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Effect of improved medication adherence on health care costs in osteoporosis patients

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Abstract

Osteoporosis is a chronic disease that requires continuous health care spending for pharmacotherapy and examinations. Osteoporotic fractures are a major economic burden. However, little is known about the economic effects of osteoporosis and osteoporotic fractures in Korea.

The purpose of this study was to determine the predictors of osteoporosis-related health care costs and to evaluate the economic effects of fracture prevention through medication adherence among osteoporosis patients.

Using the Korea National Health Insurance Claims Database (KNHICD), we identified osteoporosis patients aged 50 years and older from 2011 to 2012. Annual health care costs of osteoporosis were analyzed from the insurer's perspective and compared between patients with fractures and those without fractures. Adherents were defined as patients with a medication possession ratio of ≥80%. A generalized linear model (GLM) was used to estimate the predictors of osteoporosis-related health care costs.

The major predictors of osteoporosis-related health care costs were age, medication adherence, and the occurrence of fractures ($P < .001$). The proportion of fractures among non-adherents was approximately 1.1 times the proportion among adherents. Health care costs per patient with fractures were 3.8 times the costs per patient without fractures. Patients with fractures had higher health care costs due to hospitalization and outpatient costs but lower pharmacy costs than non-adherents. We estimated that about $5 million of health insurance expenses could be saved annually if all non-adherents became adherents.

Improved osteoporosis medication adherence can reduce osteoporosis-related health care costs by preventing fractures. Persistent pharmacotherapy for osteoporosis is necessary to prevent osteoporotic fractures and to reduce osteoporosis-related health care costs.

Abbreviations: CCI = Charlson Comorbidity Index, GLM = Generalized Linear Model, ICD-10 = International Classification of Diseases, 10th revision, KNHICD = Korea National Health Insurance Claims Database, KRW = Korean Won, MPR = medication possession ratio, NHIS = National Health Insurance Service, OTC = over-the-counter, SD = standard deviation, SERMs = selective estrogen receptor modulators, USD = United States dollar, VIF = variance inflation factor.

Keywords: generalized linear model, health care cost, medication adherence, osteoporosis, osteoporotic fractures

1. Introduction

Osteoporosis can lead to numerous clinical and health-related consequences, including fractures, and becomes a greater concern as an individual ages.[1] With rapid aging of the population, the prevalence of osteoporosis has increased.[2–4] Between 2005 and 2008, the prevalence of osteoporosis increased by 34.6% for females and 42.7% for males in Korea.[5]

Osteoporosis is the main risk factor for fractures.[6,7] Fractures reduce quality of life by decreasing mobility and limiting daily and social activities.[8] Moreover, fractures have been reported to greatly increase excess mortality.[4,6,7] The mortality rate due to osteoporotic fractures within a year has been reported to be 21.0% for males and 15.0% for females.[9] Osteoporotic fractures are also known to impose a huge economic and social burden.[10–12] There are many studies on health care costs of osteoporotic fractures in Asia and other countries.[11,13–18] In Korea, the societal costs of osteoporotic fractures increased from $88.8 million in 2007 to $149.3 million in 2011.[19] Another study in Korea reported that total health care costs of osteoporotic fractures of the elderly increased by 31.6% from $549 million in 2008 to $722 million in 2011.[20]

Medication adherence among osteoporosis patients is low although osteoporosis medication significantly reduces the risk of fractures.[15,21,22] Adherents to the medication have higher drug costs than non-adherents but adherence can lower the disease-

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related health care costs associated with fractures, such as inpatient service and surgery.[13,15] Nonetheless, research on the predictors that increase the cost burden and the economic effects of high adherence to osteoporosis medication is lacking.[5,13,23] Therefore, the present study sought to compare health care costs of osteoporosis according to the incidence of fractures. Moreover, this study aims to identify the predictors of osteoporosis-related health care costs and to evaluate the economic effects of medication adherence.

2. Methods

2.1. Data source

We used the Korea National Health Insurance Claims Database (KNHICD) for the 2011 to 2012 periods. Korea has a mandatory national health insurance system that covers 97% of the population. The remaining 3% of the population is covered under the Medical aid, a publicly funded medical assistance program for the poor. The KNHICD contains information on inpatient or ambulatory services, prescriptions, diagnoses, costs, and patient characteristics for almost all South Korean patients who utilize medical services, with the exception of procedures that are not covered by insurance, such as cosmetic surgery.[5,24,25] Diagnoses are coded according to the International Classification of Diseases, 10th revision (ICD-10).

