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Author/s:

Talevski, J;Sanders, KM;Busija, L;Beauchamp, A;Duque, G;Borgstrom, F;Kanis, JA;Svedbom, A;Connaughton, C;Stuart, AL;Brennan-Olsen, SL

Title:

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Date:

2021-02

Citation:

Talevski, J., Sanders, K. M., Busija, L., Beauchamp, A., Duque, G., Borgstrom, F., Kanis, J. A., Svedbom, A., Connaughton, C., Stuart, A. L. & Brennan-Olsen, S. L. (2021). Health Service Use and Quality of Life Recovery 12 Months Following Major Osteoporotic Fracture: Latent Class Analyses of the International Costs and Utilities Related to Osteoporotic Fractures Study (ICUROS). *JOURNAL OF BONE AND MINERAL RESEARCH*, 36 (2), pp.252-261. <https://doi.org/10.1002/jbmr.4181>.

Persistent Link:

<https://hdl.handle.net/11343/276332>

Talevski Jason (Orcid ID: 0000-0001-9180-8758)
Sanders Kerrie (Orcid ID: 0000-0002-2718-6592)
Duque Gustavo (Orcid ID: 0000-0001-8126-0637)

Health Service Use and Quality of Life Recovery 12-months Following Major

Osteoporotic Fracture: Latent Class Analyses of the International Costs and Utilities

Related to Osteoporotic Fractures Study (ICUROS)

Jason Talevski (BHLthSci)^{1,2}, Kerrie M Sanders (PhD)^{1,2,12}, Ljoudmila Busija (PhD)³, Alison Beauchamp (PhD)^{1,2,4}, Gustavo Duque (PhD)^{1,2}, Fredrik Borgström (PhD)^{6,7}, John A Kanis (PhD)^{5,8}, Axel Svedbom (PhD)¹⁰, Catherine Connaughton (PhD)⁹, Amanda L Stuart (PhD)¹¹, Sharon L Brennan-Olsen (PhD)^{1,2,12,13}

¹Department of Medicine – Western Health, The University of Melbourne, Victoria, Australia

²Australian Institute for Musculoskeletal Science (AIMSS), The University of Melbourne and Western Health, Victoria, Australia

³School of Public Health and Preventive Medicine, Monash University, Victoria, Australia

⁴School of Rural Health, Monash University, Victoria, Australia

⁵Mary McKillop Institute for Research, Australian Catholic University, Victoria, Australia

⁶Quantify Research, Stockholm, Sweden

⁷Department of Learning, Informatics, Management and Ethics, Medical Management Centre, Karolinska Institute, Stockholm, Sweden

⁸Centre for Metabolic Bone Diseases, University of Sheffield, Sheffield, United Kingdom

⁹Melbourne Academic Centre for Health, The University of Melbourne, Victoria, Australia

¹⁰ICON Plc, Stockholm, Sweden

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1002/jbmr.4181](https://doi.org/10.1002/jbmr.4181)

¹¹The Institute for Mental and Physical Health and Clinical Translation (IMPACT), School of Medicine, Deakin University, Geelong, Victoria, Australia

¹²School of Health and Social Development, Deakin University, Geelong, Victoria, Australia

¹³Institute for Health Transformation, Deakin University, Geelong, Victoria, Australia

Running title: Quality of life post-fracture

Corresponding author

Mr. Jason Talevski

Address: Department of Medicine-Western Health, University of Melbourne

C/- Western Health, Sunshine Hospital, WCHRE Building,

176 Furlong Road,

St Albans, Victoria 3021, AUSTRALIA

Email: jason.talevski@student.unimelb.edu.au

Phone: +61 3 8395 8085

Disclosures: The authors declare no conflicts of interest. The data for this analysis was accessed from the International Costs and Utilities Related to Osteoporotic fractures Study (ICUROS) central database. Access to this database should be requested from the data custodians (Prof. John Kanis and Prof Fredrik Borgström) and the principal investigators of each participating country (<http://www.icuros.org/>).

Authors' roles: JK, FB and AS are integral to the ICUROS international study protocol and are Principal Investigators and members of the ICUROS Steering Committee. JT, KMS, LB and SB-O were involved in study conception and design; JT, KMS and CC were involved in data acquisition; JT, LB and SB-O were involved in data analysis; JT led the interpretation of findings with input from the all authors; and JT drafted the manuscript, which was critically revised by all authors, who approved the final version and agree to be accountable for it. JT accepts responsibility for the integrity of the data and its analysis.

Abstract: Major osteoporotic fractures (MOFs) are associated with a rapid decline of health-related quality of life (HRQoL), however there is limited knowledge about which health care services positively affect HRQoL post-fracture. This study aimed to identify specific combinations of health service use associated with recovery of HRQoL 12-months post-MOF. The analyses included 4126 adults aged ≥ 50 years with a MOF (1657 hip, 1354 distal forearm, 681 vertebrae, 434 humerus) participating in the International Costs and Utilities Related to Osteoporotic fractures Study (ICUROS) – a multinational observational study (Australia, Austria, Estonia, France, Italy, Lithuania, Mexico, Russia, Spain, UK). HRQoL at pre-fracture and 12-months post-fracture was measured using the EuroQoL questionnaire (EQ-5D-3L). Health service use data were collected via participant interviews and medical record reviews including in-hospital care; outpatient care; community services and medication use. Data analyses involved two stages: 1) latent class analyses to identify different combinations of health service use (“classes”); and 2) logistic regression to assess effects of classes on HRQoL recovery. Analyses were repeated excluding hip fractures (non-hip MOFs). Overall, 2057 MOF participants (49.9%) recovered to their pre-fracture HRQoL at 12-month follow-up; this proportion was higher for non-hip MOFs (n=1439; 58.3%). Several distinct classes were identified across countries (range: 2-5 classes). Classes that were associated with increased odds of HRQoL recovery at 12-months were characterized by a combination of hospital presentations without admission; outpatient department visits; allied health visits; vitamin D/calcium supplementation; and/or non-opioid analgesic use. Similar classes were observed for non-hip MOFs. Understanding country-specific health care service pathways that influence greater recovery of HRQoL, particularly services that are

uncommon in some countries and routine in others, could improve post-fracture care on a global scale.

