

Disease Burden of Fractures in Patients with Osteoporosis in Japan

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INTRODUCTION

- Osteoporosis is a systemic disease which affects the skeleton and is characterized by low bone mass, deterioration of microarchitecture of bone tissue and bone fragility increase with consequent susceptibility to fracture [1].
- A total of 15 million people were estimated to have osteoporosis in Japan. Despite this high prevalence, osteoporosis remains underdiagnosed and undertreated [2].
- Bone fractures are the most frequent complications imposing heavy burden on individuals and the society as they often lead to a variety of physical and psychological consequences, including future fractures, depression, functional impairment, pain, health related quality of life (HRQoL), and disability as well as societal burden with respect to mortality and economic costs [3, 4].
- Currently there is a gap in our knowledge of the burden of fractures in osteoporosis patients aged 50 years or older in Japan. The present study sought to address this gap.

OBJECTIVE

- To investigate the disease burden of fractures, as well as incremental fractures in osteoporosis patients (≥50 years old) in Japan with respect to health status, work productivity and activity impairment (WPAI), and healthcare resource utilization.

METHODS

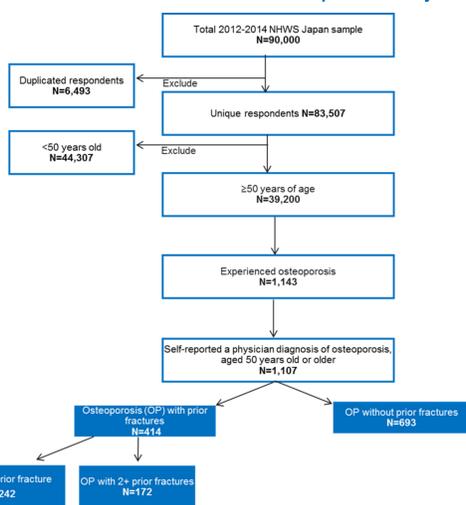
Data source

- This is a cross-sectional analysis which uses an existing database of survey responses to the Japan National Health and Wellness Survey (NHWS; Kantar Health, New York, NY).

- The NHWS is a self-administered, internet-based questionnaire from a nationwide sample of adults aged 18 or older. A stratified random sample framework with quotas based on gender and age was used to ensure representative samples.

- The current study used data from the 2012-2014 Japan NHWS. Multiple years of data were used to increase sample size and statistical power.

Figure 1. Flow chart for the selection of NHWS samples for analysis.



Measures

- Disease of interest. Self-reported fractures:** Among respondents who reported a diagnosis of osteoporosis, the number of fractures experienced was asked. A summary score of the number of fractures 0, 1 and 2+ were recorded for each osteoporosis patients.
- Demographics.** Sex, age, marital status, education level, income level, health insurance and employment status were assessed for all respondents.
- Health characteristics.** Smoking status, alcohol use, exercise behaviour, body mass index (BMI) group and Charlson Comorbidity Index [5] (CCI), which is a score for comorbid burden, were assessed for all respondents.

Health outcomes.

- Health related quality of life (HRQoL).** HRQoL was assessed using the physical (PCS) and mental component summary (MCS) scores from the Short Form-36 version 2 (SF-36v2). Health utility scores, derived from the SF-36v2 were also included (Short Form-6 Dimensions [SF-6D]).
- Work productivity and activity impairment (WPAI).** This was assessed using the Work Productivity and Activity Impairment – General Health (WPAI-GH) questionnaire that consists of four metrics:

WPAI metrics	
Absenteeism	% work time missed due to one's health in the past 7 days
Presenteeism	% impairment while at work due to one's health in the past 7 days
Overall work productivity loss	% overall work impairment due to one's health (absenteeism + presenteeism)
Activity impairment	% impairment in daily activities due to one's health in the past 7 days

- Healthcare resource utilization.** This was assessed in terms of the number of visits in the last 6 months to healthcare providers, the emergency room (ER), and hospitalizations.

