Arthroplasty for Femoral Neck Fractures

Paul Theodorus Petrus Wilhelmus Burgers

The publication of this thesis was supported by:
Anna Fonds|NOREF Leiden
Chipsoft
Erasmus MC afdeling Heelkunde
Heraeus medical
implantcast
Nederlandse Orthopaedische Vereniging
Nederlandse Vereniging voor Traumatologie
Oudshoorn chirurgische techniek B.V.
Van Wijk Voet & Zorg

Layout and printed by: Optima Grafische Communicatie, Rotterdam, the Netherlands (www.ogc.nl)

Logo design by: Studio Van Laar, Motion & Graphic design, Eindhoven, the Netherlands

ISBN: 978-94-6361-007-0

Funding for the research of this thesis was provided by the Netherlands Organization for Health Research and Development (ZonMw, research grant number 17088.2503)

Arthroplasty for Femoral Neck Fractures

Arthroplastiek voor collum femorisfracturen

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de
Rector magnificus
Prof.dr. H.A.P. Pols
en volgens besluit van het College voor Promoties

De openbare verdediging zal plaatsvinden op
vrijdag 27 oktober 2017 om 11:30 uur

door

Paul Theodorus Petrus Wilhelmus Burgers
geboren te Eindhoven

Erasmus University Rotterdam

Erasmus

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Voor mijn ouders, Caroline, Janne, Sven en Nils

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General introduction
and outline of this thesis

INTRODUCTION

"*Sometimes fracture of the neck of the femur occurs at the hip joint, which I saw when called to treat a good woman. Seeing that the leg was shorter than the other, with a prominence the trochanter makes externally and below the joint of the ischium, I assumed this was the head of the bone, dislocated and not fractured. Then I pulled and set the bone, it seemed, in its socket, after which the two legs were equal in length and contour, and I dressed and treated it as a dislocation. Two days later I found her in great pain, the leg short again and the foot turned inward. I removed the bandages and found that the prominence had reappeared. Then I tried again to replace the bone in its socket and I felt the bone crepitate. Then I found there was no joint cavity, so I knew this was a fracture and not a dislocation.*"

This first report in medical literature of a femoral neck fracture was written by Ambroise Paré (1510-1590) and published in 1575 (1). Besides being the first and the notification of the inward turned foot (mostly the foot is turned outward), also notable in this report is Paré's transparency about the initial misdiagnosis. An even longer delay in diagnosing a femoral neck fracture is in the probably oldest documented case: a woman living in the XIIth Dynasty (1990–1786 B.C.) in Egypt, who was diagnosed by researchers about 4000 years after the fracture (2). The discovery of X-rays in 1895 by the first winner of the Nobel Prize in physics (1901), Wilhelm Conrad Röntgen (1845-1923), made it substantially easier to identify femoral fractures. Another landmark in hip fracture history is the creation of the first classification in 1822 by Sir Astley Cooper (1768-1841). He classified proximal femoral fractures in intra- and extracapsular fractures on specimens (3). Nowadays the intracapsular fractures are classified on X-rays as undisplaced (type 1 and 2) and displaced (type 3 and 4), according to Robert Symon Garden (1910-1982) (Figure 1) (4).

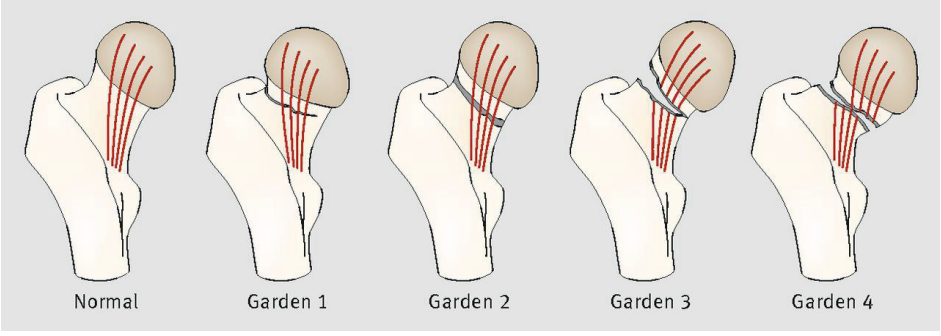

Figure 1. Classification according to Garden (4).

Almost 60% of all proximal femoral fractures are femoral neck fractures of which 80% is displaced (5).

The optimal individual treatment is under scientific debate and the famous term "the unsolved fracture", introduced by Kellog Speed (1879-1955) in 1935, is still accepted (6). The individual characteristics of both the fracture and the patient together with the preference of the surgeon determine the treatment mostly being either internal fixation or arthroplasty. This thesis focuses on the treatment of elderly patients with a displaced femoral neck fracture using arthroplasty. Surgical options for arthroplasty include total hip arthroplasty (THA) and hemi-arthroplasty (HA). The variable practice is demonstrated by a survey among an international group of orthopedic trauma surgeons (7). In order to identify the most favorable type of arthroplasty and finally develop an evidence based practice guideline the HEALTH trial (NCT00556842) was started in 2008. This international multicenter randomized controlled trial compares THA and HA by evaluating secondary interventions, complications, functional outcome and quality of life of 1,434 elderly patients with a displaced femoral neck fracture (8). Appendix 1 provides a summary of the aims and the protocol of the HEALTH trial. Data of the Dutch subset of the HEALTH trial form the base of this thesis. In general, hospitalization, long term rehabilitation, reduced quality of life, large healthcare expenses, and a high one year mortality make hip fractures a major public health issue. Despite declining trends for hip fractures in Western countries (9-13), a continued worldwide increase is expected because of the aging of populations by improving global healthcare and increasing industrialization and urbanization (14). Another important societal focus is on the health care related costs of femoral neck fractures. Hospital stay is one of the most important direct cost determinants in the treatment of femoral neck fractures (15). The implementation of multidisciplinary clinical pathways is related to with positive effects on mortality, postoperative complications, and in-hospital stay, leading to reduced costs (16-18). Consequently, the Dutch Ministry of Health, Welfare and Sport propagates early transfer to medical rehabilitation facilities (15).

AIMS OF THIS THESIS

The aim of this thesis is threefold. The first aim is to study the cumulative incidence of bilateral femoral neck fractures and the use of two types of arthroplasty for these fractures. The second aim is to investigate the reliability and validity of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) in a femoral neck fracture population. Finally, the third aim is to evaluate health care costs and functional results after treatment with arthroplasty for femoral neck fractures.

OUTLINE OF THIS THESIS

Chapter 2 includes the results from time trends in numbers and incidence rates of hip fracture related hospitalizations and admission time in the older Dutch population from 1981 throughout 2008 using the National Hospital Discharge Registry. It is known that a first hip fracture is a risk factor for a second, contralateral fracture. Data on the similarity of the treatment of bilateral femoral neck fractures are however only scarcely available. This information can be relevant to inform patients about the measures to be taken in order to minimize the risk of a second fracture in the future. Chapter 3 describes the cumulative incidence of non-simultaneous bilateral femoral neck fractures, including patient and treatment characteristics. There is still no consensus on the optimal type of arthoplasty, despite multiple clinical comparative studies. Therefore, a systematic review and meta-analysis of data from randomized trials concerning THA versus HA is included in chapter 4. This chapter forms another important base for the rationale of performing the multicenter HEALTH trial. Multicenter trials can be organized in different ways. For the Dutch sites most study tasks were managed by a central trial coordinator (central coordination), Canadian and US sites used local study coordinators (local coordination). Chapter 5 describes the results of a prospective observational study that analyses how these different strategies affected trial performance.

The main question when treating patients is to what extent patients are able to regain the functional ability they had prior to the fracture. Traditionally, objective determinants like mortality, complications, and revision surgery were used to assess treatment outcomes after hip fracture surgery. Nowadays, methods to assess the patient's perspective of treatment results are gaining importance as an indicator of the quality of care. These subjective functional outcomes and quality of life are quantified using patient reported outcome measures (PROMs). A validated questionnaire in the hip fracture population however was not available. Chapter 6 aims to determine the reliability, validity, and responsiveness of the WOMAC, compared with a known functional outcome questionnaire (SF-12) and a quality of life questionnaire (EQ-5D), in elderly patients who sustained a femoral neck fracture.

Quality of care of patient populations can be improved by implementing clinical pathways. Chapter 7 describes the effect of the implementation of a clinical hip fracture pathway on admission duration and complication rates in a Dutch teaching hospital. Cost awareness be-comes more important in today's healthcare. In times of financial distress, surgeons are ex-pected to have a general idea about the costs of the treatments they provide. Chapter 8 is a comprehensive overview of the costs of Dutch patients with a femoral neck fracture treated with arthroplasty.

Chapter 9 summarizes the main results and conclusions of the studies in this thesis, a Dutch translation is provided in chapter 10. Finally, chapter 11 provides a general discussion of the main findings in this thesis and its consequences on treatment of patients with a femoral neck fracture, including future perspectives.

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Chapter 2

The Epidemic of Hip Fractures: Are We on the Right Track?

PLoS One. 2011;6:e22227

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

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 of this study 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 in 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 20.5%, 95% CI: 20.7; 20.3), 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-morbidities.

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 to prevent falls and fractures. However, the true cause of the observation is unknown.

Funding: Grants from the Netherlands Organization for Health Research and Development (ZonMw, project number 170.885.607 and 170.882.503) and a grant from NutsOhra (project number T-0602-43) were received. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: A grant from NutsOhra (project number T-0602-43) was received. This does not alter the authors' adherence to all the PLoS ONE policies on sharing data and materials.

INTRODUCTION

Fall incidents and fall related injuries among older people are a major public health problem in 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 microarchitectural 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 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 $34.8 billion in 1990, and are expected to rise to an estimated $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 data of 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 Registry. 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, 9th 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 accessible database, containing anonymous data on admissions, which cannot be traced to individuals.

Numbers of hospitalizations due to hip fractures 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 the index year 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 crude incidence rate increased, from 46.4 per 10,000 older adults in 1981 to 66.5 per 10,000 in 2008 (an increase of 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 (an increase of 43.3%) and for older women from 59.5 to 86.8 (an increase of 46.0%) from 1981 to 2008 respectively.

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 when comparing 2008 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 aged ≥75 years showed growth of one sixth to a quart.

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 (an increase of 20.6%).

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 (*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 (n)	7,614	9,958	12,565	14,508	14,810	15,249	16,049
- males (n)	1,857	2,281	2,879	3,326	3,385	3,845	4,105
- females (n)	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.

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 to men (27.9 per 10,000 older men in 1981 and 37.8 in 2008).

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

	65-69 year		70-74 year		75-79 year		80-84 year		85-89 year		90-94 year		≥95 year	
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.

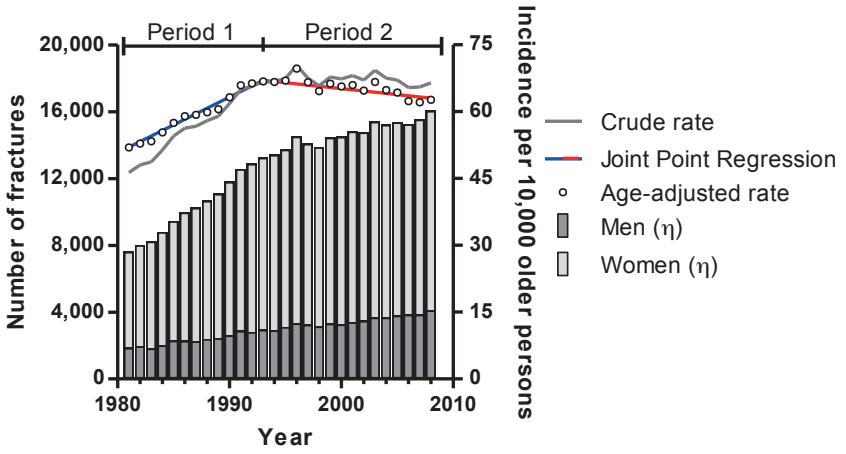

Figure 1. Numbers, crude and age-specific incidence rates of hip fracture-related hospitalizations in the Dutch population ≥65 years (1981-2008) . Period 1 (blue line): 1981-1993, percentual annual change 2.30%, (95% CI: 2.00; 2.59). Period 2 (red line): 1994-2008, percentual annual change -0.50% (95% CI: -0.70; -0.30).

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 nega-tive annual growth of 20.34% (CI 95%: 20.86; 0.19) in men and 20.64% (CI 95%: 20.83; 20.46) 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 over 60% in male and female patients of 65–79 years. Reduction in LOS was 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-beddays 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 (a decrease of 20%). For all men aged ≥65 years, the total number of hospital days decreased with 8% (from 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 (from 94,903 days in 1981 to 43,474 days in 2008). In women aged ≥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 (21%) the total number of hospital days in 1981 (123,513 days).

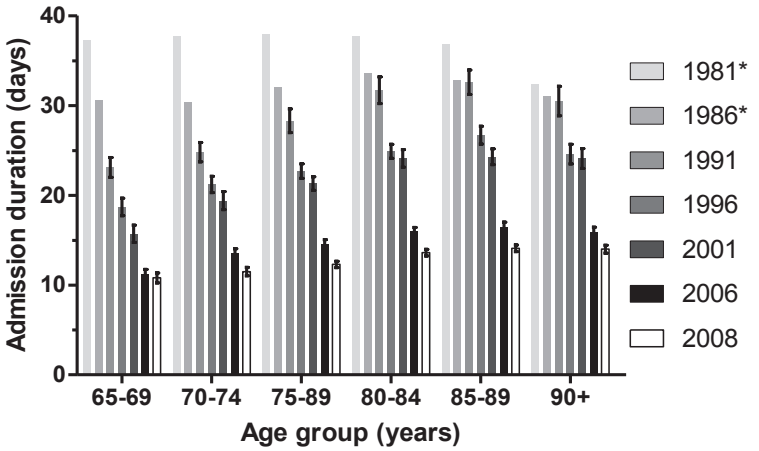

Figure 2. Mean hospital admission duration in persons aged ≥65 years in the Netherlands between 1981-2008. * No SD data were available before 1991.

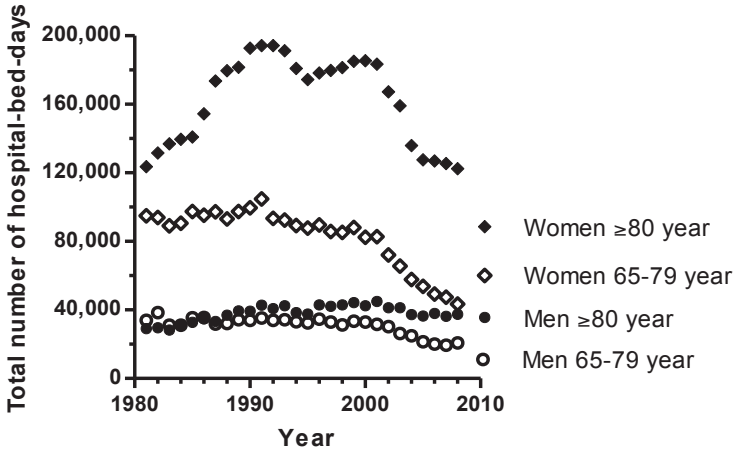

Figure 3. Total number of hip fracture-related hospital-bed-days in persons of ≥65 years in the Netherlands between 1981-2008.

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.

Comparable trends of decreasing incidence rates for hip fracture-related hospitalizations since the mid-nineties have been reported in several countries around the globe, 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). Since most studies on hip fracture incidence from multiple countries point in the same direction, there might be a causal explanation for this observation. However, 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 possibility 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 has increased in the Dutch population (33). An increased Body Mass Index is associated with a lower fracture risk (36).

A remarkable difference was observed between the younger and older age-groups. Whereas 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 past decades, resulting in a smaller gap in life expectancy between men and women (40). Consequently, men have 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 past decades (2, 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 per hip fracture in an individual patient (43). Therefore, a reduced LOS is necessary 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 to designated rehabilitation places and 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 populationbased 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 nearly complete national coverage in a highly accurate electronic database. Throughout the study period, the coding system of the National Medical Registry did not change 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 is that these data describe the situation in 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, comorbidity, 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 at the most 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 between 1981 and 1993, and the incidence rates started to decrease over the last 14 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

Cumulative incidence and treatment of non-simultaneous bilateral femoral neck fractures in a cohort of 1250 patients

Int Orthop. 2014;38:2335-42.

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ABSTRACT

Purpose: In the Netherlands, over 20,000 patients sustain a hip fracture yearly. A first hip fracture is a risk factor for a second, contralateral fracture. Data on similarity of the treatment of bilateral femoral neck fractures are only scarcely available. The objectives of this study were to determine the cumulative incidence of non-simultaneous bilateral femoral neck fractures and to describe the patient characteristics and treatment characteristics of these patients. Methods: A database of 1,250 consecutive patients with a femoral neck fracture was available. Patients with a previous contralateral femoral neck fracture were identified by

27 reviewing radiographs and patient files. Patient characteristics, previous fractures, hip fracture type and details on treatment were collected from the patient files.

Results: One hundred nine patients (9 %, 95 % confidence interval 7–10 %) had sustained a non-simultaneous bilateral femoral neck fracture. The median age at the first fracture was 81 years; the median interval between the fractures was 25 months. Overall, 73 % was treated similarly for both fractures in terms of non-operative treatment, internal fixation or arthroplasty. In patients with identical Garden classification (30 %), treatment similarity was 88 %.

Conclusions: The cumulative incidence of non-simultaneous bilateral femoral neck fractures was 9 %. Most patients with identical fracture types were treated similarly. The relatively high risk of sustaining a second femoral neck fracture supports the importance of secondary prevention, especially in patients with a prior wrist or vertebral fracture.

INTRODUCTION

Hip fractures are a global public health problem. In the Netherlands, over 20,000 patients sustain a hip fracture annually (1). The incidence of hip fractures is expected to increase, mainly due to the aging of the population. A first hip fracture is a risk factor for sustaining a second hip fracture at the contralateral side. Other reported predictors for a second hip fracture include age, female gender, living alone, alcoholism, any prior fracture, functional status, dementia, and osteoporosis (2-6).

Despite a declining trend in hip fractures in western countries (7-11), a worldwide increase is expected as a result of aging of populations by improving health care globally and increasing industrialization and urbanization (12). An increase in incidence of the first hip fracture implies that an increase in incidence of a subsequent hip fractures is to be expected as well. The latter is associated with an increased mortality risk; the one-year mortality ranges from 9 % to 27% following a first hip fracture and 8% to 32% after a second hip fracture (2, 13, 14). The 5-year mortality rate after a first and second hip fracture is 46% and 67%, respectively (2).

The overall cumulative incidence of non-simultaneous bilateral hip fractures, regardless of fracture location or subtypes, is reported to range from 2% to 15% (2-4, 6, 15-22). The reported interval between both fractures is 2-5 years (2-4, 6, 13, 15, 18, 21, 22). In 60-81% of the patients with bilateral hip fractures the second fracture is of the same type as the first hip fracture (*i.e.,* trochanteric or femoral neck) (3, 4, 13, 14, 18, 21, 23). Most reports on characteristics of bilateral hip fractures involved patients with both trochanteric and femoral neck fractures. A minority of patients with a primary trochanteric fracture sustains a subsequent contralateral femoral neck fracture. The opposite, a femoral neck fracture as a second fracture with a first trochanteric fracture, is even rarer (14, 17). Especially the treatment of non-simultaneous femoral neck fractures has received little attention in previous studies.

Controversy on the treatment of active patients with a displaced femoral neck fracture still exists, particularly on the type of implant (*i.e.*, sliding hip screw or cannulated screws) or prosthesis (*i.e.*, hemi-arthroplasty or total hip arthroplasty). One would expect that two fractures of the same type in patients with unchanged characteristics would be treated the same. In addition to these patient and fracture characteristics, preferences of the surgeon may also contribute to the treatment selection. Detailed information on the treatment of patients with non-synchronous femoral neck fractures is limited, to the best of our knowledge.

Therefore, the objectives of this study were to determine the cumulative incidence of non-simultaneous bilateral femoral neck fractures and to describe patient characteristics, mortality and treatment characteristics of these patients.

PATIENTS AND METHODS

This study was conducted as a multicenter retrospective cohort study of patients who sustained non-simultaneous bilateral femoral neck fractures. The study was approved by the local medical research ethics committee (ref. No MEC-2011-419, approval date November 4, 2011). In a previous retrospective multicenter study a database was developed, containing data for 1,250 consecutive patients with a femoral neck fracture who were treated in 14 Dutch hospitals between February 2008 and August 2009 (24). Patients were identified by searching the electronic hospital databases for DBC code (Diagnosis Treatment Combination; comparable to the North-American Diagnosis Related Groups), surgical codes and ICD-codes (International Classification of Diseases, version 9 and 10).

Two investigators (PTPWB and AKEM) independently assessed pelvic and hip X-rays of all patients for the presence of any sign of a previous fracture at the contralateral side (*i.e.* implant, arthroplasty, or healed fracture). Presence of a non-simultaneous bilateral femoral neck fracture was confirmed with data in the patient files.

Patients were eligible for enrolment if details on the treatment (*i.e.*, non-operative treatment, type of implant or arthroplasty) of both femoral neck fractures were available from radiographs or medical correspondence. Pathological fractures, simultaneous bilateral fractures, and fractures following a high energetic trauma were excluded.

The following data were collected for both fractures:

- Patient characteristics: age at fracture, gender, ASA (American Society of Anesthesiologists) class, prior and concomitant fractures;
- Fracture characteristics: Garden classification (*i.e.*, undisplaced or displaced);
- Treatment characteristics: type of treatment, and for internal fixation: quality of reduction and positioning of the implant (*i.e.*, acceptable or unacceptable);
- Post-treatment details: length of hospital stay and in-hospital mortality.

The Garden classification was assessed independently by two senior trauma surgeons (MJH and MHJV) from blinded preoperative, peroperative and postoperative X-rays; classifications were done according to the description made in 1961 (25). These surgeons also rated the quality of reduction and positioning of the implant (for internal fixation), using the criteria as defined in the guideline of the Association of Surgeons of the Netherlands (26) (Table 1), as described elsewhere (24). If two out of three criteria were met, fracture reduction and positioning of implants were scored as 'acceptable'. Disagreement was solved by a third senior trauma surgeon (GRR), who independently reviewed the X-rays in order to reach a final decision.

Table 1. Criteria for acceptable reduction and positioning of the implant for internal fixation of a femoral neck fracture, according to the guideline of the Association of Surgeons of the Netherlands (26).

Acceptable reduction	Varus- valgus dislocation: maximum Garden index: 160–180° +
	Femoral neck shortening neutralized+
	Dorsoventral dislocation: maximum 10° retroversion - 5° anteversion++
Acceptable position cannulated screws	One screw placed caudally over the calcar femoris+
	One screw placed over the dorsal cortex++
	Screws positioned into the subchondral bone (maximum distance between screw tip and femoral head lining: 5-10 mm)+
Acceptable position sliding hip screw	Screw positioned in the central or caudal 1/3 part of femoral head+
	Screw positioned in the central or dorsal part of femoral head++
	Screw positioned into the subchondral bone (maximum distance between screw tip and femoral head lining: 5-10 mm)+

+ On AP (Anterior-Posterior) view. ++ On axial view.

Statistical Analysis

Statistical analyses were conducted using SPSS (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc). Normality of continuous data was tested with the Shapiro Wilk test and by inspecting frequency histograms (Q-Q plots).

All continuous variables were non-parametric and are therefore presented as medians with the first and third quartiles. Categorical variables are presented as numbers with percentages. The traditional Wald confidence interval formula for proportions was used for calculating the 95% confidence interval around the cumulative incidence of bilateral femoral neck fractures. Descriptive analyses were performed in order to describe the patient, treatment and post-operative variables for the first and second fracture. An additional analysis of treatment was performed for a subgroup of patients in whom the Garden class of the first and second fracture were of the same type.

RESULTS

Patient demographics

The total population consisted of 1,250 patients with a femoral neck fracture. Of these, 176 patients showed radiographic signs of bilateral femoral neck fractures. After reviewing the medical files, 67 patients were excluded; 29 patients underwent arthroplasty because of arthrosis rather than a fracture, 32 patients had a subtrochanteric or pertrochanteric fracture, and six patients were treated for another reason than for osteoporotic femoral neck fracture (Figure 1). In the remaining 109 patients the occurrence of non-simultaneous bilateral femoral neck fractures (9%, 95% CI 7 to 10%) was confirmed.

Patient characteristics of these 109 included patients are shown in Table 2. The median age was 81 years (P_{25}-P_{75} 74-86 years) at the time of the first fracture and 86 years (P_{25}-P_{75}

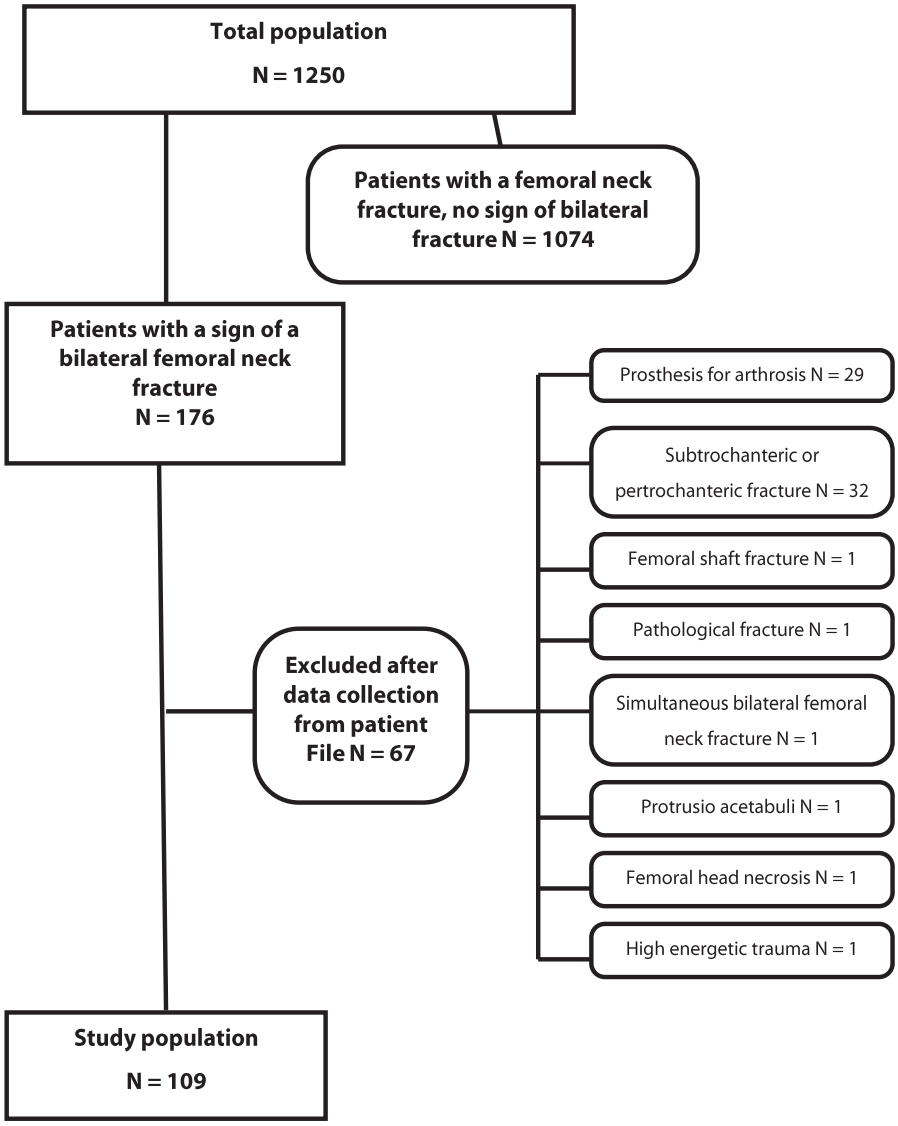

Figure 1. Flowchart of enrolled patients.

79-89 years) at the time of the second fracture. Seventy-six patients (70%) were female. The median time between the first and the second fracture was 25 months (P_{25}-P_{75} 12-62 months). The shortest interval between the two fractures was three days (and occurred following a fall) and the longest was 20 years. The right hip was the first affected side in 51 patients (47%). At the time of the first fracture 30 of 41 patients (73%) for whom data were available lived at home. At the time of the second fracture 49 of 80 patients (61%) lived at home. Concomitant fractures were found in 5% of patients at the time of the first

fracture and in 7% of patients at the time of the second fracture. Twenty-two patients (20%) had sustained another type of fracture prior to the second femoral neck fracture, with a median interval of seven years . Especially fractures of the wrist (6%), humerus (7%), spine (1%), rib (2%), olecranon (2%), and foot (2%) were found. The median hospital length of stay was 10 days (P_{25}-P_{75} 7-17 days) after the first fracture and nine days (P_{25}-P_{75} 5-13 days) after the second. One patient (1%) died during admission for treatment of the second fracture. Of the 1141 excluded patients, 42 (3.7%) died in hospital.