Key words: Aging, Fractures; Health Services Research; Quality of Life; Osteoporosis

INTRODUCTION

An estimated 200 million people aged 50 years or older are currently diagnosed with osteoporosis,^(1,2) making it the most common skeletal condition worldwide.⁽³⁾ A fragility fracture of the hip, distal forearm, vertebrae or humerus – collectively referred to as major osteoporotic fracture (MOF) – is the most prevalent clinical outcome of osteoporosis. It is well-documented that hip fractures are the most severe type of MOF, incurring higher treatment costs^(4,5) and imposing a greater burden on health-related quality of life (HRQoL)⁽⁶⁾ and physical function.⁽⁷⁾ However, fractures at other osteoporotic sites – distal forearm, vertebrae and humerus – also produce a significant burden on patients and the healthcare system. Non-hip MOFs are associated with substantial pain, limitations in physical functioning and reduced HRQoL.^(6,8) Moreover, an increased risk of mortality and subsequent fracture risk has been documented after vertebrae fractures.^(10,11) Collectively, MOFs account for over 90% of all fracture-related healthcare costs.⁽⁵⁾

Implementation of clinical care pathways for post-fracture management, commonly referred to as Orthogeriatric Services or Fracture Liaison Services, have been expanding globally over the last decade.⁽¹²⁾ They are interdisciplinary services combining orthopedic surgery, geriatric care, primary care and ancillary services such as physical therapy,⁽¹³⁾ and aim to ensure patients aged ≥ 50 years who present to hospital with a MOF receive the appropriate evaluation and treatment for osteoporosis in accordance with clinical guidelines.⁽¹⁴⁾ Clinical care pathways have shown improvements in recovery of basic activities of daily living,⁽¹⁵⁾ decreased re-fracture rates,⁽¹⁴⁾ and improved HRQoL in hip

fracture patients compared to usual care;⁽¹⁶⁾ however, there is significant variability among these care pathways in terms of the health care and community services offered to patients.

Limited knowledge is available on which health care and community services, major components of clinical care pathways, can improve the long-term health of older people following a MOF, specifically in non-hip MOF patients. Therefore, the aim of this study was to identify combinations of health care and community service use associated with recovery of HRQoL 12-months post-MOF, using data from the International Costs and Utilities Related to Osteoporotic fractures Study (ICUROS).

MATERIALS AND METHODS

Study design and population

The ICUROS study design has been described elsewhere,⁽⁶⁾ however in brief, ICUROS is a multi-national observational study, undertaken from 2008 to 2014, that aimed to quantify the HRQoL impact and cost consequences of fragility fractures across 11 countries (Australia, Austria, Estonia, France, Italy, Lithuania, Mexico, Russia, Spain, the UK and the USA). Identical study designs were applied in all countries. ICUROS adhered to the Declaration of Helsinki and was approved by the relevant research ethics committees in each country. Patients were enrolled in ICUROS if they: were aged ≥ 50 years; sustained a low-energy fracture that was not caused by a comorbidity (e.g., cancer) and confirmed via imaging; were recruited within 2 weeks after the fracture; and lived in their own home prior to the fracture. Patients residing in long-term care prior to the fracture; with cognitive impairment; or who sustained a new fracture during the follow-up period were excluded.

Study data

Approval for use of ICUROS data was obtained from the principal investigators in each participating country and Melbourne Health Human Research Ethics Committee (2010.115). Data for the current analyses were extracted from the ICUROS central database for each of the participating countries, with the exception of the USA (data on health care and community service use were unavailable). Participants who sustained a hip, distal forearm, clinical vertebral, or humeral fracture with complete 12-month data were included in analyses.

Participant demographic and fracture details were collected at the baseline interview (within 2 weeks after the fracture) and included: age (years at time of fracture); sex; highest level of educational attainment (primary, secondary, post-secondary); individual income (low, middle, high; country-specific cut-offs); living status (alone, with someone); hospitalization due to the fracture; and fracture history from the previous five years.

Data on health care and community service use ‘as a consequence of the fracture’ during the 4-months post-fracture were collected via telephone interviews and described as in-hospital care (hospital presentations/admissions, inpatient rehabilitation); outpatient care (outpatient clinics, fracture clinics, rehabilitation centers, allied health care, general practitioner [GP]/primary care center visits, health professional home visits); supported living (e.g. residential aged care); community care (phone counselling, formal home help, informal home help from family/friends, home and equipment modifications); medication use (osteoporosis-related, calcium or vitamin D supplements, opioid analgesics, non-opioid

analgesics, anti-depressant/anti-anxiety medications); and imaging (including dual-energy x-ray absorptiometry [DXA]).

Changes in HRQoL were assessed using the EuroQoL questionnaire (EQ-5D-3L)⁽¹⁷⁾ at baseline (including recall of the patient's HRQoL prior to fracture), 4-months and 12-months post-fracture. The EQ-5D-3L measures five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) at three levels of severity (no problem, some problems, major problems) giving 243 possible health state combinations.⁽¹⁷⁾ To determine the utility index score of the EQ-5D-3L, we used the weights most relevant to each individual country. The UK value set of preference weights were applied for countries where no specific weights have been developed, as recommended.⁽¹⁸⁾ Utility index scores were fixed at 1 (full health) and 0 (dead) with values below 0 indicating a state worse than death. Change in HRQoL over 12 months was calculated according to the following formula:

$$\text{HRQoL change} = \text{EQ-5D-3L utility score}_{(12\text{-months})} - \text{EQ-5D-3L utility}_{(\text{pre-fracture})}$$

HRQoL change was then dichotomized (recovered/not recovered), where a score ≥ 0 was classified as 'recovered' and a score < 0 was classified as 'not recovered'.

Statistical analyses

The statistical analyses involved two stages: 1) identifying the most common combinations of health care and community service use (hereafter referred to as 'health service use'); and 2) analyzing the associations between the identified combinations of health service use and HRQoL recovery 12-months post-MOF.

In stage one, latent class analysis (LCA) was used to classify participants into mutually exclusive groups based on their health service use (categorical indicator variables). These groups are referred to as 'classes' and represent different combinations of health service use.⁽¹⁹⁾ The LCA was undertaken without a priori assumption regarding the optimal number of classes; consistent with LCA best practice.⁽²⁰⁾ We began the class enumeration procedure by estimating a one-class model, and the number of classes was then increased in a stepwise fashion until the optimal number of classes was achieved in the final model (i.e. optimal model fit). There is no single indicator reflecting optimal model fit, therefore this was determined based on a combination of the lowest Bayesian Information Criterion (representative of the most parsimonious solution) and highest entropy value (indicative of clearest separation of individuals in each class).⁽¹⁹⁾ Qualitative assessment of the final classes were also undertaken to determine meaningfulness of the classes (i.e. were the classes different enough in terms of health service use). Health service use data were dichotomous (yes/no) and analyses were performed individually for each country using the statistical software Mplus (version 7.3).⁽²¹⁾

In stage two, we analyzed the association between each class and recovery of HRQoL at 12 months post-MOF using logistic regression. Associations were evaluated for MOFs and non-hip MOFs and presented as odds ratios (ORs) with 95% confidence intervals (CIs). Variables which were significantly associated with either HRQoL recovery or latent class membership in univariate analyses were added simultaneously to multivariable regression models. Multiplicative interaction terms were also included in the models to identify potential

effect modification between age and sex. A p-value of <0.05 was considered statistically significant. These analyses were performed using STATA statistical software (version 16).⁽²²⁾

