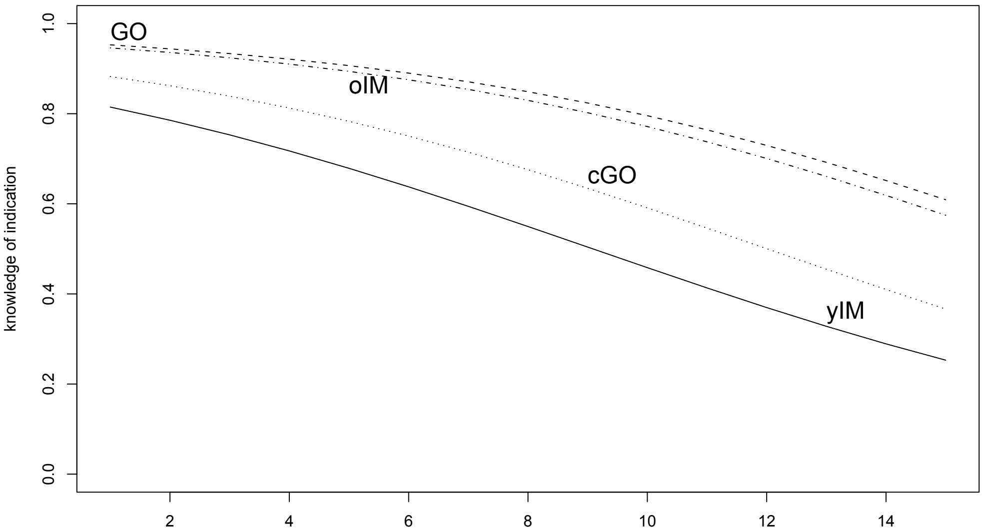
In all groups, poorer knowledge of the indication was significantly associated with a higher number of drugs (p=0.003) (Figure 2). There was no significant association between the number of drugs and knowledge of the name or the administration frequency. There was no significant association between drug knowledge and years of education or gender.

Table 2. Drug knowledge, comparison between older and younger patients (caregivers were excluded)

Knowledge of the†	Internal Medicine and Geriatric outpatients ≥65 years (η=83)	Internal Medicine outpatients <65 years (η=40)	*p*-value
- name, η (%)	22 (26)	36 (89)	<0.001
- indication, η (%)	51 (62)	36 (89)	0.002
- administration frequency, η (%)	57 (69)	39 (37)	<0.001
- dosage, η (%)	7 (9)	14 (35)	0.002

†Shown percentages (95% confidence interval). Prevalences, with 95%CI, were estimated with a multilevel analysis

Figure 2. Association between the Number of Drugs and Knowledge of the Indication



Older IM: Older (≥65 years) internal medicine outpatients (η=40), younger IM: Younger (<65 years) internal medicine outpatients (η=40), GO: Geriatric outpatients without dementia (η=43), caregivers GO: Main caregivers of geriatric outpatients with dementia (η=37).

Discussion

In this study, drug knowledge of patients was analyzed by a standardized interview in the outpatient clinics of the departments of Internal Medicine and Geriatric Medicine. Patients below the age of 65 years were best in recalling their medication. In older patients (aged 65 years and older) the knowledge was limited for all items (name, indication, dosage, and administration frequency). Only 62% of all interviewed older patients knew the indication for their drugs. However, caregivers of dementia patients were generally quite well informed, comparable with the younger IM group. Knowledge of the dosage was poor in all groups, but was especially poor among the older patients (9%).

Previous studies in other countries have reported a poor knowledge of the drug name,[10] indication,[17-19] and dosages,[17] especially in older patients. This is in line with our results. A statistically significant negative association was found between the number of drugs and the knowledge of the indication, which was in accordance with findings of other studies.[20, 21]

As far as we are aware from the literature, this study is the first to describe medication knowledge in The Netherlands. A new finding of this study is that the knowledge (about used drugs) of the caregivers of patients with dementia (*e.g.* older partners) was relatively good, and almost reached the level of the younger patients. This finding suggests that it is well possible to educate older persons about pharmacotherapy. A possible explanation for this finding might be that the caregivers of patients with dementia are very closely involved in the daily care of the patient.

A risk of being unfamiliar with the drug usage may result in an increased risk of an Adverse Drug Reaction. Approximately 50% of all serious ADR requiring hospitalization is preventable.[22] The majority of those hospitalizations are due to wrong usage of the drugs by the patients.[22] Another risk factor is the usage of multiple drugs, and especially older adults are the main consumers of multiple drugs. Therefore this age-group is at increased risk of both mild and serious ADR due to the use of an increased number of drugs. Both factors contributed most likely to the rapidly increasing trend of ADR-related Emergency Department visits and hospitalizations in the USA,[23] Australia[24] and The Netherlands[25] over the last decades.

A strength of this study was that there were no refusals to participate, and that patients were unaware of the study before their outpatient visit. Consequently, patients were not able to prepare themselves for any of the questions. This gives a reliable reflection of the real life situation. If the patient forgets his or her medication list or box in an acute situation, information provided by the patient is the only information available for the first hours or longer.

A limitation of this study might be that the study population consisted of a small group of outpatients of a university hospital, which might affect the generalizability of the findings. However, most patients in this study population (87%) used three or more drugs, with a mean of 5.9 drugs, which is consistent with other studies.[26]

Several patient education programs have been developed.[15, 27, 28] Effective methods include written medication instructions for the patient, simplified medication regimens and a self medication program, which instructs patients how to manage their medication.[29] These strategies have been shown to improve drug knowledge. Such education strategies should be further implemented and become a standard part of the physician and pharmacist consultation with older patients.

In conclusion, our study demonstrates that better drug knowledge was associated with the use of fewer drugs, and that drug knowledge of older caregivers can be equal to that of younger people, if they are well-instructed. This study implies that the number of drugs of older patients should be reduced where possible, and that patient education about medication remains needed in all age groups.