Table 2. Patient characteristics by first and second fracture

Characteristic	Overall N= 109	First Fracture N=109	Second fracture N=109
Age [1] (year)		81 (74-86)	86 (79-89)
Female gender [2]	76 (70)		
Right side affected [2]		51 (47)	58 (53)
Additional injuries at presentation[2]		5 (5)	8 (7)
Wrist/hand fracture		4 (4)	1 (1)
Humeral fracture		0 (0)	3 (3)
Tibia fracture		0 (0)	1 (1)
Head injury/wound		1 (1)	3 (3)
Not documented		34 (31)	3 (3)
Prior other fracture [2]	23 (21)		
Not documented	27 (25)		
Pre-operative ASA-class [2]			
ASA I-II		21 (19)	65 (57)
ASA III-IV		12 (11)	34 (31)
Unknown		76 (70)	13 (12)

1 Data are displayed as median, with the first and third quartile given within brackets;
2 Patient numbers are displayed with percentages within brackets

Fracture and treatment characteristics of the first and second femoral neck fracture

Details of the fractures and treatments of the total population of 109 patients are shown in Table 3. Data on the Garden classification of the first fracture were available in 50% of the patients. In patients for whom data were available, the first fracture was displaced in 72% of the patients (39 of 44); the second fracture (with 90% data availability) was displaced in 68% (67 of 98). Arthroplasty was performed in 65% of the first fractures and in 70% of the second fractures. The majority was treated with a hemi-arthroplasty (92% and 99% of the first and second fractures, respectively). Internal fixation was applied in 35 patients for the first fracture (32%) and in 30 patients (28%) for the second fracture. In these patients, cannulated hip screws (CHS) were then used in 49% of the first fractures and 70% of the second fractures. A sliding hip screw (SHS) was used in 49% and 30% of the first and second fractures, respectively.

Table 3. Fracture and treatment characteristics by first and second fracture

Characteristic	First fracture N=109	Second fracture N=109
Garden classification		
Non-displaced (Garden I-II)	15 (14)	31 (28)
Displaced (Garden III-IV)	39 (36)	67 (62)
Missing*	55 (51)	11 (10)
Therapy		
Non-operative treatment	3 (3)	3 (3)
Internal Fixation	35 (32)	30 (28)
Cannulated screws	17 (16)	21 (19)
Sliding hip screw	17 (16)	9 (8)
PFN-A	1 (1)	0 (0)
Arthroplasty	71 (65)	76 (70)
Hemi-arthroplasty	65 (60)	75 (69)
Total hip arthroplasty	6 (6)	1 (1)
Internal fixation: Reduction		
Adequate	20 (57)	28 (93)
Not adequate	0 (0)	2 (7)
Not able to determine	4 (11)	0 (0)
Missing	11 (31)	0 (0)
Internal fixation: Implant position		
Adequate	19 (54)	26 (87)
Not adequate	1 (3)	4 (13)
Not able to determine	4 (11)	0 (0)
Missing	11 (31)	0 (0)
Implant position Cannulated screws		
Adequate	8 (47.1)	17 (81.0)
Not adequate	1 (5.9)	4 (19.0)
Not able to determine	2 (11.8)	0 (0.0)
Missing	6 (35.3)	0 (0.0)
Implant position Sliding Hip Screw		
Adequate	11 (64.7)	9 (100.0)
Not adequate	0 (0.0)	0 (0.0)
Not able to determine	1 (5.9)	0 (0.0)
Missing	5 (29.4)	0 (00.0)

Patient numbers are displayed, with the percentages given within brackets.

* Garden classification could not be determined if adequate diagnostic images were not available, e.g., if trauma diagnostic had been done at another hospital.

An overview of similarity in characteristics and treatment of the first and second fracture is shown in Table 4. Data are presented for the entire group of 109 patients as well as for a subgroup of 33 patients in whom both fractures had the same Garden classification. This subgroup was treated identically in 88% of the patients in terms of non-operative treatment, internal fixation or arthroplasty. When the type of implant and arthroplasty were also taken into account, bilateral fractures of the same Garden classification were treated similarly in 73%. If arthroplasty was used, the same type of device was used in 100% of patients, whereas only in two out of seven patients (27%) treated with internal fixation the same type of implant was used. Table 5 shows the relation between Garden classification and treatment for the total population of 109 patients. Undisplaced fractures were mostly treated with internal fixation; 67% of the first fractures, 58% of the second fractures. Displaced fractures were treated with arthroplasty in 82% of first and in 81% of second fractures.

Table 4. Identical characteristics and treatment of first and second fracture

	Entire group (N=109)	**Same Garden classification for both fractures (N=33)**
	N (%)	**N (%)**
ASA classification	15/109 (14)	10/33 (30)
Garden class	33/109 (30)	N.A.
Treatment[a]	62/109 (57)	24/33 (73)
Treatment[b]	80/109 (73)	29/33 (88)
Type of prosthesis[c]	54/60 (90)	22/22 (100)
Type of implant[c]	8/20 (40)	2/7 (29)
Reduction[c]	11/20 (55)	5/7 (71)
Position implant[c]	9/20 (45)	6/7 (86)
Position cannulated screws[c]	2/4 (50)	2/2 (100)
Position SHS[c]	2/4 (50)	N.A.

Data are shown as numbers with the percentage within brackets.
N.A.; not applicable.a Treatment separated into non-operative, CHS, SHS, PFN-A, hemiarthroplasty and total hip arthroplasty.b Treatment separated into non-operative, internal fixation, and arthroplasty.c Data are shown for the subgroup of patients (denominator) where this applies to and for which data were available for both fractures.

Table 5. Association between the Garden classification and treatment (all 109 patients)

Treatment	Garden I-II	Garden III-IV	Unknown
First fracture	N=15	N=39	N=55
Non-operative	2	0	1
Internal fixation	10	7	18
Arthroplasty	3	32	36
Second fracture	N=31	N=67	N=11
Non-operative	1	1	1
Internal fixation	18	12	0
Arthroplasty	12	54	10

Data are shown as numbers.

DISCUSSION

Out of 1,250 patients with a femoral neck fracture, 109 had previously sustained a contralateral femoral neck fracture. The cumulative incidence of non-simultaneous bilateral fractures was 9%. This result is comparable with the recent literature, reporting a cumulative incidence of bilateral proximal femur fractures between 2% and 20% depending on the follow up period (2-6, 13, 15, 17). These studies however included both trochanteric and femoral neck fractures, implying that the cumulative incidence of bilateral femoral neck fractures in these studies had been lower than the percentages reported.

The median time between the first and second fracture in the current study was 25 months (P_{25}-P_{75}: 12.4-61.8 months). This is in line with literature data, where intervals from 2 to 5 years between the first and second hip fracture are reported (2, 4, 6). Given this short period, substantial changes in patient characteristics were not very likely.

Additional injuries, especially fractures, are likely to impair postoperative rehabilitation, to prolong hospital stay, and to increase the total health care costs. In the current study concomitant additional significant injuries such as a wrist fracture, head injury, or humeral fracture were seen in 5% and 7% of the patients at the time of the first and second hip fracture, respectively. Approximately a quarter of patients had already had a fracture in their medical history, prior to their femoral neck fracture (28%), which corresponds with a previous study on non-simultaneous bilateral femoral neck fractures (30%) (16). These results emphasize the vulnerability of this population, as a prior fracture increases the risk of a hip fracture and the occurrence of a first hip fracture increases the risk of subsequent (hip) fracture (5, 23). In the growing, fragile population that often suffers from multiple risk factors for falling and sustaining subsequent fractures, there might be great potential for multidisciplinary secondary prevention strategies. In this retrospective study documentation of osteoporosis screening was found in only 19% of the patients and anti-osteoporosis medication was prescribed in only 24% (data not

shown). This indicates too little attention has been paid to osteoporosis screening and management. Although circumstances and protocols differ between hospitals, there is a clear need for better compliance to the Dutch guideline on osteoporosis and fracture prevention (27). Regular evaluation of the local progress of the implementation should ensure a stricter protocol compliance and ultimately a better quality of fracture care (28). Also, independent community dwelling elderly have an increased risk of sustaining a second hip fracture (2). This emphasizes that the environment of the patient (*i.e.*, modifications in their home) and adequate rehabilitation (*i.e.*, appropriate use of walking aids and physical therapy) deserve attention to minimize the risk of falling and sustaining a new fracture as much as possible.

Over 80% of the displaced fractures were treated with arthroplasty and about 60% of the undisplaced fractures were treated with internal fixation. It seems that trauma and orthopedic surgeons generally agree on the treatment of the different types of femoral neck fractures, as 88% of the patients with a bilateral femoral neck fracture with similar Garden classification were treated similarly in terms of a non-operative treatment, internal fixation, or arthroplasty.

However, heterogeneity in the use of the specific type of implant or prosthesis remains. This is supported by the finding that in only 27% of the patients with an identical Garden classification of both fractures the type of treatment was not the same when the type of implant/ arthroplasty was also considered. Heterogeneity was especially high in the use of implant for internal fixation. This was not unexpected, as insufficient evidence on the use of implant or arthroplasty type for femoral neck fractures is known (29). It was however unexpected, that the controversy in the essential details of treatment seemed larger in undisplaced fractures (67 versus 58% internal fixation in first and second fracture), than in displaced fractures (82 versus 81% arthroplasty in first and second fracture). Diverging treatment decisions may however partially be explained by other variables such as coxarthrosis, comorbidity, surgeons preferences, material availability.

The strength of the current study is that a database of a large number of 1,250 consecutive patients treated in fourteen different hospitals was used (24). However, due to the retrospective design data were incomplete from a substantial number of patients. Data concerning the first fracture were often missing for patients in whom the first fracture was treated at another hospital. In addition, some radiographs were not available, *e.g.*, when they were made analogous, during external storage, or during digital exportation. There are no indications for a selective pattern of missingness of data. As a consequence, a reliable multivariable analysis was not possible. For the same reason the one year mortality could not be calculated, therefore the in-hospital mortality was used as a relevant alternative. Moreover, as no data on the cumulative incidence in a matched control cohort were available, it was not possible to carry out a risk assessment. Due to the relatively small number of patients per hospital, a subgroup analysis of similarity

of management for both fractures if treated at the same hospital was not possible. It is unfortunate that data on osteoporosis or osteoporosis treatment were often not documented. As discussed above, attention for osteoporosis screening and treatment can still be improved. For this reason, osteoporosis guidelines have been implemented in 1999 and were revised in 2002 and 2011 (28). Despite duplicate assessment of radiographic images, non-operatively treated fractures or fractures in which implants are removed could have been missed. However, if only the slightest doubt existed patient files were checked; in none of those patients a previous fracture was confirmed. Therefore it is unlikely that bilateral fractures were missed.

CONCLUSION

In a population of 1,250 patients who sustained a femoral neck fracture during the study period, 9% had previously sustained a femoral neck fracture at the contralateral side. The median time interval between both fractures was 25 months. If both fractures were undisplaced or both were displaced, the same treatment was applied in 88% of patients. Surgeons generally agreed on the use of internal fixation or arthroplasty for the different types of femoral neck fractures. The relatively high risk of sustaining a second femoral neck fracture supports the importance of national secondary prevention guidelines, especially in patients with a prior wrist or vertebral fracture.

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Chapter 4

Total hip arthroplasty versus hemiarthroplasty for displaced femoral neck fractures in the healthy elderly: a meta-analysis and systematic review of randomized trials

Int Orthop. 2012;36:1549-60

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ABSTRACT

Purpose: Displaced femoral neck fractures in healthy elderly patients have traditionally been managed with hemiarthroplasty (HA). Recent data suggest that total hip arthroplasty (THA) may be a better alternative.

Methods: A systematic review of the English literature was conducted. Randomized controlled trials comparing all forms of THA with HA were included. Three authors independently extracted articles and predefined data. Results were pooled using a random effects model.

Results: Eight trials totalling 986 patients were retrieved. After THA 4 % underwent revision surgery versus 7 % after HA. The one-year mortality was equal in both groups: 13 % (THA) versus 15 % (HA). Dislocation rates were 9 % after THA versus 3 % after HA. Equal rates were found for major (25 % in THA versus 24 % in HA) and minor complications (13 % THA versus 14 % HA). The weighted mean of the Harris hip score was 81 points after THA versus 77 after HA. The subdomain pain of the HHS (weighted mean score after THA was 42 versus 39 points for HA), the rate of patients reporting mild to no pain (75 % after THA versus 56 % after HA) and the score of WOMAC (94 points for THA versus 78 for HA) all favored THA. Quality of life measured with the EQ-5D favored THA (0.69 versus 0.57).

Conclusions: Total hip arthroplasty for displaced femoral neck fractures in the fit elderly may lead to higher patient-based outcomes but has higher dislocation rates compared with hemiarthroplasty. Further high-quality randomized Total hip arthroplasty for displaced femoral neck fractures in the fit elderly may lead to higher patient-based outcomes but has higher dislocation rates compared with hemiarthroplasty. Further high-quality randomized clinical trials are needed to provide robust evidence and to definitively answer this clinical question.

INTRODUCTION

The optimal surgical management of displaced femoral neck fractures in the elderly is the subject of an ongoing scientific and clinical debate (1, 2). About 50 % of the total hip fracture population has a displaced femoral neck fracture. Determining the optimal therapy is important as in the year 2000 an estimated 1.6 million hip fractures occurred (3), and this incidence is expected to increase to over six million hip fractures worldwide by the year 2050 (4). Reported causes are the changing demography and an increasing contribution of developing countries (5).

Patients with a hip fracture have high mortality and disability (6). As a consequence these fractures have a significant impact both on the patients' personal dependence, mobility and quality of life as well as on global economic health costs. Especially, the one-year mortality after a femoral neck fracture, even in selected patients, ranges from 14 % to 36 % (7), so the actual numbers are even higher. Moreover, worldwide 4.5 million persons are living with disability from hip fractures yearly. This number is expected to increase to 21 million persons in the next 40 years. The costs of treating a hip fracture patient are about three times higher than those of caring for a patient without a fracture (8). The worldwide direct and indirect annual costs of hip fractures in 1990 were estimated at US$34.8 billion (9).

Hemiarthroplasty (HA) and total hip arthroplasty (THA) remain as widely accepted methods of hip replacement after fracture. In the long run some patients treated with HA require conversion to THA because of activity limiting thigh pain due to acetabulum wear. Reported advantages of HA compared with THA are reduced dislocation rates, less complex surgery, shorter operation times, less blood loss, and lower initial costs (10). Therefore, a number of authors prefer HA for displaced femoral neck fractures (11-13). In contrast, evidence is accumulating to support better function and superior patient satisfaction for patients treated with THA(10, 14-17). Consequently, after weighing the pros and cons other authors advocate THA as preferable treatment for displaced fractures in the elderly (18-20). In two previous systematic reviews (2, 21) it was concluded that large well-designed randomized trials are needed in order to draw a definitive conclusion as the scientific evidence is still insufficient. Since the publication of these reviews, data of the largest trial (N= 250) (13) became available; these are included in the present study.

The aim of the present study was to conduct a systematic review and meta-analysis using the best available evidence in order to determine primarily the outcomes of reoperations; secondary outcomes were dislocation rates, mortality rates, complications, function, and pain of total hip arthroplasty versus hemiarthroplasty for displaced femoral neck fractures in the healthy elderly.

MATERIALS AND METHODS

The present review and meta-analysis were reported according to the PRISMA statement (22). Methods used for the analysis, search strategy, and inclusion criteria were specified in advance and documented in an unpublished protocol.

Search strategy

An electronic search of the literature was independently performed in duplicate by two clinical librarians at different time points from inception to February 22, 2011 in the following databases: MEDLINE (PubMed), EMBASE, World of Science and Cochrane Central Register of Controlled Trials. The electronic search was individually tailored to each database aiming at maximizing the sensitivity of the search when identifying studies having terms relevant to "hemiarthroplasty", "total hip arthroplasty" and "intracapsular hip fracture." The complete search terms are shown in Appendix 1. In addition, bibliog raphies were reviewed of all selected full text articles to identify additional articles. In order to evaluate any ongoing randomized trials, the international trial registries (www.clinicaltrials.gov, www.trialregister.nl and www.apps.who.int/ trialsearch) were accessed (last visit: March 11, 2011).

Eligibility criteria

Three reviewers (PTPWB, ARG and BB) independently identified titles and abstracts relevant to total hip arthroplasty versus hemiarthroplasty for dislocated femoral neck fractures. Full text published articles and unpublished data of completely finished and analysed studies were included. Authors of studies for which only the abstract was available were contacted for availability of study data. The following eligibility criteria had to be met: (1) use of (quasi) random allocation of treatments, (2) patients aged 50 years or older with a displaced femoral neck fracture, (3) inclusion of a treatment arm receiving any form of hemiarthroplasty, (4) inclusion of a treatment arm receiving any form of total hip arthroplasty, and finally all papers had to report data on the primary outcome, being revision surgery. No restrictions related to the length of follow-up or languages were defined. The reviewers obtained consensus on inclusion status with any found discrepancies.

The primary endpoint was defined as revision surgery within the different study periods. Secondary outcomes were mortality, dislocation, major and minor complications, functional outcome, pain, and quality of life. The minor and major complications were arbitrarily defined by two authors (PTPWB and ARG) as specified in Appendix 2.

Data extraction and analysis

Three reviewers (PTPWB, ARG and BB) independently extracted the inclusion criteria data from each study meeting. Data included demographics, methodology, details on intervention, and reported outcomes. Data for the primary and secondary outcomes were extracted and collected on a predefined standardized electronic data collection form. In case of differences, the reviewers discussed this item in order to meet consensus; if no agreement could be reached, a third author (RWP) decided. Methodological study quality was gauged by noting the specifics of randomization, concealment of allocation, blinding, adherence to the intention to treat principle and the extent of follow-up (Table 2) (23). Review Manager software (RevMan Version 5.0.22, Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration, 2008.) was used for statistical analysis and for generating figures. For combining the results found in the different trials the statistical method of Mantel-Haenszel with random effects method was used for dichotomous outcomes, and risk ratios for THA variance method was used with random effects analysis model and mean differences were calculated. Heterogeneity between studies was assessed by using I2 statistics. The quality of the individual parameters was assessed with Grade profiler software (GRADEpro. Version 3.2.2. for Windows. Jan Brozek, Andrew Oxman, Holger Schünemann, 2008) (24).

RESULTS

After applying the search strings 628 potentially eligible articles were identified, of which 473 were excluded based upon title, and 52 studies were duplicates of these reports. Another 67 manuscripts were excluded after reviewing the abstract. Contact with the author of one abstract revealed that the trial was still actively recruiting patients. In the next phase of the selection procedure 35 full articles were reviewed of which 24 articles did not meet the predefined eligibility criteria. Two studies were published twice (10, 16, 25, 26). One report was considered the index report, the other article was searched for additional information. Data from both articles were included in this study. One manuscript was a 13-year follow-up (27) of a previously conducted RCT (28). Data from both reports were included in the analysis. In conclusion, a total of 11 articles about eight studies were included for the present review and meta-analysis which involved a total of 986 patients (13-17, 25-29) (Figure 1). Tables 1, 2, 3 and 4 summarize the methodological quality, the methodological characteristics, the characteristics of the interventions and the characteristics of individual studies. Two studies had also included a third (internal fixation) arm (17, 27, 28). These data were not taken into account, as internal fixation was not assessed in the present study. In all studies inclusion and exclusion criteria were clearly defined prior to the study in order to select patients with an ambulatory and cog-

Table 1. Methodological quality of individual selected studies

		Quality assessment				
No of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**
1 year mortality						
6[1]	randomized trials	very serious[2]	no serious inconsistency[3]	serious[4]	serious[1,5]	none[3]
revision surgery						
8[3]	randomized trials	very serious[2]	no serious inconsistency[3]	serious[4]	serious[6]	none[3]
Dislocation						
6[7]	randomized trials	very serious[2]	no serious inconsistency[3]	serious[4]	serious[8,9]	none[3]
Major complications						
5[10]	randomized trials	very serious[2]	no serious inconsistency[3]	serious[4]	serious[10,11]	none[3]
Minor complication						
5[12]	randomized trials	very serious[2]	no serious inconsistency[3]	serious[4]	serious[12,13]	none[3]

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Date: 2010-09-20
Question: Should Total hip vs hemiarthroplasty be used for displaced femoral neck fractures?
Settings: in the elderly
Bibliography: Burgers PTPW, Van Geene AR, Van den Bekerom MPJ, Van lieshout EMM, Blom B, Aleem IS, Bhandari M, Poolman RW. Total Hip Arthroplasty versus HemiArthroplasty for displaced femoral neck fractures in the healthy elderly: A meta-analysis and systematic review of randomized trials
1 Two out of eight studies did not adequately provide numbers of death after one year follow up
2 Allocation concealment: 3/8 study used sealed envelopes, 1/8 hospital number, 2/8 computerized, 1/8 order of admission, 1/8 not specified blinding: none of studies blinded the patients, only 3/8 studies report on a blinded outcome assessor failure to adhereto the intention to treat principle: 5/8 studies. 3 No explanation was provided.

Summary of findings					
No of patients		Effect		Quality	Importance
Total hip	hemiarthroplasty	Relative (95% CI)	Absolute		
53/393 (13.5%)	64/423 (15.1%) 13.6%	RR 0.91 (0.65 to 1.27)	14 fewer per 1000 (from 53 fewer to 41 more) 12 fewer per 1000 (from 48 fewer to 37 more)	VERY LOW	CRITICAL
19/472 (4%) 7.1%	36/514 (7%)	RR 0.59 (0.32 to 1.09)	29 fewer per 1000 (from 48 fewer to 6 more)	VERY LOW 29 fewer per 1000 (from 48 fewer to 6 more)	IMPORTANT
33/369 (8.9%)	14/411 (3.4%) 0%	RR 2.53 (1.05 to 6.1)	52 more per 1000 (from 2 more to 174 more) 0 more per 1000 (from 0 more to 0 more)	VERY LOW	IMPORTANT
76/302 (25.2%)	80/330 (24.2%) 8.2%	RR 1.07 (0.76 to 1.5)	17 more per 1000 (from 58 fewer to 121 more) 6 more per 1000 (from 20 fewer to 41 more)	VERY LOW	IMPORTANT
38/302 (12.6%)	45/330 (13.6%) 7%	See comment	10 fewer per 1000 (from 60 fewer to 40 more) 5 fewer per 1000 (from 31 fewer to 20 more)	VERY LOW	IMPORTANT

4 In the different trials, different approaches and materials, eg: cement vs uncemented were used. This may have had some effect eg. pain, function, or dislocation. 5 Total (cumulative) sample (size =117) is lower than the calculated optimal information size(OIS) (64/423=0.15-->needed: RRR 25%: 500). 6 Total (cumulative) sample (size =55) is lower than the calculated optimal information size(OIS) (36/514=0.07-->needed: RRR25%: 600). 7 Two out of eight studies did not adequately provide information on dislocation rates. 8 Two out of eight studies did not provide clear numbers of dislocation at all. 9 Total (cumulative) sample (size =47) is lower than the calculated optimal information size (OIS) (14/411=0.03-->needed: RRR25%: 600). 10 Three out of eight studies did not adequately provide information on major complications. 11 Total (cumulative) sample (size = 156) is lower than the calculated optimal information size(OIS) (45/330=0.24-->needed: RRR 25%: 500).

12 Three out of eight studies did not adequately provide information on minor complications. 13 Total (cumulative) sample (size =83) is lower than the calculated optimal information size (OIS) (45/330=0.1-->needed: RRR 25%: 500)

nitive fit pre-fracture status. The quality of the individual parameters ranged from low to very low (Table 1). In three studies, sealed envelopes were used as randomization system (14-16, 26); one of which was stated as block randomization(16). A fully automated computerized allocation system was used in two studies (10, 13). Other methods used for treatment allocation were by hospital number (29), fixed treatment sequence (28), and according to the order of admission (17) . The outcome assessor was blinded for the al-

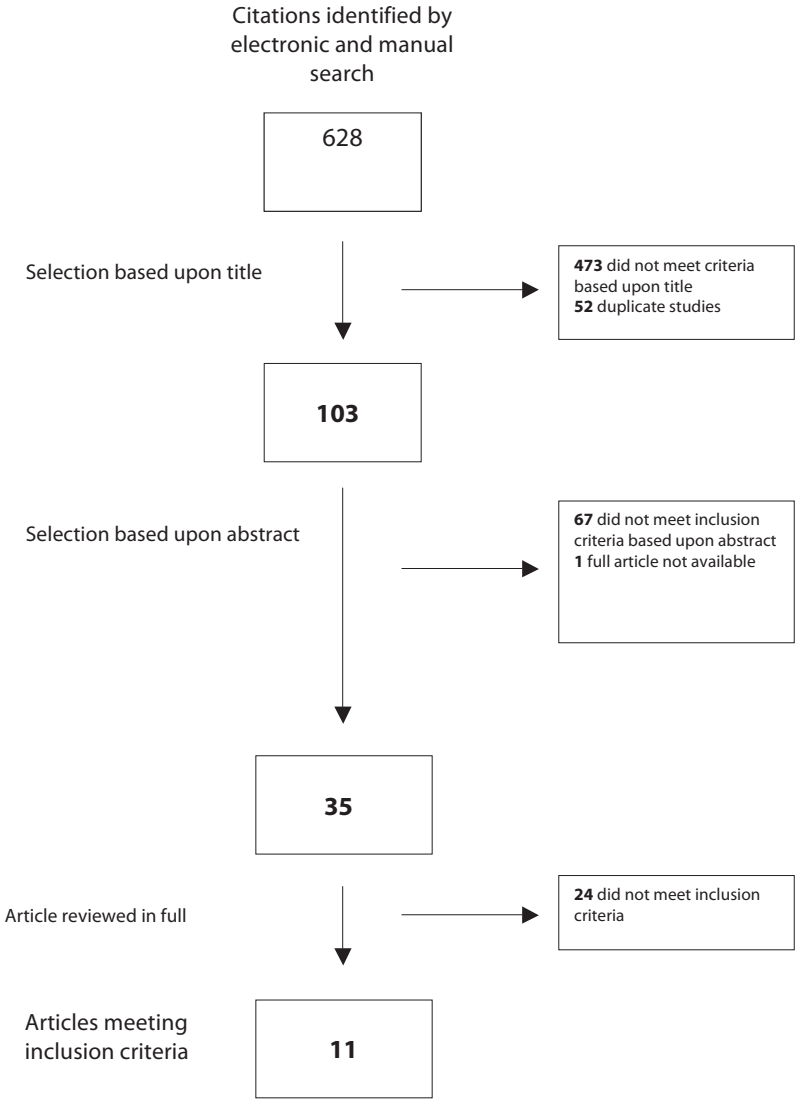

Figure 1. Flow diagram for selection process for randomized controlled trials evaluating the effect of Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly.

located treatment in only one study (17). Patients were not blinded for treatment in any of the studies. Three studies (10, 15, 16, 25, 26) stated an intention to treat analysis, one a per protocol analysis (13) and four studies did not specify the data analysis method (14, 17, 27-29). For all eight studies (13-17, 25-29) the follow-up period was at least one year (Table 2). All patients in the THA arm were treated with a cemented stem, except in one study (16) where both cemented and uncemented stems were used. For patients treated with hemiarthroplasty in two studies (16, 29) both cemented and uncemented stems were used; in one study (17) cementing of the stem was not specified. In four studies cemented stems were used; in one study uncemented stems were used. In three studies (13, 14, 28) only unipolar heads were used, in three studies (10, 15, 29) only bipolar heads were used, in one study (16) both types of heads were used and one study (17) did not specify the polarity of the head component of the hemiarthroplasty (Table 3).

Table 2. Methodological characteristics of individual selected studies

Study	Type of randomization	Allocation concealment	Patient blinding	Intention to treat	Follow-up period (years)
Baker(14)	Sealed envelopes	NS	No	NS	3
Blomfeldt(15)	Sealed envelopes	No	No	Yes	1
Dorr(29)	Hospital number	No	No	NS	4
Keating(10)	Computerized	No	No	Yes	2
Macaulay(16)	Sealed envelopes	NS	No	Yes	2
Mouzopuolos(17)	Order of admission	Yes	No	NS	4
Skinner(28)	Day of the week	No	No	NS	1
Van den Bekerom(13)	Computerized	No	No	Per protocol	5

Table 3. Intervention characteristics of individual selected studies

Study	THA	HA	Type	Surgical approach	Surgeon's grade
Baker(14)	Cemented	Cemented	Unipolar	lateral	Staff and residents
Blomfeldt(15)	Cemented	Cemented	Bipolar	anterolateral*	Staff
Dorr(29)	Cemented	Cemented or uncemented	Bipolar	posterior	NS
Keating(10)	Cemented	Cemented	Bipolar	Posterior or lateral	Staff, residents and SHO
Macaulay(16)	Cemented or uncemented	Cemented or uncemented	Uni- or bipolar	Posterolateral or anterolateral*	Staff and fellows
Mouzopuolos(17)	Cemented	NS	NS	NS	NS
Skinner(27)	Cemented	Uncemented	Unipolar	Posterolateral	Registrars and consultans and SHO's
Van den Bekerom(13)	Cemented	Cemented	Unipolar	Posterolateral, lateral or anterolateral	Staff and residents

NS, Not specified; *via Modified Hardinge; SHO, senior house officers NS= Not specified

The exact recruitment period was not specified in three studies (14-16). The number of patients per arm ranged from 17 to 137. Three studies (15, 28, 29) used a single center design; five studies (10, 13, 14, 16, 17) were performed with a multicenter approach (Table 4).