RESULTS

Study population

In total, 6604 participants were enrolled in ICUROS. After removing participants from the USA (n=256) and excluding ineligible participants such as those who sustained a fracture at a non-MOF site (n=698), 5650 participants were potentially eligible for these analyses. Among them, a further 1524 participants were excluded based on lost to follow-up (n=486), withdrawal from the study (n=351); sustaining a new fracture during follow-up (n=192), death (n=246), or other reasons (n=249). Therefore, a total of 4126 participants with a MOF were eligible from Australia (n=524), Austria (n=525), Estonia (n=146), France (n=466), Italy (n=494), Lithuania (n=340), Mexico (n=278), Russia (n=831), Spain (n=283) and the UK (n=239). The mean age of the total population was 71.5 years – participants with a distal forearm fracture were the youngest (n=1354; mean age: 67.1 years) and hip fracture participants the oldest (n=1657; mean age: 76.6 years); Russia had the lowest mean age (66.0 years); and Estonia had the highest mean age (77.2 years). The total sample were predominately female (n=3446; 83.5%) and less than 20% of participants experienced a previous fracture within the preceding five years in each country except for Estonia (24.7%) and Russia (42.1%). Similar characteristics were observed for non-hip MOF participants (n=2469), although mean age was significantly lower compared to all MOF participants (67.1

vs. 71.5 years; $p < 0.001$). Participant characteristics are presented in Table 1 by country and fracture group.

Health service use

Country-specific health service use post-MOF is presented in Supplementary Table 1. In terms of in-hospital care, participants from Russia had the highest number of hospital presentations without admission (58.7%); the highest number of hospitalizations were reported in Estonia (97.9%) and Mexico (90.3%); and admission to a rehabilitation ward was the most common in Mexico (40.3%). Outpatient department visits were least common in Russia (32.0%); fracture clinic visits were infrequent across all countries except for the UK (45.6%); and participants from Estonia reported a considerably lower amount of allied health visits (8.2%) compared to all other countries. A higher proportion of participants reported health professional home visits from France, Italy, and the UK (47.0%, 44.1% and 38.1%, respectively); and phone counselling was uncommon across all countries except for Italy (25.3%). France had the highest proportion of participants admitted to a residential aged care facility post-fracture (31.6%). Medication use varied between countries. Participants from Russia reported the highest use of osteoporosis-related medications and vitamin D/calcium supplements (62.7% and 81.1%, respectively) while participants in Mexico reported the lowest use (4.3% and 16.2%, respectively). Opioid analgesic use was the highest in Australia (42.9%) and the lowest in Lithuania and Estonia (both 0%); and all countries had a moderate-high proportion of participants using non-opioid analgesics – highest in Russia (84.1%) and the lowest in Lithuania (34.7%). All countries had a low proportion of participants using anti-

depressant/anti-anxiety medication (range: 0-2.1%). DXA scans post-fracture were uncommon in all countries (<10%), except in Russia (40.9%).

Health-related quality of life

Mean HRQoL utility scores at each follow-up point are shown in Supplementary Table 2 by country. HRQoL utility scores (mean \pm SD) before study fracture were the highest in Italy (0.95 \pm 0.12) and the lowest in Estonia (0.67 \pm 0.31) and Mexico (0.67 \pm 0.33). Mean HRQoL substantially improved across all countries at 12-month follow-up, although it remained below the pre-fracture HRQoL mean. Participants from Austria and the UK were most improved (mean change: -0.04), while Lithuania was the least improved (mean change: -0.22). Similar patterns in HRQoL trajectories were seen in non-hip MOF participants.

The proportion of participants who recovered HRQoL 12-months post-fracture is illustrated in Figure 1, by country and fracture group. Overall, 2057 participants (49.9%) recovered to their pre-fracture HRQoL at 12-month follow-up. France had the lowest proportion of participants with full HRQoL recovery (39.3%), and the UK had the highest (60.3%). For non-hip MOFs, the proportion of participants with full HRQoL recovery at 12-months was higher across all countries (n=1439; 58.3%) compared to all MOF participants. Similarly, France had the lowest proportion of participants with full HRQoL recovery (49.5%) and the UK had the highest (78.1%).

Latent class analysis (LCA)

Tests of the LCA models and optimal model fit statistics and are summarized in Supplementary Table 3, by country and fracture group. Estimated probabilities of using a particular health service in each class are shown in Supplementary Tables 4 and 5 (MOFs and non-hip MOFs, respectively) and summarized in Figure 2. Results from the logistic regression analyses of participants' class membership and odds of HRQoL recovery are presented in Table 2 and discussed below for each country.

In Australia, a 3-class model was deemed the most optimal model fit for MOF participants. Class 2 was associated with increased odds of HRQoL recovery at 12-months post-fracture following adjustment for age, sex, education, income, and pre-fracture HRQoL (adjusted OR=1.48; 95% CI: 1.00-2.17; p=0.049). Conversely, class 1 was associated with decreased odds of HRQoL recovery (adjusted OR=0.37; 95% CI: 0.23-0.61; p<0.001). No associations between classes and HRQoL recovery post-MOF were observed for participants with non-hip MOFs, noting that a 2-class model was deemed to have the most optimal model fit (Table 2).

In Austria, a 4-class model was deemed the most optimal model fit for MOF participants. Class 4 was associated with increased odds of HRQoL recovery at 12-months (adjusted OR=2.64; 95% CI: 1.65-4.21; p<0.001), whereas class 2 was associated with decreased odds of HRQoL recovery (adjusted OR=0.39; 95% CI: 0.24-0.64; p<0.001). Similar associations between classes and HRQoL recovery were observed for participants with non-hip MOFs (Table 2).

In Estonia, a 2-class model had the best fit for MOF participants. There were no significant associations between classes and HRQoL recovery 12-months post-fracture in

unadjusted ($p=0.694$) and fully adjusted ($p=0.946$) models. There were no analyses for MOF excluding hip fracture as all participants in Estonia suffered a hip fracture (Table 2).

In France, a 3-class model was the most optimal fit for MOF participants. Class 1 was associated with increased odds of HRQoL recovery at 12-months post-MOF following adjustment for age, education, income, and pre-fracture HRQoL (adjusted OR=2.69; 95% CI: 1.59-4.54; $p<0.001$). Conversely, class 2 was associated with decreased odds of HRQoL recovery in the fully adjusted model (adjusted OR=0.27; 95% CI: 0.15-0.51; $p<0.001$). Similar associations between classes and HRQoL recovery were found for participants with non-hip MOFs (Table 2).

In Italy, a 4-class model was the most optimal fit for participants with a MOF. Class 3 was associated with increased odds of HRQoL recovery at 12-months post-MOF after adjustment for age, education, income, and pre-fracture HRQoL (adjusted OR=3.85; 95% CI: 2.50-5.93; $p<0.001$). Classes 1, 2 and 4 were associated with a decreased odds of HRQoL recovery in fully adjusted models [(OR=0.51; 95% CI: 0.32-0.80; $p=0.003$) (OR=0.46; 95% CI: 0.25-0.84; $p=0.011$) (OR=0.29; 95% CI: 0.11-0.76; $p=0.012$), respectively]. Similar associations between classes and HRQoL recovery were observed for participants with non-hip MOF, noting that a 2-class model was the most optimal model fit (Table 2).