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Chapter 6

General discussion & summary

Chapter 6.1

General discussion

General discussion

Falls and subsequent fall-related injuries represent a major public health problem in ageing populations worldwide.[1-5] Currently, falls are the leading cause of injuries among persons aged 65 years and older. It has been estimated that the senior population will double in the coming decades worldwide,[6] including in The Netherlands.[7] Age-related problems, such as falls, are predicted to increase accordingly. In order to cope with those age-related issues, insights into these inevitable changes are needed for the allocation of healthcare resources and preventative measures in the near future. However, at this moment there is a lack of knowledge concerning the actual and precise burden of fall- and drug-related healthcare consumption in the older Dutch population. The aim of this thesis was to provide information on and gain insight in the magnitude of fall-related injuries, drug related admissions, and the related societal consequences in an ageing population. The following topics were studied and analysed, and are reported in this thesis:

- The current burden of healthcare consumption due to falls: Emergency Department visits, hospital admissions, and related costs.
- Trends in the consequences of fall incidents in older populations (fall-related hospitalizations, type of injury, and mortality).
- Adverse Drug Reaction related admissions, and knowledge of drugs in the older population.
- A study design for a randomized controlled trial aiming to determine the effect of withdrawal of fall-risk increasing drugs in older adults.

The main results on the topics mentioned above will be discussed in this chapter. Furthermore, methodological and theoretical matters regarding the main study outcomes will be explained. Finally, implications for healthcare professionals and recommendations for future research are presented.

Main findings

The burden of falls
It is already known that falls are an important public health problem among older persons. Our studies explored the impact of specific fall-related injuries and related healthcare costs. It was demonstrated that there is a difference in injury patterns between both genders, and that these injury patterns shifted to more severe injuries with increasing age. Besides hip fractures, falls also frequently result in high numbers of superficial injuries, upper extremity fractures, and head injuries.

Falls are leading to high numbers of major and minor injuries. All injuries, including minor injuries, have a negative impact on the quality of life in the older population. Because the affected health domains have been identified, improvement of injury treatment can be started to optimize the quality of life. The large burden of fall-related healthcare consumption results in high annual healthcare expenses. Costs per fall-related injury among the oldest old were very high, due to the high hospitalization rates and the demand for long term care in this age-group.

Time trends in the consequences of fall incidents in older populations

There is a strong increase in fall-related hospitalizations over the last three decades, which can not be explained by demographic population changes alone. However, when trends for specific fall-related injuries were determined, a divergence between different fall-related trends was noticed. The course of the hip fracture incidence rate was relatively favorable (recent decline in incidence rate), however, the incidence of fall-related head injuries showed a rapid accelerating increase. Acute vertebral fractures showed a stable increase in incidence rate over time. The differences in fall-related injury trends demonstrate that different injuries have developed different patterns over time. In specific age-groups, it was found that the overall rising fall incidence was primarily caused by the increasing incidence rates among the oldest old. The development of these trends was more pronounced in men than in women. As a result of this development, the difference between both genders is disappearing. This was not only found for hospitalization rates, but also for mortality rates. Despite a strong reduction in fall-related mortality since the mid-sixties, the mortality rates were stable in women and rising for older men since the mid-nineties. This indicates that nowadays falls are not only an important issue for older women, but also for older men.

Adverse Drug Reaction related admissions, and their knowledge of drugs in the older population

A known drawback of drug use is the risk of an Adverse Drug Reaction (ADR). Nearly 75% of older persons use one or more drugs. Despite the improvement of awareness of ADR, the number of ADR-related hospitalizations has increased over the last decades in The Netherlands. In addition to the rising numbers and incidence rates, the type of drugs related to the ADR-related hospitalization has changed over time. Although the ADR incidence is still rising, there is evidence that the increase is slowing down since the mid-nineties. Patients with an ADR often present with atypical symptoms, such as a bleeding, peptic ulcer, dehydration, or a fall, which are not always recognized as an ADR. A known risk factor for the occurrence of ADR is poor drug knowledge. It was found that drug knowledge was especially poor among older patients, which place them at high risk for an ADR. With an increasing number of drugs, the knowledge concerning indication, intake frequency, and dosage has decreased. Therefore, especially older adults with polypharmacy are at risk for an ADR.

The effect of withdrawal of fall-risk increasing drugs in older adults

In order to reduce the number of falls in senior populations in the near future, effective falls-prevention programs are needed. Withdrawal of fall-risk increasing drugs might be an important intervention in such a prevention program. However, before these interventions can be implemented as routine care, the effect of this intervention should be known. This can be achieved in a randomized controlled trial. Therefore, the design of a prospective multicenter randomized controlled trial aiming to reduce falls is presented. The effect of withdrawal of fall-risk increasing drugs in older persons who visited an

Emergency Department after a fall will be assessed. After the Emergency Department visit, patients will be assessed at the research outpatient clinic. In the intervention group the fall-risk increasing drugs will be withdrawn if possible. No medication changes will be made in the control group. After the outpatient clinic visit the number of new falls in a one-year follow-up period will be documented.

Methodological and theoretical issues

Strengths

The results of all presented studies in this thesis are based on three high quality electronic databases (the National Hospital Discharge Registry, Official-Cause-of-Death-Statistics, and the Dutch Injury Surveillance System). The databases were used independently from each other and in different studies. All studies showed similar results, pointing in the same direction: falls are an increasing public health problem. Another major quality of these databases was that they contained very accurate in-hospital data and mortality statistics over an extensive period with nearly complete national coverage in The Netherlands. The Netherlands is one of the few countries in the world with such unique databases. Absolute numbers of hospitalizations and mortality statistics in The Netherlands were recorded by using the international coding system of the World Health Organization (International Classification of Diseases - ICD) throughout the study period. The accurate data which was accumulated over an extensive period, made it possible to gather reliable population-based data for trend analysis on specific topics.