2.2. Study population

The study participants were patients with osteoporosis aged 50 years and older. Using the KNHICD, we identified osteoporosis patients who met both of the following criteria: an ICD-10 code of osteoporosis: M80 (osteoporosis with pathological fracture), M81 (osteoporosis without pathological fracture), or M82 (osteoporosis in diseases classified elsewhere); the prescription of anti-osteoporosis drugs (bisphosphonate, bisphosphonate complex, selective estrogen receptor modulators [SERMs], and calcitonin). The index date was set as the date on which patients received their first prescription in 2011. To define new users, we excluded patients who had received anti-osteoporosis drugs in one year prior to the index date,[26–28] and patients with Paget disease, rare disorders, cancer, dementia, or cerebral infarction (Fig. 1).

2.3. Variables

2.3.1. Osteoporosis-related health care costs. Osteoporosis-related health care costs include costs for hospitalization, outpatient visits, and pharmacy associated with osteoporosis and osteoporotic fractures in 2011. Costs of hospitalization and outpatient visits include medical procedures, treatments and surgeries. Pharmacy costs include drug costs and prescription fees. Claims amounts for the first visit and follow-up treatments for 1 year were tallied for each patient. We included anti-osteoporosis drug, anti-inflammatory agents, and analgesic agents used for fractures.

We estimated the annual health care costs from the insurer's perspective. When clinics or hospitals performed treatment and medical procedures, they request reimbursement of medical costs from the Korea National Health Insurance Service. Non-covered services such as caregivers' service, assistive devices, over-the-counter (OTC) drugs, and long-term care facilities were not included in the KNHICD and therefore excluded from our analysis.

The estimated annual costs were inflation-adjusted to the 2012 Korean Won (KRW) unit cost except drug costs and then

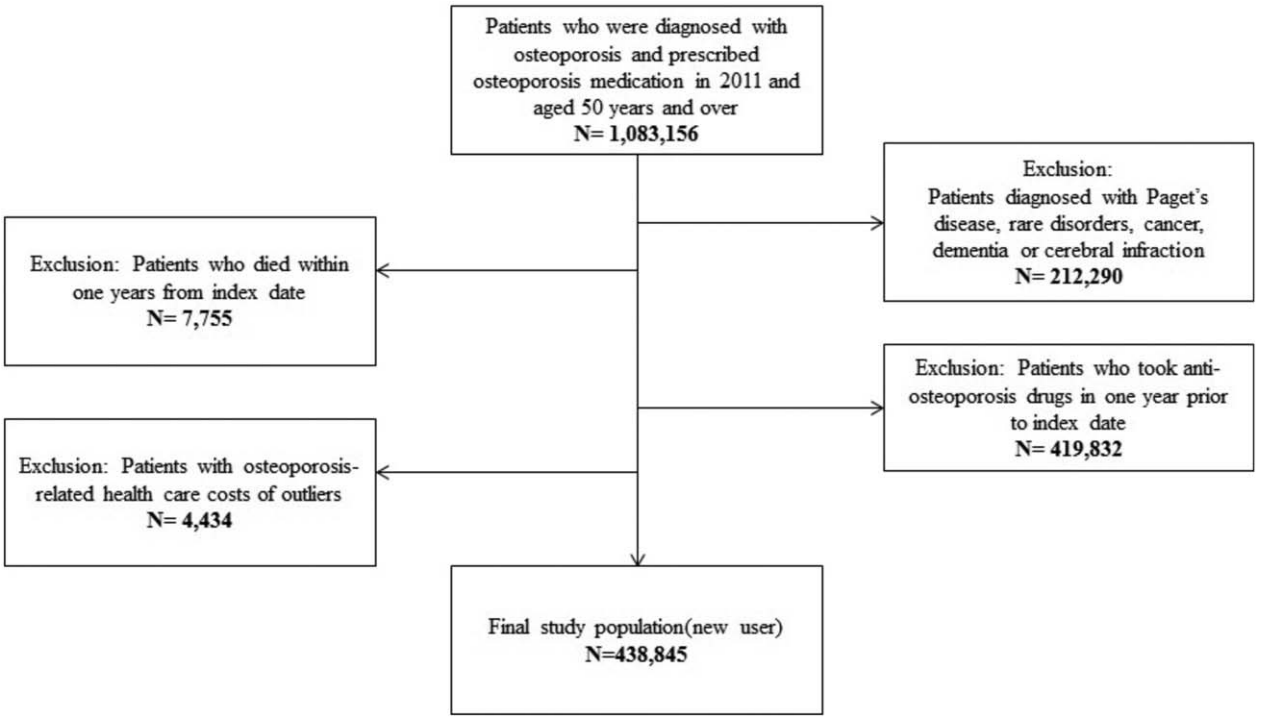

Figure 1. Selection of the study population.

converted to United States dollars (USD) by using the 2012 average conversion rate of 1126 KRW per 1 USD (http://ecos/bok.or.kr).