In Lithuania, a 4-class model had the most optimal fit for MOF participants. Class 1 was associated with increased odds of HRQoL recovery at 12-months post-MOF in the fully adjusted model (adjusted OR=4.90; 95% CI: 1.70-6.83; $p<0.001$). Conversely, classes 2 and 4 were associated with a decreased odds of HRQoL recovery in fully adjusted models [(OR=0.41; 95% CI: 0.23-0.74; $p=0.003$) (OR=0.14; 95% CI: 0.07-0.30; $p<0.001$),

respectively]. Similar associations between classes and HRQoL recovery were observed for participants with non-hip MOF (Table 2).

In Mexico, a 3-class model was the most optimal fit for MOF participants. Class 3 was associated with increased odds of HRQoL recovery at 12-months post-MOF after adjustment for age, sex, education, income, and pre-fracture HRQoL (adjusted OR=1.87; 95% CI: 1.15-3.89; p=0.045). Class 2 was associated with decreased odds of HRQoL recovery at 12-months in fully the adjusted model (OR=0.25; 95% CI: 0.09-0.68; p=0.006). Similar associations between classes and HRQoL recovery were observed for participants with a non-hip MOF (Table 2).

In Russia, a 5-class model was the most optimal fit for MOF participants. Class 4 and class 5 were both associated with increased odds of HRQoL recovery at 12-months post-fracture following adjustment [(adjusted OR=18.88; 95% CI: 11.10-32.30; p<0.001) (adjusted OR=2.39; 95% CI: 1.56-3.65; p<0.001), respectively]. Conversely, classes 1, 2 and 3 were associated with a decreased odds of HRQoL recovery at 12-months [(adjusted OR=0.44; 95% CI: 0.27-0.72; p<0.001) (adjusted OR=0.16; 95% CI: 0.10-0.25; p<0.001) (adjusted OR=0.13; 95% CI: 0.08-0.21; p<0.001), respectively]. Similar associations between classes and HRQoL recovery were observed for participants with a non-hip MOF (Table 2).

In Spain, a 3-class model was the most optimal fit for MOF participants. Class 3 was associated with increased odds of HRQoL recovery at 12-months following adjustment for age, education, income, and pre-fracture HRQoL (adjusted OR=2.00; 95% CI: 1.05-3.83; p=0.036). Conversely, class 2 was associated with a decreased odds of HRQoL recovery at 12-months post-MOF (adjusted OR=0.55; 95% CI: 0.31-0.95; p=0.034). For non-hip MOF

participants, there were no significant associations between classes and HRQoL recovery in both unadjusted and adjusted models (Table 2).

In the UK, a 3-class model was the most optimal fit for MOF participants. Class 3 was associated with increased odds of HRQoL recovery at 12-months post-MOF after adjustment for age, sex, and pre-fracture HRQoL (adjusted OR=2.92; 95% CI: 1.58-5.41; $p<0.001$). Conversely, class 2 was associated with a decreased odds of HRQoL recovery (adjusted OR=0.24; 95% CI: 0.13-0.47; $p<0.001$). Similar associations were observed for participants with a non-hip MOF within a 2-class model (Table 2).

DISCUSSION

Previous publications based on ICUROS data described trajectories of HRQoL for individual fracture sites from 11 different countries, combined⁽⁶⁾ and country-specific,^(8,23) and showed that fractures incur substantial loss in HRQoL for at least 12-months. The current analyses identified several distinctive health service use pathways that are associated with improved HRQoL recovery 12-months post-MOF across individual countries. Understanding country-specific health service use pathways and their association with HRQoL recovery may facilitate improvements in managing patients following MOF on a global scale.

A total of 34 health service pathways (or 'classes') were observed for MOF participants across countries. Most countries identified one class that was associated with increased odds of HRQoL recovery 12-months and one class associated with decreased odds of HRQoL recovery. Interestingly, the health service use pathways with the greatest proportion of participants were not always associated with increased odds of HRQoL

recovery. This was observed for Australia, Austria, Italy, Mexico, Spain, and the UK, suggesting that common combinations of health service use post-MOF in these countries may not be appropriate to achieve HRQoL recovery. Classes that were associated with increased odds of HRQoL recovery were characterized by individuals with hospital presentations without admission (7 classes); outpatient department visits (8 classes); allied health visits (8 classes); vitamin D/calcium supplementation (8 classes); and/or non-opioid analgesic use (7 classes). It was not surprising that allied health care and non-opioid analgesics were associated with increased HRQoL recovery. Allied health services (e.g. physiotherapy) play a key role in early mobilization and functional recovery after MOF in many countries,^(24,25) and non-opioid analgesics are widely known to be efficient in reducing pain – pain being a dimension of the EQ-5D-3L utility score used to calculate HRQoL in this study.⁽²⁶⁾

Conversely, classes that were associated with decreased odds of HRQoL recovery in MOF participants were characterized by inpatient care (hospitalization, inpatient rehabilitation); outpatient department visits; both formal and informal home care; and home and equipment modifications. It was not unexpected that hospitalization was associated with decreased HRQoL recovery, as hospitalization can be an indicator of a fracture with severe injury. Participants who were hospitalized for their MOF had a lower rate of HRQoL recovery at 12-months compared to those who were not (41.9% vs. 67.1%; unpublished data). Furthermore, previous studies have shown that people hospitalized with a hip⁽²⁷⁾ or vertebral⁽²⁸⁾ fracture have worse trajectories of HRQoL post-fracture than patients not admitted. Similarly, formal home care services may also be an indicator of a patient with poorer health or greater physical frailty, given that these services are only available for those

with more complex care needs. Admission to long-term aged care facilities were associated with decreased odds of HRQoL recovery in France and Italy, driven by hip fracture participants. There is a lack of data for HRQoL of residents of aged care facilities,⁽²⁹⁾ although residents are typically physically frailer than the general older population,⁽³⁰⁾ thereby impacting their HRQoL. Future research should explore factors that influence HRQoL in people living in long-term aged care facilities post-fracture.

Health service use substantially differed between countries as expected, given the geographic variation in healthcare system structure. A variety of factors could also have affected health care-seeking behaviors in participants, including availability of universal health care (i.e. no out-of-pocket expenses) or proximity and availability to health services. The low proportion of osteoporosis-related medication use across most countries implies that a large proportion of participants were not assessed for osteoporosis – confirming the ‘osteoporosis care gap’.⁽³¹⁾ Research has highlighted that pharmacological treatments for osteoporosis are effective at reducing risk of fractures,⁽³²⁾ with some studies also showing they can improve HRQoL post-fracture.⁽³³⁻³⁵⁾ Opioid analgesic use was quite low across countries possibly due to the controversial nature of prescribing opioids for post-fracture care.^(36,37) However, given that pharmaceutical regulations vary between countries, care should be taken when interpreting these proportions. There was infrequent attendance to fracture clinics across all countries except for the UK, which may be due to the introduction of Fracture Liaison Services (intimately linked with fracture clinics) in the UK in the early 2000s. Phone consultations by a healthcare professional following hospitalization was uncommon across countries except for Italy; which was a component of the class associated

with improved HRQoL recovery. Understanding the country-specific health care services that promote recovery of HRQoL could improve post-MOF care worldwide, particularly for health care services uncommon in some countries, yet routine in others.

