The International Costs and Utilities Related to Fractures Study (ICUROS) - Quality of Life During the First 4 Months After Fracture

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Abstract

Introduction: The International Costs and Utilities Related to Osteoporotic fractures Study (ICUROS) was initiated in 2007 with the objective of estimating costs and quality of life related to fractures in several countries worldwide. The ICUROS is ongoing and enrolls patients in 11 countries (Australia, Austria, Estonia, France, Italy, Lithuania, Mexico, Russia, Spain, UK and the US). The objective of this paper is to outline the study design of ICUROS and present results regarding the QoL (measured using the EQ-5D) during the first 4 months after fracture based on the patients that have been thus far enrolled ICUROS.

Methods: ICUROS uses a prospective study design where data (costs and quality of life) are collected in four phases over 18 months after fracture. All countries use the same core CRFs. Quality of life was collected using the EQ-5D instrument and a time-trade off questionnaire.

Results: The total sample for the analysis was 2,808 patients (1,273 hip, 987 distal forearm and 548 vertebral fracture). For all fracture types and countries, the QoL was reduced significantly after fracture compared to pre-fracture QoL. A regression analysis showed that there were significant differences in the QoL-loss between countries. Also, a higher level of QoL prior to the fracture significantly increased the QoL-loss and patients who were hospitalised for their fracture also had a significantly higher loss compared to those who were not.

Conclusions: The findings in this study indicate that there appear to be important variations in the QoL decrements related to fracture between countries.

Key words: *Osteoporosis, Fracture, Quality of life, Costs*

Introduction

Osteoporosis causes more than 8.9 million fractures annually worldwide – approximately 1,000 per hour [1]. Fracture rates are higher in the western world than in other regions so that, despite the lower population, slightly more than one-third of all osteoporotic fractures occur in Europe. The disease predominantly affects postmenopausal women, in whom the lifetime fracture risk is 40-50% [2-6]. However, the specifics of the burden of fractures differ by fracture type, from substantial pain and suffering, disability and even death associated with hip fractures [3] to less serious and often transient effects following, for example, a distal forearm fracture. Because of the high associated risk of fractures in osteoporotic patients, osteoporosis is a major public health problem, posing a significant burden on both the individual and the society [7].

Burden of disease analyses provide useful information concerning the costs that society has to carry for managing the disease of interest. From a health economic perspective, the burden of disease encompasses both the cost related to the disease and its morbidity consequences (i.e. quality of life and survival). Costs and quality of life (QoL) related to a disease is also required information for the economic evaluation of medical interventions (e.g. cost-effectiveness analysis). When conducting such studies, it is preferable to use country specific data but, in the case of osteoporosis, there are empirical data gaps with regards to the consequences of these fractures in terms of cost and reduction in quality of life in many countries. As a result, expert opinion or the transfer of data across countries has been used to substitute missing data, which leads to uncertainty and decreased validity of health economic analyses.

With the purpose of estimating the burden and to fill parts of the data gap related to fracture consequences in Sweden, a prospective observational study (the KOFOR-study) collected data on the societal costs and QoL related to fractures up to 18 months after the fracture event [8,9]. Whereas the KOFOR-study provided a deeper insight on the burden associated with osteoporotic fractures in Sweden, the results cannot be directly transferred to other countries as there are differences in health care systems and price levels across countries, affecting the resource use, costs and outcomes. Therefore, it is important to investigate the costs and health effects of fractures in countries other than Sweden.

The International Costs and Utilities Related to Osteoporotic fractures Study (ICUROS) was initiated in 2007 through the International Osteoporosis Foundation with the objective of estimating the costs and quality of life related to fractures in a number of countries across the

world, based on a similar study design as used in the KOFOR-study. A multinational study approach has the advantage of enabling direct comparisons of the health economic impact of an osteoporotic fracture among different countries. It also increases the awareness of consequences of osteoporosis on an international level, creating a more widespread knowledge base of the true burden of the disease worldwide. The ICUROS is ongoing and has enrolled about 5,869 patients with fracture (as of May 2012) in 11 countries (Australia, Austria, Estonia, France, Italy, Lithuania, Mexico, Russia, Spain, UK and the US). The study is still recruiting patients and may be expanded to additional countries.

The objective of this paper is to outline the study design of ICUROS and present results regarding the QoL (measured using the EQ-5D) during the first 4 months after fracture based on the patients that have been thus far enrolled ICUROS.