2.4. Fracture

We identified osteoporotic fractures including fractures in the hip (S72.0 [fracture of neck of femur], S72.1 [pertrochanteric fracture], and seven procedures [open reduction of fractured extremity-femur, closed pinning-femur, external fixation-pelvis/femur, closed reduction of fractured extremity-pelvis/femur, bone traction, skin traction, hemiarthroplasty-hip]), the spine (S22.0 [fracture of the thoracic vertebra], S22.1 [multiple fractures of the thoracic spine], S32.0 [fracture of lumbar spine and pelvis], M48.4 [fatigue fracture of vertebra] and M48.5 [collapsed vertebra, NEC]), wrist (S52.5 [fracture of lower end of radius], and S52.6 [fracture of lower end of both ulna and radius]), and the humerus (S42.2 [fracture of upper end of humerus] and S42.3 [fracture of shaft of humerus]) by using all claims records of outpatient visits or hospital admissions of patients from the KNHICD in the study period.[29] Multiple fractures were defined as more than 1 fracture within the study period.

2.5. Medication adherence

Medication adherence was calculated using the medication possession ratio (MPR). The MPR is defined as the ratio of the number of days for which a patient is supplied with medication to the total number of days in the study period.[25] On the basis of previous studies, we used 80% as the cutoff point to classify patients as adherents or non-adherents.[30–33] Adherents were defined as patients with an MPR of ≥80%. Some studies have suggested that an MPR of 80% or higher allows patients with chronic disease to receive the benefits of their medication.[32,33]

2.6. Other covariates

We include relevant confounders that could affect health care cost related osteoporosis: gender, age, area of residence, type of health coverage, medical institution, fracture history, anti-osteoporosis drugs, and Charlson Comorbidity Index (CCI). Age was categorized into 50 to 64 years, 65 to 74 years, and 75 years and over. To consider the availability of medical institutions by region, we classified area of residence into metropolis, small to medium sized cities, and rural areas. The type of health insurance was included as a variable describing the socioeconomic status of the patient and out of pocket money. Medical Aid beneficiaries have low or no income and qualify for low or no out-of-pocket payment. As medical care costs can vary depending on the medical care institutions used, the type of medical institution was considered and defined as the institution which the patient used most often during the 1 year for the treatment of osteoporosis or osteoporotic fractures. Medical institutions were classified into general hospitals, hospitals, and clinics/public health centers. We also included anti-osteoporosis drugs as a covariate. The type and severity of comorbidities experienced by patients can influence osteoporosis-related health care costs and thus need to be adjusted for.[34] Comorbidities were measured by using the CCI, which was converted into ICD-9 and ICD-10.[34] We calculated the CCI, based on previous studies using national health insurance claims data, and scored it as 0, 1, 2, and 3 or over.[25,34] We also included history of fractures as a covariate because it can also influence osteoporosis-related health care costs. History of fractures was defined as experience of receiving treatment due to fractures within 2 years prior to the index date. We assessed the gender, age, area of residence, and type of health coverage for the index date. Medical institution and anti-osteoporosis drugs were assessed 1 year after the index date, and the CCI were assessed within one year prior to the index date, in order to identify predictors of osteoporosis-associated health care costs.

We tested and confirmed that there was no problem of multicolinearity for all variables (variance inflation factor, VIF < 10).

2.7. Statistical analysis

Characteristics of non-adherents and adherents were tested by using χ^2 tests and *t* test, respectively. We then compared, by using the *t* test and ANOVA, the average health care between patients with fractures, and patient without fractures. In addition, we used a generalized linear model (GLM) with a gamma distribution and log link function to analyze the association between osteoporosis-related health care costs and predictors such as medication adherence and fractures according to patient demographics and clinical characteristics.[21,35] The GLM was used to take into consideration the skewed distribution of the dependent variable, health care costs.[36–38]

Using the GLM, we estimated the cost of osteoporosis treatment. The estimated osteoporosis treatment costs were then multiplied by the number of excess fractures among non-adherents. The number of excess fractures was determined as the difference in the number of fractures between non-adherents and adherents. The product is viewed as the amount of health care costs that could be saved if non-adherents become adherents and thus the economic effects of maintaining a high level of medication adherence.

All statistical analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC) and a 2-tailed level of statistical significance was defined as a $P < .05$.