Limitations

ICUROS is the largest multi-country observational study on HRQoL consequences of fractures conducted to date where all variables in the study are captured using the same protocol. Because of the identical study design applied in all countries, ICUROS provided a unique opportunity to assess associations between different combinations of health service use and HRQoL recovery post-MOF across different countries. However, our study has some limitations. In terms of the ICUROS dataset, HRQoL prior to fracture was determined by recall, therefore, there is a potential risk for recall bias. However, it has been reported that patients can accurately recall their HRQoL up to 6 weeks following surgery.⁽³⁸⁾ Further to this, mean pre-fracture HRQoL utility scores were similar to reported EQ-5D index population norms,⁽³⁹⁾ so substantial recall bias is not likely. Results may not be applicable to several important subpopulations (e.g. those with dementia, those living in residential aged care) due to the exclusion criteria of the ICUROS. In terms of our analyses, we were unable to comment on other factors that may influence HRQoL recovery in older adults, for instance multimorbidity. We were unable to complete the analyses by individual fracture site as sample sizes were insufficient to reliably carry out LCA;⁽¹⁹⁾ however, this provided motivation for completing the analyses excluding hip fractures. Given that different fractures incur different disutility, care should be taken when interpreting results as the proportion of

fractures at different skeletal sites varied in countries. Finally, there was a high loss to follow-up/drop-out rate in ICUROS (approximately 21%), which may reflect that the ICUROS population was, on average, elderly and frail. We did not include these patients in our analyses as it was impossible to impute health service use data beyond this. However, the original ICUROS investigators performed analyses that included data for participants who were lost to follow-up, which produced similar results for trajectories of HRQoL⁽⁶⁾, indicating that these participants may not have substantially impacted our results.

Conclusions

HRQoL 12-months post-MOF typically does not return to pre-fracture levels in older adults. We identified several, distinct country-specific health service use pathways associated with improved HRQoL recovery. Given that HRQoL encompasses both physical and mental functioning, which are imperative to healthy ageing, incorporating our findings into existing clinical practice may result in care pathways that optimize HRQoL recovery for patients with a MOF. Future research should focus on determining the causality of these associations.

ACKNOWLEDGEMENTS

JT is supported by an Australian National Health and Medical Research Council (NHMRC) Postgraduate Scholarship (1151089) and SLB-O is supported by a NHMRC Career Development Fellowship (1107510). We are grateful to the Quality of Life and Epidemiology Working Group of the Committee of Scientific Advisors for the International Osteoporosis Foundation (IOF) under whose supervision this study was undertaken. At the international

level, the ICUROS was sponsored by Amgen, Eli Lilly, Medtronic (Kyphon), Novartis, Sanofi-Aventis Wyeth and Servier. We acknowledge the Quality of Life and Epidemiology Working Group: Jonathan Adachi, Frederik Borgström, Patricia Clark, Cyrus Cooper (co-chair), Manuel Diaz Curiel, Hans Peter Dimai, Mickaël Hiligsmann, John Kanis (co-chair), Edith Lau, Paul Lips, Mickael Lewiecki, Roman Lorenc, Eugene McCloskey, Sergio Ortolani, Alexandra Papaioannou, Stuart Silverman and Pawel Szulc. In Australia, the study was supported by the NHMRC (628422) with subsidiary funding support from Merck Australia Pty Ltd. In Austria, the study was sponsored by Central Association of Austrian Social Security Institution, the Austrian Society for Bone and Mineral Research (AuSBMR), Merck Sharp & Dohme, Nycomed, Roche and Daiichi-Sankyo GmbH. In Mexico, the study was supported by the National Council of Science and Technology (CONACyT) grant El 2008-01-87106. In Lithuania, the study was supported by the National Osteoporosis Center. In Estonia, the study was supported by Estonian Science Foundation (Grant 9368).

FIGURE LEGENDS

Figure 1: Proportion (%) of participants who recovered to their pre-fracture quality of life at 12-months, by country and fracture group

Figure 2: Health care and community service use profiles ('classes') for MOF and non-hip MOF participants, by country

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Table 1: Participant characteristics, by country

	Australia		Austria		Estonia		France		Italy		Lithuania		Mexico		Russia		Spain		UK	
	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF	MOF	Non-Hip MOF
No. of participants	524	374	525	267	146	-	466	303	494	257	340	272	278	120	831	603	283	127	239	146
Age, mean (SD)	70.2 (11.2)	67.6 (10.6)	73.7 (9.0)	70.7 (8.9)	77.2 (10.7)	-	71.9 (11.3)	69.4 (11.0)	75.5 (10.2)	71.3 (9.8)	69.0 (10.3)	67.8 (10.1)	73.5 (11.2)	68.1 (10.4)	66.0 (9.3)	64.9 (8.9)	76.5 (10.9)	70.6 (9.6)	72.0 (10.7)	68.7 (10.3)
Female, n (%)	415 (79.2)	298 (79.7)	426 (81.1)	224 (83.9)	105 (71.9)	-	392 (84.1)	263 (86.8)	464 (93.9)	236 (91.8)	292 (85.9)	237 (87.1)	235 (84.5)	109 (90.8)	676 (81.3)	515 (85.4)	241 (85.2)	112 (88.2)	200 (83.7)	132 (90.4)
Education, n (%)																				
Primary	38 (7.3)	20 (5.3)	217 (41.4)	116 (43.4)	54 (37.0)	-	162 (37.0)	93 (33.8)	320 (65.0)	133 (52.2)	71 (20.9)	50 (18.4)	142 (60.2)	52 (47.7)	58 (7.0)	31 (5.1)	244 (86.5)	100 (79.4)	22 (9.2)	13 (8.9)
Secondary	284 (54.3)	186 (49.7)	225 (42.9)	106 (39.7)	69 (47.2)	-	144 (33.0)	89 (32.4)	136 (27.6)	94 (36.9)	159 (46.7)	131 (48.2)	52 (22.0)	33 (30.3)	380 (45.8)	248 (41.1)	20 (7.1)	13 (10.3)	176 (73.9)	105 (71.9)
Post-secondary*	201 (38.4)	168 (44.9)	82 (15.7)	45 (16.9)	23 (15.8)	-	131 (30.0)	93 (33.8)	36 (7.4)	28 (11.0)	110 (32.4)	91 (33.5)	42 (17.8)	24 (22.0)	392 (47.2)	324 (53.7)	18 (6.4)	13 (10.3)	40 (16.9)	28 (19.2)
Income, n (%)#																				
Low	244 (46.6)	159 (42.5)	195 (37.1)	92 (34.5)	129 (88.4)	-	122 (26.2)	70 (23.1)	232 (47.0)	96 (37.4)	9 (2.6)	8 (2.9)	194 (69.8)	66 (55.0)	178 (21.4)	93 (15.4)	207 (73.1)	83 (65.4)	66 (27.7)	37 (25.3)