Method and materials

Study design and data collection

ICUROS used a prospective study design similar to the previous KOFOR-study and is published elsewhere [9]. Only minor changes were made to the study protocol and case report forms (CRFs) used in the KOFOR-study. All countries use the same core CRFs, with minor changes to allow for adaptation to local conditions. In brief, patients with fracture were enrolled at their first contact with a health care agency for their fracture and an interview should be undertaken within two weeks after fracture. In the US, this post-fracture enrollment window was extended to 6 weeks. The data were collected in four phases over 18 months after fracture. Phase I refers to immediately after fracture (baseline) where patient characteristics, background information and perceived health related QoL before (recollected) and after the fracture event were collected. Phase II to IV took place at 4 months, 12 months and 18 months after the fracture event, at which time current health status and fracture-related resource use since the last interview were documented. The information for Phase I was primarily collected by interview while the patient still was at the health care institution receiving care for their fracture but, in some instances, undertaken by telephone interview. Reported resource use and QoL data for the following phases were collected mainly through telephone interviews with patients but also during routine physician visits, whereas data on hospitalizations were retrieved from hospital charts and/or administrative billing data.

ICUROS included patients sustaining a fracture of the hip, vertebra (confirmed by x-ray) or distal forearm from all countries participating in the study. A few centres chose to extend the study to include other fracture sites, such as humeral and ankle fractures. ICUROS was not based around a hypothesized effect size, thus a formal statistical power calculation was not applicable. Based on the results in the KOFOR-study a total of 200 patients of each fracture type and country were judged to be an appropriate target sample size to produce stable cost and QoL estimates and to facilitate analysis of differences in costs and QoL for main patient characteristics such as age and gender in each country.

To be eligible for inclusion in the study, patients had to be diagnosed with a low-energy induced fracture and be at least 50 years old. Patients with multiple fractures and fractures caused by co-morbidities (such as cancer induced fractures) were excluded as well as patients who were deemed unable to complete the questionnaires because of dementia or other psychological problems. Institutionalized patients were also excluded because of their high resource consumption prior to the fracture, making it difficult to assess the resource use due to the fracture event. Additionally, patients that sustained a new fracture during the study period were withdrawn from the study.

The study was approved by the relevant research ethics committees in each participating country. All patients provided their informed consent to participate and the patients could withdraw from the study at any time on their own request.

Patient characteristics

General background information and patient characteristics were collected during Phase 1, including age, sex, level of education, level of income, living arrangements before fracture, work status and previous fractures during the last 5 years.

Resource use

Fracture-related resource use was collected with the objective of estimating the costs from a societal perspective. Data were collected through patient records and by asking the patient. The resources were categorised into direct medical costs (hospitalisations, outpatient care and pharmaceutical intervention), direct non-medical costs (community care, investments such as home modifications and informal care) and indirect costs (i.e. loss of production related to sick

leave and early retirement). Community care consisted of special living arrangements, home care and transportation. Patient-reported resource use in the month prior to interview (community care and informal care) and resources lost, i.e. indirect costs, were recorded. The one month recall period was used to minimize recall bias.

Quality of life measurement

Health-related quality of life is estimated using two instruments in ICUROS: The EQ-5D and a Time Trade-Off question (TTO). However, in this study, only results from the EQ-5D questionnaire is reported.

The EQ-5D is a generic QoL instrument consisting of two components. The first component is the descriptive system which is a questionnaire covering five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension is divided into three levels of severity: no problem, some problems and major problems, resulting in 243 possible health states (3^5 combinations) [10]. These health states can be translated into utilities on a unison scale using a population based value set derived through a TTO valuation technique. In this study we used the value set presented by Dolan [10] which is based on the preferences of a UK population.

The EQ-5D also includes visual analogue scale (VAS) measurement which is a vertical scale between 0 (worst imaginable health state) and 100 (best imaginable health state). It is a comparatively simple method where the patient can rate their current health status by drawing a line from a box stating "your own health state today" to the appropriate point on the VAS scale.

Estimating quality of life following an osteoporotic fracture

QoL related to fracture presented in this article was based on the EQ-5D (descriptive system) questionnaire for patients who had a full four months of follow-up, by fracture site (hip, vertebra or distal forearm). For the estimation of the loss in quality of life associated with a fracture during the first four months, it was assumed that the patient would have remained at their pre-fracture level of quality of life had the fracture not occurred. In order to obtain an estimate of the QoL loss that accounts for the initial drop in QoL after fracture and the subsequent improvement during the ensuing four months, the accumulated QoL loss in the 4-

months follow-up after fracture was calculated as the area under the curve using the trapezoid method [11].

Analysis sample

The data set for the analyses was extracted from the ICUROS database on October 15th 2010 for all countries except the US where the data extraction was conducted in February 2011. The cut-off for inclusion in the analysis was data from any country that had recruited 30 patients or more at any fracture site (hip, vertebrae or distal forearm) that had also completed Phase II (4 months after fracture). Additionally, the Swedish patients in the KOFOR-study were also included in the analysis [8,9].