Methodological issues

However, the use of link administrative databases, which have been used to analyze Emergency Department visits, hospitalizations, and mortality statistics, also have several limitations. First of all, the data are only accurate within the limitations of the coding system. The accuracy of the hospital information is likely to be dependent on the accuracy of the data in the medical records and the recognition of the injuries and trauma mechanisms, in the first instance by the patient's physician writing the record and secondly by the clerk coding the diagnosis into the database. In order to minimize coding errors and variation, official coding clerks translate the information to the ICD codes. A recent quality survey showed a high accuracy of coded injury data (correctly coded in 91% of cases and incomplete in 9% of cases). This provides support for the validity of the data used on hospitalizations due to external causes as extracted from these databases. The accuracy is comparable to the registration in New Zealand (period 1996–98).

A second important limitation of the link administrative databases is that the databases do not contain information regarding underlying diagnosis, co-morbidities, treatments, injury severity, life style, drug(s), medication compliance, and clinical details of the individual patients. Therefore, it was not possible in the presented studies to draw conclusions regarding specific high risk groups, such as the fall-risk for patients with polypharmacy. This restricts the interpretation of causal mechanisms behind the observed trends, such as the rapid rise in head injuries. The causal mechanism behind the trends found should be explored to determine new preventative strategies.

Third limitation is that most of the data were based on the national situation in one country. The Netherlands is a country with a full healthcare insurance coverage system and access for the whole population during the study period, and our findings might therefore not be directly applicable to other countries. However, comparable increasing temporal trends for fall- and ADR related-hospitalizations were found in other countries around the world. It therefore seems likely that the incidence of injury related hospital admissions will progress similarly in other developed countries. Additional studies are required to confirm if these trends in hospital admissions are comparable with those in other populations.

Fourth limitation is the absence of patients who were not seen at an Emergency Department or were not admitted to the hospital. These patients are not registered in the databases used and, consequently, are not included in this study. Therefore, this thesis mainly reflects trends regarding the incidence rates of serious fall-related injuries and excludes isolated minor fall-related injuries treated exclusively in the primary care setting. The actual societal impact of all fall-related injuries, both major and minor, is presumably even larger than the burden described in this study.

Implications

Despite these limitations, our findings show comparable results with studies from other countries around the globe.[8-11] Due to worldwide ageing, age-related issues, such as falls, are expected to lead to an increasing healthcare demand. Based on the exploration of injury type, incidence rates, and the identification of specific high risk age-groups, predictions could be made to calculate the expected fall-related healthcare demand for the near future. Considering the limited healthcare resources and a rising healthcare demand, changes have to be made in order to keep the healthcare sector accessible for all inhabitants, including the oldest old.

To reduce the fall-related healthcare consumption, the causal mechanisms behind the rising incidence of falls and related healthcare usage should be determined. Once the causal mechanisms are known, targeted intervention programmes can be developed and implemented. Possible factors which have been suggested to contribute to the rising fall-related healthcare demand could be that older adults have a more active lifestyle than 30 years ago. Another potential cause could be the rising life expectancy of the population. Older persons are getting older, and live longer with multiple co-morbidities, increasing their risk of falling. Furthermore, a lower admission threshold after Emergency Department visits might also contribute to a rising incidence rate of fall-related hospitalizations. However, the effects of these and other factors, should be explored in further research.

The majority of fall-related injuries was, and is still seen in women, but men are catching up.[3, 11] For example, fall-related mortality rates in both genders have become equal. This indicates that falls are not an exclusive issue of older women anymore, but of all older adults. However, the type of injury still remains different between men and women.

The question arises why men present more often with severe head injuries in old age, and why women present more often with fractures of the upper arm.[12] A potential cause could be the post-menopausal osteoporosis, which makes older women more vulnerable for fractures. Hip fractures in old age are the no. 1 reason for hospitalization after a fall incident. It is common knowledge that hip fractures may have long term consequences. But also less severe injuries, such as a “simple” wrist fracture, might be the difference between independent living and the need for social care in older adults.

There are multiple options to reduce the burden of fall-related healthcare use. An option to lower the burden of healthcare use after a fall is by reducing the length of hospital stay. Over the last three decades the admission duration has been reduced by approximately two-thirds. Despite the rapid increase in the number of fall-related hospitalizations, the total number of required hospital-bed-days in older persons did not increase, due to a reduced length of hospital stay. However, it will become more difficult to achieve such spectacular reduction in length of hospital stay again over the coming decades, because a minimum length of hospital stay will always be required. And it seems that we have almost reached the minimum length of hospital stay. The rising incidence and changing demographics make it likely that the required number of hospital bed days will increase till 2050.[13] Therefore other options to reduce the burden of fall-related healthcare consumption should be found.

Major and minor fall-related injuries result in a reduced quality of life. A reduced quality of life is leading to a higher healthcare consumption. Therefore, improvement of the initial treatment of fall-related injuries might contribute to a lower healthcare consumption, and to a reduction in the need for social care over a long period. A fall in older adults is not as simple as it sounds, and progress in treatment improvement should be made.

The options mentioned above are only focussed on reducing the healthcare consumption per fall-related injury. However, the key in reduction of fall-related healthcare consumption should be found in the reduction of fall risk and fall incidence among older adults. The burden of fall-related healthcare use can be substantially lowered, only when there are fewer people with fall-related injuries. This goal might be realized if falls prevention programs for older adults will be implemented. Based on risk factors which have been identified after extensive research over the last three to four decades[5, 14-18], multiple falls prevention strategies have been developed. However, not all falls prevention programmes are equally effective, so a careful selection of the most effective falls prevention measures and programmes should be made.[19-22]

Future research

New research should focus on the effectiveness of the different falls prevention programs. For example what is the effect of medication withdrawal, muscle strength training, or education on the fall-risk of the individual patient. Only measures which have been proven to be effective should be implemented.[21] Further studies should also explore why the trends for injuries are showing divergent trends for type of injury and for gender.

The important problem in research of older adults is the fact that they are often not included, or represent a minimal subsample of a study population.[23] Low participation of seniors in falls prevention studies makes it difficult to develop the best policy. Based on our experience, we recommend that research among oldest old should be designed differently. For example, in studies of older fallers we recommend to visit the patients at home or arrange transport to the research facility.