Mid-high	248 (47.3)	194 (51.9)	297 (56.6)	157 (58.8)	17 (11.6)	-	167 (35.8)	98 (32.3)	157 (31.8)	117 (45.5)	330 (97.1)	263 (96.7)	81 (29.1)	53 (44.2)	614 (73.9)	477 (79.1)	62 (22.0)	41 (32.3)	149 (62.3)	100 (68.5)
Refused to answer	32 (6.1)	21 (5.6)	33 (6.3)	18 (6.7)	0 (0.0)	-	177 (38.0)	135 (44.6)	105 (21.2)	44 (17.1)	1 (0.3)	1 (0.4)	3 (1.1)	1 (0.8)	39 (4.7)	33 (5.5)	14 (4.9)	3 (2.4)	24 (10.0)	9 (6.2)
Lives alone, n (%)	159 (30.8)	103 (27.8)	225 (43.4)	103 (39.3)	65 (44.5)	-	217 (47.2)	134 (44.7)	128 (26.7)	62 (24.9)	105 (31.1)	77 (28.5)	32 (11.5)	15 (12.5)	132 (16.5)	94 (16.2)	63 (23.3)	23 (18.9)	97 (41.8)	49 (34.0)
Fracture in previous 5 years, n(%)	84 (16.0)	59 (15.8)	82 (15.6)	41 (15.4)	36 (24.7)	-	89 (19.1)	55 (18.2)	81 (16.4)	50 (19.5)	34 (10.0)	28 (10.3)	34 (12.2)	10 (8.3)	350 (42.1)	295 (48.9)	42 (14.8)	16 (12.6)	30 (12.6)	18 (12.3)
Study fracture site, n (%)																				
Hip	150 (28.6)	-	258 (49.1)	-	146 (100)	-	163 (35.0)	-	237 (48.0)	-	68 (20.0)	-	158 (56.8)	-	228 (27.4)	-	156 (55.1)	-	93 (38.9)	-
Distal forearm	261 (49.8)	261 (69.8)	109 (20.8)	109 (40.8)	0 (0.0)	-	163 (35.0)	163 (53.8)	129 (26.1)	129 (50.2)	182 (53.5)	182 (66.9)	58 (20.9)	58 (48.3)	242 (29.1)	242 (40.1)	83 (29.3)	83 (65.4)	127 (53.1)	127 (87.0)
Vertebrae	61 (11.6)	61 (16.3)	82 (15.6)	82 (30.7)	0 (0.0)	-	79 (17.0)	79 (26.1)	116 (23.5)	116 (45.1)	90 (26.5)	90 (33.1)	34 (12.2)	34 (28.3)	191 (23.0)	191 (31.7)	27 (9.5)	27 (21.3)	1 (0.5)	1 (0.7)
Humerus	52 (9.9)	52 (13.9)	76 (14.5)	76 (28.5)	0 (0.0)	-	61 (13.0)	61 (20.1)	12 (2.4)	12 (4.7)	0 (0.0)	0 (0.0)	28 (10.1)	28 (23.3)	170 (20.5)	170 (28.2)	17 (6.1)	17 (13.4)	18 (7.5)	18 (12.3)
First contact post-MOF, n (%)																				
Primary care centre	80 (15.3)	75 (20.1)	39 (7.4)	27 (10.1)	2 (1.4)	-	40 (8.6)	28 (9.2)	21 (4.3)	12 (4.7)	36 (10.6)	35 (12.9)	48 (17.3)	29 (24.2)	65 (7.8)	61 (10.1)	19 (6.7)	10 (7.9)	20 (8.4)	19 (13.0)

/GP																				
Hospital/ ED	444 (84.7)	299 (79.9)	486 (92.6)	240 (89.9)	144 (98.6)	-	426 (91.4)	275 (90.8)	473 (95.7)	245 (95.3)	304 (89.4)	237 (87.1)	230 (82.7)	91 (75.8)	766 (92.2)	542 (89.9)	264 (93.3)	117 (92.1)	219 (91.6)	127 (87.0)
Admitted to hospital, n (%)	300 (57.3)	153 (40.9)	425 (81.0)	173 (64.8)	144 (98.6)	-	383 (82.2)	221 (72.9)	325 (65.8)	90 (35.0)	148 (43.5)	81 (29.8)	200 (71.9)	68 (56.7)	346 (41.6)	157 (26.0)	209 (73.9)	58 (45.7)	116 (48.5)	25 (17.1)

For education, data were missing for 78 patients (1.9% of total cohort).

*Includes university degree, certificates, Technical and Further Education (TAFE) and professional diplomas

#Different cut-off points for income levels were defined by each participating country

MOF=Major osteoporotic fracture; SD=Standard deviation; n=Number of participants; GP=General Practitioner; ED=Emergency Department; -=Not applicable

Table 2: Logistic regression models showing the association between class membership and odds of recovery of health-related quality of life recovery at 12 months post-fracture, unadjusted and fully adjusted models

	MOF					Non-hip MOF				
	N	Unadjusted		Adjusted		N	Unadjusted		Adjusted	
		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value		Odds Ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Australia[‡]										
Class 1	157	0.35 (0.23-0.55)	<0.001	0.37 (0.23-0.61)	<0.001	198	0.82 (0.55-1.24)	0.354	0.82 (0.54-1.25)	0.350
Class 2	176	1.59 (1.10-2.29)	0.014	1.48 (1.00-2.17)	0.049	176	1.22 (0.80-1.84)	0.354	1.22 (0.80-1.87)	0.350
Class 3	191	1.44 (0.95-2.17)	0.085	1.32 (0.87-2.02)	0.197	-	-	-	-	-
Austria[‡]										
Class 1	102	0.94 (0.56-1.56)	0.806	0.87 (0.50-1.51)	0.625	117	1.59 (0.96-2.63)	0.071	1.99 (1.14-3.47)	0.015
Class 2	175	0.72 (0.48-1.07)	0.105	0.39 (0.24-0.64)	<0.001	86	0.57 (0.34-0.97)	0.036	0.63 (0.35-0.83)	0.020
Class 3	91	0.88 (0.56-1.38)	0.564	0.96 (0.58-1.61)	0.888	64	1.06 (0.60-1.90)	0.839	0.64 (0.32-1.27)	0.151
Class 4	157	1.68 (1.10-2.57)	0.016	2.64 (1.65-4.21)	<0.001	-	-	-	-	-