Statistical analysis

To identify determinants of QoL reduction after hip, vertebral and wrist fractures, multivariate ordinary least square (OLS) regression analyses was carried out using demographic characteristics and different disease characteristics as predictors. The variables included were: quality of life at baseline, country, age, gender, hospitalization in connection to the fracture, fractures during the previous five years, time between the index fracture and first interview, and interaction terms between country and the other variables. A stepwise regression approach was used and the cut-off statistical significance for keeping variables in the regression was set at 10%. All statistical analyses were performed using STATA 10.0 for Windows (Statsoft, Tulsa, OK).

Results

Patient characteristics

At the time of data extraction, 3,915 patients had been enrolled in the ICUROS. Of the 3,915 patients, 419 had been withdrawn from the study prior to first follow-up and a further 1,553 were yet to complete first follow-up, resulting in 1,943 patients eligible for analysis. Combining the 1,943 patients from ICUROS with the 865 patients eligible for analysis from the KOFOR study resulted in a total sample of 2,808 patients (1,273 hip, 987 distal forearm and 548 vertebral fracture) from 36 centers in ten countries (Table 1). Estonia was the only country with too few patients followed up to 4 months to be included in the analysis. Patient characteristics by fracture site and country are shown in Table 2. Overall, 83% of the patients

were women with a mean age of 72.2 years, distal forearm fracture patients were the youngest (mean age: 67.6 years) and hip fracture patients were the oldest (mean age: 75.9 years). The mean age was lower in Russia compared to other countries for all fracture types. Almost all patients were hospitalized in relation to the hip fracture except in Mexico and Russia where 80 and 88% were hospitalized respectively. There were some notable country differences in the hospitalization rates for distal forearm and vertebral fracture. For example, in France 81% of all distal forearm fracture patients were admitted compared to 10% in Sweden and 9% in the US; for vertebral fracture patients, 71% were admitted in France compared to 10% in Russia. There were also differences between fracture sites and countries in the proportion of patients that had sustained a previous fracture within the last 5 years. In all, 24% of the patients had a previous fracture, though, in Russia the proportion of patients with a previous fracture was 44%.

Quality of life

The estimated EQ-5D QoL before, just after and at 4 months after fracture per country and fracture type is shown in Table 3. Overall, QoL prior to vertebral fracture (0.88) was higher than prior to hip (0.77) or distal forearm fracture (0.77). For all fracture types and countries, the QoL was reduced significantly after fracture compared to pre-fracture QoL. The mean decrease was largest for patients with hip fracture followed by vertebral and distal forearm fracture. The QoL after fracture was higher in the US compared to the other countries.

At four months, the average quality of life had significantly increased, although it was still below the pre-fracture level. The mean accumulated loss in QoL over 4 months (Table 3) related to hip fracture varied between countries. In Austria and Spain the QoL-loss was estimated at 0.11 whereas the loss was almost twice as high in Lithuania (0.21) and Italy (0.20). There were also marked differences in the loss of QoL for vertebral fracture with USA (0.05), Austria (0.08) and Russia (0.09) at the lower end and Italy at the higher end (0.19). For distal forearm fractures the QoL-loss ranged from 0.07 in Australia, Sweden and the US to 0.11 in Italy.

Regression analysis

The observed differences in the country mean values of the QoL-loss could be related partly to differences in patient characteristics. In the multivariate regression analysis shown in Table 4 the impact of different factors on the loss of QoL is shown. Models including interaction terms between the countries and the variables of interest were also constructed. However, the Akaike information criterion indicated that the models with the interaction terms were inferior to the

models without the interaction terms (results not shown). Therefore, the models without the interaction terms are presented. The results show that there were significant differences in the QoL-loss between countries. The QoL-loss after hip fracture was significantly lower in Austria (which was set as reference case in the regression) compared to all countries except Sweden and Spain. With the exception of the US, Austria was also found to have lower QoL-loss related to vertebral fractures compared to the other countries included in the analysis. The differences were smaller for distal forearm fractures but the QoL-loss was significantly ($p<0.05$) lower in Australia and Sweden, although higher in France compared to Austria. The QoL-loss increased with higher age ($p <0.05$) for hip but not for vertebral or distal forearm fractures. Men with distal forearm fracture had a significantly lower QoL-loss than women. There was no significant difference between sexes for hip and vertebral fracture. Further, a higher level of quality of life prior to the fracture significantly increased the quality of life loss. As might be expected, patients who were hospitalised for their fracture also had a higher loss compared to those who were not.

A comparison between countries regarding the estimated QoL-loss during the first four months following the fracture is presented in Figure 1, derived from a regression including all countries as explanatory variables. For this illustration, it was assumed that the patient was a 70 year old woman with a previous fracture. The pre-fracture quality of life weight was set to 0.8, and it was assumed that all hip fractures led to hospitalization whereas distal forearm fractures did not. Variations in QoL-loss between countries ranged from 0.12 to 0.21 for hip fractures, 0.05 to 0.18 for vertebral fractures (with higher values for hospitalized patients) and 0.05-0.08 for distal forearm fracture patients.