Both clinical practice and healthcare policy may benefit from studies dedicated to modifiable variables which can be applied in a falls prevention program. Important variables are: personal health perception, coping style of fall-risk, availability of personal aids, and the provision of preventative healthcare services. Research of falls in the older population requires further attention. Despite the complexity of age-related problems, due to co-morbidities, age-related issues, and pharmacotherapy in older adults, much is to be gained for the individual patients, healthcare services, and healthcare policy makers.

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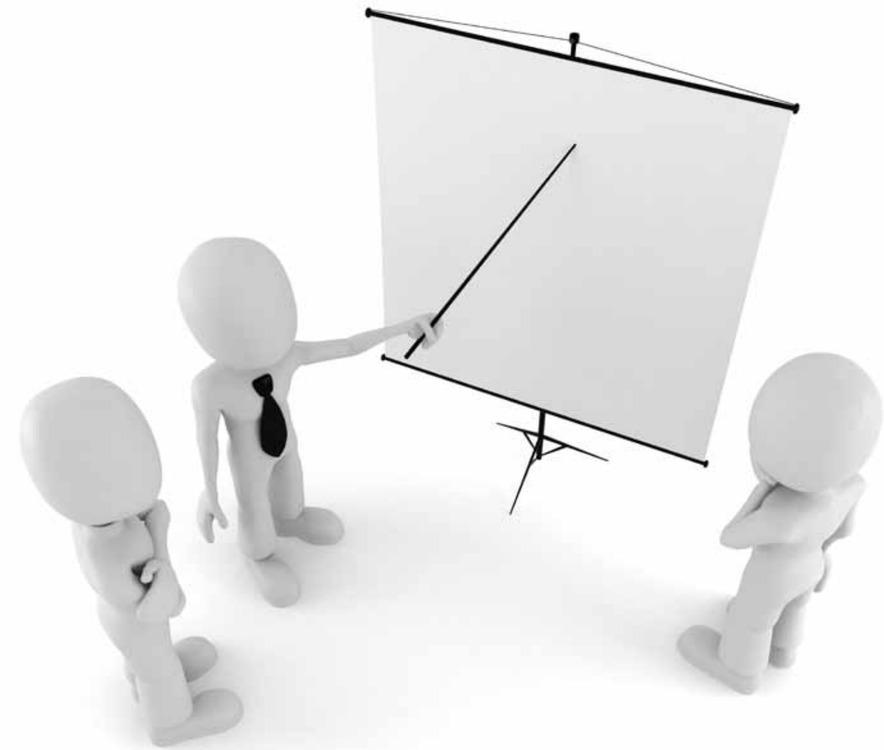
Chapter 7

Chapter 7.1



Summary and conclusions

Summary and conclusions

Falls represent a major public health problem among older persons in western countries, since approximately a third of all persons aged 65 years and older experience at least one f–all per year. Over the last decades the awareness of falls and related injuries has increased. However, the true magnitude of falls and adverse drug reactions among older persons is not known. Therefore, time trends and healthcare consumption as a result of falls and drugs in the older Dutch population were analyzed.

Chapter 1 gives a general introduction on the research topics of this thesis. **Chapter 2** provides an overview of fall-related injuries and healthcare expenses in The Netherlands, including fall-related Emergency Department visits and hospital admissions. In **Chapter 2.1** the total number of fall-related Emergency Department visits per year was calculated. Between 2005 and 2007, approximately 70,000 Emergency Department visits per year were due to a fall in the older population, with fractures being the most common presentation. Injuries were different for men and women, and varied with age. The oldest old presented with more often with severe injuries, such as hip fractures and head injuries, compared to younger adults. Furthermore, the quality of life after an injurious fall is reduced, short term as well as long-term. Nine months after a fall, the quality of life was still decreased. The healthcare expenses related to of falls are shown in **Chapter 2.2**. The total healthcare costs due to falls, including nursing home care, and hospital costs were over €674 million in 2007. Hip fractures were the most expensive type of injury, and because of the high incidence rate accounted for 40% of all fall-related healthcare costs. The costs per case among the oldest old were higher; due to an increased injury severity, this age group frequently requires hospitalization and long-term care. For hospitalized patients, the majority of healthcare costs were acquired due to prolonged stay in a long-term care facility, after discharge from the hospital. In **Chapter 2.3** the total number of fall-related hospitalizations is presented. Between 1981 and 2008, the number of fall-related hospital admissions increased by 137% to 34,091 hospitalizations in 2008. Main injury categories requiring admission were hip fractures, superficial injuries, and head injuries. Despite the fact that the number of admissions more than doubled during the study period, the total number of hospital bed days remained stable due a reduction of over 50% in the length of hospital stay per admission. The rapid increase in fall-related admissions is not only seen in The Netherlands. Similar findings were reported for the United States which is stated in **Chapter 2.4**. In concordance with the findings from The Netherlands, the incidence rate of fall-related hospitalizations increased in all age-groups for persons aged 65 years and older. The highest incidence rates were found for the oldest old, *i.e.*, aged 80 years and over.

Chapter 3 covers secular trends on hospitalizations due to hip fractures, head injuries, and vertebral fractures. In **Chapter 3.1** the number of hip fractures is presented. The incidence of hip fractures increased rapidly until the mid-nineties. Since then the increase in incidence rates of hip fractures has slowed down. In addition the incidence rate has started to decrease over de last decade. The mechanism for this finding is not known yet. However, a similar pattern has been found in other western countries as well. Besides the