Estonia*										
Class 1	74	0.85 (0.39-1.89)	0.694	0.97 (0.39-2.44)	0.946	-	-	-	-	-
Class 2	72	1.17 (0.53-2.60)	0.694	1.03 (0.41-2.60)	0.946	-	-	-	-	-
France†										
Class 1	228	2.44 (1.57-3.80)	<0.001	2.69 (1.59-4.54)	<0.001	54	0.75 (0.41-1.38)	0.359	0.95 (0.48-1.87)	0.878
Class 2	181	0.41 (0.26-0.65)	<0.001	0.27 (0.15-0.51)	<0.001	63	0.72 (0.38-1.34)	0.295	0.35 (0.15-0.82)	0.016
Class 3	57	0.89 (0.50-1.58)	0.689	0.99 (0.52-1.91)	0.982	186	1.54 (0.92-2.56)	0.100	1.81 (1.02-3.29)	0.049
Italy†										
Class 1	193	0.51 (0.34-0.77)	<0.001	0.51 (0.32-0.80)	0.003	95	0.51 (0.30-0.85)	0.010	0.49 (0.28-0.84)	0.010
Class 2	91	0.40 (0.22-0.70)	0.001	0.46 (0.25-0.84)	0.011	162	1.96 (1.17-3.29)	0.010	2.06 (1.19-3.58)	0.010
Class 3	163	4.70 (3.15-7.02)	<0.001	3.85 (2.50-5.93)	<0.001	-	-	-	-	-
Class 4	47	0.24 (0.10-0.54)	0.001	0.29 (0.11-0.76)	0.012	-	-	-	-	-
Lithuania‡										
Class 1	141	5.98 (4.88-11.03)	<0.001	4.90 (1.70-6.83)	<0.001	27	0.08 (0.02-0.33)	0.001	0.08 (0.02-0.32)	0.001
Class 2	76	0.41 (0.23-0.74)	0.003	0.41 (0.23-0.74)	0.003	44	0.36 (0.20-0.68)	0.001	0.37 (0.17-0.80)	0.012

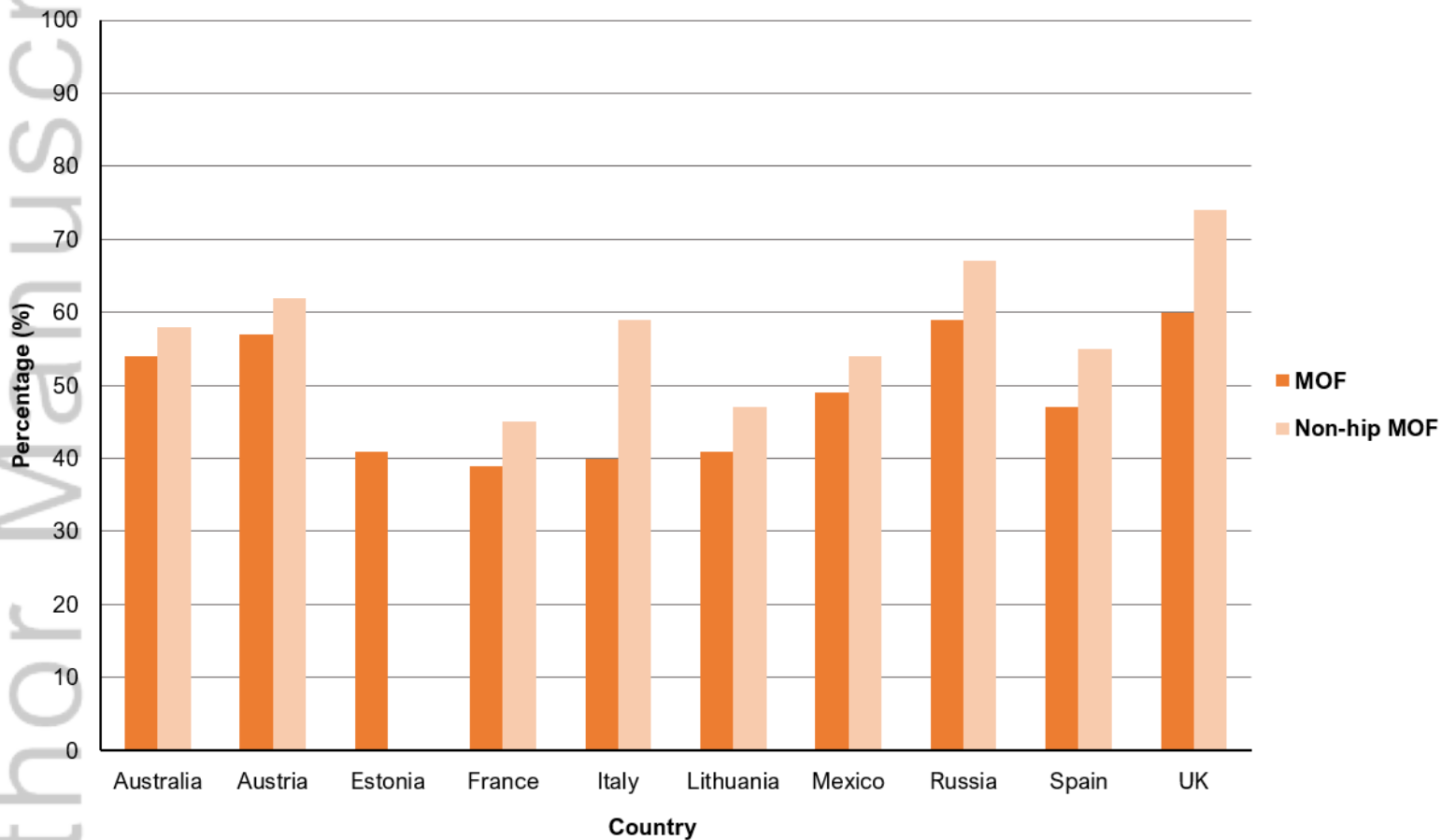
Class 3	44	0.51 (0.25-1.02)	0.057	0.47 (0.22-1.01)	0.052	141	6.60 (3.87-11.25)	<0.001	6.89 (3.88-12.23)	<0.001
Class 4	79	0.15 (0.07-0.30)	<0.001	0.14 (0.07-0.30)	<0.001	60	0.38 (0.20-0.71)	0.002	0.39 (0.21-0.74)	0.004
Mexico[‡]										
Class 1	204	1.02 (0.60-1.73)	0.956	1.23 (0.64-2.35)	0.534	93	4.74 (1.82-12.34)	0.001	5.25 (1.86-14.85)	0.001
Class 2	27	0.33 (0.14-0.81)	0.015	0.25 (0.09-0.68)	0.006	27	0.21 (0.09-0.55)	0.001	0.17 (0.07-0.54)	0.001
Class 3	47	1.87 (0.98-3.55)	0.057	1.87 (1.15-3.89)	0.045	-	-	-	-	-
Russia[‡]										
Class 1	96	0.52 (0.33-0.81)	0.004	0.44 (0.27-0.72)	<0.001	264	18.8 (10.8-32.5)	<0.001	18.2 (10.1-32.8)	<0.001
Class 2	143	0.15 (0.10-0.24)	<0.001	0.16 (0.10-0.25)	<0.001	66	0.13 (0.07-0.23)	<0.001	0.17 (0.09-0.33)	<0.001
Class 3	138	0.12 (0.08-0.19)	<0.001	0.13 (0.08-0.21)	<0.001	42	0.20 (0.10-0.41)	<0.001	0.18 (0.08-0.39)	<0.001
Class 4	280	22.40 (13.4-37.6)	<0.001	18.88 (11.1-32.3)	<0.001	161	0.88 (0.60-1.30)	0.529	1.29 (0.83-1.99)	0.255
Class 5	175	1.50 (1.04-2.15)	0.029	2.39 (1.56-3.65)	<0.001	70	0.10 (0.05-0.19)	<0.001	0.09 (0.05-0.18)	<0.001
Spain[†]										
Class 1	59	1.02 (0.57-1.82)	0.959	1.16 (0.58-2.31)	0.685	27	0.85 (0.34-2.09)	0.715	0.82 (0.30-2.26)	0.703
Class 2	156	0.55 (0.34-0.89)	0.014	0.55 (0.31-0.95)	0.034	37	0.66 (0.30-1.47)	0.313	0.69 (0.28-1.70)	0.422