Discussion

In this article the general study design of ICUROS is presented. The study is, so far, the largest prospective observational study with the objective of estimating the consequences of osteoporotic fractures in terms of costs and quality of life in an international perspective. By applying the same methodology in all countries participating, comparisons can be performed between countries and the results will eventually enable estimates of the total burden of osteoporosis.

The results from the interim analysis presented in here support previous research that fractures are associated with a substantial decrement in quality of life which varies between fracture

types [12-20]. For hip fracture, mean QoL just after fracture fell below 0.05 in Italy, Mexico, Lithuania, Russia and Spain, an estimate close to death on the 0 (death) to 1 (full health) QoL scale used in this study. Whilst comparisons to other studies are difficult reflecting discrepancies in methodology, valuation technique, and respondents; a few studies eliciting QoL using the EQ-5D shortly after and / or approximately after four months have reported on the size of the QoL decrement. In a systematic review (incorporating the KOFOR study), hip fractures were associated with a QoL decrement of approximately 0.50 shortly after fracture and 0.20 four months after fracture [16]. Similarly, vertebral fractures were associated with a QoL decrement of approximately 0.37 shortly after fractures and 0.03 after four to six weeks after fracture [16]. In a more recent study conducted in Japan, hip, vertebral, and wrist fractures were associated with QoL decrements of 0.42, 0.35 and 0.22 at two weeks after fracture [21].

Additionally, the results suggest that there are differences in the magnitude of the quality of life reduction after fracture between countries. This could be related to factors such as differences in management and treatment of fracture patients, different perceptions and valuations of quality of life and differences in the ascertainment processes used to include patients in the study.

In the US, QoL weights after fracture were higher compared to other countries. A potential reason for this could be that the QoL data in the US after fracture were –on average – collected later than in other countries. However, in the models of mean accumulated loss in QoL, time-to-interview was not significant (see above). Another potential reason is ascertainment bias, i.e. the recruitment of milder cases.

There are differences between countries concerning the way fracture patients are managed and treated. This could be either due to economic reasons or different standards of practice which, in turn, is likely to have an impact on patient outcomes such as quality of life. For example, in Mexico and Russia only 80% and 88%, respectively of patients were hospitalized for hip fracture whereas in the other countries all patients were hospitalized. The observed differences between countries in terms of e.g. hospitalization rates and QoL for vertebral and distal forearm fractures could also be explained by differences in the ascertainment processes used to identify and enroll patients rather than actual differences in the patterns of care.

The quality of life before fracture in this study was estimated using the EQ-5D social value set from a UK population and applied to all countries. The reason for this is that the UK value set is the most commonly used and country specific value sets are available for only a few countries [22,23]. However, comparisons between value sets have shown differences between countries in how they value the EQ-5D health states in terms of quality of life [24]. Thus, the present study could either under or overestimate the utility loss associated with fracture in the various countries. When and if EQ-5D value sets for the countries included in ICUROS become available it will be important to re-assess the quality of life related to fractures. Another cause for country variations could be that the sample size used in this interim analysis (30 or more patients per fracture and country) is not yet sufficient to be fully representative for the fracture population.

Other studies have indicated that there is an additional decrement in quality of life in patients with a past history of previous fracture [13,19,25,26]. The effect is more marked for vertebral fractures in patients with a previous fracture [27,28]. These observations could not be fully supported by the findings in this study where a prior fracture had a significant impact (at a 5% level) on the QoL-loss for only hip fractures when controlling for other variables.

Previous studies of vertebral fractures have shown that those hospitalized at the time of fracture have a worse quality of life one year after the fracture than those patients that are not admitted related to fracture [27]. This is to be expected since hospitalization is a marker of a fracture with more severe clinical consequences. This finding is supported by the results from our regression analysis, where patients with a fracture who were hospitalized at the time of fracture had a significantly higher quality of life loss.

A potential limitation of the chosen study design for ICUROS is that patients were asked for their pre-fracture quality of life after the fracture event, which may incur a recall bias if the patient perceives the pre-fracture quality of life better than it actually was. This may overestimate, therefore, the QoL-loss after a fracture. In the KOFOR-study, a sensitivity analysis was performed when using normal population based quality of life as proxy for pre-fracture quality of life. The results from this analysis were inconclusive and no strong evidence for overestimation was found.