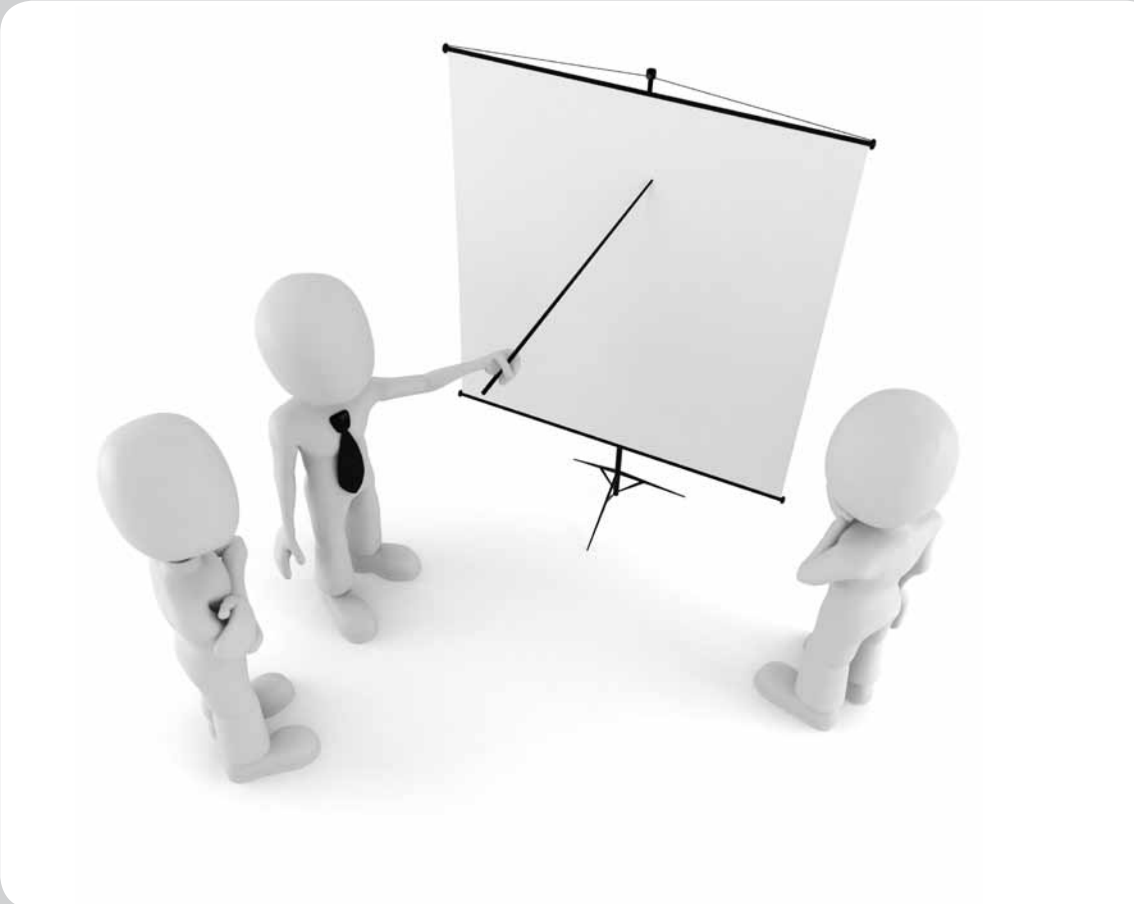
change in hip fracture incidence rates, a change in admissions for fall-related head injuries was also found. The incidence of head injuries increased gradually till the year 2000, but accelerated over the last decade **(Chapter 3.2)**. The total number of older patients admitted with fall-related head injuries tripled over the past decade, which might be due to be to an increased awareness of brain damage in older persons, improved radiologic possibilities, increasing life expectancy, and the introduction of new guidelines for traumatic head injuries. Vertebral fractures were studied, and the results are shown in **Chapter 3.3**. The majority of acute vertebral fractures leading to an Emergency Department visit were caused by a fall. The incidence rate of this type of injury is also increasing.

In **Chapter 4** fall-related mortality rates are presented. Over the past four decades the fall-related mortality rates dropped rapidly. During the mid-seventies the mortality rates were at least twice as high in women compared to men. Over the last decades, the gender difference disappeared and mortality rates for older men and women became comparable over the last decades. Despite the strong reduction, mortality rates have stopped decreasing and have started to increase in men.

In **Chapter 5** drugs, knowledge of drugs and hospitalizations due to adverse drug reactions are discussed. Pharmacotherapy is commonly used to treat medical conditions, but it is well known that side effects increase with an increasing number of drugs. Since older patients have multiple comorbidities, they are at high risk of polypharmacy. Some drugs are associated with an increased fall-risk. Therefore, we designed the IMPROveFALL study, which is presented in **Chapter 5.1**. In order to determine the effect of withdrawal of fall-risk increasing drugs on older fallers a randomized controlled trial will be conducted. The patients will be randomized for withdrawal of fall-risk increasing drugs versus "care as usual". The primary outcome will be the number of future falls in a one-year follow-up period. A case series on drug levels of fall-risk increasing drugs in older fallers is presented in **Chapter 5.2**. Several mechanisms make older adults more prone to side effects of drugs. Data on adverse drug reactions are scarce. In **Chapter 5.3** a description of registered adverse drug reactions related hospital admissions in The Netherlands is presented. It was found that the incidence of Adverse Drug Reactions related admissions increased with age. However, over the last decades the type of drugs contributing to the admission has changed. A known risk factor for an adverse drug reaction is poor drug knowledge. **Chapter 5.4** covers the drug knowledge of older adults, which was dependent on the number of drugs used. Moreover, the drug knowledge, including indication, name, dosage, and intake frequency was poorer in older persons compared with younger persons.

In **Chapter 6**, the general discussion, the main findings of this thesis are discussed and put in a broader perspective. The results indicate that falls prevention is needed in order to cope with the rising fall-related healthcare demand and to limit the healthcare consumption in an ageing population. Therefore, evidence based interventions should be implemented in the near future.

Chapter 7.2



Samenvatting en conclusies

Samenvatting en conclusies

Valincidenten bij ouderen zijn een groot maatschappelijk gezondheidsprobleem in westerse landen. Ongeveer een op de drie personen van 65 jaar en ouder valt jaarlijks. In de laatste decennia is de aandacht voor valincidenten en gerelateerde letsels sterk toegenomen. Desondanks is de totale omvang van valincidenten en onbedoelde geneesmiddelen reacties niet bekend. Daarom werden tijdreeksen, kosten, en zorggebruik door valincidenten en geneesmiddelen in de oudere Nederlandse populatie bepaald en geanalyseerd.