Table 4. Study characteristics of individual selected studies

Study	Recruitment period	THA number (N)	HA number (N)	Single-/ multicenter (N of sites)	THA mean age	HA mean age
Baker(14)	NS	40	41	Multicenter (3)	74	76
Blomfeldt(15)	NS	60	60	Single-Center	81	81
Dorr(29)	March 1980- July 1982	39	50	Single-Center	69	
Keating(10)	Sep 1996 - June 2000	69	69	Multicenter (11)	75	75
Macaulay (16)	18 months (NS)	17	23	Multicenter (5)	82	77
Mouzopoulos(17)	April 1999-April 2002	43	43	Multicenter (NS)	73	74
Skinner (27)	Dec. 1984- Dec. 1986	89	91	Single-Center	81	82
Van den Bekerom(13)	Jan 1995-Dec. 2001	115	137	Multicenter (8)	82	80

NS, Not specified

Clinical outcomes

Revision surgery

Data on revision surgery and reported planned revision surgery were pooled, totaling 986 patients and 55 events (5 %). Revision surgery was performed in 4 % in the THA-arm versus 7 % in the HA-arm (Figure 2).

There was low evidence of heterogeneity across the studies (I2=9 %, P= 0.36). No statistically significant difference in revision sur gery between the two groups (relative risk, RR 0.59, 95 % confidence interval CI 0.32–1.09, absolute risk difference, ARD –0.02, 95 % CI –0.06 to 0.01) could be found. However, the pooled data showed a trend towards less revision surgery for patients who had undergone total hip arthroplasty compared with those who had undergone hemiarthroplasty.

One-year mortality

Data for mortality at one year were pooled. Six out of the eight selected studies provided adequate data on one-year mortality (10, 13, 15-17, 28) which involved a total of 816 patients and 117 deaths (overall 14 %; Figure 3). The one-year mortality was 13 % in the THA-arm versus 15 % in the HA-arm. There was no evidence of heterogeneity (I2=0 %, P= 0.79). The pooled one-year mortality data did not differ between patients who had undergone total hip arthroplasty or hemiarthroplasty (RR 0.91, 95 % CI, 0.65–1.27, ARD –0.01, 95 % CI –0.05 to 0.03).

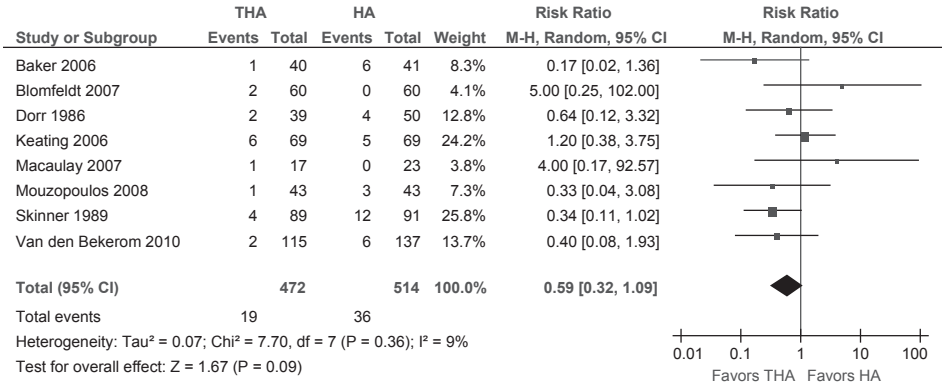

Figure 2. Forest plot comparing risk ratios of revision and planned revision surgery after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Mantel-Haenszel statistical method was used with the 'random effects' analysis method for dichotomous data.
M-H, Mantel-Haenszel; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

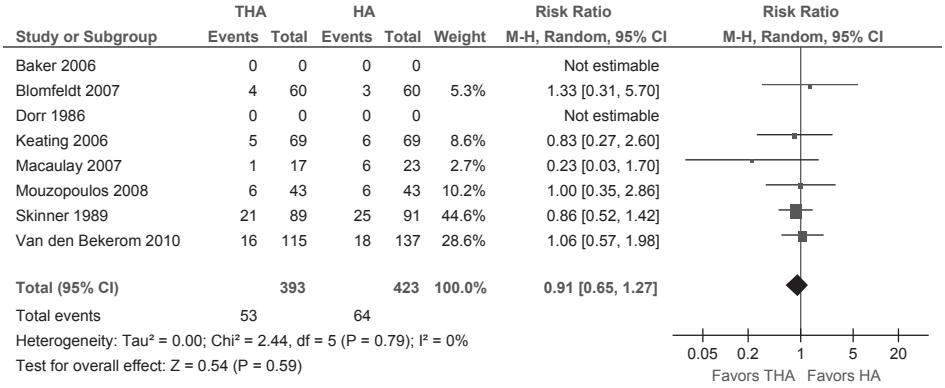

Figure 3. Forest plot comparing risk ratios of one year mortality after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Mantel-Haenszel statistical method was used with the 'random effects' analysis method for dichotomous data. M-H, Mantel-Haenszel; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

Dislocation

Six of the included studies provided data on dislocation (10, 13, 14, 16, 28, 29) (Figure 4). Another study did not report on dislocation (17), and one study reported that in both treatment arms there were no cases of dislocation (15). The risk of dislocation was 9 % in the THA-arm versus 3 % in the HA-arm. There was low evidence of heterogeneity across the studies (I2=30 %, P= 0.21). Pooling the data of these 780 patients and 47 events (6 %) revealed a significant risk for dislocation after treatment with total hip arthroplasty for dislocated femoral neck fractures (RR 2.53, 95 % CI 1.05–6.10, ARD 0.05, 95 % CI 0.02–0.08).

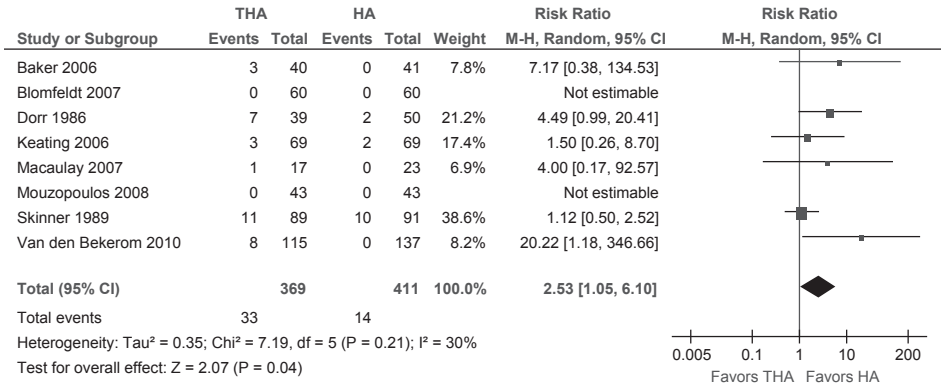

Figure 4. Forest plot comparing risk ratios of dislocation after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Mantel-Haenszel statistical method was used with the 'random effects' analysis method for dichotomous data.
M-H, Mantel-Haenszel; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

Complications (Appendix 2)

Data on major complications were retrieved from five studies (10, 13-16) (Figure 5). In addition, one study reported data on both minor and major complications, and these data had to be excluded as these were not specified to both treatment groups (29). The outcome measures of two other studies were focused on functional recovery only and data on general complications were not presented (17, 28). In 25 % major complications were found after THA versus 24 % after performing HA. No significant difference in major complication rates was found after either form of arthroplasty (RR 1.07, 95 % CI 0.76–1.50, ARD 0.00 95 % CI −0.08 to 0.08). Heterogeneity across the studies was 17 % (P=0.31). The same five studies described in the section above on major complications presented data on general minor complications (10, 13-16) (Figure 6).

Heterogeneity across the five studies was 39 % (P=0.16). In 13 % minor complications were found after THA versus 14 % after performing HA. After excluding the mentioned three studies for analysis, pooled data for general complications showed no significant difference in general minor complications (RR 0.94, 95 % CI 0.56–1.58, ARD −0.01, 95 % CI −0.08 to 0.07).

Functional outcome

Four studies reported the Harris hip score after total follow-up (13, 15-17). The Harris hip score ranges from 0 to 100 points and include function, pain, deformity and the range of motion. The weighted mean HHS was 81 (weighted mean SD 11) versus 77 (12) for THA and HA, respectively. A difference was found for the total score of this specific hip score (mean difference, MD 5.12, 95 % CI 2.81–7.42). Patients treated with THA reported statistically significantly higher Harris hip Scores. Heterogeneity across the studies was 0 % (P=0.46) (Figure 7).

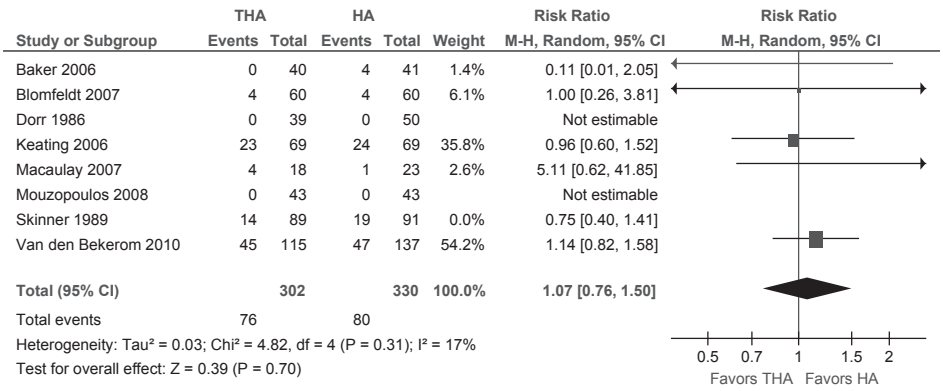

Figure 5. Forest plot comparing risk ratios of major complications (as defined in Appendix 2) after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Mantel-Haenszel statistical method was used with the 'random effects' analysis method for dichotomous data.
M-H, Mantel-Haenszel; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

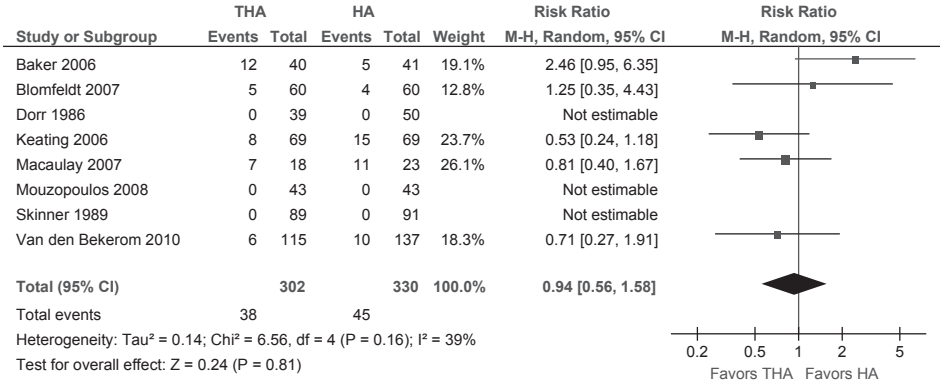

Figure 6. Forest plot comparing risk ratios of minor complications (as defined in Appendix 2) after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Mantel-Haenszel statistical method was used with the 'random effects' analysis method for dichotomous data.
M-H, Mantel-Haenszel; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

From two papers it was possible to calculate separately the pain subdomain of the Harris hip score (13, 15). The weighted mean score for the pain subdomain of the HHS was 42 (weighted mean SD 2) versus 39 (3) for THA and HA, respectively. A significant difference was found favouring this score after treatment with THA (MD 2.62, 95 % CI 0.18–5.05) (Figure 8). Two studies (10, 28) reported pain in categories mild to no pain (with no analgesia) after total follow-up. No to mild pain was reported in 75 % after THA and in 56 % after HA. These pooled data also showed a significant difference in favour of the THA group (RR 1.36, 95 % CI 1.20–1.54. Heterogeneity across studies was 0 % (P=0.39) (Figure 9).

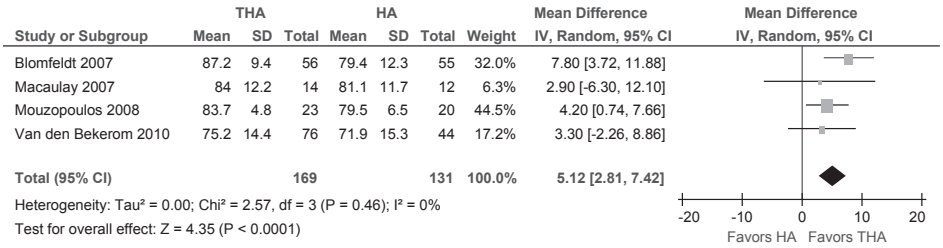

Figure 7. Forest plot comparing risk ratios of total Harris Hip Score after Total Hip Arthroplasty versus Hemi-Arthroplasty in displaced femoral neck fractures in the healthy elderly. Inverse variance statistical method was used with the 'random effects' analysis method for continuous data.
IV, Inverse Variance; THA, Total Hip Arthroplasty; HA, HemiArthroplasty
Pain

One study (16) separately showed the results of pain as scored with the Western Ontario and McMaster Universities Osteoarthritis Index questionnaire (WOMAC). The calculated mean difference was 16.60 points (THA 94.4, SD 6.8 versus HA 77.8, SD 20.9; 95 % CI 5.00–28.20, P=0.005) favouring THA (Figure 10).

Quality of life

Two European studies measured the quality of life with the EuroQol-5 Dimensions questionnaire at the final follow-up at one and two years respectively (10, 15). The weighted mean EQ-5D score was 0.69 (weighted mean SD 0.28) versus 0.57 (0.48) for THA and HA, respectively. A difference was found favouring THA (MD 0.13, 95 % CI 0.03–0.23, P=0.01). Heterogeneity across the studies was 0 % (P=0.33) (Figure 11).

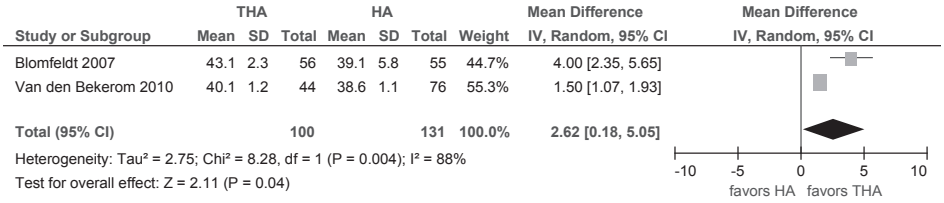

Figure 8. Forest plot comparing risk ratios of Harris Hip Score pain section after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Inverse variance statistical method was used with the 'random effects' analysis method for continuous data.
IV, Inverse Variance; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

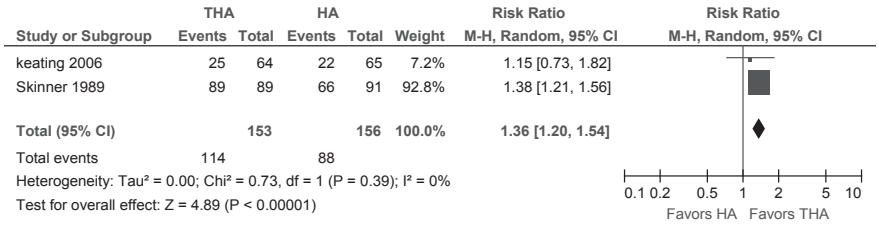

Figure 9. Forest plot comparing risk ratios of no-to-mild pain after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Mantel-Haenszel statistical method was used with the 'random effects' analysis method for dichotomous data. M-H, Mantel-Haenszel; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

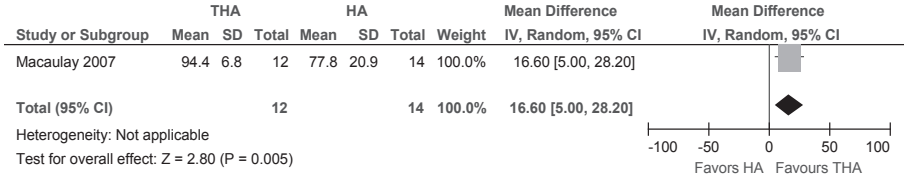

Figure 10. Forest plot comparing risk ratios of WOMAC pain score after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Inverse variance statistical method was used with the 'random effects' analysis method for continuous data. IV, Inverse Variance; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

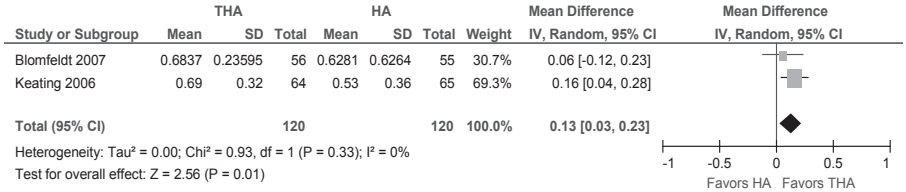

Figure 11. Forest plot comparing risk ratios of Quality of lifederived from the EQ-5D after Total Hip Arthroplasty versus HemiArthroplasty in displaced femoral neck fractures in the healthy elderly. Inverse variance statistical method was used with the 'random effects' analysis method for continuous data. IV, Inverse Variance; THA, Total Hip Arthroplasty; HA, HemiArthroplasty

DISCUSSION

Revision surgery rates and mortality rates were similar after THA and HA treatment for displaced femoral neck fractures in healthy elderly. None of these treatment options appeared to be superior with respect to postoperative minor or major complications. Risk of dislocation favoured HA. Estimates for function, pain and quality of life are less clear, but tend to be in favour of THA. The first debate on the management of selected displaced hip fractures started in the 70s and the question is still valid, as is illustrated by the flow of publications with expert opinions, experiences and reviews. In the last

three years two systematic reviews were published (21, 30), and the Cochrane review was recently updated (2), yet the question has still not been resolved.

Goh et al. performed a meta-analysis published in 2007 including three studies totaling 407 patients (10, 28, 29). In summary, no differences were found for revision surgery, mortality and dislocation rates. Significantly less pain was reported for patients with THA after one year of follow-up. It was concluded that for a subgroup of healthy patients with a good prefracture mobility THA might be considered as primary surgical treatment (30).

Hopley et al. concluded in their extensive analysis with four randomized, three quasi-randomized and eight retrospective cohort studies that patients treated with total hip arthroplasty for intracapsular hip fractures may obtain better outcomes than those treated with HA (21). In addition, they concluded that advantages with THA must be traded off against a slightly higher risk of dislocations and general complications.

From the latest Cochrane review on this topic including the same seven randomized trials as in the article by Hopley et al. it was concluded that although dislocation was more common with THA, there was a general trend towards better functional outcome scores for those treated with THA (2).

Data from the "ARTHRO trial" (13) were not included in the above-mentioned manuscripts. Beyond revision outcomes, this methodological well-designed trial provided new data on functional outcomes not previously available. Adding data from the 250 patients from this trial resulted in a 34 % increase in total population from randomized trials. The present analysis provides important new insights. First, our estimates of functional outcomes and pain suggest that patient-based results after THA may be better than that reported in previous meta-analyses. Also, our estimate of the difference in dislocation rates is less pronounced than previously reported. The overall mortality rate of 14 % as found in this study is lower than the frequently reported 20–25 %; this may be due to the relatively healthy patients that were included in the individual trials.

Study limitations

The present review has some limitations. The published individual trials were generally of low methodological quality (I). For example, the methods of allocating participants to a treatment were not all strictly randomized (e.g., hospital record number, order of admission, and day of the week). Also, the method of data analysis was not specified in three studies. Different outcome parameters and methods of reporting the results were used. Consequently, interesting parameters could not be analysed, for example, the 30-day mortality. In addition, the studies meeting the inclusion criteria were individual trials with a small sample size without an adequate power calculation.

The total number of available randomized trials is still small, however they jointly involve almost 1,000 patients. Although definitive conclusions cannot be drawn from these results, there seems to be a more prominent and beneficial role for total hip ar-

throplasty over hemiarthroplasty in the growing group of selected patients with femoral neck fractures.

Implications for future research

Although there is a growing awareness of the possibility of better results for selected patients treated with THA for displaced femoral neck fractures, a randomized trial is needed to definitively answer this long-lasting controversy in trauma surgery. One such unique international collaborative initiative (IHFRC; www.ihfrc.ca) is currently actively en-rolling patients in a multinational trial comparing revision surgery, functional outcome and quality of life after THA versus HA in elderly patients who sustained a displaced femoral neck fracture (31). This study would allow further assessment of the clinical relevance of the relatively small differences in pain and functional outcome found in the present study. This trial is important because it has the potential to substantially change surgical practice for the management of femoral neck fractures (32).

CONCLUSION

This review, including the most recent evidence, shows that total hip arthroplasty may be advantageous over hemiarthroplasty in a selected group of patients suffering displaced femoral neck fractures. Ultimately, only large, well designed and well conducted studies will result in improvements in the outcomes of treatment and resolve the long-standing controversy of whether total hip arthroplasty or hemiarthroplasty is the preferred treatment modality for this common fracture.

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APPENDIX 1. LAST SEARCHES CARRIED OUT: 22-2-2011

PubMed: N=211

(hip fractures[mesh] OR hip fracture*[tw] OR femoral neck fractures[mesh] OR femoral neck fracture*[tw] OR femur neck fracture*[tw] OR femoral collum fracture*[tw] OR femur collum fracture*[tw] OR intracapsular hip fracture*[tw] OR subcapital hip fracture*[tw] OR intracapsular collum fracture*[tw] OR subcapital collum fracture*[tw] OR intracapsular neck fracture*[tw] OR subcapital neck fracture*[tw]) AND (arthroplasty[mesh] OR arthroplast*[tw] OR hemiarthroplast*[tw] OR hip replace*[tw] OR hip prosthe*[tw]) AND random*[tw] NOT (animals[mesh] NOT humans[mesh])

EMbase: N=121

(' femur neck fracture '/syn OR (('femoral neck' OR 'femur neck' OR 'femoral collum' OR 'femur collum' OR 'intracapsular hip' OR 'subcapital hip' OR 'intracapsular collum' OR 'subcapital collum' OR 'intracapsular neck' OR 'subcapital neck') NEAR/3 fracture*):ti,ab,de) AND ('hip arthroplasty'/syn OR hemiarthroplast*:ti,ab,de OR (hip NEAR/3 (replace* OR prosthe*)):ti,ab,de) AND random*:ti,ab,de NOT (animal/de NOT human/de)

WoS: N=774

(hip fracture* OR femoral neck fracture* OR femur neck fracture* OR femoral collum fracture* OR femur collum fracture* OR intracapsular hip fracture* OR subcapital hip fracture* OR intracapsular collum fracture* OR subcapital collum fracture* OR intracapsular neck fracture* OR subcapital neck fracture*) AND (arthroplast* OR hemiarthroplast* OR hip replace* OR hip prosthe*) AND random* NOT (animal* NOT human*)

APPENDIX 2

Minor complications included all reported cases of:
Anemia
Ileus
Superficial Wound infect
Urinary tract infection
Deep venous trombosis
Bloodtransfusion
Atrial fibrilation
Pneumonia
Decubitus
Hart failure
Post operative confusion
Other infection

Major complications included all reported cases of:
Myocardial infarction
Deep infection
Stroke
Pulmonary embolism
Sepsis
Hematemesis
Re-operation (not revision)
GI bleeding

Chapter 5

Central coordination of a multicenter randomized trial as an alternative for payment per patient: experience from the HEALTH trial

Ned Tijdschr Traum. 2012;20:2-8

P.T.P.W. Burgers, R.W. Poolman, S.Culgin, T.A.Einhorn, M. Bhandari, P. Patka, E.M.M. van Lieshout, on behalf of the HEALTH trial investigators

ABSTRACT

Objective: Different strategies can be used for the organization of multicenter clinical trials. Multiple sites participated in the HEALTH trial (Hip Fracture Evaluation with ALternatives of Total Hip Arthroplasty versus Hemi-Arthroplasty). For the Dutch sites all trial-related tasks are managed by a central trial coordinator, whereas the sites in Canadian and the US have local study coordinators. The aim of this study was to analyze how these strategies affected trial performance.

Design: Prospective, observational study.

Method: Data related to obtaining ethics approval, trial start-up time, inclusion rate, and percentage of completed follow-ups were collected for each hospital and compared. Data from pre-trial screening were compared with actual inclusion rates.

Results: The median start-up time of the trial after obtaining ethics approval was shorter in the Netherlands than in Canada/US (4.6 versus 11.6 weeks). The inclusion rate was similar in both groups (0.62 versus 0.64/month). The median percentage of enrolled patients in the Netherlands was 27.3% versus 17.0% in Canada/US. The actual inclusion rates were lower than expected from pre-trial screening. The percentage of effectuated follow-up visits was > 90% in both groups.

Conclusion: In this study, central trial coordination contributed to faster trial start-up and higher inclusion rates, but had no effect on the effectuated follow-up visits. Central coordination is therefore a suitable alternative for appointing these tasks to local research assistants and per patient payment. Central coordination enables non-academic hospitals to participate in clinical trials. Limiting conditions for central coordination are budget availability, a manageable number of patients, and a manageable distance between participating sites.

Funding**:** Grants from the Netherlands Organization for Health Research and Development (ZonMw, project number 170.882.503), Canadian Institute of Health Research (CIHR; project number MCT-90168) and a grant from the National Institute of Health (NIH; project number 1R011AR055130-01A1) were received. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

INTRODUCTION

Feasibility of clinical studies largely depends on the required sample size (1-3). A multicenter trial can be used in order to reduce the inclusion period. Such a design also has the advantage of better generalizability of the results (4,5). However, multicenter clinical trials require a complex logistic organization, especially for international trials (6). Coordination is critical to obtaining a good trial infrastructure and to make the study a success with reliable results (3, 7-10).

In multicenter research the local principal investigator is responsible for carrying out the trial in his/her hospital. Traditionally, local coordination has been the standard method; the local investigator has to organize everything by himself. A research assistant or research nurse may support in obtaining ethics approval, patient recruitment, and data collection. Especially in industry-sponsored studies, the research team receives financial compensation. However, the availability of support often outweighs any financial compensation in deciding whether or not to participate in a clinical trial (11-13). Most university hospitals have access to research assistance. Community hospitals often lack this support, while the patient volume is generally bigger in those hospitals.

Currently, central coordination method is increasingly used as an alternative to local coordination. A physician-researcher performs almost all tasks in all participating hospitals in a restricted geographical area. Participating centers do not receive any financial compensation. The central coordinator carries out the study tasks on behalf of and in close cooperation with the local principal investigator, who remains ultimately responsible. In order to ensure independency, the central coordinator may not be involved in obtaining informed consent. The goal of central coordination is a faster ethics approval process, a faster trial start-up, and improved data quality.

In the HEALTH Trial (Hip Fracture Evaluation of Alternatives with Total Hip Arthroplasty Versus Hemi Arthroplasty), an international randomized controlled trial (RCT) in hip fracture patients, both central and local trial coordination methods were used. The trial has been initiated by the International Hip Fracture Research Collaborative (IHFRC; www.ihfrc.ca) (14). The primary aim of the HEALTH trial is to compare revision rates after total hip arthroplasty and hemi-arthroplasty for femoral neck fractures in the elderly. In the Netherlands, central coordination is used, while sites in Canadian and the US use local coordinators.

The aim of this study was to analyze how central and local coordination have influenced the progress of the HEALTH trial.

PATIENTS AND METHODS

HEALTH trial Characteristics

In the Netherlands the 14 participating sites started between December 15, 2008 and January 6, 2011. On February 14, 2011 the anticipated sample size of 150 patients was reached. In Canada five sites participated. These started between January 7 and December 14, 2009. On October 30, 2010 the target number of 36 patients was reached. In the US eleven sites participated and their start was between October 16, 2009 and November 12, 2010. In the US, the inclusion period is not yet complete. Patients with a dislocated femoral neck fracture who could not be included, were recorded. A distinction was made between excluded and missed patients.

Prior to the trial, seven sites also participated in a pre-trial screening period, with the aim to get an estimation of the number of eligible patients and thus the feasibility of the trial.

In the HEALTH trial two different coordination strategies are used: in the Netherlands, the trial is coordinated centrally from Erasmus MC. The central trial coordinator, who was funded by an external grant, was authorized by all principal investigators in the participating centers to carry out local study tasks. Ethics approval was centrally coordinated, in close cooperation with the local centers. These sites were responsible for patient screening and obtaining informed consent, and the central coordinator was responsible for collecting follow-up data. The maximum one-way distance from the coordinating site was 125 km. Sites received no fee for their participation. Sites in Canada and the US had a local research assistant and all study tasks were carried out by local staff. As compensation these sites received payment per enrolled patient.

Data

Until April 1, 2011, the following data were collected for each hospital:

- Basic characteristics (hospital type and method of research coordination);
- Ethics approval process (date of submission and date of approval, number and nature of revisions);
- Pre-trial screening period (start and end date, and number of screened and eligible patients);
- trial period (start and end dates, number of enrolled, excluded, and missed patients, and number of completed follow-ups).

Data analysis

All data were analyzed using the Statistical Package for the Social Studies version 16.0 (SPSS Inc., Chicago, IL, USA). Data of the centrally coordinated sites (the Netherlands) were compared with locally coordinated sites (Canada/US). Continuous variables are expressed as median with quartiles, and tested using a Mann-Whitney U-test. Categori-

cal variables are expressed as number of percentage and tested using a Chi-squared or Fisher's Exact test. A p-value <0.05 was considered statistically significant.

RESULTS

Characteristics of participating sites

In the Netherlands 50% of the participating centers were non-academic, non-teaching hospitals, while in Canada and the US 69% of the centers were non-academic, teaching hospitals (p = 0.022; Figure 1).