A further limitation lies in the calculation of the QoL-loss during the 4 months after fracture. We assumed a linear improvement in the QoL level from the time of first assessment up to the 4-month measurement. This might overestimate the loss slightly, since patients are likely to

improve their health status at a faster rate during the first month after the fracture than in the following months. For example, for distal forearm fractures, if one assumes that the US patients sustain the same reduction in QoL immediately after fracture as observed in the other countries and that the only difference between QoL is due to the timing of the interview (on average about 4 weeks after fracture), this would imply that about 70% of the improvement over the 4 months occurred during the first month after fracture.

Also, to be noted is that the QoL-loss is estimated for patients that had survived up to 4 months. For these patients the QoL-loss coincides with the quality-adjusted life-years (QALY) lost during this period. The average QALY lost for a fractured patient would be higher if deaths were to be considered during these 4 months. In the Swedish KOFOR-study there was no significant difference in QoL-loss in the first 4 months between patients who died during months 5–18 of the study and those who survived for 18 months [8]. When data with longer follow-up are available from ICUROS it will be important to analyse more thoroughly differences in QoL between patients that die after fracture and those that do not.

The fracture patient sample included in the present study comprised patients living at home before fracture. This can be considered a sub-sample since some fracture patients are in sheltered accommodation at the time of fracture. On average, about 10-30% (varying by age and country) of all hip fracture patients come from sheltered accommodation at the time of fracture. One reason for not including patients from sheltered accommodation is that studies have shown that these patients, except for the initial acute costs (e.g. hospitalisation, surgery), do not incur any major additional costs when comparing resource use the year after with the year before fracture [29,30].

In addition, the most cognitively impaired and/or demented were excluded from the study sample, which will give a somewhat skewed sample of the real population of fracture patients (especially hip fracture). Estimates of the prevalence of cognitive impairment/dementia in hip fracture patients vary widely in the literature (10-60%) [31-34]. These patients have difficulty in completing the self reported parts of the case report form, and the cognitively impaired are more frequently institutionalized. In a study by Formiga et al. [35] it was shown that the prevalence of dementia in institutionalised patients pre-fracture was more than 3 times higher than in patients admitted from home. Also, those cognitively impaired are also likely to have a higher level of resource consumption prior to the fracture, indicating a lower fracture related cost.

The patient characteristics of the sample included in the study may not reflect the real situation in all countries. The sample depends on the institutions and centres in which the study was conducted. For example in France, all centres were university hospitals and these patients are on average likely to be frailer compared with patients in private institutions. A higher proportion of frail patients in some countries may lead to higher hospitalization rates. Furthermore, the low number of centres in certain countries in the sample at hand – only one in each of Italy, Spain and Lithuania– may hamper the generalization of the results on a country basis.

The findings in this study indicate that there appear to be important variations in the QoL decrements related to fracture between countries. Should these results be confirmed in subsequent analyses with more patients and with longer follow-up, it will be important to account for these differences in health economic evaluations of treatments for osteoporosis since they may have a significant impact on the cost-effectiveness.

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Table 1 Patients by centre and fracture type used for analysis

	Hip fracture	Vertebral fracture	Distal forearm fracture
Austria			
Hanusch Krankenhaus, Wien	29	19	46
Lorenz-Böhler Krankenhaus, Wien	31	1	9
Medical University of Graz	29	3	14
Orthopaedisches Spital Speising, Wien-Hietzing	-	14	-
Universitaetsklnik für Unfallchirurgie, Graz	9	4	2
Unfallkrankenhaus Graz	61	5	25
Unfallkrankenhaus Meidlind, Wien	87	23	10
Wilhelminenspital Wien	20	2	7
Subtotal	266	71	113
Australia			
Austin Health, VIC	-	-	15
Barwon Health, VIC	-	-	22
Menzies, TAS	-	-	6
Sir Charles Gairdner, WA	-	-	7
Subtotal	-	-	50
Spain			
Fundación Jiménez Díaz ,Madrid	46	-	-
Subtotal	46	-	-
France			
CHU-Amiens	38	13	21
CHU-Edouard Herriot, Lyon	36	10	24
CHU-Lille	14	7	5
CHU-Saint Etienne	38	14	42
Hospital Cochin, Paris	50	5	32
Hospital Lariboisiere ,Paris	21	27	44
Subtotal	197	76	168
Italy			
5 Centers* Subtotal	112	47	30
Lithuania			
National Osteoporosis Center, Vilnius	34	-	-
Subtotal	34	-	-
Mexico			
Hospital de Traumatología y Ortopedia Lomas Verdes, Naucalpan	23	-	-
Instituto Nacional de Rehabilitación, Tlalpan	21	-	-
Subtotal	44	-	-
Russia			
Irkutsk Institute of Postgraduate Training	19	113	68
Institute of Rheumatology, Moscow	19	19	7
Rostov-on-Don State Medical University	108	13	30
Ural State Medical Academy		47	20
Vreden Institute of Trauma and Orthopedics	57	1	17
Yaroslavl State Medical Academy	16	4	60
Subtotal	219	197	202
USA			
Geisinger Clinic, Pennsylvania	-	13	9
Marchfield Clinic, Winsconsin	-	16	14
Reliant Medical Center, Massachusetts	-	8	11
Subtotal	-	37	34
Sweden			
Helsingborgs Lasarett	26	8	62
Hässleholms Sjukhus	28	12	42
Lund Universitetssjukhus	64	51	73
Malmö Universitetssjukhus	81	14	79
Norrlands Universitetssjukhus	19	18	33
Södersjukhuset	94	2	17
Ystad Lasarett	43	15	84
Subtotal	355	120	390
Total	1273	511	953