Hoofdstuk 1 geeft een algemene introductie op de onderwerpen die in dit proefschrift worden besproken. **Hoofdstuk 2** beschrijft de aard van de letsels en de gezondheidskosten die het gevolg zijn van valincidenten bij ouderen, inclusief Spoedeisende Hulp bezoeken en ziekenhuisopnamen. In **Hoofdstuk 2.1** wordt het totale aantal valgerelateerde Spoedeisende Hulp bezoeken in Nederland geanalyseerd. Tussen 2005 en 2007 bezochten jaarlijks 70.000 ouderen de Spoedeisende Hulp na een valincident, waarbij een botbreuk de meest voorkomend diagnose was. Letselpatronen waren verschillend voor mannen en vrouwen, en veranderden met leeftijd. De oudste ouderen presenteerden zich vaker met ernstiger letsel, zoals een heupfractuur en hoofdletsel, in vergelijking met jongere senioren. Letsel na een valincident gaat gepaard met een langdurige afname in de kwaliteit van leven. Negen maanden na de val is de kwaliteit van leven nog altijd verlaagd. De valgerelateerde zorgkosten zijn weergegeven in **Hoofdstuk 2.2**. In 2007 bedroegen de totale valgerelateerde zorgkosten, inclusief verpleeghuiszorg en ziekenhuisopnamen, €674 miljoen. De kosten per letsel waren het hoogste voor een heupfractuur. Door het grote aantal heupfracturen is dit type letsel verantwoordelijk voor 40% van alle valgerelateerde zorgkosten in Nederland. De kosten per letsel stegen met de leeftijd van de patiënt doordat de letsels ernstiger waren, doordat vaker ziekenhuis- en verpleeghuisopname noodzakelijk was en een langere opnameduur. Het totale aantal valgerelateerde ziekenhuisopnamen in Nederland bij ouderen wordt vermeld in **Hoofdstuk 2.3**. Tussen 1981 en 2008 steeg het aantal valgerelateerde ziekenhuisopnamen met 137% tot 34.091 opnamen per jaar in 2008. Het merendeel van de valgerelateerde ziekenhuisopnamen was in verband met een heupfractuur, oppervlakkig letsel, en hoofdletsel. Ondanks het feit dat het totale aantal ziekenhuisopnamen meer dan verdubbelde gedurende de studieperiode, bleef het totale aantal ligdagen in het ziekenhuis gelijk. Dit was een gevolg van een verkorting van de opname duur van meer dan 50% per opname. De snelle toename in valgerelateerde ziekenhuisopnamen werd niet alleen gezien in Nederland. Een soortgelijke bevinding werd gedaan in de Verenigde Staten, zoals is weergeven in **Hoofdstuk 2.4**. Bij Amerikanen van 65 jaar en ouder steeg de incidentie van valgerelateerde ziekenhuisopnamen in alle leeftijdsgroepen. De hoogste incidentie werd waargenomen bij de oudste ouderen (personen boven de 80 jaar).

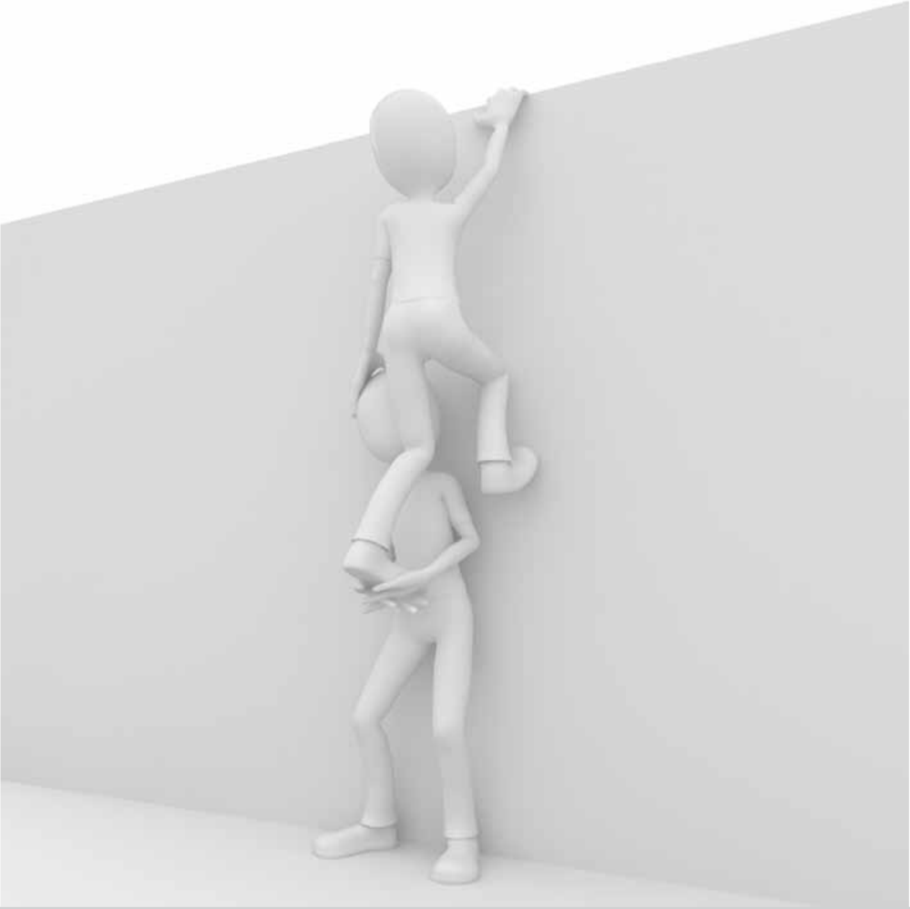
Hoofdstuk 3 richt zich op de ontwikkeling van specifieke letsels, zoals heupfracturen, hoofdletsels, en wervelfracturen gedurende een langere periode. In **Hoofdstuk 3.1** wordt het aantal heupfracturen gepresenteerd in Nederland. De incidentie van heupfracturen steeg sterk tot en met halverwege de jaren negentig, en sindsdien nam de stijging geleidelijk af. Gedurende het laatste decennium daalde de incidentie van heupfracturen zelfs licht.