- Direct and indirect costs.** Annualized unit costs for physician visits, emergency room visits, and hospitalizations were used to derive direct costs. For each employed respondent, hours lost due to either absenteeism or presenteeism was multiplied by their estimated wage (based on age and gender, Japan Basic Survey on Wage Structure, 2011) to estimate total annualized indirect costs.

METHODS (Continued)

Statistical analysis

- The difference in demographic, health characteristics and health outcomes was compared for:
 - Osteoporosis patients with prior fracture (N = 414) versus those without prior fracture (N = 693)
 - Osteoporosis patients with multiple fractures (2+ fractures, N = 172) versus those with single fracture (N = 242)
- Demographic and health characteristics difference was assessed using Pearson's chi-square test for categorical variables and ANOVA test for continuous variables.
- Multivariate generalized linear models were used to examine the difference in health outcomes adjusting for potential confounding effects of demographic and health characteristic variables.

RESULTS

- Osteoporosis is more prevalent in females aged above 60 years old.
- A total of 414 (37.4%) osteoporosis patients were found to have prior fractures. Of the osteoporosis patients with prior fractures (n=414), 242 (58.5%) patients were found to have single fracture, and 172 (41.5%) patients were found to have multiple fractures.
- Osteoporosis patients with single fracture were more likely to be in the lowest income group compared to those with no fracture or multiple fractures.
- Osteoporosis patients with multiple fractures were older, less likely to be married or living with partner, and had more comorbidity burden.

Table 1. Demographics and health characteristics of the study population with osteoporosis by fracture subgroup

	Total, N (%) (N = 1,107)	No prior fracture (N = 693)	Single fracture (N = 242)	Multiple fractures (N = 172)	P-value	
	Mean (SD)/ N (%)					
Age (Mean, SD)	66.6 ± 6.3	66.1 ± 6.6 _b	67.1 ± 6.1 _{a,b}	68.2 ± 5.3 _b	<0.001	
Gender	Female	1,014 (91.6)	633 (91.3)	222 (91.7)	159 (92.4)	0.89
Marital Status	Married/ living with partner	770 (69.6)	507 (73.2) _a	158 (65.3) _{a,b}	105 (61.0) _b	0.002
Education	University degree	296 (26.7)	194 (28.0)	64 (26.4)	38 (22.1)	0.29
Employment status	Employed	250 (22.6)	160 (23.1)	56 (23.1)	34 (19.8)	0.63
Insurance type	National Health Insurance	783 (70.7)	473 (68.3)	179 (74.0)	131 (76.2)	0.11
	Social Insurance	254 (22.9)	177 (25.5)	48 (19.8)	29 (16.9)	
	Late Stage Elderly Insurance	46 (4.2)	26 (3.8)	12 (5.0)	9 (4.7)	
	Other	14 (1.3)	12 (1.7)	1 (0.4%)	1 (0.6)	
	None of the above	10 (0.9)	5 (0.7)	2 (0.8%)	3 (1.7)	
Income	<¥3m	257 (23.2)	138 (19.9) _a	77 (31.8) _b	42 (24.4) _{a,b}	0.006
	¥3m to <¥5m	323 (29.2)	213 (30.7) _a	54 (22.3) _b	56 (32.6) _{a,b}	
	¥5m to <¥8m	203 (18.3)	131 (18.9)	49 (20.2)	23 (13.4) _a	
	¥8m or more	190 (17.2)	123 (17.7)	39 (16.1)	28 (16.3)	
	Declined answer	134 (12.1)	88 (12.7)	23 (9.5)	23 (13.4)	
CCI (Mean, SD)	0.35 ± 1.24	0.29 ± 0.69 _a	0.30 ± 0.72 _a	0.64 ± 2.67 _b	0.003	
BMI category	Obese	107 (9.7)	63 (9.1)	22 (9.1)	22 (12.8)	0.26
	Normal	810 (73.2)	507 (73.2)	179 (74.0)	124 (72.1)	
	Underweight	176 (15.9)	115 (16.6)	35 (14.5)	26 (15.1)	
	Declined answer	14 (1.3)	8 (1.2)	6 (2.5)	0 (0.0)	
Smoking	Current smoker	115 (10.4)	73 (10.5)	25 (10.3)	17 (9.9)	0.89
	Former smoker	196 (17.7)	122 (17.6)	47 (19.4)	27 (15.7)	
	Non-smoker	796 (71.9)	498 (71.9)	170 (70.2)	128 (74.4)	
Alcohol	Consume alcohol	621 (56.1)	385 (55.6)	144 (59.5)	92 (53.5)	0.43
Exercise behaviour	Regularly exercise	572 (51.7)	353 (50.9)	136 (56.2)	83 (48.3)	0.23