*IstitutoAuxologico Italiano IRCCS, Milano (Dr. M.L. Bianchi, coordinator); Istituto Ortopedico Gaetano Pini - Milano (Prof. C. Verdoia, Dr. C. Costantini); Ospedale Casa Sollievo della Sofferenza IRCCS - S. Giovanni Rotondo (Prof. G. Guglielmi); Ospedale Nuovo San Gerardo – Monza (Prof. G. Zatti); Policlinico Tor Vergata - Roma (Prof. U. Tarantino)

Table 2 Patient characteristics

	Austria	Australia	Spain	France	Italy	Lithuania	Mexico	Russia	Sweden	USA
Hip fracture										
Patients	266	-	46	197	112	34	44	219	355	-
Age mean (sd)	76.2 (8.3)	-	80.4 (10.6)	776.7 (10.6)	79.4 (8.9)	74.9 (9.7)	78.8 (9.2)	68.9 (9.9)	77.5 (8.7)	-
% men	24	-	22	22	4	21	18	30	21	-
% hospitalized in relation to fracture	98	-	100	99	100	100	80	88	100	-
% with previous fracture last 5 yrs	19	-	33	19	15	9	14	25	22	-
% working	4	-	2	8	5	18	11	15	3	-
Level of education (%) - primary	40	-	89	43	70	41	67	11	NA	-
secondary	47	-	9	33	26	44	18	59	NA	-
university	7	-	2	21	5	15	15	29	NA	-
post graduate	7	-	-	3	-	-	-	-	NA	-
Level of income – low	45	-	89	36	61	-	82	37	NA	-
Middle	51	-	11	44	19	82	14	58	NA	-
High	2	-	-	8	3	18	5	5	NA	-
Declined to answer	2	-	-	13	18	-	-	1	NA	-
Days from first HC contact to interview mean (sd)	10.1 (25.5)	-	16.1 (19.6)	4.8 (3.1)	11.6 (9.5)	4.5 (3.4)	5.2 (5.2)	3.3 (4.1)	4.7 (3.4)	-
Distal forearm fracture										
Patients	113	50	-	168	30	-	-	202	390	34
Age mean (sd)	67.9 (8.3)	68.1 (10.4)	-	68.4 (10.5)	75.0 (8.6)	-	-	62.6 (8.2)	69.2 (10.2)	69.3 (9.6)
% men	8	14	-	10	13	-	-	14	9	18
% hospitalized in relation to fracture	37	36	-	81	17	-	-	23	10	9
% with previous fracture last 5 yrs	18	12	-	16	7	-	-	40	13	44
% working	12	36	-	27	0.00	-	-	33	24	47
Level of education (%) - primary	46	8	-	30	43	-	-	6	NA	15
secondary	39	50	-	31	43	-	-	46	NA	27
university	11	28	-	33	13	-	-	48	NA	43
post graduate	4	14	-	7	-	-	-	-	NA	6
Level of income – low	35	49	-	32	38	-	-	13	NA	
Middle	56	31	-	49	41	-	-	76	NA	
High	5	18	-	6	7	-	-	10	NA	
Declined to answer	5	2	-	13	14	-	-	1	NA	
Days from first HC contact to interview mean (sd)	15.1 (40.0)	11.5 (5.3)	-	5.6 (4.4)	16.8 (26.4)	-	-	2.5 (3.6)	8.3 (4.1)	29.8 (8.4)
Vertebral fracture		-	-			-	-			
Patients	71	-	-	76	47	-	-	197	120	37
Age mean (sd)	72.5 (9.6)	-	-	72.1 (11.5)	72.7 (9.4)	-	-	67.8 (8.6)	76.5 (9.7)	75.8 (9.3)
% men	21	-	-	28	2	-	-	11	20	27
% hospitalized in relation to fracture	62	-	-	71	26	-	-	10	70	16
% with previous fracture last 5 yrs	13	-	-	25	26	-	-	70	19	62
% working	8	-	-	11	6	-	-	19	8	14
Level of education (%) - primary	54	-	-	40	34	-	-	6	NA	19
secondary	32	-	-	34	45	-	-	33	NA	32
university	9	-	-	18	17	-	-	62	NA	46
post graduate	6	-	-	8	4	-	-	-	NA	3
Level of income – low	40	-	-	43	30	-	-	16	NA	
Middle	50	-	-	49	45	-	-	72	NA	
High	6	-	-	2	9	-	-	12	NA	
Declined to answer	4	-	-	6	17	-	-	-	NA	
Days from first HC contact to interview mean (sd)	24.2 (24.1)	-	-	22.22 (52.3)	11.6 (13.9)	-	-	2.8 (5.1)	6.7 (7.2)	28.6 (12.8)