Welke achterliggende reden hiertoe heeft geleid is nog niet precies bekend, maar toch wordt dit patroon gezien in meerdere landen wereldwijd. Niet alleen een verandering in de incidentie van heupfracturen werd gevonden, maar ook in ziekenhuisopnamen als gevolg van valgerelateerde hoofdletsels. De incidentie voor hoofdletsel steeg marginaal tot aan het jaar 2000. Sindsdien versnelde de groei in incidentie in de afgelopen 10 jaar **(Hoofdstuk 3.2)**. Het totale aantal ouderen dat werd opgenomen met een hoofdletsel na een val is verdrievoudigd in de laatste 10 jaar tijd, wat mogelijk verklaard kan worden aan de hand van een toegenomen alertheid op schedel/hersenletsel bij ouderen, verbeterde beeldvormende technieken, hogere levensverwachting, en de invoering van nieuwe richtlijnen met betrekking tot mild schedel hersenletsel. Ook wervelfracturen werden onderzocht, en de resultaten worden getoond in **Hoofdstuk 3.3.** Het merendeel van de acute wervelfracturen dat werd gediagnosticeerd op de Spoedeisende Hulp werd veroorzaakt door een val. Ook van dit type letsel steeg de incidentie geleidelijk.

In **Hoofdstuk 4** worden valgerelateerde sterftecijfers gepresenteerd. Het aantal sterfgevallen als gevolg van een valincident is sinds 1969 sterk afgenomen. Waren de sterftecijfers in de jaren '70 nog tenminste tweemaal zo hoog voor vrouwen vergeleken met mannen, nu is dat verschil helemaal verdwenen. De relatieve sterftecijfers voor mannen en vrouwen zijn inmiddels gelijk geworden. Ondanks de sterke afname in valgerelateerde sterfte, is de afname afgevlakt, en zijn de getallen voor vrouwen stabiel. De relatieve sterftecijfers voor mannen echter lopen langzaam op.

Hoofdstuk 5 gaat in op geneesmiddelen, geneesmiddelenkennis, en ongewenste geneesmiddelenreacties. Geneesmiddelen worden gebruikt voor de behandeling van bepaalde aandoeningen. Het is bekend dat de kans op ongewenste neveneffecten stijgt bij het gebruik van een groter aantal geneesmiddelen. Omdat het aantal aandoeningen stijgt met de leeftijd, komt het gebruik van polyfarmacie (gebruik van drie of meer geneesmiddelen) het meeste voor bij ouderen. Een aantal geneesmiddelen is in verband gebracht met een verhoogd valrisico. Om die reden werd de IMPROveFALL studie ontworpen, zoals is gepresenteerd in **Hoofdstuk 5.1**. Om het effect te bepalen van het verlagen of stoppen van valrisico verhogende geneesmiddelen is een gerandomiseerde studie opgezet. De deelnemers worden middels loting verdeeld over de interventie- of controle groep. In de interventiegroep wordt getracht om valrisico verhogende geneesmiddelen te verlagen of te stoppen als dat (veilig) mogelijk is. Patiënten in de controlegroep ontvangen de "huidige standaard zorg" zonder extra geneesmiddelaanpassing. Het aantal nieuwe valincidenten in het aankomende jaar wordt gebruikt als belangrijkste uitkomstmaat. In een serie patiënten die na een valincident gezien werden, is de bloedspiegel bepaald van valrisico verhogende geneesmiddelen **(Hoofdstuk 5.2)**. Meerdere onderliggende mechanismen zorgen ervoor dat ouderen gevoeliger zijn voor ongewenste geneesmiddelenreacties. In **Hoofdstuk 5.3** wordt beschreven hoeveel ziekenhuisopnamen er jaarlijks in Nederland geregistreerd worden als gevolg van een ongewenste geneesmiddelreactie. Niet alleen het geneesmiddelgebruik is leeftijdsafhankelijk, ook het aantal ziekenhuisopnamen ten gevolge van een ongewenst effect steeg met de leeftijd. Wel werd gezien dat het soort geneesmiddelen die leidde tot de opnamen gedurende de laatste 30 jaar zijn veranderd. Een bekende risicofactor is slechte kennis betreffende het geneesmiddel en het gebruik hiervan bij de patiënt. **Hoofdstuk 5.4** gaat in op de kennis van geneesmiddelen die patiënten gebruiken. Naar mate personen meer geneesmiddelen gebruikten, nam de kennis met betrekking tot naam, inname frequentie, dosering, en indicatie af. Daarnaast was de kennis bij ouderen minder goed in vergelijking met jongere patiënten.

De belangrijkste bevindingen van dit proefschrift worden in een breder perspectief geplaatst in **Hoofdstuk 6**. De gepresenteerde resultaten geven aan dat valpreventie noodzakelijk is om het toenemende valgerelateerde zorggebruik in de hand te houden in een vergrijzende samenleving. Daarom zullen effectieve valpreventie maatregelen verder geïmplementeerd moeten gaan worden in de nabije toekomst om de zorg voor iedereen goed toegankelijk te houden en het beperkte zorgaanbod het meest efficiënt te gebruiken.