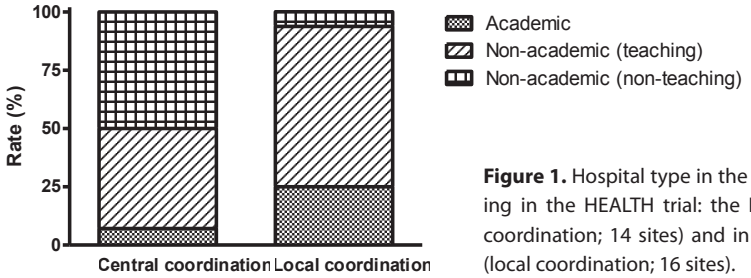

Figure 1. Hospital type in the countries participating in the HEALTH trial: the Netherlands (central coordination; 14 sites) and in Canada and the US (local coordination; 16 sites).

Ethics approval process

The median duration for obtaining ethics approval was 10.1 weeks in the Netherlands versus 10.3 weeks in Canada/US (p = 0 .810; Table 1). In the Netherlands, two of the 14 ethics boards had requested to adapt trial documents: one time additional information had to be added to the patient information folder and two times language corrections were requested. In Canada/US, six of the sixteen Institutional Review Boards (IRBs) requested adjustments; two asked for additional information, two for language corrections in the patient information folder, and two for additional information for the study protocol. Five IRBs asked for an explanation of study procedures in the protocol (Table 1).

Pre-trial screening period

Three Canadian, five American and two Dutch sites participated in the pre-trial patient screening**.** The median duration of this screening period in the Netherlands was 7.8 weeks (P_{25}-P_{75} 7.3-8.3 weeks) versus 8.3 weeks (P_{25}-P_{75} 7.7-10.2 weeks) in Canada/US. The cumulative screening period, calculated by a summation of screening times per center, was 3 months for the Netherlands versus 17 months in Canada/US.

In the Netherlands, 17 patients were evaluated, of whom 10 (58.8%) were found eligible for participation. In Canada/US 93 patients were assessed (median 10 per center; P_{25}-P_{75} 3-19), of whom 41 (44.1%) were found eligible for participation. Based on these

data the expected inclusion number in the Netherlands was 2.78 per month (10 in 3.6 months) versus 2.40 patients in Canada/US (41 patients in 17.1 months).

Table 1. Data concerning the process of obtaining ethics/IRB approval of sites participation in the HEALTH trial by coordination strategy

	Central coordination (n=14)	Local coordination (n=16)	p-value
Time needed for ethics/IRB approval[1] (weeks)	10.1 (5.8-19.2)	10.3 (7.0-18.7)	0.810[+]
Resubmission rounds[1]	0 (0-0)	0 (0-1)	0.145[+]
Type of revisions requested:			
– Patient information folder: add information[2]	1 (7.1)	2 (12.5)	1.000[++]
– Patient information folder: change wording[2]	2 (14.3)	2 (12.5)	1.000[++]
– Protocol: add information[2]	0 (0.0)	2 (12.5)	0.485[++]
– Protocol: explain procedures [2]	0 (0.0)	5 (31.2)	0.045[++]

The numbers in the headers represent the number of sites.
1 Data are presented as median with P25-P75 given between brackets; 2 data are presented as number with percentages between brackets; + Mann-Whitney U-test; ++ Fisher exact test.

Inclusion

The median time between the ethics approval and the start of the trial in the Netherlands was 4.6 weeks; this was significantly shorter than in Canada/US (11.6 weeks, p= 0.011; Table 2). In the Netherlands, the overall inclusion period was longer than in Canada/US (median 89.9 versus 36.5 weeks). Dutch and Canadian sites stopped enrolling since they reached the targeted population size. In the US 84% of target enrolment was achieved on that date.

During a cumulative enrolment period of 240 months, 150 Dutch patients were enrolled, which is 0.62 inclusions per month. In Canada/US 90 patients were enrolled in a cumulative period of 140 months, which is 0.64 patients per month. The centers that participated in the pre-trial screening enrolled 29 patients in 51 months (0.57 per month) in the Netherlands versus 64 patients in 90 months (0.71 per month) in Canada/US.

In all centers, more patients were excluded than included. The median percentage of patients included in the Netherlands was 10% higher than in Canada/US (Table 2). In the Netherlands, relatively fewer patients were excluded (64.2% versus 78.5% in Canada/US). Less than 5% of patients were missed for inclusion.

Follow-up

Follow-up data were collected at seven time points: at the outpatient department (1 and 10 weeks, and 6, 12, 24 months after surgery) or by telephone (9 and 18 months). The rate of completed follow-ups within the predefined acceptable time window was 91% in the Netherlands and 92% in Canada/US (Table 2).

Table 2. Characteristics of the enrolment and follow-up period of the HEALTH-trial by coordination strategy

	Central coordination (n=14)	**Local coordination (n=16)**	**p-value**
Time between ethics approval and trial start (weeks)	4.6 (1.0-9.1)	11.6 (6.0-54.4)	0.011
Duration of enrolment period (weeks)	89.9 (39,3-108,1)	36.5 (25.8-49.3)	n.v.t.
Included patients (number)	9 (6-15)	6 (1-9)	n.v.t.
Excluded patients (number)	26 (15-48)	14 (3-42)	n.v.t.
Missed patients (number)	2 (0-5)	0 (0-0)	n.v.t.
Included patients (% of total)	27.3 (15.5-30.9)	17.0 (8.1-33.6)	0.124
Excluded patients (% of total)	64.2 (55.9-69.9)	78.5 (53.6-91.9)	0.081
Missed patients (% of total)	4.4 (0.0-8.2)	0.0 (0.0-0.0)	0.023
Completed follow-ups (%)	91.2 (79.5-95.5)	92.3 (75.0-100.0)	0.631

Numbers in the headers represent the number of sites. Data are represented as median with P25-P75 between brackets. Data are analyzed with Mann-Whitney U-test

DISCUSSION

Central coordination of the HEALTH trial resulted in better trial progress. In the Netherlands, where a central trial coordinator conducted virtually all tasks for the participating sites, the startup-time after obtaining ethics approval was shorter and inclusion progress was better than in Canada and the US, where local research assistants were appointed at individual sites. The rates of completed follow-ups were equally good in both coordination systems.

The process of obtaining ethics approval can be time-consuming and stressful and may result in diverse responses from review ethics committees (8-13). Despite procedural differences between the two regions, the duration of the review process for the HEALTH trial was similar for both groups. In the Netherlands, a central ethics committee performs a full review of the submitted study documents. Subsequently, this central committee approves the participation of other sites, upon receipt of a 'declaration of local feasibility' signed by the local Board of Directors. In Canada and the US, the IRB at each individual site performs a full review of trial documents. The IHFRC, initiator of the trial, had prepared all the trial documents and provided them to all center for ethics review. Given the small number of needed revisions, these documents proved to be of high quality. The high quality of study documents clearly contributed positively to the relatively short review time.

The start-up phase in the Netherlands took about one month. The longer start-up phase in Canada/US had a financial reason. In the Netherlands, a grant was available and each center could start immediately after obtaining ethics approval and an initiation visit. Unlike Dutch sites, sites in Canada and the US received financial compensation for

each enrolled patient. The contract negotiations took place after obtaining IRB approval and prior to trial start-up. This has significantly delayed the start-up process in Canada/US. Apart from these procedural differences between countries, the focused activities and actions of the central trial coordinator may have contributed positively to a more efficient and speedy start-up in the Netherlands.

Interestingly, the inclusion rate was 10% higher in the Netherlands than in Canada and the US ($p > 0.05$). Several factors may have contributed to this difference. In the Netherlands, more general hospitals participated. These hospitals treat more patients with a femoral neck fracture than university hospitals. Using central trial coordination allowed these centers, which often do not have a research infrastructure, to participate in the trial. The relatively low (administrative) costs for staff and assistants were of eminent importance to most Dutch site principal investigators in their decision to participate.

In addition, cultural differences contributed to differences in trial progress. In Canada and the US orthopedic trauma surgeons are responsible for the care of patients with a femoral neck fracture; they perform both hemi-arthroplasty and total hip arthroplasty. In the Netherlands, the care for these patients is provided by both general orthopedic surgeons (20-25% trauma duty) and general and trauma surgeons (75-80% trauma duty). In the Netherlands, total hip implantation is restricted to orthopedic surgeons; consequently, centers could only participate if at least the orthopedic surgeons participated. At four sites general and trauma surgeons participated. Participation of all surgical departments could have shortened the inclusion period in the Netherlands.

Based upon the screening data, the number of inclusions was much lower than was expected. Although disappointing, this was consistent with a previous study, which demonstrated that retrospective screening is more likely to give a reliable assessment than prospective screening (15). Prospective screening may be useful to motivate local staff and give awareness for future trial participation, but it has no predictive value for trial progression. The rate of completed follow-up visits was independent from the coordination strategy; both central and local coordination resulted in excellent follow-up performance, with > 90% of follow-ups being completed.

This study has some limitations. Many of the results of this study were multifactorially influenced. Legislation, health care and insurance systems differed in the participating countries. As a result, not all observed differences may be attributable to the difference in coordination strategy.

Central trial coordination strategy is compliant to the recently tightened requirements of Good Clinical Practice (16). Moreover, this strategy facilitates trial participation of general hospitals, which adds to the feasibility of performing randomized surgical trials in the Netherlands as well as to the participation in international research. In addition, generalizability is higher when general hospitals participate as well. Important

conditions are the availability of sufficient funds to cover costs for the salary and travel expenses of the coordinating investigator.

CONCLUSION

Results of this study showed that central coordination of a multicenter trial is a suitable alternative for local coordination. The strategy with a centrally funded trial coordinator enables high-volume hospitals to participate, thus improving the trial progression, compared with local trial coordination combined with per patient payment. Both strategies resulted in similar, high quality follow-up data. The feasibility of central coordination depends upon the size of the study population, the availability of sufficient budget for salary and travel expenses of the coordinator, and the distance between the participating sites. If these aspects are adequately taken into account, the central coordination approach for the management of multicenter trials should be considered. Given the restricted geographical area of the Netherlands, this concept can be very promising for future multicenter studies in our country.

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Chapter 6

Reliability, validity and responsiveness of the Western Ontario McMaster Osteoarthritis Index (WOMAC) in the elderly population with a femoral neck fracture

JBJS Am. 2015; 97:751-7

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ABSTRACT

Background: The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) has been extensively evaluated in groups of patients with osteoarthritis, yet not in patients with a femoral neck fracture. This study aimed to determine the reliability, construct validity, and responsiveness of the WOMAC compared with the Short Form-12 (SF-12) and the EuroQol 5D (EQ-5D) questionnaires for the assessment of elderly patients with a femoral neck fracture.

Methods: Reliability was tested by assessing the Cronbach alpha. Construct validity was determined with the Pearson correlation coefficient. Change scores were calculated from ten weeks to twelve months of follow-up. Standardized response means and floor and ceiling effects were determined. Analyses were performed to compare the results for patients less than eighty years old with those for patients eighty years of age or older.

Results: The mean WOMAC total score was 89 points before the fracture in the younger patients and increased from 70 points at ten weeks to 81 points at two years postoperatively. In the older age group, these scores were 86, 75, and 78 points. The mean WOMAC pain scores before the fracture and at ten weeks and two years postoperatively were 92, 76, and 87 points, respectively, in the younger age group and 92, 84, and 93 points in the older age group. Function scores were 89, 68, and 79 points for the younger age group and 84, 71, and 73 points for the older age group. The Cronbach alpha for pain, stiffness, function, and the total scale ranged from 0.83 to 0.98 for the younger age group and from 0.79 to 0.97 for the older age group. Construct validity was good, with 82% and 79% of predefined hypotheses confirmed in the younger and older age groups, respectively. Responsiveness was moderate. No floor effects were found. Moderate to large ceiling effects were found for pain and stiffness scales at ten weeks and twelve months in younger patients (18% to 36%) and in the older age group (38% to 53%).

Conclusions: The WOMAC showed good reliability, construct validity, and responsiveness in both age groups of elderly patients with a femoral neck fracture who had been physically and mentally fit before the fracture. The instrument is suitable for use in future clinical studies in these populations.

Clinical Relevance: The results are based on two clinical trials. The questionnaires used concern pure, clinically relevant issues (ability to walk, climb stairs, etc.). Moreover, the results can be used for future research comparing clinical outcomes (or treatments) for populations with a femoral neck fracture.

Funding: Research grants were received from Stichting NutsOhra, the Netherlands (project number T-0602-43) and the Netherlands Organization for Health Research and Development (ZonMw, the Netherlands, project number 170.885.607 and 170.882.503). These funding sources had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Level of Evidence: Diagnostic studies, level I

INTRODUCTION

The problem in assessing quality of care for patients with a hip fracture is the complex assortment of issues related to their care, including baseline health and frailty, social isolation and support, mental status, and joint function and pain. Different constructs can be assessed in the evaluation of hip fracture treatment. A frequently used disease-specific patient-reported outcome measure is the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) (1). To also cover the complexity of issues, the SF-12 (Short Form-12) and the EQ-5D (EuroQol 5D) are used for evaluating general health and health-related quality of life (2-5).

The WOMAC is a disease-specific twenty-four-item questionnaire (scored on a 5-point Likert scale) measuring three domains: pain, stiffness, and function. The WOMAC was designed for patients with osteoarthritis of the hip and knee (6). Translation and cross-cultural validation were performed for different countries, including the Netherlands (7-10). The WOMAC has frequently been used for orthopaedic patients, including those with a hip fracture (11-13). It has been extensively validated in patients who underwent knee and hip arthroplasty because of osteoarthritis, but measurement properties in patients with a hip fracture are undetermined.

The aim of this study was to determine the reliability, validity, and responsiveness of the WOMAC compared with the SF-12 and EQ-5D questionnaires for the assessment of elderly patients who sustained a femoral neck fracture.

MATERIALS AND METHODS

Patients

Between March 3, 2008, and February 14, 2011, 400 patients with a femoral neck fracture were enrolled in two multicenter trials. One hundred and fifty patients were enrolled in the Dutch branch of the HEALTH (Hip Fracture Evaluation with ALternatives of Total Hip arthroplasty versus hemiarthroplasty) trial (ClinicalTrials.gov identifier NCT00556842; fourteen hospitals), and 250 were enrolled in the FAITH (Fixation using Alternative Implants for the Treatment of Hip fractures) trial (ClinicalTrials.gov identifier NCT00761813; fourteen hospitals). Adult patients (fifty years of age or older) with a low-energy femoral neck fracture without other major trauma who were able to walk before the fracture were considered eligible. Patients with a suspected pathological fracture, associated major injuries of the lower extremities, retained hardware or infection around the hip, a bone metabolism disorder other than osteoporosis, cognitive impairment, dementia, or Parkinson disease as well as patients who were not likely to be able to complete follow-up were excluded. Data on sex, age, American Society of Anesthesiologists (ASA) clas-

sification (14), walking status, and living situation were collected. The ethics committees approved this study, and all patients provided signed informed consent.

Questionnaires

All 400 patients were asked to complete the three multidimensional questionnaires—the WOMAC, SF-12, and EQ-5D—in the hospital and at each visit to the outpatient department.

The SF-12 score ranges between 0 and 100 (best) and consists of a Physical Component Summary (PCS-12) and Mental Component Summary (MCS-12) (2). The SF-12 represents a plausible alternative to the larger thirty-six-item SF-36 for measuring health status, especially in large-scale studies with a need to reduce questionnaire length. The reliability and validity were determined in different populations (2) and countries, including the Netherlands (3). The EQ-5D is a reliable and valid instrument for assessing health-related quality of life for elderly patients with a femoral neck fracture (4). The mobility, self-care, daily activities, pain, and anxiety domains are tested on a 3-point Likert scale, resulting in a utility score (EQ-US) that ranges from 0 to 1 (maximum) (5). In addition, patients scored their health status on a visual analog scale (EQ-VAS) that ranged from 0 (indicating worst possible health) to 100 (indicating best possible health) (5).

Data about the prefracture status were gathered during visits within one week after surgery, and other follow-up visits were at ten weeks and at six, twelve, and twenty-four months after surgery. Questionnaires were also completed during a telephone interview at nine and eighteen months. Patients did not receive any assistance in completing the questionnaires and did not consider the burden of completion too high. If necessary (e.g., due to physical status early in recovery), interviewer-administered versions were used.

Data analysis

Data were analyzed with SPSS software (version 20.0; IBM SPSS Statistics for Windows; IBM, Armonk, New York). Data are reported using the COSMIN (COnsensus-based Standards for the selection of health status Measurement INstruments) checklist (15).

Outcome scores for each follow-up visit for all instruments and subdomains were calculated. Unless mentioned otherwise, all further analyses were performed for two age groups (i.e., less than eighty years old and eighty years of age or older) and for ten weeks and twelve months.

The reliability of the WOMAC instrument was tested by determining the Cronbach alpha as a measure of internal consistency. The Cronbach alpha was used as a reliability parameter as there was no repetition of measurement by different observers or at different follow-up times. Questionnaires aimed at measuring the same construct (WOMAC pain, SF-12 pain, and EQ-Pain) were used as repetition measurement (16,17). A Cronbach alpha within the range of 0.70 to 0.90 was considered acceptable (16).

In the absence of a gold standard for the assessment of hip function after a hip fracture, construct validity was determined by calculating the Pearson correlation coefficient. Construct validity refers to the extent to which scores on a particular measure relate to other measures in a manner that is consistent with theoretically derived hypotheses concerning the concepts being measured (17). Only questionnaires for which the WOMAC total score was available were included. Hypotheses for construct validity were defined before data analysis (see Appendix). Correlation coefficients of 0.1 to 0.3 were considered weak; 0.3 to 0.6, moderate; and >0.6, strong (18).

Responsiveness is the ability of a questionnaire to detect clinically important changes over time (17). Change scores of the instruments were calculated from ten weeks to twelve months of follow-up. To assess responsiveness, standardized response means were calculated by dividing the mean change by the standard deviation of this change. Effect estimates were interpreted according to Cohen: a standardized response mean of 0.2 to 0.4 was considered a small effect; 0.5 to 0.7, a moderate effect; and 0.8, a large effect (19).

A floor or ceiling effect was considered present if >15% of the patients in a sample size of fifty patients achieved the lowest or highest possible score (17).

Missing data

As the raw data for individual items were analyzed, missing data were not imputed.

RESULTS

Population

Of all 400 included patients, 275 were less than eighty years old and 125 were eighty years of age or older (Table 1); 251 patients (62.8%) were female and 386 (96.5%) lived independently. This was similar in both age groups. Before the fracture, 325 patients (81.3%) walked without aid; they included 248 (90.2%) of those in the younger age group and seventy-seven (61.6%) of those in the older age group. Of the total group, 289 patients (72.3%) were categorized as ASA class 1 or 2; they included 223 (81.1%) of those in the younger age group and sixty-six (52.8%) of those in the older age group. The dominant treatment was internal fixation in the younger age group (199 patients; 72.4%) and arthroplasty in the older age group (eighty-three patients; 66.4%).

Outcome scores

Patients who were less than eighty years old had a mean WOMAC total score (and standard deviation) of 89 ± 15 points before the fracture, 70 ± 22 points at ten weeks after the fracture, and 81 ± 20 points after twenty-four months (see Appendix). In the older age group, the corresponding scores were 86 ± 16, 75 ± 21, and 78 ± 18 points. Similar

changes in scores were reported for WOMAC stiffness, WOMAC pain, and WOMAC function (see Appendix).

SF-12 PCS scores decreased after the fracture and increased again over time (see Appendix), yet SF-12 MCS scores remained more stable over time (see Appendix). Likewise, EQ-US scores decreased after the fracture and increased again over time (see Appendix), whereas EQ-VAS scores remained more stable over time (see Appendix).

Table 1. Demographic data on the study group according to age group

		Total (N=400)	Age <80 years (N=275)	Age ≥ 80 years (N=125)
Female		251 (62.8%)	173 (62.9%)	78 (62.4%)
Mean age (years)		74 (10)	69 (8)	85 (4)
ASA I/II		289 (72.3%)	223 (81.1%)	66 (52.8)
Walking without aids prefracture		325 (81.3%)	248 (90.2%)	77 (61.6%)
Living independently prefracture		386 (96.5%)	268 (97.5%)	118 (94.4%)
Treatment:	internal fixation	241 (60.3%)	199 (72.4%)	42 (33.6%)
	hemiarthroplasty	92 (23.0%)	48 (17.5%)	44 (35.2%)
	total hip arthroplasty	67 (16.8%)	28 (10.2%)	39 (31.2%)

SD, standard deviation; ASA, American Society of Anesthesiologists.
Data are shown as number (%) or as mean (SD).

WOMAC reliability

The Cronbach alpha for the domains of pain, stiffness, function, and the total scale were between 0.83 and 0.98 for the younger group and between 0.79 and 0.97 for the older group (Table 2)

Table 2. Reliability of the WOMAC instrument at ten weeks and twelve months for patients who had a femoral neck fracture, according to age group

WOMAC domain	Number of items	Cronbach's alpha (N)			
		Age <80 years (N=275)		Age ≥ 80 years (N=125)	
		10 weeks	12 months	10 weeks	12 months
Stiffness	2	0.83 (229)	0.83 (204)	0.79 (113)	0.79 (95)
Pain	5	0.92 (191)	0.92 (186)	0.85 (67)	0.83 (70)
Function	17	0.97 (107)	0.97 (130)	0.97 (22)	0.93 (36)
Total scale	24	0.98 (105)	0.98 (128)	0.97 (21)	0.94 (35)

N; number of available questionnaires with all items completed per domain and with all items completed. The Cronbach's alpha is given with the number of patients included in the analysis between brackets.

Construct validity

All Pearson correlations were significant at $p < 0.01$ (two-tailed; Table 3). In six main hypotheses, twenty-eight components were predicted, of which twenty-three (82%) were

Table 3. Construct validity of the WOMAC domains and WOMAC Total score and the domains of the SF-12 and EQ-5D instruments at ten weeks , according to age group

		WOMAC							
		Age <80 years (N=275)				Age ≥ 80 years (N=125)			
		Stiffness	Pain	Function	Total score	Stiffness	Pain	Function	Total score
SF-12 PCS	***r***	**0.35**	**0.56**	**0.71**	**0.70**	**0.41**	**0.52**	**0.74**	**0.710**
	95% CI	**(0.23-0.46)**	**(0.46-0.65)**	**(0.62-0.77)**	**(0.61-0.77)**	**(0.24-0.55)**	**(0.37-0.64)**	**(0.61-0.83)**	**(0.58-0.81)**
	N	222	218	177	177	110	110	72	72
SF-12 MCS	***r***	**0.41**	**0.47**	**0.51**	**0.52**	**0.45**	**0.59**	**0.57**	**0.64**
	95% CI	**(0.29-0.51)**	**(0.36-0.57)**	**(0.40-0.61)**	**(0.40-0.62)**	**(0.29-0.59)**	**(0.46-0.70)**	**(0.39-0.71)**	**(0.47-0.76)**
	N	222	218	177	177	110	110	72	72
SF-12 Pain	***r***	0.55	**0.74**	**0.77**	**0.79**	0.51	**0.78**	**0.59**	**0.66**
	95% CI	(0.45-0.63)	**(0.68 -0.80)**	**(0.70-0.82)**	**(0.72-0.84)**	(0.36-0.63)	**(0.70-0.84)**	**(0.42-0.72)**	**(0.50-0.77)**
	N	228	224	179	179	113	112	73	73
SF-12 Total	***r***	0.50	**0.67**	**0.78**	**0.78**	0.55	0.71	**0.81**	**0.84**
	95% CI	(0.39-0.59)	**(0.59-0.74)**	**(0.71-0.83)**	**(0.71-0.83)**	(0.40-0.67)	(0.60-0.79)	**(0.71-0.88)**	**(0.75-0.90)**
	N	222	218	177	177	110	110	72	72
EQ-US	***r***	0.42	0.74	**0.76**	**0.78**	0.52	0.72	**0.77**	**0.80**
	95% CI	(0.30-0.52)	(0.67-0.79)	**(0.69-0.82)**	**(0.71-0.83)**	(0.37-0.64)	(0.61-0.80)	**(0.66-0.85)**	**(0.70-0.87)**
	N	228	223	179	179	113	112	73	73
EQ-Pain	***r***	0.44	**0.80**	**0.72**	**0.75**	0.49	**0.75**	**0.53**	**0.60**
	95% CI	(0.33-0.54)	**(0.74-0.84)**	**(0.64-0.78)**	**(0.68 -0.81)**	(0.34-0.62)	**(0.65-0.82)**	**(0.34-0.68)**	**(0.43-0.73)**
	N	229	224	179	179	113	112	73	73
EQ-VAS	***r***	**0.39**	**0.51**	**0.66**	**0.65**	**0.41**	**0.55**	**0.63**	**0.66**
	95% CI	**(0.27-0.49)**	**(0.41-0.60)**	**(0.57-0.73)**	**(0.56-0.73)**	**(0.25-0.56)**	**(0.40-0.67)**	**(0.47-0.75)**	**(0.50-0.77)**
	N	229	224	179	179	112	111	72	72

N; number of available questionnaires with all items completed per domain and with all items completed.
The Pearson correlation coefficient (r) is given with its 95% confidence interval in brackets.
Correlation is significant at the 0.01 level (2-tailed) for all comparisons.
Correlations that were predicted correctly are given in boldface.

correctly hypothesized a priori in the younger age group and twenty-two (79%), in the older age group. Unconfirmed predictions were mainly underestimations (hypothesis 3; see Appendix). WOMAC stiffness correlated moderately (r > 0.35 to 0.55) with all other scores, while weak correlations (r = 0.1 to 0.3) were expected. WOMAC pain correlated strongly with EQ-US (r = 0.74 in the younger age group and 0.72 in the older age group), whereas moderate correlation (r = 0.3 to 0.6) was expected.

Responsiveness

Descriptive statistics and responsiveness are presented in Table 4. The standardized response mean was moderate for WOMAC function (0.64) and the WOMAC total score (0.66) for the younger age group. WOMAC subscales for stiffness and pain showed small standardized response means, ranging from 0.21 to 0.30 in the younger age group.

Table 4. Responsiveness of the WOMAC domains and WOMAC Total score, according to age group

	Age <80 years (N=275)				Age ≥ 80 years (N=125)			
	10 weeks Mean (SD)	12 months Mean (SD)	Change Mean (SD)	SRM (N)	10 weeks Mean (SD)	12 months Mean (SD)	Change Mean (SD)	SRM (N)
WOMAC Stiffness	67 (24)	74 (23)	5.5 (25.5)	0.21 (185)	80 (22)	81 (20)	-0.3 (25.2)	-0.01 (93)
WOMAC Pain	76 (23)	85 (20)	6.9 (22.8)	0.30 (184)	84 (22)	91 (16)	5.1 (19.4)	0.26 (92)
WOMAC Function	68 (24)	80 (21)	11.7 (18.2)	0.64 (145)	71 (24)	79 (18)	5.0 (19.1)	0.26 (54)
WOMAC Total score	70 (22)	80 (20)	10.8 (16.4)	0.66 (144)	75 (21)	82 (15)	4.1 (16.6)	0.24 (54)

Scores at 10 weeks and at 12 months as well as the difference between these scores (change), are shown as median with SD.
The Standardized Response Mean (SRM) is given with the number of patients used in the analysis between brackets.

Table 5. Ceiling effect of the WOMAC domains and WOMAC Total score, according to age group

	Age <80 years (N=275)			Age ≥ 80 years (N=125)		
	N	10 weeks N (%)	12 months N (%)	N	10 weeks N (%)	12 months N (%)
WOMAC Stiffness	224	40 (17.9%)	72 (35.6%)	112	43 (38.4%)	50 (52.6%)
WOMAC Pain	229	46 (20.1%)	53 (26.1%)	113	48 (42.5%)	38 (40.0%)
WOMAC Function	179	7 (3.9%)	26 (13.7%)	73	3 (4.1%)	8 (10.3%)
WOMAC Total score	179	2 (0.1%)	13 (6.9%)	73	2 (2.7%)	7 (9.0%)

The number of patients reporting the maximum score of 100 points are given with the percentage given in brackets. N represents the total number of questionnaires used for the analysis. None of the instruments demonstrated a floor effect (i.e., 0 points).

Floor and ceiling effects

None of the WOMAC domains or the total score showed a floor effect. No ceiling effects were found for the function domain or the total score in either of the age groups (Table 5). Pain and stiffness showed a ceiling effect at ten weeks and twelve months postoperatively for the younger age group (18% to 36%) as well as for the older age group (38% to 53%).

DISCUSSION

The present study was the first to determine the reliability, validity, and responsiveness of the WOMAC compared with the SF-12 and EQ-5D for the assessment of elderly patients who sustained a femoral neck fracture and who had been physically and mentally fit before the fracture. The results indicated that the WOMAC is a reliable and valid patient-reported outcome measure for patients who are less than eighty years old and for those who are eighty years of age or older. Responsiveness was also sufficient, indicating the instrument can be used for measuring changes in scores over time.