Osteoporosis patients with vs. without prior fractures

- After adjusting for demographic and health characteristics, osteoporosis patients with prior fractures reported significantly lower PCS (adjusted relative difference: -2.38; 95% confidence interval [CI] -3.33 to -1.43), MCS (adjusted relative difference: -1.98; 95% CI -3.20 to -0.76), and health state utility scores (adjusted relative difference: -0.04; 95% CI -0.05 to -0.02), than those without prior fractures.
- Osteoporosis patients with prior fractures were also found to have significantly higher overall work impairment (adjusted relative risk (RR): 1.36; 95% CI 1.01 to 1.83), and activity impairment (adjusted RR: 1.18; 95% CI 1.04 to 1.35).
- Osteoporosis patients with prior fractures had significantly higher number of healthcare provider (HCP) visits (adjusted RR: 1.22; 95% CI 1.07 to 1.39), emergency room (ER) visits (adjusted RR: 1.66; 95% CI 1.18 to 2.33) and hospitalizations (adjusted RR: 2.95; 95% CI 2.41 to 3.62) along with significantly higher indirect costs (adjusted RR: 1.43; 95% CI 1.06 to 1.92), and direct costs (adjusted RR: 2.78; 95% CI 2.41 to 3.21).

Osteoporosis patients with single vs. multiple fractures

- After adjusting for demographic and health characteristics, osteoporosis patients with multiple fractures reported significantly lower MCS (adjusted relative difference: -3.87; 95% CI -5.93 to -1.82), and health state utility scores (adjusted relative difference: -0.03; 95% CI -0.06 to -0.01), than those with single fracture (Figure 2).
- Osteoporosis patients with single fractures were also found to have significantly higher absenteeism (adjusted RR: 9.2; 95% CI 2.7 to 31.9), and activity impairment (adjusted RR: 1.30; 95% CI 1.05 to 1.60; Figure 3).

RESULTS (Continued)

Figure 2. Adjusted relative difference in HRQoL-related outcomes compared between osteoporosis patients with single and multiple fractures. Points represent the mean adjusted relative difference with bars representing the 95% CIs, with the single fracture group as the reference.