Note: NA – Not Available

Table 3 Estimated quality of life (EQ-5D) before, after and 4 months after fracture

	Hip fracture		Vertebral fracture		Distal forearm fracture	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
Austria						
Before fracture	0.75	(0.72-0.79)	0.78	(0.71-0.84)	0.86	(0.83-0.90)
After fracture	0.19	(0.16-0.22)	0.37	(0.3-0.45)	0.49	(0.44-0.54)
4 months after fracture	0.65	(0.61-0.68)	0.67	(0.6-0.74)	0.76	(0.72-0.81)
Accumulated QoL-loss	0.11	(0.10-0.12)	0.08	(0.06-0.11)	0.08	(0.07-0.09)
Australia						
Before fracture	-	-	-	-	0.91	(0.86-0.95)
After fracture	-	-	-	-	0.61	(0.55-0.67)
4 months after fracture	-	-	-	-	0.78	(0.72-0.85)
Accumulated QoL-loss	-	-	-	-	0.07	(0.05-0.09)
Spain						
Before fracture	0.66	(0.55-0.76)	-	-	-	-
After fracture	0.03	(0-0.06)	-	-	-	-
4 months after fracture	0.64	(0.58-0.7)	-	-	-	-
Accumulated QoL-loss	0.11	(0.07-0.14)	-	-	-	-
France						
Before fracture	0.79	(0.76-0.82)	0.66	(0.59-0.74)	0.83	(0.79-0.86)
After fracture	0.09	(0.06-0.11)	0.15	(0.1-0.21)	0.37	(0.33-0.41)
4 months after fracture	0.57	(0.53-0.61)	0.50	(0.43-0.58)	0.70	(0.67-0.74)
Accumulated QoL-loss	0.15	(0.14-0.16)	0.11	(0.09-0.13)	0.10	(0.08-0.11)
Italy						
Before fracture	0.85	(0.81-0.89)	0.93	(0.88-0.98)	0.94	(0.90-0.98)
After fracture	0.04	(0.01-0.07)	0.12	(0.05-0.18)	0.46	(0.35-0.58)
4 months after fracture	0.45	(0.40-0.50)	0.62	(0.55-0.69)	0.78	(0.68-0.88)
Accumulated QoL-loss	0.20	(0.19-0.21)	0.19	(0.17-0.21)	0.11	(0.08-0.13)
Lithuania						
Before fracture	0.80	(0.75-0.86)	-	-	-	-
After fracture	0.01	(0-0.010)	-	-	-	-
4 months after fracture	0.36	(0.27-0.45)	-	-	-	-
Accumulated QoL-loss	0.21	(0.19-0.22)	-	-	-	-
Mexico						
Before fracture	0.64	(0.55-0.74)	-	-	-	-
After fracture	0.01	(0-0.03)	-	-	-	-
4 months after fracture	0.46	(0.37-0.55)	-	-	-	-
Accumulated QoL-loss	0.14	(0.11-0.17)	-	-	-	-
Russia						
Before fracture	0.71	(0.68-0.74)	0.79	(0.76-0.81)	0.88	(0.86-0.91)
After fracture	0.03	(0.02-0.05)	0.32	(0.28-0.36)	0.45	(0.41-0.49)
4 months after fracture	0.43	(0.38-0.47)	0.69	(0.65-0.73)	0.81	(0.78-0.84)
Accumulated QoL-loss	0.16	(0.15-0.17)	0.09	(0.08-0.10)	0.09	(0.08-0.09)
Sweden						
Before fracture	0.80	(0.77-0.82)	0.74	(0.7-0.79)	0.90	(0.88-0.92)
After fracture	0.18	(0.16-0.2)	0.20	(0.15-0.25)	0.56	(0.53-0.58)
4 months after fracture	0.62	(0.59-0.64)	0.50	(0.44-0.56)	0.83	(0.81-0.85)
Accumulated QoL-loss	0.13	(0.12-0.14)	0.13	(0.12-0.15)	0.07	(0.06-0.08)
USA						
Before fracture	-	-	0.75	(0.67-0.83)	0.87	(0.81-0.93)
After fracture	-	-	0.57	(0.47-0.65)	0.64	(0.54-0.72)
4 months after fracture	-	-	0.65	(0.55-0.73)	0.68	(0.57-0.77)
Accumulated QoL-loss	-	-	0.05	(0.02-0.07)	0.07	(0.04-0.10)