Subscores of all patient-reported outcome measures showed similar patterns over time. The scores reduced (most likely immediately) after surgery; from ten weeks after surgery onward, a gradual increase over time was noted. After two years, the scores approximated the prefracture scores, indicating a small residual decrease in mental and physical functioning. Due to differences in symptom evolution, the clinimetric results from groups of patients with osteoarthritis are not readily applicable to groups with a hip fracture. The minimal clinically important change (MIC) for patients with a hip fracture has not been reported, yet changes in WOMAC pain and function were larger than the MIC reported for hip replacement after osteoarthritis (10 points for pain and 8 to 9 points for function) (20,21). There may be two reasons that changes in the mean WOMAC over time were smaller than those observed after hip replacement for osteoarthritis (from 53 points at baseline to 94 points two years after surgery for pain and from 50 to 92 points, respectively, for function) (22). First, true baseline scores for patients with a hip fracture (i.e., scores between fracture and surgery) would have been much lower. Although these scores are unknown (as asking patients to complete questionnaires before surgery is not feasible), we expect these scores to be even lower than preoperative scores in patients with osteoarthritis (22). Calculating changes in WOMAC scores relative to baseline would have resulted in much larger changes over time. Second, at the first follow-up visit (at ten weeks), rehabilitation likely has progressed considerably already in the majority of patients, as participation required patients to be fit before the fracture.

The construct validity of the WOMAC instrument was good, with 82% (patients less than eighty years old) and 79% (patients eighty years or older) of the predefined hypoth-

eses being true. In particular, the strong correlations of the WOMAC function and total score with the SF-12 PCS, SF-12 total score, and EQ-US support the preferred use of the WOMAC for assessing functional recovery in this population.

The responsiveness of the WOMAC instrument as a whole was moderate for patients less than eighty years old, as the standardized response mean was 0.66. In the older age group, the standardized response mean was small (0.24). For patients with a hip fracture, the standardized response mean has not been shown before. However, for patients with hip osteoarthritis, the standardized response mean of the WOMAC exceeded 1.0 (23,24), which was mainly due to much larger changes in scores between the two measurements. Larger changes for those patients are expected, as the WOMAC score is at the lowest point prior to the hip replacement. These true baseline scores cannot be determined for patients with a hip fracture. The Dutch version of the non-hip-specific Short Musculoskeletal Function Assessment questionnaire (SMFA) appeared to be moderately responsive (standardized response means for subscales, 0.17 to 0.47) for patients with a variety of musculoskeletal disorders (25). In different Swedish patient groups with a hip fracture, the standardized response means were moderate to large (0.76 to 0.96) for the SMFA and small to large for the non-disease-specific instruments EQ-5D (0.01 to 1.14) and Nottingham Health Profile questionnaire (0.09 to 0.98) (26,27).

There was no evidence for any floor effect of the WOMAC instrument or for a ceiling effect of WOMAC function and total score. In contrast, moderate to large ceiling effects (18% to 53%) were found for pain and stiffness at ten weeks and twelve months in both age groups, which is similar to that reported in other studies (28-30). It may reflect the narrow discriminating capacity of these WOMAC domains in the studied population. Some selection bias might have played a role, as patients had to be physically and mentally fit to participate. Participants were able to walk and lived independently before the fracture.

The WOMAC has been used previously for assessing functional outcomes and quality of life for patients with a hip fracture (31,32). In the current study, it was validated for the first time in a group of patients with a hip fracture. We consider the novelty of validating the WOMAC for patients with a hip fracture to be a strength of our study. Moreover, we consider the studied groups to be representative of patients with a hip fracture seen in daily practice and believe the results apply to generally fit patients with a hip fracture. Whether the WOMAC is also valid for use in frail elderly patients remains unknown, as patients who were not able to walk before the fracture and patients with other disorders, e.g., Parkinson disease, pathological fractures, and dementia, were excluded. Another strength of the study was the built-in, very short period, only several days after fracture, for the self-reported, preinjury disability evaluation to be completed, minimizing the risk of recall bias (33).

The sample size of the present study was not large enough to analyze the effect of complications on the results. The occurrence of complications, especially those resulting in revision surgery, may have affected the crude questionnaire scores, but that applies to all three instruments used. An association between the occurrence of complications and the validity of the WOMAC instrument seems unlikely and has never been reported in the literature before as far as we know.

One limitation could be the use of arbitrary hypotheses for construct validation, although they were predefined in compliance with clinimetric evaluation guidelines (15). Second, some selection bias might have led to overestimation of the outcomes, especially ceiling effects. This effect is also known from the Harris hip score, which is frequently used in orthopaedic research, but no gold standard exists for functional evaluation of patients with a hip fracture (34,35).

Third, data completeness was not 100% at each time point. One can imagine that patients were not able to complete the forms, especially if they were in poor condition. The 36% of the items that were missing, which caused a missing WOMAC total score, might have influenced the outcomes, resulting in the present, more favorable, mean outcome scores and large ceiling effects.

In conclusion, the WOMAC, a widely used disease-specific questionnaire, shows adequate reliability and construct validity for patients fifty years of age or older with a femoral neck fracture who had been physically and mentally fit before the fracture. Responsiveness was better for younger patients than for patients eighty years of age or older. It is therefore a suitable instrument for use in future clinical studies in this population.

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Chapter 7

Implementing a clinical pathway for hip fractures; effects on hospital length of stay and complication rates in 526 patients

Int Orthop. 2014;38:1045-50

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ABSTRACT

Purpose: Modern management of the elderly with a hip fracture is complex and costly. The aim of this study was to compare the treatment-related hospital length of stay (HLOS) before and after implementing a clinical pathway for patients undergoing hip fracture surgery.

Methods: Retrospective, before-and-after study. The first period ranged from June 21, 2008 to November 1, 2009 (N= 212), the second was from January 7, 2010 to July 7, 2011 (N= 314). The electronic hospital system and patients records were reviewed for demographics, HLOS, mortality, complications and readmissions.

Results: In the first period 53% had a femoral neck fracture, of which 57% was treated with hemiarthroplasty. In the second period this was 46% and 71%. Pertrochanteric fractures were treated with a Gamma nail in 85% in the first period, 92% in the second period. The median HLOS decreased from nine to six days ($p<0.001$). For the hemiarthroplasty group HLOS decreased from nine to seven days ($p<0.001$), for internal fixation there was no significant difference (five versus six days, $p=0.557$) and after Gamma nailing it decreased from ten to six days ($p<0.001$). For mortality no statistically significant difference was found (6% versus 5%, $p= 0.698$). Complications decreased for the Gamma nail group (44% versus 31%, $p= 0.049$). Readmissions for the total group were not different (16% versus 17%, $p= 0.720$).

Conclusions: Implementing a clinical pathway for hip fractures is a safe way to reduce the HLOS and it improves the quality of care.

INTRODUCTION

Optimal modern management of the elderly with a hip fracture is complex and costly. The incidence of hip fractures increases exponentially with age, resulting in a 1-year incidence of 1% in women aged 80 years in Western countries (1). An expected increase in life expectancy, higher activity levels of the elderly and a subsequent higher risk of falling, cause hip fractures to be an increasing challenge for health care systems (1, 2).

The total costs of health care for hip fractures in 2007 in the Netherlands were €378 million, of which 54% was generated during the in-hospital stay (3). Over 40% of the patients, admitted from their home setting are not able to return to their home setting after surgery (4). Waiting lists for medical rehabilitation facilities and nursing homes result in prolonged hospital stay and associated increasing costs (3).

To reduce these health care costs the Dutch Ministry of Health, Welfare and Sport propagates an early transfer to medical rehabilitation facilities (4). Implementing a multidisciplinary clinical pathways may improve the logistic management of the growing population of elderly patients with a hip fracture. It tends to have positive effects on mortality, postoperative complications, and in-hospital stay, consequently leading to reduced costs (5, 6). The aim of this study was to compare the treatment-related hospital length of stay before and after implementing a clinical pathway for all patients undergoing hip fracture surgery.

PATIENTS AND METHODS

Study

A retrospective single-center before-and-after study. The first period ranged from June 21, 2008 to November 1, 2009. The second period was from January 7, 2010 to July 7, 2011.

Clinical pathway

The clinical pathway was developed by a multidisciplinary team and adapted to the local needs and circumstances. The team consisted of trauma surgeons, an anesthesiologist and a geriatrician, a physiotherapist, the unit coordinator and team leaders of the surgical ward, a representative of the emergency department, the head of the hospital logistic department and of the department for patient education and the managers of the rehabilitation centers involved. This team was responsible for training and implementing the pathway per stage on the different departments. Five stages were defined: pre-, peri-, post-operative, transfer and follow-up. The primary goal was to reduce the hospital length of stay. The standardized protocol covered the emergency department

(ED) with a rapid assessment of the patient, immediate video assisted education for patient and relatives about recommended treatment and prognosis. Other medical disciplines should be consulted preoperatively on the ED if necessary. The protocol continues on the clinical ward with consulting supportive disciplines such as physical therapists and a geriatrician. It also includes appointments with three surrounding rehabilitation facilities aiming at transferring the patient to a patient-centered destination as soon as possible. This pathway was standard of care from November 2, 2009 onwards.

Patients

All patients admitted to the department of surgery of the IJsselland Ziekenhuis, Capelle aan den IJssel, the Netherlands for fractures of the proximal femur were included. Patients were identified by searching the electronic hospital database for CTG Code (Centraal orgaan Tarieven Gezondheidszorg; CTG38565 hemiarthroplasty; CTG38533 internal fixation for proximal femoral fracture (IF); CTG38535 internal fixation for pertrochanteric fracture. Pathologic fractures and treatments with total hip arthroplasty were excluded. The following data were collected from the electronic patient files:

- Patient characteristics: gender, date of birth, date of fracture, date and time of admission, date and length of surgery, ASA classification (American Society of Anesthesiologists).
- Treatment characteristics: use of cancellous screws (Synthes, Paoli, USA), sliding hip screw (Synthes, Paoli, USA), Thompson hemiarthroplasty (Stryker, Newbury, United Kingdom), (Long) Gamma3^{TM} nail (Stryker, Schönkirchen, Germany), specialty of surgeon (trauma surgeon, general surgeon or surgical resident). The type of treatment was determined by the (supervising) surgeon.
- Post-surgery characteristics: re-admission date, date and type of complications categorized by: superficial wound infection, deep wound infection with or without re-operation, revision surgery, implant removal, death, neurologic complications, cardiac complications, miscellaneous (*e.g.*, delirium, medication related, urinary tract infection, pneumonia, etc.), date and cause of death.

Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 16.0 (SPSS Inc. Released 2007, SPSS for Windows, Chicago, SPSS Inc). Normality of continuous data was assessed by frequency histograms (Q-Q plots). Descriptive analysis was performed for describing patient-, fracture and treatment-related variables. Continuous variables were all non-parametric and are shown as medians with the first and third quartiles. Categorical variables are presented as numbers with percentages. Differences between the two periods were compared using a Mann-Whitney U-test (continuous data) or a Chi-squared test (categorical data). A p-value <0.05 was considered statistically significant.

RESULTS

Patient demographics, fracture and treatment characteristics

In total 526 patients were admitted, 212 in the first period and 314 in the second. Patient characteristics are shown in Table 1. The median age was 84 years (P_{25}-P_{75} 78-89 years) and 391 patients were woman (74%). Two-hundred ninety one patients were classified as ASA class II (55%) and 181 as ASA class III (34%). The median age (p= 0.512), gender (p=0.919) and pre-operative ASA class (p=0.366) did not differ. In the first period 53% of the patients had sustained a femoral neck fracture, in the second period this was 46% (p=0.110). In the first period 57% of the patients were treated with a Thompson hemi-arthroplasty versus 71% in the second period (p=0.024). Of the population with a per-trochanteric fracture 85% was treated with a Gamma Nail, 8% with a Long Gamma Nail, and 7% with a SHS. In the second period these rates were 92%, 7%, and 1% (p=0.062).

Table 1. Patient, fracture and treatment characteristics before and after the implementation of the clinical pathway

Characteristic	Total	Before	After	p-value
N	526	212	314	
Female gender[1]	391 (74)	157 (74)	234 (75)	0.919
Age[2]	84 (78-89)	84 (77-89)	84 (79-89)	0.512
Pre-operative ASA-score [1]				
ASA I	39 (7)	19 (9)	20 (6)	0.366
ASA II	291 (55)	130 (61)	161 (51)	
ASA III	181 (34)	60 (28)	121 (39)	
ASA IV	12 (2)	1 (1)	11 (4)	
Unknown	3 (1)	2 (1)	1 (0)	
Fracture type[1]				
Femoral Neck	255 (48)	112 (53)	143 (46)	0.110
Pertrochanteric	271 (52)	100 (47)	171 (54)	
Surgical procedure[1]				
Femoral Neck				
Hemiarthroplasty	166 (65)	64 (57)	102 (71)	0.024
Internal fixation	89 (35)	48 (43)	41 (29)	
Pertrochanteric				
SHS	9 (3)	7 (7)	2 (1)	0.032
Gamma nail	242 (89)	85 (85)	157 (92)	
Long Gamma nail	20 (7)	8 (8)	12 (7)	

1 Patient numbers are displayed, with the percentages given within brackets;
2 Data are displayed as median, with the first and third quartile given within brackets

Hospital length of stay

Table 2 shows the median hospital length of stay (HLOS), which for the total group was nine versus six days (p<0.001). For patients treated with hemiarthroplasty the median HLOS was two days shorter (nine versus seven days, p<0.001). For the IF group no difference was found (median HLOS: five versus six days, p=0.557). For patients treated with Gamma nail it was four days shorter (ten versus six days, p<0.001).

Table 2. Median hospital length of stay in days by type of fracture, treatment and period

	Total	Before	After	p-value
Total	7 (5-10)	9 (5-14)	6 (5-8)	<0.001
Femoral neck	7 (7-4)	8 (4-12)	6 (4-8)	0.024
Hemiarthroplasty	8 (5-10.25)	9 (6-14)	7 (5-8.25)	<0.001
Internal Fixation	5 (3-9)	5 (3-10.5)	6 (4-7.50)	0.557
Pertrochanteric	7 (5-11)	10 (6-16)	6 (5-8)	<0.001
SHS	9 (6-13)	9 (7-10)	15 (3-15)	1.000
Gamma nail	7 (5-10)	10 (5-17)	6 (4-8)	<0.001
Long Gamma nail	10 (7-12)	10 (11-16)	8 (6-10)	0.014

Data are displayed as median, with the first and third quartile given within brackets

Mortality

Detailed mortality rates are shown in Table 3. No statistically significant difference was found for the 30-day mortality (6 versus 5%, p= 0.698). None of the patients treated with SHS for pertrochanteric fractures died within 30 days after admission.

Table 3. Mortality within 30 days after admission by type of fracture, treatment and study period

	Total	Before (N= 212)	After (N= 314)	p-value
Total	29/ 526 (6)	13/ 212 (6)	16/ 314 (5)	0.698
Femoral neck	18/ 255 (7)	6/ 112 (5)	12/ 143 (8)	0.462
Hemiarthroplasty	15/ 166 (9)	4/ 64 (6)	11/ 102 (11)	0.411
Internal Fixation	3/ 89 (3)	2/ 48 (4)	1/ 41 (2)	1.000
Pertrochanteric	11/ 271 (4)	7/ 100 (7)	4/ 171 (2)	0.106
SHS	0/ 9 (0)	0/ 7 (0)	0/ 2 (0)	1.000
Gamma nail	9/ 242 (4)	7/ 85 (8)	2/ 157 (1)	0.010
Long Gamma nail	2/ 20 (10)	0/ 8 (0)	2/ 12 (17)	0.495

Patient numbers are displayed, with the percentages given within brackets

Complications

Tables 4 and 5 show the post-operative complications. A total of 214 (41%) patients had at least one complication. Ninety-five patients had a complication in the first period and 119 in the second period (45 vs 38%, p=0.124). The complication occurred within 30 days after admission for 54 patients in the first period and for 73 patients in the second period (57 vs 61%, p=0.576).

In patients treated with hemiarthroplasty, 69 (42%) had a post-operative complication. No difference was found between the two periods (41 versus 42%, p=0.873). Forty six complications (67%) occurred within 30 days after surgery, which was similar for both periods (65 versus 67%, p=1.000). Of the IF group 48% developed a complication in the first period versus 51% in the second period (p=0.833). Thirty four percent of complications occurred within 30 days after surgery, which was similar for both periods (26% versus 43%, p=0.342). For hemiarthroplasty surgical site infections were the main hip-related complication (31%). Implant removal and conversion surgery accounted for 71% of the complications after internal fixation for femoral neck fratcures.

A complicated course was found in 85 patients (35%) treated with a Gamma nail. In the second period a reduction was found for complication rates (44% versus 31%, p= 0.049). Fifty-six complications (67%) occurred within 30 days after surgery, which was similar for both periods (65 vs 67%, p=1.000).

Table 4. Complication rate by type of treatment and study period

Characteristic	Total	Before	After	p-value
Total	214/ 526 (41)	95/ 212 (45)	119/ 314 (38)	0.124
Femoral Neck	113/ 255 (44)	49/ 112 (44)	64/ 143 (45)	0.237
Hemiarthroplasty	69/ 166 (42)	26/ 64 (41)	43/ 102 (42)	0.873
Internal fixation	44/ 89 (49)	23/ 48 (48)	21/ 41 (51)	0.833
Pertrochanteric	101/ 271 (37)	46/ 100 (46)	55/ 171 (32)	0.027
SHS	3/ 9 (33)	2/ 7 (29)	1/ 2 (50)	1.000
Gamma nail	85/ 242 (35)	37/ 85 (44)	48/ 157 (31)	0.049
Long Gamma nail	13/ 20 (65)	7/ 8 (88)	6/12 (50)	0.158

Patient numbers are displayed, with the percentages given within brackets

Table 5. Rate of complications within 30 days after surgery by type of treatment and study period

Characteristic	Total	Before	After	p-value
Total	127/ 214 (59)	54/ 95 (57)	73/ 119 (61)	0.576
Femoral Neck	61/113 (54)	23/ 49 (47)	38/ 64 (59)	0.253
Hemiarthroplasty	46/ 69 (67)	17/ 26 (65)	29/ 43 (67)	1.000
Internal fixation	15/ 44 (34)	6/ 23 (26)	9/ 21 (43)	0.342
Pertrochanteric	66/ 101 (65)	31/ 46 (67)	35/ 55 (64)	0.834
SHS	2/ 3 (67)	2/ 2 (100)	0/1 (0)	0.333
Gamma nail	56/ 85 (66)	24/ 37 (65)	32/ 48 (67)	1.000
Long Gamma nail	8/ 13 (62)	5/ 7 (71)	3/ 6 (50)	0.592

Patient numbers are displayed, with the percentages given within brackets

Readmissions

Readmission rates are shown in Tables 6 and 7. In total, 86 patients (16%) were readmitted, without difference between the two periods (16% vs 17%, p= 0.720). The readmission rate within 30 days after discharge was higher in the second period (18 vs 43%, p= 0.020). The readmission rate after hemiarthroplasty was not significantly different between the periods (16 vs 21%, p= 0.540). No significant difference was found for the readmission rate within 30 days after hemiarhtroplasty (50 vs 62%, p= 0.701). After IF no difference was found in the total readmission rate (33% vs 44%, p= 0.383) nor in the readmission rate within 30 days (6 vs 33%, p= 0.090). After Gamma nail treatment six patients were readmitted in the first period and 12 in the second period (7 vs 8%, p=1.000). None of the patients in the Gamma nail group was readmitted within 30 days in the first period, but four patients were readmitted in the second period (0 vs 33%, p= 0.245).

Table 6. Readmission rate by type of fracture, treatment and study period

Characteristic	Total	Before	After	p-value
Total	86/ 526 (16)	33/ 212 (16)	53/ 314 (17)	0.720
Femoral Neck	65/ 255 (25)	26/ 112 (23)	39/ 143 (27)	0.474
Hemiarthroplasty	31/ 166 (19)	10/ 64 (16)	21/ 102 (21)	0.540
Internal fixation	34/ 89 (38)	16/ 48 (33)	18/ 41 (44)	0.383
Pertrochanteric	21/ 271 (8)	7/ 100 (7)	14/ 171 (8)	0.817
SHS	1/ 9 (11)	0/ 7 (0)	1/ 2 (50)	0.222
Gamma nail	18/ 242 (7)	6/ 85 (7)	12/157 (8)	1.000
Long Gamma nail	2/ 20 (10)	1/ 8 (13)	1/ 12 (8)	1.000

Patient numbers are displayed, with the percentages given within brackets

Table 7. Rate of readmission within 30 days after discharge by type of fracture, treatment and study period

Characteristic	Total	Before	After	p-value
Total	29/ 86 (34)	6/ 33 (18)	23/ 53 (43)	0.020
Femoral Neck	25/ 65 (38)	6/ 26 (23)	19/ 39 (49)	0.043
Hemiarthroplasty	18/ 31 (58)	5/ 10 (50)	13/ 21 (62)	0.701
Internal fixation	7/ 34 (21)	1/ 16 (6)	6/ 18 (33)	0.090
Pertrochanteric	4/ 21 (19)	0/ 7 (0)	4 /14 (29)	0.255
SHS	0/ 1 (0)	0/ 0 (0)	0/ 1 (0)	1.000
Gamma nail	4/ 18 (22)	0/ 6 (0)	4/ 12 (33)	0.245
Long Gamma nail	0/ 2 (0)	0/ 1 (0)	0/ 1 (0)	1.000

Patient numbers are displayed, with the percentages given within brackets

DISCUSSION

Implementing a clinical pathway for the treatment of patients with a proximal femoral fracture is efficient and safe. It resulted in a significant reduction of the median hospital length of stay by three days, without significantly influencing the rates of mortality, complications, and readmissions.

To streamline the increasing demand for beds for patients with proximal femoral fractures, these results are of importance. Findings from a previous study (1996) showed a mean hospital stay of 21 days for these patients (7). In 2002, Van Balen *et al.* reported a reduction of the median hospital stay from 18 to 11 days after implementing an "early discharge regimen" in the same geographical area (8). The British national audit report described a 5% reduction in average hospital stay between 2011 and 2012 (9). In contrast, the current study showed a 33% reduction of HLOS. This difference cannot solely be explained by "natural reduction" as found by the audit, which itself might be partly caused by the increase in use of clinical pathways for hip fracture patients. The comparison with only the clinical pathway as a variable, consistency of the findings with literature and the explicable underlying mechanism jointly support causality.

Literature on effects of clinical pathways for hip fractures generally shows positive results, although some publication bias cannot be excluded (10-13). A recent review by Leigheb *et al.* showed similar reductions in the hospital length of stay in eight out of twelve studies (6). Three studies reported a longer hospital stay (14-16) and one did not find any difference after implementing a clinical pathway (17).

The main strength of the current study is that it is one of the first to report differences per treatment subgroup of a hip fracture population. The median age of the IF group was almost 10 years younger compared to the other treatment groups (77 versus 85 and

86 years, respectively). These younger patients were likely in better physical and mental condition and thus sooner fit for discharge to their own house. They had no waiting time for rehabilitation at all. In contrast, Hommel *et al.* did not find any significant differences between patients with different kind of operation types (15).

The total number and percentage of patients primarily treated with total hip arthroplasty was very small and did not contribute substantially to the total group. Moreover these patients were treated on another ward and by the orthopedic surgical team. For these reasons this small group was not taken into account in the current analysis. Hemiarthroplasty was used more frequently in the second period despite similar patient characteristics and relative frequency of femoral neck fractures. Participation in an internal fixation randomized trial during the first period could have led to a lower threshold for applying internal fixation (18). Other known variables that may influence the choice of treatment (*e.g.* membership of the supervising staff, internal hospital procedures, daily ward affairs and procurement of medical supplies) did not change during the study. Moreover, the fact that people treated with hemiarthroplasty had a longer HLOS would rather have led to an underestimation of the effects. It is very unlikely that potential unknown or unmeasured changes have influenced the outcomes of this order. Therefore the clinical pathway seems to be responsible for the changes in HLOS.

The unchanged readmission and complication rates (decreased from 45 to 38%) support the safety of the implemented care pathway. The observed difference in type of treatment did not influence the complication rates as the treatment-related complication rates were the same in both groups. For a major part this was due to the decreasing rate in the Gamma nail group. This observation lacks a clear clarification in view of the implementation. The rate of complications within 30 days was also unchanged between the periods. The total complication rates were comparable with rates found in literature (19). The safety of implementing a clinical pathway for hip fractures is further supported by a meta-analysis of nine studies (involving 4637 patients), focusing on co-morbidities and postoperative complications (20). It was found that complications during hospitalization in patients with hip fractures be treated in a clinical pathway were less prevalent. A third parameter for safety would be mortality. Due to the low mortality rate within 30 days after surgery, no definitive conclusions can be drawn on the effect of the clinical pathway on this parameter. However, the 30-day mortality rates (6% versus 5%) are in accordance with those from the meta-analysis. The combined in-hospital/ 30-day mortality was reported 8% (118 of out 1520 patients) in the pathway group and 9% (141 out of 1522 patients) in the non-pathway group (20).

In the current study, the majority of complications after hemiarthroplasty (72%) and Gamma nail (75%) occurred within 30 days after surgery, whereas only a minority of complications after IF (32%) occurred early after surgery. General complications such as delirium, urinary tract infection, and medication related complications occurred most

frequently (53%) after treatment with Gamma nail. These data can inform patients and their relatives about what clinical outcomes and problems they may expect after surgery. The type of surgeon: general surgeon, trauma surgeon, or surgical resident did not influence the complication rates (data not shown), which is also reported in literature (21). Moreover, the same brand and type of materials were used for all standardized surgical procedures during the entire study period.

This study had a few limitations. Although multiple digital hospital systems and patient files were used to identify complications, a slight underestimation due to the retrospective design of the study cannot be ruled out. Secondly, some interesting parameters, such as long term follow up, functional recovery by patient reported outcome measures, costs and total duration of institutionalization could not be investigated due to the retrospective design. Van Balen *et al.* found no reduction in total costs after implementation of an early discharge regimen, with a shift from the hospital to the nursing home. However, they reported in 2002 a median total hospital stay of 26 days (8).

Despite these limitations, the study provides evidence that in our institute implementing the clinical pathway has led to a higher level of organisation and improvement of the quality of care for patients with a fracture of the proximal femur.

CONCLUSION

Implementing a clinical pathway for proximal femoral fractures resulted in a significant reduction of hospital length of stay for patients treated with hemiarthroplasty or Gamma Nail but not after treatment with internal fixation. No differences were found for rates of mortality, complication and readmission. The use of a clinical pathway for hip fractures is a safe way to reduce the hospital length of stay and it contributes to improvement of quality of care of this fragile population.

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Chapter 8

Total medical costs of treating femoral neck fracture patients with hemi- or total hip arthroplasty: a cost analysis of a multicenter prospective study

Osteoporos Int. 2016; 27:1999–2008

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ABSTRACT

Purpose: The absolute number of hip fractures is growing and increases the already significant burden on society. The aim of this study was to determine the mean total medical costs per patient for treating displaced femoral neck fractures with hemi- or total hip arthroplasty in fit elderly patients.

Methods: The population was the Dutch sample of an international randomized controlled trial relating to femoral neck fracture patients treated with hemi- or total hip arthroplasty. Patient data and health care utilization were prospectively collected during a total follow-up period of two years. Costs were separated into costs for hospital costs during primary stay, costs for clinical follow-up, and costs generated outside the hospital during rehabilitation. Multiple imputation was used to account for missing data.

Results: Data of 141 participants (mean age 81 years) were included in the analysis. The 2-year mortality rate was 19%. The mean total costs per patient after ten weeks of follow-up were €15,216. After one and two years of follow-up the cumulative mean costs were €23,869 and €26,398, respectively. Rehabilitation was the main cost determinant, and accounted for 46%. Primary admission days accounted for 22% of the total costs, index surgery for 11% and physical therapy for 7%.

Conclusions: The main determinants for the mean total costs (€26,398 per patient until two years) for arthroplasty after treatment of displaced femoral neck fractures were rehabilitation and nursing homes. Most of the costs were made in the first year. Reducing costs after hip fracture surgery should focus on improvements of the duration and efficiency of the rehabilitation phase.

INTRODUCTION

The major complication of osteoporosis is the clinical manifestation of hip fractures. Based upon global trends and demographic changes the world-wide number of hip fractures is assessed to be over 7.3 million patients in the year 2050 (1, 2). In the Netherlands the number of patients sustaining a hip fracture since 1981 has more than doubled to almost 19,000 patients in 2012 (3). Almost 60% of all proximal femoral fractures concern femoral neck fractures, of which 80% are displaced (4). The Garden classification is frequently used to describe femoral neck fractures in the elderly. Garden type 3 and 4 represent displaced fractures. Femoral neck fractures can be treated using a non-operative approach, internal fixation, or arthroplasty. The arthroplasty group can further be divided into hemi-arthroplasty and total hip arthroplasty. Approximately 62% of patients aged 65 years or older are primarily treated with arthroplasty; hemi-arthroplasty is performed in this group in 78% of patients on average (5). Different insights into the preferred treatment of femoral neck fractures is subject of ongoing international debate (6). An international survey revealed that primary arthroplasty was for 75% of the responding surgeon's the preferred treatment for patients over 60 years of age with a displaced fracture. For patients under 60 years of age with a displaced fracture (Garden type 3 or 4) hemi-arthroplasty was preferred by 11% and 25% of respondents, respectively (6). Despite the higher initial costs compared with internal fixation, arthroplasty has been proven to be a cost-effective therapy (7-10).

According to data of the Dutch Ministry of Health care, Welfare and Sports, hip fracture associated crude total costs in 2011 in the Netherlands were 471.5 million euro (11). Insight into health care use and associated costs is gaining importance as the burden of health care costs threatens to exceed the financial resources available. Such insight may reveal options for cutting down health care expenses. Although surgeons are expected to have a general idea about the costs for treatments they provide, these data are not easily available (12-14). Recently data came available of the total medical costs of femoral neck fracture patients treated with internal fixation in the Netherlands (15). To the best of our knowledge, detailed analysis of the costs of arthroplasty for femoral neck fractures in the Netherlands has not been published before. Therefore the aim of this study was to provide a detailed overview of the costs of patients with a femoral neck fracture treated with arthroplasty.