Class 3	68	2.19 (1.25-3.83)	0.006	2.00 (1.05-3.83)	0.036	63	1.52 (0.75-3.07)	0.243	1.50 (0.68-3.29)	0.318
UK*										
Class 1	42	1.62 (0.77-3.40)	0.203	1.28 (0.59-2.79)	0.535	52	0.23 (0.10-0.50)	<0.001	0.22 (0.10-0.49)	<0.001
Class 2	101	0.22 (0.13-0.39)	<0.001	0.24 (0.13-0.47)	<0.001	94	4.40 (2.00-9.67)	<0.001	4.63 (2.04-9.50)	<0.001
Class 3	96	3.51 (1.97-6.26)	<0.001	2.92 (1.58-5.41)	<0.001	-	-	-	-	-

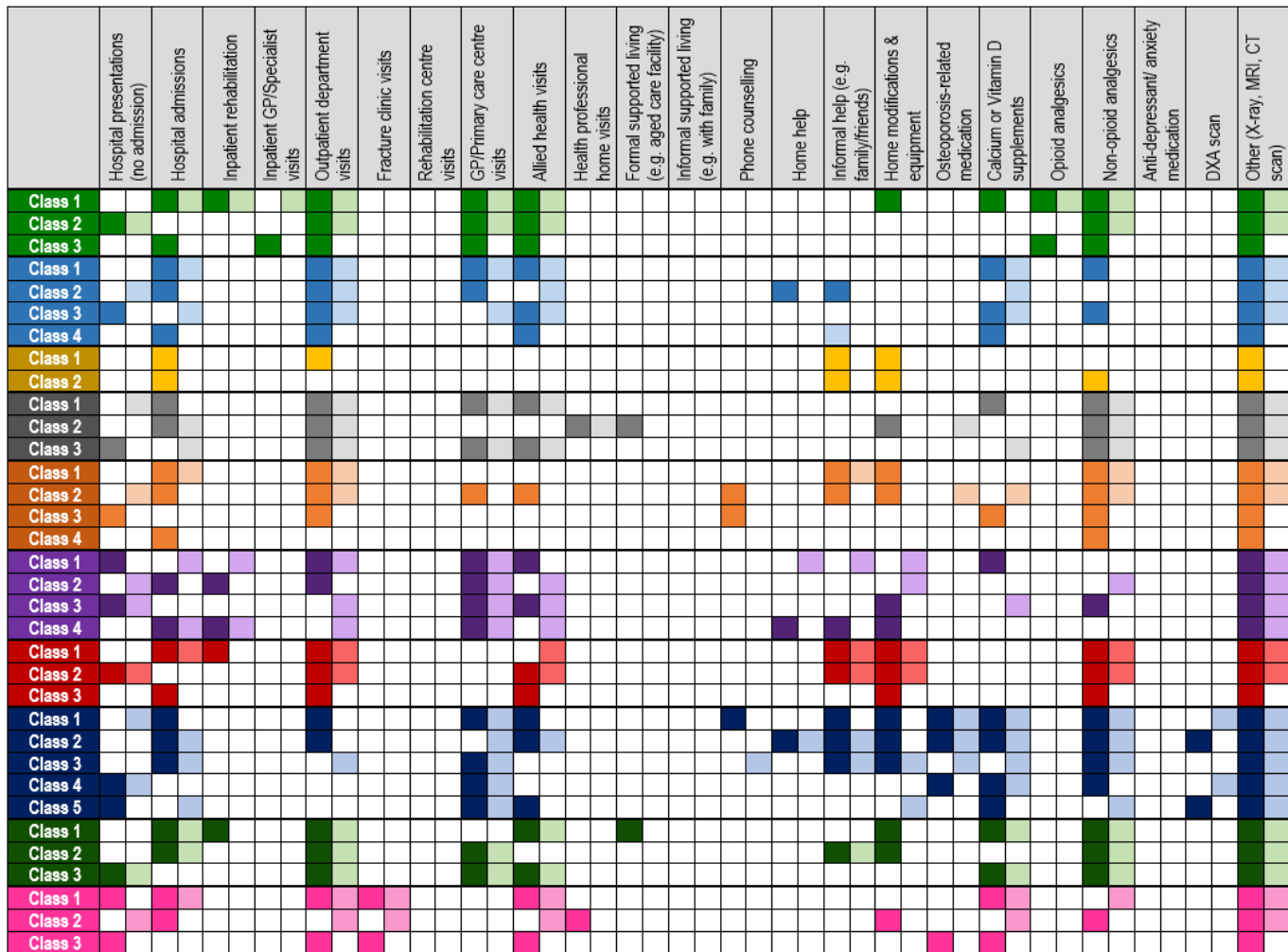
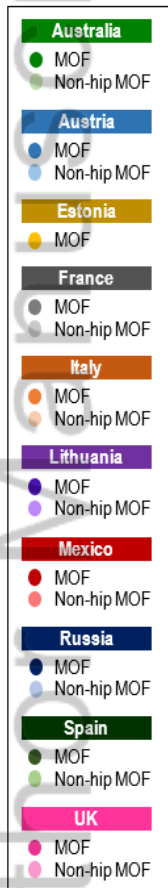
*Adjusted for age, sex, and pre-fracture EQ-5D utility score

†Adjusted for age, education, income level and pre-fracture EQ-5D utility score

‡Adjusted for age, sex, education, income level and pre-fracture EQ-5D utility score



JBMR_4181_Figure 1.tif



JBMR_4181_Figure 2.tif