Table 4 Regression analysis of quality of life loss over 4 months after fracture

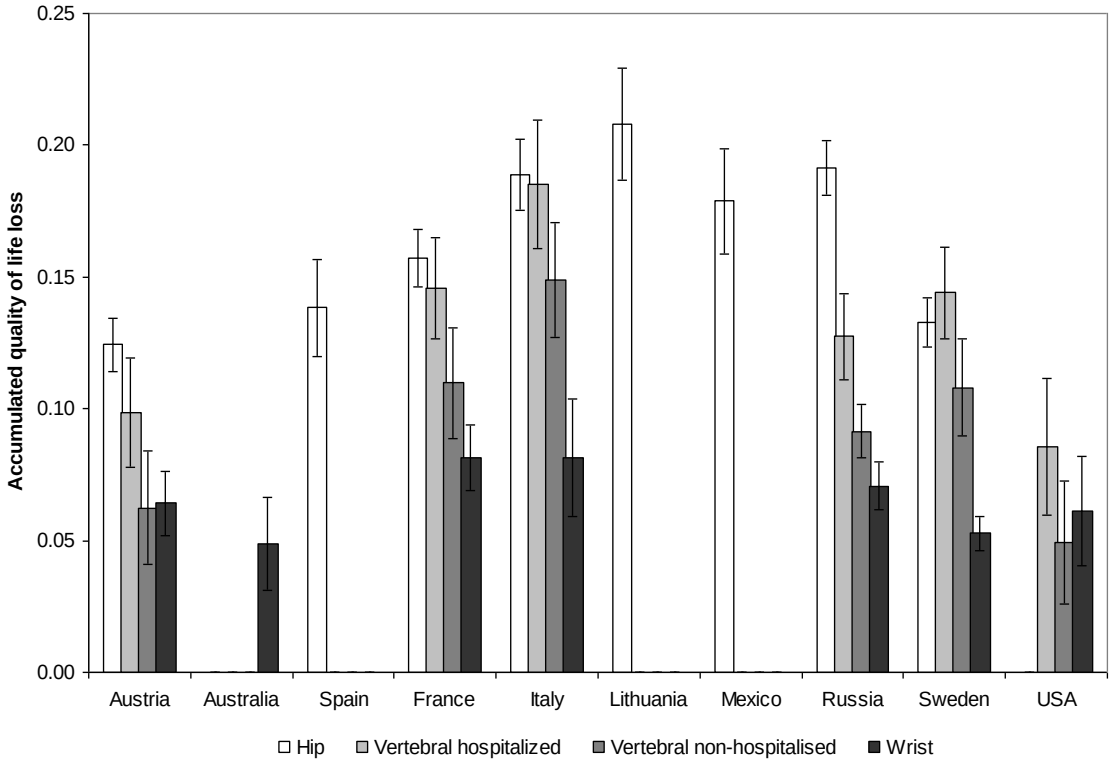
	Hip		Vertebral		Distal forearm	
Variable	Coefficient	p-value	Coefficient	p-value	Coefficient	p-value
Australia	-		-		-0.020	0.03
Spain	*		-		-	
France	0.027	<0.01	0.051	(<0.01)	0.013	(0.04)
Italy	0.059	<0.01	0.094	<0.01	*	
Lithuania	0.078	<0.01	-		-	
Mexico	0.049	<0.01	-		-	
Russia	0.062	<0.01	0.035	<0.01	*	
Sweden	*		0.055	<0.01	-0.016	<0.01
US	-		*		*	
Baseline quality of life	0.236	<0.01	0.193	<0.01	0.179	<0.01
Male					-0.023	<0.01
Age	0.001	<0.01	*		*	
Fracture last 5 years	0.008	<0.01	*		*	
Hospitalised	0.031	<0.01	0.043	<0.01	0.014	<0.01
Job before fracture	*		-0.015	0.08	*	
Time to interview	*		*		*	
Constant	-0.162	<0.01	-0.094	<0.01	-0.075	<0.01
Number of patients	1271		548		987	
F-value	165		62.5		51.2	
R2 adjusted	0.537		0.44		0.234	

Note: Austria was a reference case in the regression

- indicates that no observations from this country was included

* Variable was excluded due to non-significance at 10% level or lower

Figure 1 Estimated quality of life loss over four months by country following a fracture at the sites shown for a woman aged 70 years with a history of previous fracture



Note: the bars indicate 95% confidence intervals

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