PATIENTS AND METHODS

This cost study was conducted as a cohort study alongside the Dutch sample of the HEALTH trial (Hip Fracture Evaluation with ALternatives of Total Hip Arthroplasty ver-

sus Hemi-Arthroplasty, NCT00556842), an international randomized controlled trial comparing total hip arthroplasty and hemi-arthroplasty on revision surgery and quality of life in patients with a displaced femoral neck fracture. The local Medical Research Ethics Committees of all participating centers approved the study. Informed consent was obtained from all individual participants included in the study.

Population

In the Netherlands 14 hospitals participated and enrolled 150 patients between December 2008 and January 2011. Patients were eligible if they: 1) were adults aged ≥50 years, 2) had a (radiologically confirmed) displaced femoral neck fracture (ICD-10 code S72.0; Garden type 3 and 4) after a low energy impact and no other major trauma, 3) had operative treatment within three days of presenting to the emergency room, and 4) were ambulatory pre-fracture (with or without aid). Patients or proxies provided informed consent. Patients were excluded if they 1) were not suitable for treatment with arthroplasty (i.e., inflammatory arthritis, rheumatoid arthritis, pathologic fracture, or severe osteoarthritis of the hip), 2) had infection or retained hardware around the affected hip, 3) had a bone metabolism disorder other than osteoporosis, 4) were moderately or severely cognitively impaired pre-fracture, 5) had dementia or Parkinson's disease severe enough to compromise the rehabilitation process, or 6) were not likely to be able to complete follow-up.

Treatment and follow-up

Medical optimization was warranted for all included patients before surgery. Within 72h after presenting to the Emergency Department, patients were treated with arthroplasty (i.e., hemiarthroplasty or total hip replacement). The exact treatment including material choice (cemented or uncemented and unipolar or bipolar prosthesis) was left to the treating surgeon. Thromboprophylaxis were prescribed to all patients according to the local protocols. Post-operative weight bearing was as tolerated and early mobilization was encouraged. All patients were advised to be screened and treated for osteoporosis if deemed necessary. Follow-up measurements were performed at 10 weeks and at 6, 9, 12, 18, and 24 months after the primary surgery.

Cost measurement

This study included the following categories for hip related costs; (1) hospital costs during primary hospital stay, including emergency department visit, diagnostic evaluations, surgery, and admission days; (2) hospital costs during follow-up, including diagnostic evaluations, outpatient clinic visits, diagnosis and treatment of adverse events, revision surgery, and admission days; and (3) non-hospital costs of rehabilitation and aids.

Data on health care use were collected prospectively at each scheduled follow-up contact and at the close-out visit at the end of the study. Data were collected from the study case report forms (items are listed in Electronic supplementary material (ESM) Supplemental Table 1) and from the patient's hospital file. At each follow-up contact, patients were asked to complete a questionnaire on their health care use. This questionnaire was a customized version of the 'Trimbos and iMTA questionnaire on Costs associated with Psychiatric illness' (Tic-P), which has been validated for use in health care cost studies (15, 16). An English version of the TicP questionnaire is available online (17). The questionnaire included questions on stay in a hospital, rehabilitation center or nursing facility, number of contacts with an intramural medical specialist or paramedical worker during admission and follow-up, medication use, co-morbidity and use of walking aids. Any missing data were completed during a close out visit at each hospital.

The total number of consumption units per cost category was multiplied by the unit prices. All unit prices were indexed with the national consumer price index to 2012 and are presented in Table 1. Costs for the index surgery, including time spent in the operating room, theatre personnel, overhead, anesthesia, and implant material and general equipment, was provided by two teaching hospitals and one academic hospital. Data from the teaching hospitals were averaged in order to obtain a realistic estimation of the average prices in the participating teaching hospitals. The Dutch manual on cost research, methods and standard costs in economic healthcare evaluations was used for reference cost prices of most other health care resources (18). The NZa (Nederlandse Zorgautoriteit; Dutch Healthcare Authority) is the Dutch market regulator in care and advises the Minister on healthcare costs. This institute provided the unit prices for intramural diagnostic procedures. Costs of medication were derived from the CVZ (College voor zorgverzekeringen; Health Care Insurance Board), online accessible on www.medicijnkosten.nl. Costs of rehabilitation aids were obtained from a local home care firm that is a represention of national practice. Costs of aids were calculated according to the annuity method, applying an interest rate of 4.5% and a 10-year write off period. With over 90% of the patients in the study being retired, the costs for production losses were considered of limited importance for this population, and were thus excluded. Home care was also excluded, since it was impossible to determine which proportion of the total home care received was due to the hip fracture. As done previously in a similar study on internal fixation of femoral neck fractures, costs of osteoporosis screening were included in radiology/diagnostic studies costs, costs of visits to an osteoporosis specialist were included in outpatient clinic visits costs, and costs for osteoporosis treatment were included in medication costs.

Table 1. Sources and unit costs of healthcare resources

Cost categories	Unit	Source of consumption data	Source of value	Unit price (in €)
Hospital costs – primary stay				
Emergency department visit	Visit	Hospital registry	Cost manual[a]	160,34
Radiology/Diagnostic modalities				
X-ray	X-ray	Hospital registry	NZa[b]	54,14
CT-scan pelvis	CT-scan	Hospital registry	NZa[b]	238,25
MRI scan pelvis	MRI scan	Hospital registry	NZa[b]	274,16
Ultrasound	Ultrasound	Hospital registry	NZa[b]	86,07
DEXA scan	DEXA scan	Hospital registry	NZa[b]	114,52
Skeletal scintigraphy	Scintigraphy	Hospital registry	NZa[b]	194,37
Surgery				
Surgeon	Hour	Study registry (CRF)	Cost manual[a]	143,88[c] / 109,37[d]
Operating room[e]	Hour	Study registry (CRF)	Hospital/ Industry data[f]	738,60[c]/ 885,00[d]
Equipment and implant				
Cemented hemiarthroplasty	Operation	Study registry (CRF)	Hospital/ Industry data[f]	1362,00[c] /1197,73[d]
Cemented total hip arthroplasty	Operation	Study registry (CRF)	Hospital/ Industry data[f]	1465,75[c] /1684,45[d]
Uncemented total hip	Operation	Study registry (CRF)	Hospital/ Industry data[f]	N.A. /2041,80[d]
Admission days	Day	Study registry (CRF)	Cost manual[a]	610,57[c] / 461,91[d]
Hospital costs – follow-up				
Radiology/Diagnostic modalities				As described above
Out-patient clinic visits	Visit	Hospital registry + questionnaire[g]	Cost manual[a]	136,98[c] / 67,96[d]
Adverse events				
Medication[h]	Dose per day	Hospital registry / questionnaire[g]	CVZ[i]	Variable
Emergency	Visit	Hospital registry	Cost manual[a]	160,34
Brace	Piece	Hospital registry / questionnaire[g]	Hospital/ Industry data[f]	440,39

Table 1. Sources and unit costs of healthcare resources (continued)

Cost categories	Unit	Source of consumption data	Source of value	Unit price (in €)
Admission days	Day	Study registry (CRF)	Cost manual[a]	610,57[c] / 461,91[d]
Revision surgery				
Surgeon	Hour	Study registry (CRF)	Cost manual[a]	143,88[c] / 109,37[d]
Operating room[e]	Hour	Study registry (CRF)	Hospital/ Industry data[f]	738,60[c] / 885,00[d]
Equipment and implant				
Cemented hemiarthroplasty	Operations	Study registry (CRF)	Hospital/ Industry data[f]	1362,00 [c] /1197,73 [d]
Cemented total hip arthroplasty	Operations	Study registry (CRF)	Hospital/ Industry data[f]	1465,75 [c] /1684,45 [d]
Uncemented total hip	Operations	Study registry (CRF)	Hospital/ Industry data[f]	N.A. /2041,80 [d]
Cup revision	Operations	Study registry (CRF)	Hospital/ Industry data[f]	773,09
Open fenestration/ bursectomy	Operations	Study registry (CRF)	Hospital/ Industry data[f]	524,20
Open reduction (OR)	Operations	Study registry (CRF)	Hospital/ Industry data[f]	333,96
Closed reduction (ER)	Operations	Study registry (CRF)	Hospital/ Industry data[f]	160,34
Antibiotic beads	Operations	Study registry (CRF)	Hospital/ Industry data[f]	324,83
Admission days	Days	Study registry (CRF)	Hospital/ Industry data[f]	610,57[a] / 461,91[b]
Medication[j]	Dose per day	Hospital registry / questionnaire[g]	CVZ[i]	N.A.
Costs related to rehabilitation				
Rehabilitation center/Nursing home				
Elderly home	Days	Patient questionnaire[g]	Cost manual[a]	95,57
Nursing home	Days	Patient questionnaire[g]	Cost manual[a]	252,73
Rehabilitation clinic	Days	Patient questionnaire[g]	Cost manual[a]	361,04
Home nursing day	Days	Patient questionnaire[g]	Cost manual[a]	46,72
Physical therapy (outpatient)	Hour	Patient questionnaire[g]	Cost manual[a]	
Physical therapy	Session	Patient questionnaire[g]	Cost manual[a]	38,23
Use of aids				

Table 1. Sources and unit costs of healthcare resources (continued)

Cost categories	Unit	Source of consumption data	Source of value	Unit price (in €)
Crutches	Day	Patient questionnaire[g]	Home care firm[k]	0,07
Walker	Day	Patient questionnaire[g]	Home care firm[k]	0,08-0,15
Wheelchair	Day	Patient questionnaire[g]	Home care firm[k]	0,27
Electric scooter	Day	Patient questionnaire[g]	Home care firm[k]	0,70
Extra bed	Day	Patient questionnaire[g]	Home care firm[k]	1,22
Extra toilet facilities	Day	Patient questionnaire[g]	Home care firm[k]	0,10-0,20
Extra shower facilities	Day	Patient questionnaire[g]	Home care firm[k]	0,10-0,18

Reference unit costs anno 2012 were used, or costs were adjusted to 2012 costs by using the national consumer price index
NA not applicable
a Cost manual—manual on cost research, methods and standard costs in economic health care evaluations, version 2010 [16]
b NZa; Nederlandse Zorgautoriteit (Dutch Health care Authority) standard costs
c Academic hospital
d General hospital
e Including operating room personnel, anesthesia, and overhead costs
f Hospital/industry data; costs were requested from one academic hospital, three regional hospitals, and one surgical equipment and implant firm.Means were calculated and used as an estimation of the real costs in all participating sites
g Patient questionnaire—customized version of the BTrimbos and iMTA questionnaire on costs associated with psychiatric illness^ [17]
h Mainly antibiotics and in-hospital thrombosis profylaxis
i CVZ—standard prices were used as described by the CVZ (College voor zorgverzekeringen; Health Care Insurance Board), online available on www.medicijnkosten.nl
j Hip fracture-related medication only (i.e., pain medication and anti-osteoporosis medication; see ESM Supplemental Table 2 for details)
k Home care firm; costs of aids were requested froma home care firm and costs per day were calculated based on the calculated daily annuity. These costs were used as an estimation of the real costs in all participating patients

Statistical analysis

Data were analyzed using SPSS (version 20.0, SPSS Inc., Chicago, IL, USA). Replacement of missing values for cost items was done with multiple imputation following the predictive mean matching method, using ten imputations (19). The following variables were included in the imputation model: sex, age, ASA at baseline, walking independently at baseline, treatment, costs of initial surgery and all other cost categories at 10 weeks, 6, 9, 12, 18 and 24 months. Each of the ten complete datasets were further analyzed by non-parametric bootstrapping using 1,000 bootstraps per dataset (20). The 95% confidence interval around the mean costs was determined by taking the 2.5th and the 97.5th percentile of these bootstrap replications. Costs were calculated for the total study population.

RESULTS

Demographics

The participating departments in the 14 hospitals registered 592 consecutive patients with a femoral neck fracture, of whom 181 were eligible and 150 (25%) subsequently gave informed consent (Figure 1). One withdrew consent immediately, one patient died before surgery and seven patients were treated with internal fixation rather than arthroplasty. A total of 141 patients remained for the current cost analysis, of whom 74 were treated with hemiarthroplasty and 67 with a total hip arthroplasty. The mean age was 81 (SD 7; range 57-100) years, 2 patients (1%; both females) were younger than 60 years of age. A total of 96 patients (68%) were female. The mean age was 80 (SD 8; range 57-100) years for females and 81 (SD 6; range 69-91) years in males. No patients (0%) had ASA class 1, 67 (48%) ASA class 2, 46 (33%) ASA class 3 and 2 (1%) ASA class 4 and 26 (18%) ASA 5. A total of 136 (97%) were not institutionalized before the fracture, and 102 (72%) patients were independent ambulatory before the fracture.

Clinical outcome and health care consumption

The mean hospital length of stay was 10 days (SD 8). One patient with a complicated clinical course was discharged 90 days after the initial surgery. Within 14 days, 87% (N=123) of the patients was discharged. The discharge destination was in a rehabilitation or nursing facility in 56%, and 44% of the patients went to their own house. Median stay in a rehabilitation facility was 10 (SD 28) days, in a nursing facility 14 (SD 42) days, and in an elderly home 18 (SD 62) days. During rehabilitation, patients had a mean of 52 (SD 5) physical therapy sessions.

A total of 118 adverse events (AEs) occurred and 77 patients (55%) had no AE at all. The most frequent AEs were a subsequent fracture (N= 19; 13%), superficial wound

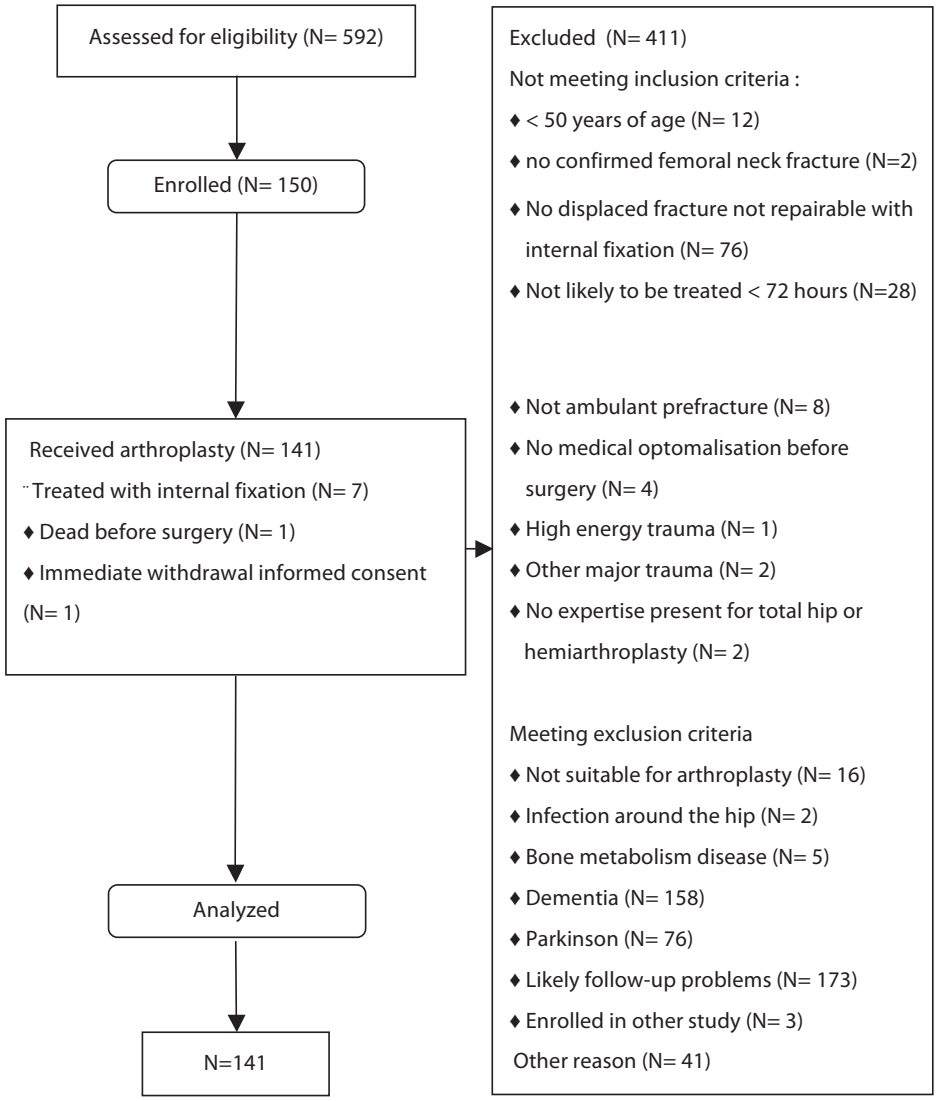

Figure 1. Flow-chart of patient enrollment process

infections (N= 11; 8%) and dislocations (N= 10; 7%). Less than ten patients had other AEs including pulmonary embolus, myocardial infarction, cerebral vascular accident, pneumonia, urinary tract infection, delirium and decubitus. A total of 18 revision surgeries were performed in 10 patients of which seven closed reductions were performed in the emergency department (Table 2). One patient had four times a reoperation because of recurrent dislocations. One patient had three times arthrotomy and joint lavage because of deep infection, reduction was performed two times closed and one time

open, two cups were reimplanted, one periprosthetic fracture was treated with plating and one conversion was performed. The mortality after ten weeks was 5% (N= 7), the 1-year mortality was 11% (N=16) and the 2- year mortality was 19% (N=27). Patients died mainly due to cancer (N= 9), cardiovascular diseases (N= 6), neurological diseases (N= 3) and the bone cement implantation syndrome (N=2). The mean duration of follow-up was 22 months (SD 9).

Costs

Table 3 shows the calculated mean costs after multiple imputation of the missing data. The overall percentage of missing data was 17.8% and the relative efficiency of the multiple imputation was 0.98. In the first 10 weeks after the fracture the mean total costs were €15,216, which was 58% of the total costs. The most important cost category was the primary hospital stay accounting for €9,026. From this category costs were predominantly related to hospital admission (€5,732) and to the index surgery (€2,915). Other important costs were made for rehabilitation facilities and nursing homes (€4,068).

After 1 year of follow-up the cumulative mean total costs per patient were €23,869 (95% CI 19,157- 30,136), this was 90% of the overall total costs. The single most contributing costs (55%) were related to rehabilitation and changes in living situation with a total amount of €13,139. Rehabilitation centers/ nursing homes (€11,694) and physical therapy at the outpatient clinic (€13,340) were the main items of expenditure. After 2 years of follow-up the total rehabilitation related costs (€14,429) still accounted for 55% of the total costs. The hospital costs for follow-up almost doubled from €1,705 (7% of the total costs) after 1 year to €2,943 (11%) after two years of follow-up. The main items were costs related to adverse events which increased with 181% from €581 to €1,052 and an increase of 204% for revision surgery from €480 to €980 (Figure 2).

Table 2. List of revision surgeries performed

	Revision surgery 1	Revision surgery 2	Revision surgery 3	Revision surgery 4
Patient 1	Conversion to THA	Closed reduction ED	Closed reduction ED	Closed reduction ED
Patient 2	Arthrotomy and joint lavage	Arthrotomy and joint lavage	Arthrotomy and joint lavage	
Patient 3	Closed reduction ED	Closed reduction ED	Plate fixation periprosthetic frx	
Patient 4	Closed reduction OR	Closed reduction ED		
Patient 5	Conversion to THA			
Patient 6	Open reduction			
Patient 7	Closed reduction ED			
Patient 8	Arthrotomy			
Patient 9	Conversion to THA			
Patient 10	Closed reduction OR			

THA, total hip arthroplasty; ED, emergency department; OR, operating room

Table 3. Mean costs of femoral neck fracture patients treated with arthroplasty (N=141)

Cost categories	Cost until 10 weeks (€)	Costs until 1 year (€)	Costs until 2 years (€)
Hospital costs – primary stay			
Emergency department visit	160 (160- 160)	160 (160- 160)	160 (160- 160)
Radiology/Diagnostic modalities	219 (206- 232)	219 (206- 232)	219 (206- 232)
Surgery	2,915 (2,798-3,023)	2,915 (2,798-3,023)	2,915 (2,798-3,023)
Admission days	5,732 (4,452- 7,966)	5,732 (4,452- 7,966)	5,732 (4,452- 7,966)
Total	9,026 (7,706- 11,295)	9,026 (7,706- 11,295)	9,026 (7,706- 11,295)
Hospital costs – follow-up			
Radiology/Diagnostic modalities	115 (103- 128)	240 (212- 270)	344 (278- 427)
Out-patient clinic visits	120 (109- 133)	297 (263- 336)	416 (355- 494)
Adverse events	200 (66- 392)	581 (280- 1056)	1,052 (568- 1,781)
Revision surgery	396 (61- 990)	480 (112- 1100)	980 (345- 1940)
Medication	82 (74- 92)	106 (93- 121)	151 (125- 182)
Total	914 (499- 1541)	1,705 (1,102- 2,563)	2,943 (1,894- 4,308)
Costs related to rehabilitation / changes in living situation			
Rehabilitation center/Nursing home	4,707 (3,627- 5,874)	11,694 (8,132- 16,350)	12,240 (8,542- 17,008)
Physical therapy (outpatient)	549 (470- 640)	1,340 (1,162- 1,537)	1,975 (1,627- 2,370)
Use of aids	20 (17- 25)	105 (78- 139)	214 (166- 270)
Total	5,276 (4,200- 6,467)	13,138 (9,486- 17,956)	14,429 (10,461- 19,552)
Total costs	15,216 (13,051- 18,323)	23,869 (19,157-30,136)	26,399 (21,101- 33,213)

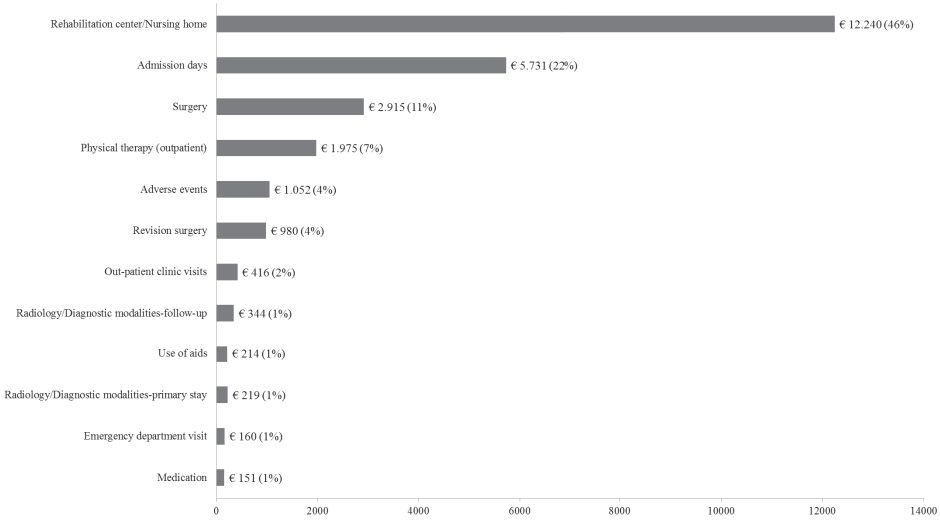

Figure 2. Relative contribution of costs categories to the total treatment costs of patients until two years follow-up

Costs are presented as mean costs at each follow-up moment with 95 % uncertainty interval between brackets
The data have been imputed. If a patient had not consumed health care, costs for that item were recorded as €0

DISCUSSION

The cumulative mean costs per patient after treatment with arthroplasty for femoral neck fracture were after 1 year €23,869 (95% CI €19,157- €30,136) and €26,398 (95% CI €21,101- €33,213) after 2 years.

These costs are in line with the range of €12,952 to €43,671 (as adjusted to 2012) found in literature (7-9, 21-25). This broad range can be explained by different variables used in the studies. All studies were performed in western countries, but with different health systems, mean length of hospitals stays, reference costs and rehabilitation facilities. The populations studied were relatively small with 32 to 180 patients. One study, based on 19,808 patients, used a Markov decision model (25). Although most of the costs are generated in the first year, the two studies with the lowest costs had a follow-up of one year (21, 23), not taking into consideration the late and costly complications. One study (8) did not include treatment with hemiarthroplasty and two studies only reviewed the costs for patients treated with hemiarthroplasty (21, 22). Also, different types of costs were calculated in previous studies, e.g., in-hospital costs only (7), the included populations differed in age, or included only women (23). The current results correspond best with the results (adjusted costs €29,834 and €29,807, respectively) of the two largest studies, both including both types of arthroplasty (9, 25).

Additionally, from a prospective cohort study of 10,275 Dutch people the estimated incremental cost of medical care the first year after a hip fracture was $9,540 (adjusted to €, 2012: €11,715) and $1,017 (€1,248) in the subsequent year (26). These incremental costs are comparable with the €14,844 (first year) and €2,529 (subsequent year) found in the current study De Laet et al. (26) found higher costs, but in that study detailed costs of adverse events, revision surgeries and costs of diagnostic modalities were not included. The in-depth method of our study can be considered more specific as the total costs are presented in more detail.

Recently a similar study was published for Dutch elderly patients with a femoral neck fracture (50 years or older) primarily treated with internal fixation (15). Both studies had the same design and used identical research methods, questionnaires, statistics. and resources, making it suitable for direct comparison. After two years of follow-up the costs, adjusted to 2012 for the total internal fixation group were €20,368 (original data: €19,425; 95% CI €5,237-€58,874). The relative contributions of the different cost categories were very comparable with respect to rehabilitation (46% of total costs for arthroplasty and 49% (for internal fixation) and admission days (both 22%), with higher absolute costs in the current arthroplasty study. These differences can be explained by

the general older population in the arthroplasty group based on baseline characteristics. In the current study, the mean age was 10 years older (81 versus 71), patients were more often ASA 3-4 (54% versus 13%), used aids prefracture more often (28% versus 13%), and had a displaced fracture more often (100% versus 46%). It is likely that older patients require more and longer rehabilitation facilities. Besides, the mean HLOS (10 versus 7 days) were longer in the arthroplasty group. Subgroup analysis of 67 patients (27%) who underwent revision to arthroplasty after primary internal fixation resulted in adjusted costs of: €28,031 (€26,733; 95% CI €9,465- €80,029), which exceeds the costs of primary arthroplasty. This emphasizes the need to carefully select the primary treatment for hip fractures as conversion from internal fixation to arthroplasty is even more costly than primary arthroplasty.

This study had some limitations. First, the population has been selected, based upon the eligibility for arthroplasty. Therefore it is a specific subset of the total population which was presented at the emergency departments of participating hospitals. The patients were relatively healthy, fit, and most were independent walkers before the fracture. Patients with dementia or Parkinson's disease were excluded. As they represent a substantial part of the general hip fracture population. These patients may have complex needs and incur higher costs, consequently leading to an underestimation of the mean costs presented. Costs are based on Dutch prices and may vary depending on the health care system used. However, we believe and have shown by comparing with published costs from other Western countries that the results are applicable to other settings as well. Secondly, the actual costs are expected to be even higher as costs for pre-hospital care, costs for routine blood analysis at the emergency department and wards, and perioperative consultation by other medical specialists and, although not routinely applied, forensic autopsy were not included. On the other hand, the number of visits for follow-up and X-rays are lower in general practice compared to a trial setting. Also, the amounts used in the manuals may differ from the actual costs. However, these costs are not expected to be substantial. Finally, costs for home care were not included as for most patients it was impossible to discriminate which part of the post-fracture home care was actually due to the hip fracture and not due to home care they already received for pre-fracture conditions. With these limitations in mind the results are in line with previous international publications.

In conclusion, the treatment of displaced femoral neck fractures with arthroplasty is costly with cumulative mean costs after one year of €23,869 and €26,398 after two years of follow-up. Rehabilitation and nursing homes accounts for almost half of the total medical costs, revision surgery and adverse events not even ten percent. Focus on improvements of the rehabilitation phase can result in reducing costs.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

FUNDING

Members of the research team received a grant from the Netherlands Organization for Health Research and Development (ZonMw; grant number 17088.2503), Canadian Institutes of Health Research (CIHR; grant number MCT-90168) and National Institutes of Health (NIH; grant number 1R011AR055130-01A1). The funding agencies were not involved in the study design, data collection, data analysis, manuscript preparations or publication decisions for this manuscript.