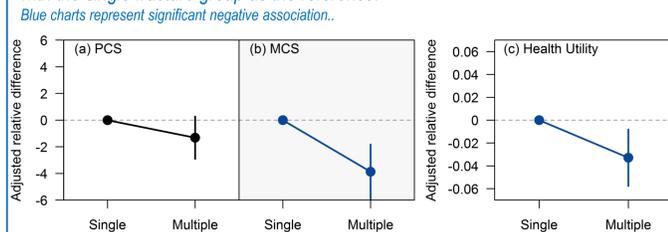
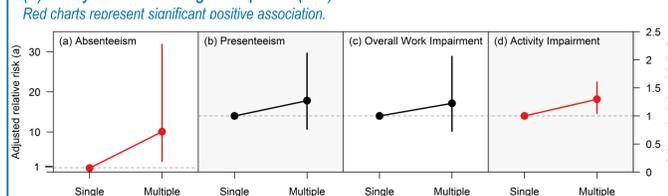
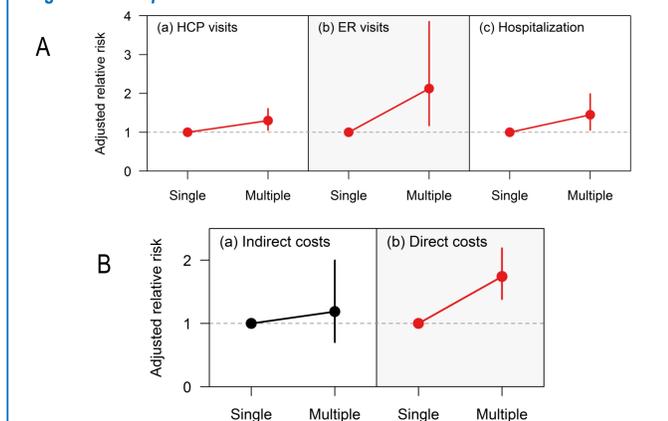


Figure 3. Adjusted relative risk (RR) for WPAI-related outcomes compared between osteoporosis patients with single and multiple fractures. Points represent the mean adjusted RRs with bars representing the 95% CIs, with the single fracture group as the reference. Please refer to the y-axis on the left for panel (a) and y-axis on the right for panel (b-d).



- Osteoporosis patients with multiple fractures had significantly higher number of HCP visits (adjusted RR: 1.30; 95% CI 1.05 to 1.61), ER visits (adjusted RR: 2.13; 95% CI 1.17 to 3.85) and hospitalizations (adjusted RR: 1.45; 95% CI 1.06 to 1.99; Figure 4A)
- Osteoporosis patients with multiple fractures had significantly higher direct costs (adjusted RR: 1.74; 95% CI 1.38 to 2.19; Figure 4B).

Figure 4. Adjusted relative risk (RR) for the number of A) healthcare visits and B) direct and indirect costs compared between osteoporosis patients with single and multiple fractures.



LIMITATIONS

- Although the NHWS is demographically representative of the adult population in Japan, it is unclear the extent to which the osteoporosis sample is representative of the adult osteoporosis population in Japan.
- The data are cross-sectional in nature and do not allow for causal explanations to be made.
- As with any survey, the data are self-reported and cannot be verified by patients' medical charts or other objective data.
- The study is limited by the data collected in the NHWS. For example, information on fracture site and time of the fracture was unavailable.

CONCLUSIONS

- Almost 40% of osteoporosis patients were found to have prior fractures. Having prior fractures imposes a significant clinical burden on osteoporosis patients, and associated with significantly higher indirect and direct costs.
- Among those with prior fractures, 42% of the patients had multiple fractures (2 and more fractures). Patients with multiple fractures had significantly lower HRQoL in mental component and mean health state, and associated with significantly higher direct costs compared with those with single fracture.
- These findings suggest a substantial unmet need for more effective osteoporosis management strategies in Japan, particularly among osteoporosis patients with multiple fractures. Better disease management could help to reduce the clinical and economic burden of osteoporosis.

DISCLOSURES

This study was funded by Amgen Astellas Biopharma K.K. Kantar Health received funding from Amgen Astellas Biopharma K.K. during the conduct of the study. Saeko Fujiwara received a consulting fee from Amgen Astellas Biopharma K.K. during the conduct of the study and received a consulting fee from Eli Lilly K.K., and has served as a speaker bureau of Alere Medical Co., Ltd. Pfizer Inc. and Asahi Kasei Pharma Corp. Dena Jaffe and Cheryl Teoh are employees of Kantar Health and received a consulting fee from Amgen Astellas Biopharma K.K. Yurie Taguchi is an employee of Amgen Astellas Biopharma K.K. and is an ISPOR Japan councillor.

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