Dankwoord / Acknowledgements

Dankwoord / Acknowledgements

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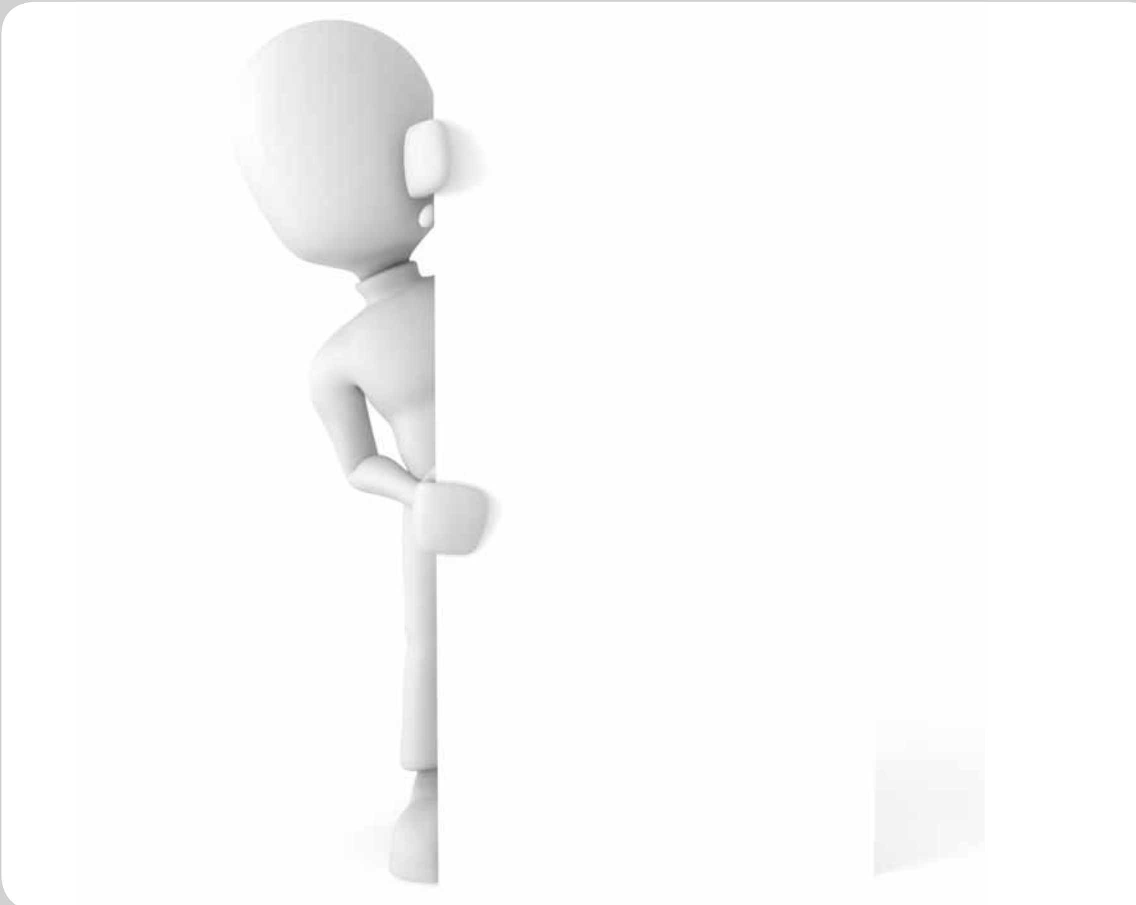

Curriculum Vitae

Curriculum Vitae

Klaas Hartholt was born on June 4th 1984 in Delft, The Netherlands. After graduating high school at the Christelijk Lyceum Delft in Delft, he started his medical training at the Erasmus University in Rotterdam in 2002. During his study he set up a research project at the Trauma Center of the South West Netherlands.

After completing his regular internships, options were used to explore healthcare services in South Africa. After organizing an internship at the Trauma Unit of the Addington Hospital in Durban, South Africa, a backpack travel tour through the inlands of several countries in the southern part of Africa was made.

In 2009, he received his degree in medicine and started working at the Erasmus MC, University Medical Center Rotterdam, as research fellow at the IMPROveFALL-study. The study, which resulted into this dissertation, concerned fall incidents among older persons, and was a cooperation between the department of Surgery-Traumatology (Prof. dr. P. Patka) and the department of Internal Medicine-section Geriatrics (dr. T.J.M. van der Cammen). In August 2011 he started as resident in the Reinier de Graaf Group in Delft.

Publication list

Publications

Click here for the most recent publications

KA Hartholt, S Polinder, EF Van Beeck, N Van der Velde, EMM Van Lieshout, P Patka, TJM Van der Cammen. End of the spectacular decrease in fall-related mortality rate: men are catching up. Am J Public Health. In Press

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PhD Portfolio

Summary of PhD-training and teaching

Name PhD student: K.A. Hartholt Erasmus MC Department: Surgery-Traumatology Research School: COEUR / MUSC	PhD Period: Dec 2008 - April 2011 Promotor: Prof.dr. P. Patka Co-promoters: dr. T.J.M. van der Cammen, dr. E.F. van Beeck		
1. PhD Training		**Year**	**Workload (ECTS)**
General courses			
- Medical statistics (NIHES summercourse ESP)		2009	4.5
- BROK ('Basiscursus Regelgeving Klinisch Onderzoek')		2009	1.5
Specific courses (*e.g.* Research School, Medical Training)			
Seminars and workshops			
- Zuid-West Nederland Overleg Traumatologie (ZWOT)		2009-2001	1.0
- CPO Minicursus voor Methodologie van Patiëntgebonden onderzoek en voorbereiding van subsidieaanvragen		2009	0.3
Presentations			
- Various presentations at research seminars and symposia of the Erasmus University Medical Center		2009-2011	10
(Inter)national conferences			
- Geriatriedagen		2009-2011	2.0
- Assistentensymposium Nederlandse Vereniging voor Traumatologie		2009-2010	1.0
- European Union Geriatric Medicine Society, Dublin		2010	2.0
- International Association of Gerontology and Geriatrics, Bologna		2011	1.0
- European Society of Trauma and Emergency Surgery, Milano		2011	1.0
- Traumadagen		2010	1.0
2. Teaching			
Lecturing			
- Lecturing for Geriatric residents		2009	1.0
- Lecturing at dept. of Surgery		2009-2011	2.0
- Lecturing for Psychiatrists		2011	1.0
- Lecturing for minor students of Geriatric Medicine		2010	1.0
Supervising practicals and excursions, Tutoring			
- Examination of Basic Life Support (EHBO) of medical students		2009-2010	1.0
Supervising master theses (three students)			
- J.J. Val		2009	2.0
- A.B.M. Elskamp		2010	2.0
- K.M.M. van Riel		2011	2.0