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Chapter 9

English summary

This thesis covers three topics related to hip fracture patients. **Part 1** comprises three chapters in which epidemiological data are analyzed. The results of these studies provide answers to the following questions:

- What were the incidence rates of hip fractures in the older Dutch population, based on historical data from 1981 to 2008? (**Chapter 2**)
- What is the cumulative incidence of non-simultaneous bilateral femoral neck fractures in the Netherlands, based on data from 14 Dutch hospitals? (**Chapter 3**)
- Is hemiarthroplasty (HA) or total hip arthroplasty (THA) the preferred treatment for displaced femoral neck fractures in fit elderly, based on randomized trials? (**Chapter 4**)

Part 2 consists of two chapters focusing on research techniques. Here, the research questions are:

- What is the preferred coordination strategy for conducting a multicenter study in the Netherlands? (**Chapter 5**)
- Is the WOMAC also a valid patient reported outcome measure (PROM) in a hip fracture population? (**Chapter 6**)

Part 3 contains two chapters on clinical and economic questions:

- What is the impact of the implementation of a clinical pathway for patients with a hip fracture admitted to a Dutch teaching hospital? (**Chapter 7**)
- What are the direct medical costs for patients treated with a prosthesis for a hip fracture, in the Netherlands? (**Chapter 8**)

PART 1

Chapter 2 describes the absolute numbers of hip fracture patients in the Dutch elderly population between 1981 and 2008. In this period, the absolute number of patients more than doubled from 7,614 to 16,049. The crude incidence rate increased from 46.4 per 10,000 older adults in 1981 to a peak in 1995 (70.4 per 10,000 older adults), and subsequently gradually decreased to 66.5 in 2008. Although no real explanation could be found, this pattern is comparable with the trends reported from several Western countries. Furthermore, the total length of stay decreased by a fifth, as in all age groups the average length of stay decreased (from an average 37 days in 1981 to 14 in 2008).

Patients sometimes fracture the contralateral hips after a first hip fracture. **Chapter 3** aims to determine the cumulative incidence of non-simultaneous, bilateral hip fractures in the Netherlands. Data were available from 1,250 consecutive hip fracture patients, who were admitted to 14 Dutch hospitals between February 2008 and August 2009. The

number of patients with a non-simultaneous bilateral hip fracture was 109 (9%). The median interval between the two fractures was 25 months. With an identical fracture type, the type of treatment was also the same in 88%. The relatively high risk for a second femoral neck fracture points out the importance of secondary prevention, particularly in patients with a previous wrist or vertebral fracture. **Chapter 4** is a systematic review with meta-analysis of eight randomized trials (between 1986 and 2010) with a total of 986 patients. In all studies, patients were randomized between HA and THA and the follow-up was at least 1 year. A non-significantly revision rate difference was found: 4% (HA) versus 7%. The dislocation rate was higher in the THA group: 3% versus 9%. The 1-year mortality did not differ significantly: 15% (HA) versus 13%. Rates of major complications, 24% (HA) versus 25%, and minor complications, 14% (HA) versus 13% were equal in both groups. Patient satisfaction measured with different patients reported outcome measures were statistically significantly better after THA. However, because these individual studies did not meet the modern quality standards, the **HEALTH trial** was designed. This is an international, randomized trial comparing HA with THA for the treatment of displaced femoral neck fractures in the fit elderly (N = 1,434).

PART 2

Chapter 5 describes the analysis of two different coordination strategies that are used to coordinate the above mentioned **HEALTH trial**. Traditionally, multicenter research is coordinated with a local coordination strategy. The local principal investigator organizes everything himself in his hospital. Assistance for procedures to obtain ethics approval, patient recruitment, and data collection is sometimes available. With the central coordination strategy, one funded coordinator conducts all tasks for the participating hospitals. Central coordination resulted in a shorter startup time (median 7 weeks) and a higher inclusion rate (median 10%), with comparable high quality and an excellent follow-up rate (> 90%). Central coordination provides, under certain conditions, non-academic, high-volume hospitals the opportunity to participate to major orthopedic trauma trials.

Nowadays, in clinical research and in modern practice, validated questionnaires are used to measure patient satisfaction for a certain treatment. Such a questionnaire is the Western Ontario and McMaster Universities Arthritis Index (WOMAC). It is frequently used since 1982 and it has been extensively studied in patients with hip and knee wear (osteoarthritis) who are treated with artificial joints. **Chapter 6** describes the validation results of the WOMAC in a total different population: patients without clinical relevant osteoarthritis, but with a hip fracture. With osteoarthritis complaints (pain) continues to increase until surgery is performed. Contrary, patients with a fracture generally have no symptoms of the hip joint until the femoral neck fracture. This study demonstrates for

the first time that the WOMAC is valid, reliable and also detects well clinically relevant changes in the hip fracture population.

PART 3

The modern treatment of patients with a hip fracture requires multidisciplinary involvement. Basic requirements include adequate pain relief, a short stay at the emergency department, emergency surgical treatment, complication prevention (decubitus, delirium, infections, etc.), adequate postoperative mobilization and subsequent rehabilitation, including osteoporosis screening. All these necessities in a frail population and taking into account the physical and psychological co-morbidities and polypharmacy. A clinical care pathway provides structure to healthcare professionals in order to achieve this optimal care for all patients. **Chapter 7** describes the effect of the introduction of a clinical pathway for hip fracture patients in a Dutch teaching, the Netherlands. The analysis of 212 patients during the period preceding the introduction (June 21, 2008 to November 1, 2009) and 314 patients after the care pathway introduction (January 7, 2010 to July 7, 2011) resulted in a decrease in admission days up to 4 days, depending on the type of surgery. The death rate (6 versus 5%) and complication rate (45 versus 38%) did not differ significantly. There was also no difference in the overall rate of readmissions (16 versus 17%). In conclusion, the introduction of a clinical care pathway proved to be a safe way to shorten the length of stay and contributes to improving the quality of care for this vulnerable population. The results described in **Chapter 8** answer the question: What are the direct medical costs of a treatment with prosthesis for a hip fracture in the Netherlands? The care trajectories of the Dutch HEALTH trial participants were closely monitored. To each component a unit price was linked and eventually a mean amount could be calculated. The indexed costs were available from financial data kindly provided by several participating hospitals, the Dutch Healthcare Authority (NZa) and the Dutch Manual for Costing: Methods and Reference Prices for Economic Evaluations in Healthcare by the Institute for Medical Technology Assessment commissioned by the Healthcare Insurance Board (CVZ, College voor zorgverzekeringen). These are the usual sources for calculating direct medical costs of treatment in healthcare. Rehabilitation (46%) and admission days (22%) accounted for the main part of the total costs per patient. The cumulative average price after one year follow-up was € 23,869 and after two years € 26,398.

Finally, **Chapter 9** is the Dutch summary and **Chapter 10** is the English summary. **Chapter 11** is the general discussion of the results described in this thesis. Future perspectives on the treatment with a prosthesis for a hip fractured are included.

Chapter 10

Nederlandse samenvatting

Dit proefschrift beschrijft onderzoek over patiënten met een "gebroken heup" en bestaat uit drie delen. **Deel 1** bestaat uit drie hoofdstukken waarin epidemiologische gegevens zijn onderzocht.
De resultaten van de onderzoeken geven antwoorden op de volgende vragen :

- Hoe is het verloop van het aantal nieuwe patiënten met een gebroken heup in Nederland, gebaseerd op historische gegevens vanaf 1981? (**Hoofdstuk 2**)
- Hoe vaak komt het beiderzijds, maar niet-simultaan breken van heupen voor in Nederland, gebaseerd op gegevens van 14 Nederlandse ziekenhuizen? (**Hoofdstuk 3**)
- Heeft een totale heupprothese of een kop-halsprothese de voorkeur in behandeling voor verplaatste heupfracturen bij fitte ouderen, gebaseerd op de resultaten van gerandomiseerde klinische studies? (**Hoofdstuk 4**)

Deel 2 beslaat twee hoofdstukken over onderzoekstechnieken. De geformuleerde onderzoeksvragen zijn hier:

- Welke coördinatiestrategie heeft de voorkeur bij het verrichten van een multicenter onderzoek in Nederland? (**Hoofdstuk 5**)
- Is de WOMAC ook een valide vragenlijst voor de follow-up van patiënten die behandeld zijn aan een gebroken heup? (**Hoofdtsuk 6**)

Deel 3 bevat twee hoofdstukken met klinisch-economische vragen:

- Welke invloed heeft de invoering gehad van een klinisch pad voor patiënten die met een gebroken heup werden opgenomen in een regionaal opleidingsziekenhuis in Nederland? (**Hoofdstuk 7**)
- Wat zijn in Nederland de direct medische kosten van patiënten met een gebroken heup, die behandeld zijn met een prothese? (**Hoofdstuk 8**)

DEEL 1

Hoofdstuk 2 beschrijft het totaal aantal nieuwe patiënten met een gebroken heup in de Nederlandse 65+ populatie tussen 1981 en 2008. Het absolute aantal patiënten verdubbelde van 7.614 naar 16.049 in deze periode. In een eerste periode steeg de incidentie van 46,4 per 10.000 ouderen tot een piek van 70,4 in 1995, waarna de incidentie afnam tot 66,5 in 2008. Een eensluidende verklaring is hiervoor niet gevonden. Dit patroon komt wel goed overeen met het patroon dat in andere westerse landen voorkomt. Verder nam het totaal aantal ligdagen met een vijfde af, doordat de gemiddelde opnameduur in alle leeftijdsgroepen verminderde (van gemiddeld 37 dagen in 1981 tot 14 in 2008).

Echter, na een eerste breuk van de heup kan ook de andere zijde breken. Bij ouderen gaat het dan vaak om een nieuwe val. Het doel van **Hoofdstuk 3** is het bepalen van de frequentie van dit beiderzijds, niet-simultaan breken van heupen in Nederland. Uit 14 Nederlandse ziekenhuizen waren de gegevens beschikbaar van alle 1.250 patiënten die tussen februari 2008 en august 2009 opgenomen werden met de diagnose "gebroken heup". Het aantal patiënten met een niet-simultane breuk van beide heupen was 109 (9%). Het mediane interval tussen de twee breuken was 25 maanden. Bij een identiek breuktype was de behandeling in 88% ook hetzelfde. Het relatief hoge risico voor een tweede dijbeenhalsbreuk benadrukt het belang van secundaire preventie, vooral bij patiënten met een eerdere pols- of wervelfractuur. **Hoofdstuk 4** beschrijft het samenvoegen van de resultaten van 8 eerder (tussen 1986 en 2010), onafhankelijk van elkaar uitgevoerde, gerandomiseerde onderzoeken met in totaal 986 patiënten. De behandeling van een patiënt met een gebroken heup hangt van veel factoren af. Wanneer gekozen wordt voor een prothese zijn hier grofweg in het algemeen 2 typen van. Een kop-halsprothese (KHP) vervangt de dijbeenhals en heupkop van de patiënt. Bij een totale heupprothese (THP) wordt ook de kom vervangen. Welke van deze twee operaties voor de patiënt beter is, is nog niet duidelijk. In de 8 onderzoeken lootten patiënten tussen KHP en THP en vervolgens vond minimaal 1 jaar follow-up plaats. Dit review met meta-analyse resulteerde in een revisiepercentage dat niet-significant groter was bij de KHP- groep: 4% versus 7%. Het percentage "uit de kom schieten" (luxatie) was bij de THP-groep hoger: 3% versus 9%. De 1-jaarsmortaliteit verschilde niet significant: 15% na een KHP versus 13% na een THP. Grote complicaties, 24% (KHP) versus 25% en kleine complicaties, 14% (KHP) versus 13% waren in beide groepen gelijk. Patiëntentevredenheid gemeten met verschillende door patiënten ingevulde vragenlijsten was beter na een THP. Echter, omdat de onderzoeksmethoden van de individuele studies niet voldoen aan moderne methodologische standaarden is de **HEALTH trial** opgezet. Dit is een internationaal, gerandomiseerde trial die KHP vergelijkt met THP voor de behandeling van verplaatste dijbeenhalsfracturen (N= 1.434).

DEEL 2

In **Hoofdstuk 5** staat de analyse beschreven van twee verschillende coördinatiestrategieën die gebruikt zijn voor het coördineren van de **HEALTH trial**. Traditioneel wordt bij multicenter onderzoek gekozen voor *lokale* coördinatie. Hierbij organiseert de lokale hoofdonderzoeker alles zelf in zijn ziekenhuis. Soms is assistentie beschikbaar voor de procedure bij de medisch ethische toetsingscommissie (METC), patiëntenrekrutering en dataverzameling. Bij *centrale* coördinatie verricht een centraal aangestelde, betaalde studiecoördinator voor alle deelnemende ziekenhuizen deze taken. Centrale coördi-

natie resulteerde in een kortere opstarttijd (mediaan 7 weken) en een hoger inclusiepercentage (mediaan 10% meer) met vergelijkbare hoge kwaliteit en een uitstekend follow-uppercentage (>90%). Centrale coördinatie biedt, onder randvoorwaarden, niet-academische, hoog-volume ziekenhuizen de mogelijkheid deel te nemen aan grote orthopedisch- traumachirurgische studies.

Bij de follow-up van patiënten wordt, zeker in onderzoeksverband, maar ook in de moderne klinische praktijk, veel gebruikt gemaakt van gevalideerde vragenlijsten. Deze door de patiënt gerapporteerde uitkomstmaten geven de belangrijkste informatie over het effect van de behandeling. **Hoofdstuk 6** beschrijft de resultaten van het onderzoek naar een vragenlijst (WOMAC), die sinds 1982 veel wordt afgenomen en uitgebreid is onderzocht bij patiënten met heup- of knie*slijtage* (artrose). Met deze lijst wordt de patiëntentevredenheid na behandeling met kunstgewrichten van deze aandoeningen gemeten. De populatie van patiënten met gewrichtsslijtage verschilt echter belangrijk met die van patiënten met een gebroken heup. Bij artrose nemen (pijn)klachten steeds verder toe bij vorderende slijtage van het gewricht, tot een moment waarop besloten wordt te opereren. Patiënten met een fractuur daarentegen hebben over het algemeen geen klachten van het heupgewricht zelf en hebben van het ene op het andere moment een dijbeenhalsbreuk en veel pijn. Daarom is het niet vanzelfsprekend dat deze vragenlijst ook gebruikt kan worden in de beenbreukpopulatie. Met dit onderzoek is voor de eerste keer aangetoond dat de WOMAC vragenlijst geldig en betrouwbaar is en bovendien klinisch relevante veranderingen goed detecteert in de heupfractuurpopulatie.

DEEL 3

De moderne behandeling van patiënten met een gebroken heup vereist vele handelingen met betrokkenheid van meerdere disciplines. Basale vereisten zijn bijvoorbeeld adequate pijnstilling, een vlotte doorstroom op de spoedeisende hulp en snelle operatieve behandeling, valanalyse, decubitus-, val- en delierpreventie, adequate postoperatieve mobilisatie en verdere revalidatie, dit alles rekening houdend met fysieke en psychische comorbiditeit en polyfarmacie. Een klinisch zorgpad geeft structuur aan zorgprofessionals om deze optimale zorg voor alle (fractuur)patiënten te bereiken. **Hoofdstuk 7** beschrijft het effect van de introductie van een klinisch zorgpad voor heupfractuurpatiënten in een regionaal opleidingsziekenhuis in Nederland. De analyse van 212 patiënten met een operatie voor een heupfractuur in de periode vóór het zorgpadgebruik (21 juni 2008 tot 1 november 2009) en 314 patiënten met het zorgpadgebruik (7 januari 2010 tot 7 juli 2011) resulteerde in een daling van de gemiddelde opnameduur van 10 tot 6 dagen, afhankelijk van het type operatie. Het overlijdenspercentage (6 versus 5%) en compli-

catiepercentage (45 versus 38%) verschilden niet wezenlijk. Ook was er geen verschil in het totale percentage heropnames (16 versus 17%). Concluderend is de introductie van een klinisch zorgpad een veilige manier gebleken om de opnameduur te bekorten en het draagt bij aan verbetering van de kwaliteit van zorg voor deze kwetsbare populatie.

De in **Hoofdstuk 8** beschreven resultaten geven antwoord op de vraag: wat kost een behandeling met een prothese voor een gebroken heup in Nederland? De zorgtrajecten van de Nederlandse **HEALTH trial** deelnemers zijn nauwkeurig gevolgd. Aan elk onderdeel van deze zorg werd een bedrag gekoppeld en uiteindelijk kon hier een gemiddelde van berekend worden. De geïndexeerde kostprijzen waren beschikbaar uit de financiële administratie van verschillende, participerende ziekenhuizen, de Nederlandse Zorgautoriteit (NZa) en uit de handleiding voor kostenonderzoek van het Instituut voor MedicalTechnology Assessment in opdracht van het college van zorgverzekeringen (CvZ). Voor het berekenen van direct medische kosten van een behandeling zijn dit gebruikelijke bronnen. Het revalidatietraject (46%) en de opnamedagen (22%) maakten samen het belangrijkste deel uit van de totale kosten per patiënt. Het cumulatieve gemiddelde bedrag na 1 jaar follow-up was € 23.869 en na 2 jaar € 26.398.

Tot slot bevat **Hoofdstuk 9** de Nederlandse samenvatting en **Hoofdstuk 10** de Engelse samenvatting. **Hoofdstuk 11** is een algemene discussie over de bevindingen beschreven in dit proefschrift en de plaats hiervan in zowel de praktijk als de literatuur. Tevens bevat het een toekomstperspectief over de behandeling van een “gebroken heup” met een prothese.

Chapter 11

General discussion

Hip fracture care must be well organized in order to achieve the best medical and logistic results for the 20,000 Dutch patients who sustain such a fracture annually. In order to optimize healthcare planning, knowledge of accurate numbers in hip fracture incidence rate and population structure are needed (**Chapter 2**). A trend break in the incidence rates of hip fracture-related hospitalizations was observed in the Netherlands around 1994. This study was performed over the period from 1981-2008. The incidence peak was in 2010 for the first time more than 20,000 patients (20,254 registered cases, 65+ population: 17,184, Figure 1).

Since 1981 a fairly stable 85% (ranges: 81-89%) of hip fractures occur in the 65+ population. The Dutch 65+ population has almost doubled since 1981 from 1.6 million (12% of total population) to more than 3 million (18%), with a steep increase since 2010 (Figure 2).

A parallel steep increase of the hip fracture incidence in the future might better be prevented. So what must be the major effort in hip fracture prevention in the Netherlands?

Although clear Dutch primary and secondary preventive guidelines exist (1-3), it has repeatedly been shown that the adherence to these guidelines is generally poor (4-8). Two aspects are crucial for fracture prevention. First, the focus should be on primary prevention of falls (9, 10). Leading activities for sustaining a fracture indoors are walking, standing, and sitting; common outdoor activities are walking and cycling (11). Key aspects of such prevention programs should include individual patient assessment, evaluation of risks around the house, safety intervention (12-14), physical exercise training to improve body balancing (15, 16) and follow-up (17). However, it is good to realize that patients themselves are not always motivated to follow these prevention strategies (18, 19).

Hip protectors, for example, probably reduce the risk of hip fractures (but not falls) in selected patients in nursing homes, but its effect is minimal due to poor acceptance and adherence particularly in the long term (20). Elderly persons increasingly use a mobility aid. Using such mobility aids can lead to substantial accidents (21, 22). The second aspect in fracture prevention is screening for osteoporosis and treating this risk factor can be an effective strategy in fracture prevention (23, 24). Bisphosphonates have shown a clinically important benefit, especially in secondary prevention (25-27). On the other hand, it is known that patient compliance and persistence with treatment for optimal fracture prevention is mandatory, but low (28). The role of vitamin D suppletion is still debated (29), but there is lacking evidence for a positive effect of supplementation on fractures or fall prevention (30). So, the use of pharmacotherapy should always be outweighed against the possible side effects (31-35). The importance of short-term sec-

ondary prevention is emphasized by the fact that recurrent fallers have poorer physical performance and quality of life than single fallers (36). These data support the results as described in **Chapter 3**. The cumulative incidence of non-simultaneous bilateral femoral neck fractures was 9 % and the median interval between the two fractures was 25 months (37). These numbers are in accordance with previous published Dutch results (38). In conclusion, primary and secondary hip fracture prevention is challenging and important in daily practice to achieve improvement.

When prevention fails and the older person falls, a displaced femoral neck fracture can be the result. Traditionally, these fractures have been treated with hemiarthroplasty and later with total hip arthroplasty, also other options exist, *e.g.*, conservative treatment (only with short life expectancy) and internal fixation (39). Both in literature (40-43) and at morning rounds (the characteristics of) these patients and their fractures are frequently discussed. Mostly the conclusion is that the preference of the surgeon is decisive for treatment. The supposed advantage of total hip arthroplasty is superior function and patient satisfaction, proponents of hemiarthroplasty emphasize shorter surgery times, reduced blood loss and lower costs (44, 45). It is good to realize that the discussion is about a subgroup of the total population, namely the elderly patient who is cognitive unimpaired and who was physically fit before the fracture (46, 47). In literature there is a trend towards better functional outcomes in patients treated with total hip arthroplasty. For example, the Cochrane review in 2001 (48) and its updates by Parker *et al.* in 2004 (49) and 2006 (50) concluded that the role of total hip arthroplasty in the treatment of displaced femoral neck fractures was uncertain. The most recent update in 2010 states that there is some evidence for better functional outcomes, against more dislocations after total hip arthroplasty than after hemiarthroplasty (51). In our systematic review and meta-analysis (**Chapter 4**) we also found similar rates for postoperative minor and major complications, revision surgery rates and mortality. Risk of dislocation favored HA. Estimates for function, pain and quality of life are less clear, but tend to be in favor of THA . Other recent reviews and cost-effectiveness analysis confirms these conclusions (52-55), also without a greater risk for mortality (56). The moderate methodological quality of the trials, which form the base of the reviews and analyses, is the reason why controversy persist (57). The results of the international HEALTH trial (N= 1,434, see appendix) aims to provide better evidence for the preferred type of arthroplasty for active elderly patients with a displaced femoral neck fracture (58). The follow-up of this trial is two years and 91% (1,302/1,434) of the participants was included in November 2016. This trial has the potential to have an important impact on the confidence in the effect estimate and to substantially change surgical practice for the modern management of femoral neck fractures, for instance in the Netherlands. Combining available data from Statistics Netherlands (http://statline.cbs.nl) and the Annual Report of the Dutch Arthro-

plasty Register (www.LROI.nl) results only in a stable 3.5% primary total hip arthroplasties for acute fracture management in 2010, 2011, and 2012 (Table 1).

On the other hand, a study from the American Board of Orthopaedic Surgery found an increase on the use of total hip arthroplasty over time from 0.7% (1999) to 7.7% (2011) (59). A nationwide study in Finland found an increase from 4.9% (1998) to even 9.2% (2011)(60).

Considering total hip arthroplasty more often potentially results not only in better patient outcomes but it also can have a positive influence on costs (61). Another interesting trial (currently recruiting patients) aims to compare total hip arthroplasty and hemiarthroplasty for displaced femoral neck fracture specifically in patients aged 80 years and over (62). Besides the type of implant other surgery related uncertainties exist, for example: is there a "best approach"(63), use cement or not for new design implants (64, 65), what is the role of large-head (≥36-millimeters) total hip implants and which patient characteristics are essential to make correct patient-based-decisions on the treatment of the femoral neck fracture in a particular patient?

Table 1. Total number of patients treated with primary total hip arthroplasty (THA) in relation to the number of all types of hip fractures in the Netherlands, divided per year (www.LROI.nl).

Year	N (total hip fractures)	N (THA for fractures)	%
2012	18,863	628	3.3
2011	19,136	624	3.2
2010	20,254	831	4.1

Research in the field of management of hip fractures requires large numbers of participating patients. These numbers can best be achieved in multicenter research, which brings logistical and regulatory challenges. Several coordination strategies can be used. **Chapter 5** describes a comparison of a strategy with a centrally-funded trial coordinator enabling high-volume hospitals to participate, thus improving trial progression, with local trial coordination combined with per patient payment. Limiting conditions for central coordination are budget availability, a manageable number of patients, and a manageable distance between participating sites. The same results were found in a comparable trial, including even 250 hip fracture patients in the Netherlands (66). Although inclusion rates were similar for both coordination strategies there was a higher enrollment rate with central coordination. Kendall *et al.* also found a positive association between site visiting coordinators and the assessed recruitment-related study milestones (67).

Traditionally, objective determinants like mortality, complications, and revision surgery were used for evaluating quality of care in clinical research. Nowadays, methods to measure the subjective patient's perspective of treatment results are gaining importance (68). These perspectives are quantified using patient-reported outcome measures (PROMs), which are available for assessing functional outcome and quality of life. In

Chapter 6 it is shown, for the first time, that a well-known disease specific questionnaire, the WOMAC, is valid and reliable in a generally fit hip fracture population. It is therefore a suitable instrument for use in future clinical studies in this population (69). Great efforts are made by the Netherlands Orthopaedic Association and Dutch Trauma Society to make PROMs part of standard of arthroplasty and hip fracture care. Implementing PROMs to the Dutch Arthroplasty Register (www.LROI.nl) and the Dutch Hip Fracture Audit aims to evaluate quality and further improve patient care. A successful stepwise introduction of such a comprehensive program was previously shown in Sweden (70).

As outlined above, the care for patients with hip fractures is complex and, especially in the frail subpopulation, outcomes depend on multidisciplinary collaboration (71). A

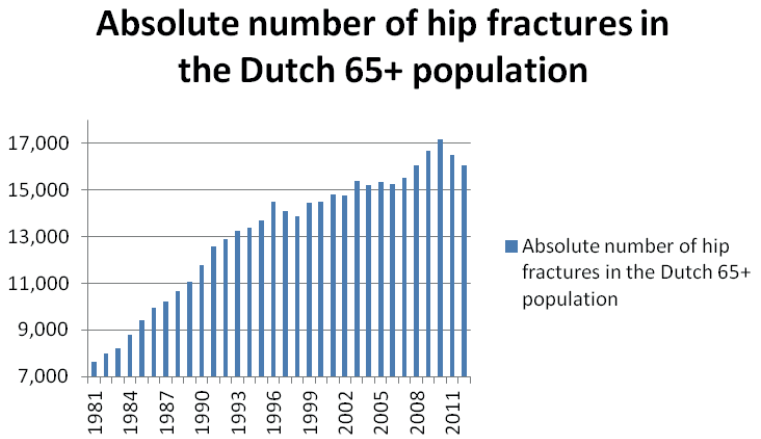

Figure 1. Absolute numbers of hip fractures in the Dutch 65+ population (available data until 2012: http://statline.cbs.nl).

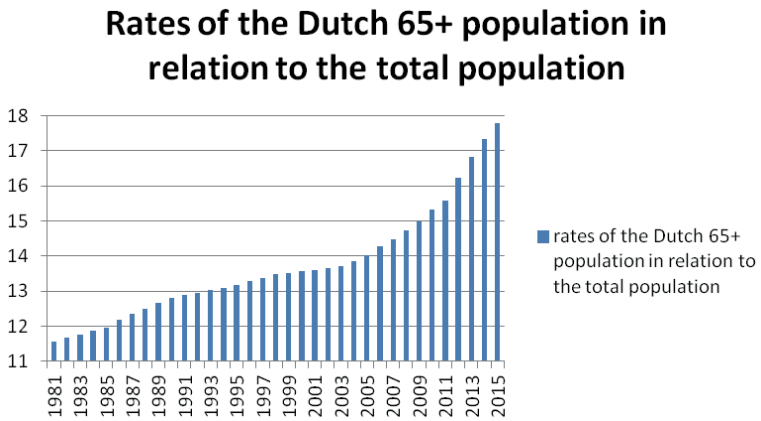

Figure 2. Rates of the Dutch 65+ population in relation to the total population (available data until 2015: http://statline.cbs.nl).

hospital specific clinical pathway is a tool for care professionals to ensure optimal care through the whole process without skipping essential steps. Pathways can have a positive effect on clinical outcomes (72, 73). The results from **Chapter 7** show the same effect in a before-and-after study. The pathway describes interdisciplinary appointments and rules regarding the five clinical stages: pre-, peri-, post-operative, transfer to surrounding rehabilitation centers and follow-up. Successful implementation of such pathways can contribute to reducing healthcare costs as propagated by the Dutch Ministry of Health, Welfare and Sport (74). Namely, health expenditure has increased continuously since 1972, from 8% to 13% of gross domestic product (GDP). Based on the trend of the past decade, different scenarios assess healthcare expenditure between 19% and 31% of GDP in 2040. Insight in healthcare costs may reveal options for cutting down health care expenses. **Chapter 8** reveals for the first time the Dutch costs for arthroplasty for the treatment of displaced femoral neck fractures in active elderly patients. The mean total medical costs of treating femoral neck fracture patients with arthroplasty were after one year € 23,869 and after two year € 26,399. The main cost determinants were rehabilitation and nursing homes. Reducing costs after hip fracture surgery should focus on improving the duration and efficiency of the rehabilitation phase.

Hip fracture care in the Netherlands is well organized. However, results from clinical research are able to better finetune the details of hip fracture management. A pivotal role is for the treating clinician whose task is to have a helicopter view and look after the optimal, individual, pre-operative preparation, timely surgery, eye for peroperative detail and to be *interested* in the patient after surgery and at the outpatient clinic.

In summary, a dedicated orthopedic trauma surgeon is not solely dependent on implant material, but should be able to achieve good clinical results and satisfied patients.

FUTURE PERSPECTIVES

Figure 3 summarizes the impact of results from this thesis on clinical practice. Future research should focus on the following topics, in order to further improve hip fracture care in the Netherlands.

First, the most important aspect of optimal hip fracture care is primary fall prevention. Therefore, increasing national awareness for fall incidents by public campaigns is necessary. Recurrent falling, especially in the 65+ population cannot be accepted by neither healthcare professionals nor family members. Different types of fall prevention strategies exist and this health topic deserves more attention. Fall prevention (number and cause(s) of falls, living circumstances, polypharmacy, etc.) is primarily a task for general practitioners and nursing homes physicians.

Hospitals in cooperation with general practitioners should organize the secondary fracture prevention. First because in the Netherlands fractures are diagnosed and treated in hospitals. Secondly, this type of prevention is time consuming, needs good follow-up structure, blood sampling and DEXA scanning. In the cases that prevention has failed and the hip fracture is a fact, the appropriate treatment must be chosen for that particular patient by shared decision making. The first question should be: osteosynthesis or arthroplasty? The definitive results from the HEALTH and FAITH trial will soon provide important data on the type of implant preference and on risks of revision surgery, complication rates and costs. Multiple options are available for arthroplasty and some clinical questions are unanswered. Future research should also focus on clinical important differences and costs when comparing different options for arthroplasty. For example, does the surgical approach (and the surgeons' experience) substantially influence postoperative function, pain and rates of dislocation? Does the use of cement substantially influence postoperative function, pain and rates of periprosthetic fractures, infection and death in the hip fracture population? When performing total hip arthroplasty in this population, what are the disadvantages of using large diameter heads (>36 mm)? Discussions and critical reviews from meta-analyses from randomized controlled trials and observational studies, answering the above mentioned questions will support the decision making for treatment of individual patients. The results from future (randomized) studies will be of more clinical value when a high volume of patients are included and when the follow-up time, depending on the subject of course, is longer (at least five year) than customary (1 or 2 years). Also, clinical hip fracture related studies without using patient reported outcome measures (PROMs) should not be planned, carried out, sponsored or approved by medical research ethics committees. PROMs are not only of importance for the results in individual studies, but also the continuation of the PROMs program (including the hip fracture populations) related to the Dutch Arthroplasty Register, involving all disciplines treating hip fractures, is essential in improving quality of hip fracture care. Study results can be compared with national standard values and geographic important variations can be detected. Also, in order to improve quality of hip fracture care it is possible to discuss and to monitor if treatment trends from literature are reflected in clinical practice. This kind of scientific support for treatment changes has been proven to be successful, an example is the Swedish National Patient Register (75). Another aspect for future investment in the care for hip fractures, based among other publications and on the outcomes described in **Chapter 7**, is to stimulate the use of dedicated care pathways and to evaluate the results of surgery, complications, admission days, secondary prevention, and follow up.

Especially the mean hospital admission days has been reduced in the last decade. This can be regarded as an important advance. However, in **Chapter 8** it is described that about half of the costs for hip fracture treatment is needed for rehabilitation facilities/

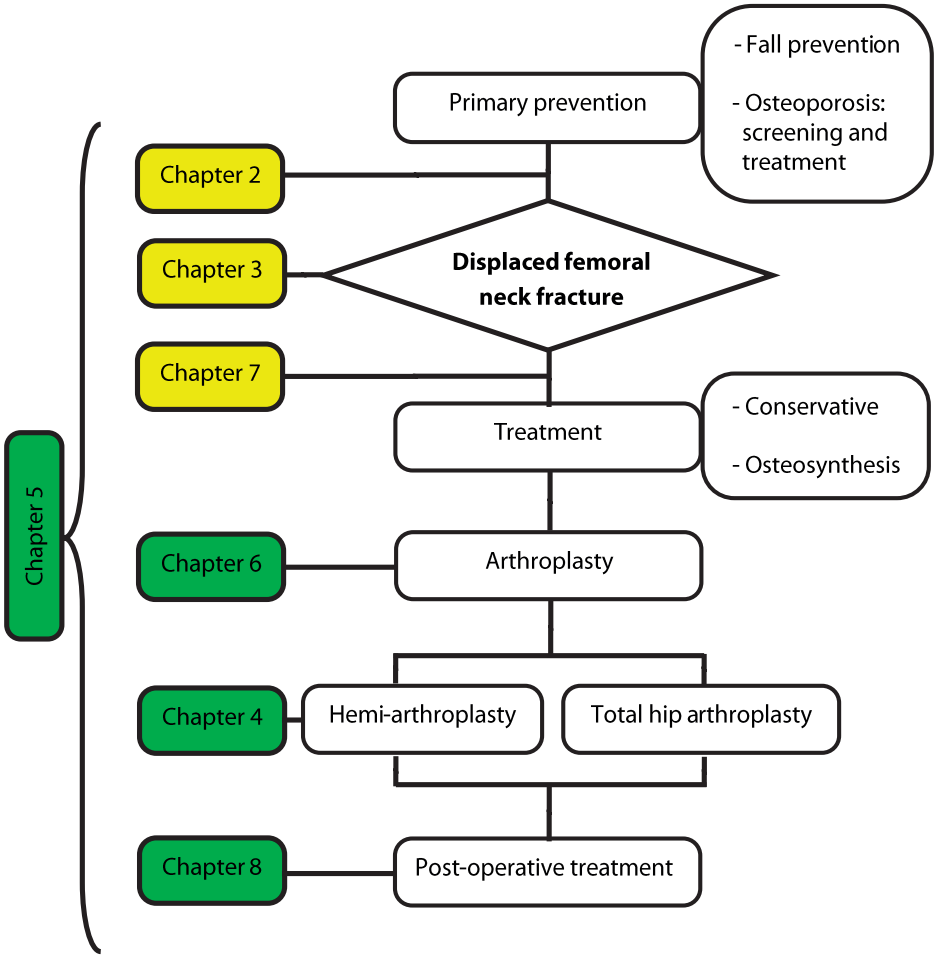

Figure 3. Relation between chapters from this thesis and the clinical course of displaced femoral neck fractures. Green blocks represent new information from study results in this thesis, which can be used in clinical practice. Yellow blocks represent information from study results in this thesis, which can confirm previously published results, without direct effect on clinical practice.

nursing homes. Reducing this length (and thus costs) would be a next step in optimizing treatment. Most rehabilitation centers, hospitals and physiotherapists have their own protocols. But no uniform national protocol exists. It would be useful to develop such a program with specific exercises and points. The Dutch concept guideline "Proximal femoral fractures" advices, based on the NICE and AAOS guidelines, to offer at least once daily in-hospital therapy and evaluate functional recovery. To start therapy on the day of surgery is part of optimal hip fracture care. Early mobilization is preferred as it reduces complications and has positive influence on the functional recovery. As a consequence hip fracture patients ideally are treated in the morning, before the

regular operative theater program. In most hospitals however, the daily practice is that hip fractures patients are operated at the end of the regular program (after 16:00). To implement morning hip fracture surgery would have major logistic consequences. After discharge intensive home therapy (at least 3x / week) is preferred over no physiotherapy and it equals therapy at the outpatient department. Alternatively, therapy is performed in rehabilitation facilities. There is no evidence on the optimal duration or discharge criteria from physiotherapy. The standard rehabilitation duration of 12 months needs to be further evaluated.

In conclusion, for the preferred early mobilization of hip fracture patients surgery in the morning can help to achieve even better patients outcomes. The length, type of exercises, evaluation methods and location (at home or rehabilitation center) of the physiotherapy in the Netherlands needs to be further evaluated with a cost analysis and development of a national protocol.

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Chapter 12

Thesis mini abstract

WHAT IS ALREADY KNOWN ON THIS TOPIC?

- Since the mid-nineties there are decreasing incidence rates for hip fracture-related hospitalizations in several, but not all, western countries (**Chapter 2**).
- The cumulative incidence of non-simultaneous proximal femur fractures is about 2-20% and the median interval is about 2-5 years (**Chapter 3**).
- The most beneficial type of arthroplasty (per patient) for displaced femoral neck fractures is not known (**Chapter 4**).
- Patient reported outcome measures are the modern way of treatment evaluation (**Chapter 6**), a well- known example is the WOMAC questionnaire, frequently used in arthritis populations.
- Cost analysis are important, but are country dependent due to different healthcare and economic systems around the world (**Chapter 8**).

WHAT THIS THESIS ADDS?

- **Chapter 2** shows a decrease in hip fracture incidence rates since 1994, also in the Netherlands.
- **Chapter 3** shows for femoral neck fractures a specific cumulative incidence of 9% and an interval of 2 years. In this population osteoporosis screening was performed in only 19%, although 28% had had a prior fracture and 5-7% had a concomitant fracture. Surgeons generally agreed on the use of internal fixation or arthroplasty for the different types of femoral neck fractures.
- The review of the most recent available evidence (**Chapter 4**) shows that total hip arthroplasty may be advantageous over hemiarthroplasty in a selected group of patients suffering displaced femoral neck fractures.
- The results in **Chapter 6** show for the first time that the WOMAC is also suitable for use in future clinical studies in hip fracture populations.
- For the first time in the Netherlands the total medical costs of treating femoral neck fracture patients with hemi- or total hip arthroplasty are calculated: € 26,399 per patient until 2 years postoperatively (**Chapter 8**).

WHAT DO WE HAVE TO CHANGE?

- Efforts to minimize hip fractures and the length of hospital stay after a hip fracture must be continued (**Chapter 2**).

- Use the results from **Chapter 3** for patient education to increase awareness of the relatively high risk of a second hip fracture in the near future. Doctors should better adhere to the national secondary osteoporosis prevention guideline (and refer all 50+-patients with a fracture for screening).
- Total hip arthroplasty should more frequently be considered in the treatment of displaced femoral neck fractures (**Chapter 4**) and without any type of delay this treatment for fracture care should be available at all times.
- PROMs should be obligatory in future hip fracture treatment evaluation research (**Chapter 6**).
- With the expected increase of the total absolute numbers of hip fractures in the near future, efforts need to be made to reduce the total medical costs (**Chapter 8**).

WHAT NEEDS FURTHER RESEARCH?

- For appropriate healthcare planning and follow-up, it would be advisable to repeat the study from **Chapter 2** in 2020.
- Further identifying risk factors for other fractures after a hip fracture with a prospective study or database. Measurements of hip fracture treatment results from a patient perspective (PROMs), also after a second fracture (**Chapter 3**).
- Research on the effect sizes of the types of arthroplasty after displaced hip fracture and further fine tuning of the national guideline on this topic. Although several randomized controlled trials have already been performed or are recruiting patients, results of more large, well-designed and well-conducted studies are needed (**Chapter 4**).
- Future research in the field of PROMs for hip fracture populations should focus on the found ceiling effects and possible redundant questions, to finally develop an optimal hip fracture specific WOMAC questionnaire (**Chapter 6**).
- As rehabilitation and nursing homes accounted for almost half of the total medical costs after treatment with arthroplasty for displaced femoral neck fractures, focus on improvements of the rehabilitation phase can result in reducing costs (**Chapter 8**).

Chapter 13

Summary HEALTH study protocol

Hip Fracture Evaluation with ALternatives of Total Hip Arthroplasty versus Hemi-arthroplasty (HEALTH): A multicenter randomized trial comparing total hip arthroplasty and hemi-arthroplasty on revision surgery and quality of life in patients with displaced femoral neck fractures

INTRODUCTION

Worldwide, 4.5 million persons are disabled from hip fractures yearly with an expected increase to 21 million persons living with disability in the next 40 years. Hip fractures are associated with a 30% mortality rate and the number of hip fractures is expected to be over 6 million patients annually by 2050.

Despite these impressive numbers, definitive standard surgical management of displaced femoral neck fractures is lacking. Current evidence suggests the use of arthroplasty; advocates of hemi-arthroplasty (HA) focus upon reduced dislocation rates, lower rates of deep vein thrombosis, shorter operating times, less blood loss, and a technically less demanding procedure. Surgeons supporting total hip arthroplasty (THA) perceive benefits in improving patient function and improving quality of life. Methodological limitations of previous studies, as well as their small sample sizes and resulting wide confidence intervals, have left the optimal operative approach unresolved.

Objective

The HEALTH trial compares revision rates at 24 months following THA versus HA in patients 50 years of age or older with displaced femoral neck fractures. Secondary outcome measures include mortality, complications, health-related quality of life (Short Form-12, SF-12), functional outcomes (Western Ontario McMaster Osteoarthritis Index, WOMAC), and health outcome (EuroQol-5D, EQ-5D).

Hypothesis

It is hypothesized that total hip arthroplasty will have similar or lower rates of revision surgery (primary outcome) and higher functional outcome scores (secondary outcome) at 24 months compared with hemi-arthroplasty.

METHODS AND ANALYSIS

In a multicenter, randomised controlled trial, 1,434 patients 50 years of age or older, with displaced femoral neck fractures from international sites are randomised to receive either THA or HA. Exclusion criteria include associated major injuries of the lower extremity, hip infection(s) and a history of frank dementia. Minimisation is used to ensure balance between intervention groups for the following factors: age, prefracture living, prefracture functional status, American Society for Anesthesiologists (ASA) Class and center number. Data analysts and the HEALTH Steering Committee are blinded to the surgical allocation throughout the trial. Outcome analysis will be performed using a $\chi 2$

test (or Fisher's exact test) and Cox proportional hazards modelling estimate. All results will be presented with 95% CIs.

RESULTS

In the Netherlands 14 participating sites started between December 15, 2008 and January 6, 2011. On February 14, 2011 the anticipated sample size of 150 patients was reached. Patients were recruited for the Dutch HEALTH trial if they (1) were adults aged ≥50 years; (2) had a radiologically confirmed displaced femoral neck fracture, were aged at least 50 years (and were not candidates for osteosynthesis); (3) had a low energetic fracture without other major trauma; and (4) were ambulatory pre-fracture (with or without aid). Patients were excluded if they; (1) had a pathological fracture; (2) had associated major injuries of the lower extremities; (3) had retained hardware around the hip; (4) had an infection around the hip; (5) had a bone metabolism disorder other than osteoporosis; (6) were moderately or severely cognitively impaired pre-fracture; (7) had dementia or Parkinson's disease severe enough to compromise the rehabilitation process; or (8) were not likely to be able to complete follow-up. These eligibility criteria did not interfere with national treatment guidelines.

Appendices

List of abbreviations

List of HEALTH and FAITH trial collaborators

List of publications

Dankwoord

Curriculum vitae

PhD portfolio

LIST OF ABBREVIATIONS

CVZ	College voor zorgverzekeringen (tegenwoordig:Zorginstituut Nederland)
EuroQol-5D/ EQ-5D	Europe Quality of Life- 5 dimensions (questionnaire)
GDP	Gross domestic product
FAITH	Fixation using Alternative Implants for the Treatment of Hip fractures
HA	Hemi-Arthroplasty
HEALTH	Hip fracture Evaluation with ALternatives of Total hip arthroplasty versus Hemi-arthroplasty (NCT00556842)
NZa	Nederlandse Zorg Autoriteit
KHP	Kop-halsprothese
METC	Medisch ethische toetsingscommissie
PROM	Patient Reported Outcome Measure
SF-12	Short Form 12 (questionnaire)
THA	Total Hip Arthroplasty
THP	Totale heupprothese
WOMAC	Western Ontario McMaster Osteoarthritis Index (questionnaire)

List of HEALTH and FAITH trial collaborators

HEALTH trial:

Research grants were received from the following: Canadian Institutes of Health Research (CIHR) (PI: M Bhandari, Co-PI: GH Guyatt), National Institutes of Health (NIH) (PI: TA Einhorn), the Netherlands Organisation for Health Research and Development (ZonMw) (PI: EMM van Lieshout), Sophies Minde Foundation for Orthopaedic Research (PI: L Nordsletten and F Frihagen), and McMaster Surgical Associates (PI: M Bhandari). Dr. Bhandari was also funded, in part, by a Canada Research Chair in Musculoskeletal Trauma which is unrelated to the present study (McMaster University, Hamilton, ON, Canada). The funding sources had no role in design or conduct of the study; the collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript. Dr. Mohit Bhandari had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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FAITH trial:

Research grants were received from the following: Canadian Institutes of Health Research (CIHR) (PI: Mohit Bhandari); Stichting NutsOhra (PI: Martin J. Heetveld), the Netherlands Organisation for Health Research and Development (PI: Esther M.M. Van Lieshout); Physicians' Services Incorporated (PI: Mohit Bhandari). Funding for the pilot phase of FAITH was supported, in part, by Stryker Inc. Dr. Bhandari was also funded, in part, by a Canada Research Chair in Musculoskeletal Trauma which is unrelated to the present study (McMaster University, Hamilton, ON, Canada). We would also like to acknowledge the support of The County Durham & Tees Valley Comprehensive Local Research Network which operates as part of the National Institute for Health Research Comprehensive Clinical Research Network in England. The funding sources had no role in design or conduct of the study; the collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript. Dr. Mohit Bhandari had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Orthopaedic Associates, LLC); Joseph R. Hsu, James Ficke, Michael Charlton, Matthew Napierala, Mary Fan **(US Army Institute of Surgical Research);** Paul Tornetta III, Chadi Tannoury, Hope Carlisle, Heather Silva **(Boston University Medical Center);** Michael Archdeacon, Ryan Finnan, Toan Le, John Wyrick, Shelley Hess **(UC Health/University of Cincinnati Medical Center);** Michael L. Brennan, Robert Probe, Evelyn Kile, Kelli Mills, Lydia Clipper, Michelle Yu, Katie Erwin **(Scott and White Memorial Hospital);** Daniel Horwitz, Kent Strohecker, Teresa K. Swenson **(Geisinger Medical Center);** Andrew H. Schmidt, Jerald R. Westberg **(Hennepin County Medical Center);** Kamran Aurang, Gary Zohman, Brett Peterson, Roger B. Huff **(Kaiser Permanente);** Joseph Baele, Timothy Weber, Matt Edison **(OrthoIndy);** Jessica McBeth **(Santa Clara Valley Medical Center);** Karl Shively, Janos P. Ertl, Brian Mullis, J. Andrew Parr, Ripley Worman, Valda Frizzell, Molly M. Moore, Erin Tobias, Emily Thomas **(Indiana University – Wishard Health Services);** Charles J. DePaolo, Rachel Alosky, Leslie E. Shell, Lynne Hampton, Stephanie Shepard, Tracy Nanney, Claudine Cuento **(Mission Hospital Research Institute);** Robert V. Cantu, Eric R. Henderson, Linda S. Eickhoff **(Dartmouth-Hitchcock Medical Center);** E. Mark Hammerberg, Philip Stahel, David Hak, Cyril Mauffrey, Douglas Gibula, Hannah Gissel, Corey Henderson **(Denver Health and Hospital Authority);** David P. Zamorano, Martin C. Tynan, Deeba Pourmand, Deanna Lawson **(University of California Irvine Medical Center);** Gregory J. Della Rocca, Brett D. Crist, Yvonne M. Murtha, Linda K. Anderson **(University of Missouri Health Care);** Colleen Linehan, Lindsey Pilling **(Covenant Healthcare of Saginaw);** Courtland G. Lewis, Stephanie Caminiti, Raymond J. Sullivan, Elizabeth Roper **(Hartford Hospital);** William Obremskey, Philip Kregor, Justin E. Richards, Kenya Stringfellow **(Vanderbilt University Medical Center);** Michael P. Dohm, Abby Zellar **(Western Slope Study Group)**

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DANKWOORD

Onderzoek verrichten is teamwork. Dit proefschrift is tot stand gekomen dankzij de gegevens en/ of persoonlijke medewerking van in totaal 358.702 **patiënten** (H2: 355.320, H3: 1.250, H4: 986, H5:370, H6: 250, H7: 526). Graag bedank ik allen en de 150 Nederlandse deelnemers aan de HEALTH studie in het bijzonder, die op het moment van de fractuur op de spoedeisende hulp de beslissing hebben gemaakt om toestemming te verlenen aan dit onderzoek.

Geachte **Professor Patka,** zo begon menig mailtje aan u. Veel later voegde ik daar pas "beste Peter" aan toe. Hartelijk dank voor de mogelijkheid voor mij om de Nederlandse HEALTH trial coordinator te zijn. Onderzoek verrichten is teamwork. Uw rust in zowel uitstraling, uw motoriek als in wijze van discussie voeren, hebben mij vaak met een enkele opmerking laten nadenken over belangrijke punten van dat momentw. Het resultaat heeft u nu in handen, geweldig bedankt!

Dr. E.M.M. van Lieshout, beste Esther. Tsja, waar moet ik beginnen? Onderzoek verrichten is teamwork. Dat heb je mij duidelijk gemaakt. Je bent de motor van ook dit proefschrift. Overal bestaat een oplossing voor en daar moet vaak hard voor gewerkt worden. Structuur, netjes archiveren, keuzes maken: onderzoek doen heb ik van jou geleerd. Ongelooflijk dat ik dit project met jou heb kunnen doen en niet in de laatste plaats, omdat je juist ook persoonlijk geinteresseerd bent in de mensen om jou heen. Wauw!

Dr. R.W. Poolman, beste Rudolf. Mijn oudste co-schap Orthopedie liep ik in het AMC, toen jij daar in opleiding was. Jaren later treffen wij elkaar bij de HEALTH studie en nu ben je mijn copromotor. Onderzoek verrichten is teamwork en er is altijd een vrolijke en zeer gedreven sfeer in het team met jouw aanwezigheid. Ontzettend bedankt dat mede dankzij jouw inbreng en uitgebreide netwerken dit proefschrift tot stand is gekomen.

Onderzoek verrichten is teamwork. Graag bedank ik dan ook de teamleden **Prof.dr. M.H.J Verhofstad, Prof.dr. R.G.H.H. Nelissen, Prof.dr. A. Van kampen, Prof.dr. T.J.M. van der Cammen** en **Dr. F.U.S. Mattace Raso** voor hun enthousiasme bij het ontvangst van het manuscript ter beoordeling en voor de tijd en moeite die genomen is om deel uit te maken van de promotiecommissie.

Graag bedank ik alle **deelnemende centra,** alle **"includeerders"** en de **lokale hoofdonderzoekers** in het bijzonder: **drs L.H.G.J. Elmans (Afdeling Orthopedie, Amphia Ziekenhuis, Breda), dr. R. Krips (Afdeling Orthopedie, Diaconessenhuis, Leiden), dr. J.P.W. van Jonbergen (Afdeling Orthopedie, Deventer Ziekenhuis, Deventer)** en **drs. A.J. Frima (Afdeling Heelkunde, Deventer Ziekenhuis, Deventer), drs. M.L.M. Falke (Afdeling Orthopedie, Flevoziekenhuis, Almere), drs. J.P. van Dijk (Afdeling Heelkunde, Ziekenhuis Gelderse Vallei, Ede), drs. H.W. Bolhuis (Afdeling Heelkunde, Gelre ziekenhuizen, Apeldoorn)** en **drs. F. Steenstra (Afdeling Orthopedie, Gelre ziekenhuizen, Apeldoorn), dr. W.P.J. Fontijne (Afdeling Orthopedie,**

IJsselland Ziekenhuis, Capelle aan den IJssel), dr. H.J.L. van der Heide (Afdeling Orthopedie, Leids Universitair medisch Centrum, Leiden), drs. S.B. Keizer (Afdeling Orthopedie, Haaglanden Medisch centrum, Den Haag), dr. R.W. Poolman (Afdeling Orthopedie, OLVG, Amsterdam), drs. R. Kooijman (Afdeling Heelkunde, Spijkenisse Medisch Centrum, Spijkenisse) en **dr. H.I.H. Lampe(Afdeling Orthopedie, Spijkenisse Medisch Centrum, Spijkenisse), dr. L. Schuman** en **dr. D. Haverkamp (Afdeling Orthopedie, Slotervaartziekenhuis, Amsterdam), dr. P.A. Nolte (Afdeling Orthopedie, Spaarne Ziekenhuis, Hoofddorp)** en **dr. H.M. Van der Vis (Afdeling Orthopedie, Tergooiziekenhuizen, Hilversum)**. Een beter voorbeeld dat onderzoek verrichten teamwork is, kan ik niet bedenken.

Dr. M. Bhandari. Performing medical research is teamwork. Therefore, I would like to thank you and your team for the opportunity to participate from the early beginning with the Dutch sites to the international HEALTH trial team.

Geachte mede trauma-onderzoekers, beste **Simon, Stephanie, Klaas, Johan, Nicole, Gijs, Steven en Kiran**. Na een rondje door Nederland gereden te hebben, was het altijd prettig om even bij jullie op de kamer wetenschappelijke verdieping op te doen (…) of flauwe grappen te maken (Simon, Stephanie, Klaas, Johan, Nicole, Gijs, Steven en Kiran). Onderzoek verrichten is teamwork en ook jullie waren het team, bedankt daarvoor.

Onderzoek verrichten is teamwork. Graag bedank ik de jongste teamleden. Beste **Diederik, Adinda, en Elle.** Als student-onderzoekers hebben jullie een belangrijke bijdrage aan verschillende publicaties geleverd. Bedankt voor de gezellige tijd met jullie.

Lieve **Sylvia,** beste **Dirk,** wat geweldig dat jullie vandaag als team achter mij staan als paranimfen.

Lieve **papa en mama**, dank jullie wel voor alle ruimte, mogelijkheden en vertrouwen die jullie altijd aan mij, onvoorwaardelijk hebben gegeven. Dank voor jullie niet aflatende interesse in mij en mijn bezigheden. Zonder jullie steun, waarvan ik altijd weet dat die er is op alle vlakken, had ik dit project niet kunnen afronden. Ik houd van jullie.

Lieve **Caroline**, ontzettend bedankt voor alles wat je mij gegeven hebt. Mede door jouw steun en inzet hebben we ook dit project kunnen afronden. Ik houd van jou en zal dat blijven doen.

Lieve **Janne, Sven en Nils**. Wat zijn jullie een prachtig team met z'n drieen. Altijd gezellig (en soms wat ongelegen…) als jullie mee kwamen typen op de computer. Ik weet waar ik het allemaal voor doe en ik ben apetrots op jullie (recent: "waarom ben jij aperots, papa?"). Jullie geven mij energie en maken mij gelukkig.

CURRICULUM VITAE

Paul Burgers was born on August 26th 1980 in Eindhoven, the Netherlands. He grew up and had a happy childhood in Nuenen, Noord-Brabant. After graduating high school at the Eckart College Eindhoven in July 1998, he did a summer course Physics at the James Boswell Institute, Utrecht. It was here where he met the love of his live, Caroline.

Academic medical training was started in September 1998 at the University of Amsterdam.

He organized to do his final internship (Dr. J. Van Olmen) for 4 months in Ndala hospital, Tanzania. Afterwards Caroline came over and they traveled for 1 month through Tanzania.

He obtained his medical degree in 2004 and Paul started his first residentship at the Waterland Ziekenhuis, Department of Orthopedic Surgery, Purmerend (Drs H. Penterman). In 2006 he moved to the Antoni van Leeuwenhoek Ziekenhuis/ Netherlands cancer Institute, Amsterdam (Dr. F. Van Coevorden) and worked there as resident and took a first step on his scientific path.

In 2008 he started as a research fellow at the Erasmus MC, University Medical Center

Rotterdam, Department of Surgery-Traumatology under Prof. dr. P. Patka. He was the Dutch study coordinator of the HEALTH trial, involving 14 Dutch hospitals. This international, randomized clinical trial concerns the treatment with two types of arthroplasty for femoral neck fractures in the elderly. His work resulted into this dissertation.

Training in general surgery started in December 2013 in the IJsselland Ziekenhuis, Capelle aan den IJssel (Dr. I Dawson). Orthopaedic training started in 2015 at the Medical Center Haaglanden, The Hague (Dr. E.R.A. van Arkel), Leiden University Medical Center, Leiden (Prof. Dr. R.G.H.H. Nelissen) and the Haga hospital, The Hague (Dr. R. Deijkers).

Paul is currently enjoying living in Rotterdam, Nesselande with his wife Caroline Burgers-Pompe and their children Janne (2009), Sven and Nils (2013).

PHD PORTFOLIO

Summary of PhD training and teaching

Name PhD student: Paul T.P.W. Burgers	PhD period: November 2008 – May 2015
Erasmus MC Department: Trauma Research Unit	Promotor: Prof. Dr. P. Patka
Department of Surgery	Co-promotors: Dr. E.M.M. Van Lieshout, Dr. R.W. Poolman

1. PhD training

	Year	Workload (ECTS)
General courses		
Biostatistics	2008	1.0
BROK ('Basiscursus Regelgeving Klinisch Onderzoek')	2009	1.0
Good Clinical Practice	2009	1.0
Minicursus methodologie van patiëntgebonden onderzoek en voorbereiding van subsidieaanvragen	2010	0.3
Specific courses (e.g. Research school, Medical Training)		
Arts en acute zorg	2011	2.0
ATLS	2013	2.0
Professioneel presenteren	2014	1.0
International conferences		
EORS Amsterdam (poster presentation)	2012	1.0
ESTES Frankfurt (oral presentation)	2014	2.0
ESTES Amsterdam (oral and poster presentation)	2015	2.5
National conferences		
ZWOT (oral presentation)	2008	1.0
ZonMW symposium: 10 jaar doelmatigheidsonderzoek (poster presentation)	2009	1.0
SEOHS (oral presentation)	2009	1.0
Assistentensymposium NVT (oral presentation)	2010	1.0
Assistentensymposium NVT (oral presentation)	2011	1.0
Traumadagen NVT (poster presentation)	2011	1.0
Springmeeting NVVH (oral presentation)	2012	1.0
Najaarsvergadering NOV (oral presentation)	2012	1.0
Traumadagen NVT (poster presentation)	2013	1.0
ZWOT (oral presentation)	2014	1.0

2. Teaching

	Year	Workload (ECTS)
Lecturing		
25 jaar LINK SP2	2009	0.5
Supervising practicals and excursions, Tutoring		
Examination Basic Life Support for medical students Co-assistentenonderwijs YSL	2009-2010	0.5
Supervising Master's theses (3 students)		
Adinda Mailuhu	2011- 2012	2.0
Diederik Van Bakel	2012-2013	2.0
Ellen Van Woensel	2013	2.0
Joost Verhelst	2013	1.0