2.8. Ethics statement

The study protocol was approved by the National Health Insurance Service (NHIS) Institutional Review Board (approval number: NHIS-2015-4-001).

3. Results

Of 438,845 osteoporosis patients included in this study, adherent patients accounted for 22.2% (97,469) of the study population and non-adherent patients 77.8% (Table 1). The average age (± standard deviation, SD) of non-adherents was higher than that of adherents (68.9 [±9.1] years vs 66.9 [±8.4] years, $P < .001$), and the greatest proportion of patients were 65 to 74 years in both groups. Males comprised 10% of non-adherents and 5% of adherents ($P < .001$). The proportion of Medical Aid beneficiaries were higher in non-adherents (10.4%) ($P < .001$). The most frequently used medical institutions were clinics/public health centers (81.8%), followed by tertiary/general hospitals (10.5%) and hospitals (7.7%). Adherents visited hospitals and bigger medical institutions ($P < .001$). The percentage of fractures were higher in non-adherents (7.6%) than in adherents (6.9%) ($P < .001$). The overwhelming majority of the patients (88%) used bisphosphonates to treat osteoporosis. The proportion of patients with a CCI of 0 was higher in non-adherents (65.9%) than in adherents (65.3%) ($P < .001$)

Table 1

Characteristics of study subjects.

		Total (n = 438,845)		Non-adherent (MPR < 80) (n = 341,376)		Adherent (MPR > = 80) (n = 97469)		
		N	%	n	%	n	%	*P*
Age, y	Mean, (±SD)	68.45	8.97	68.90	9.08	66.86	8.41	<.001
	50–64	145,032	33.05	106,485	31.2	38,547	39.5	<.001
	65–74	179,634	40.93	139,381	40.8	40,253	41.3	
	≥75	114,179	26.02	95,510	28.0	18,669	19.2	
Gender	Men	39,726	9.05	34,185	10.0	5541	5.7	<.001
	Women	399,119	90.95	307,191	90.0	91,928	94.3	
Area of residence	Metropolis	163,741	37.31	122,926	36.0	40,815	41.9	<.001
	Small to medium cities	195,616	44.58	152,561	44.7	43,055	44.2	
	Rural areas	79,488	18.11	65,889	19.3	13,599	14.0	
Type of health coverage	Health insurance	396,300	90.31	305,892	89.6	90,408	92.8	<.001
	Medical aid	42,545	9.69	35,484	10.4	7061	7.2	
Medical institution	General hospital	46,016	10.49	30,299	8.9	15,717	16.1	<.001
	Hospital	33,707	7.68	25,609	7.5	8098	8.3	
	Clinic and public health center	359,122	81.83	285,468	83.6	73,654	75.6	
Fracture history	Yes	419,372	95.56	326,332	95.6	93,040	95.5	0.07
	No	19,473	4.44	15,044	4.4	4429	4.5	
Fracture	Yes	32,828	7.48	26,057	7.6	6,771	6.9	<.001
	Hip	2788	8.49	2179	8.4	609	9.0	
	Vertebral	22,640	68.97	17,744	68.1	4896	72.3	
	Wrist	5508	16.78	4558	17.5	950	14.0	
	Humerus	964	2.94	779	3.0	185	2.7	
	Multi fractures	928	2.83	797	3.1	131	1.9	
	No	406,017	92.52	315,319	92.4	90,698	93.1	
Anti-osteoporosis drugs	Bisphosphonate	387,447	88.29	296,520	86.9	90,927	93.3	<.001
	SERM	12,780	2.91	8099	2.4	4681	4.8	
	Calcitonin	38,618	8.80	36757	10.8	1861	1.9	
MPR	Mean, (±SD)	44.69	32.49	30.88	22.11	93.05	5.85	<.001
	<80%	341,376	77.79					<.001
	≥80%	97,469	22.21					
CCI	0	288,741	65.80	225,102	65.9	63,639	65.3	<.001
	1	103,954	23.69	80,713	23.6	23,241	23.8	
	2	31,449	7.17	24,105	7.1	7344	7.5	
	3+	14,701	3.35	11,456	3.4	3245	3.3	

CCI = Charlson comorbidity index, MPR = medication possession ratio, SD = standard deviation, SERM = selective estrogen receptor modulator.

Figure 2 shows difference in the number of osteoporotic fracture patients by medication adherence. The proportion of fractures among non-adherents (7.6%) was approximately 1.1 times the proportion among adherents (7.0%). The proportion of fracture among non-adherents was 1.03 times that of adherents, the smallest difference between these groups. The proportion of fractures was 5.2% and 5.0% in non-adherents and adherents, respectively, and the proportion of vertebral fractures

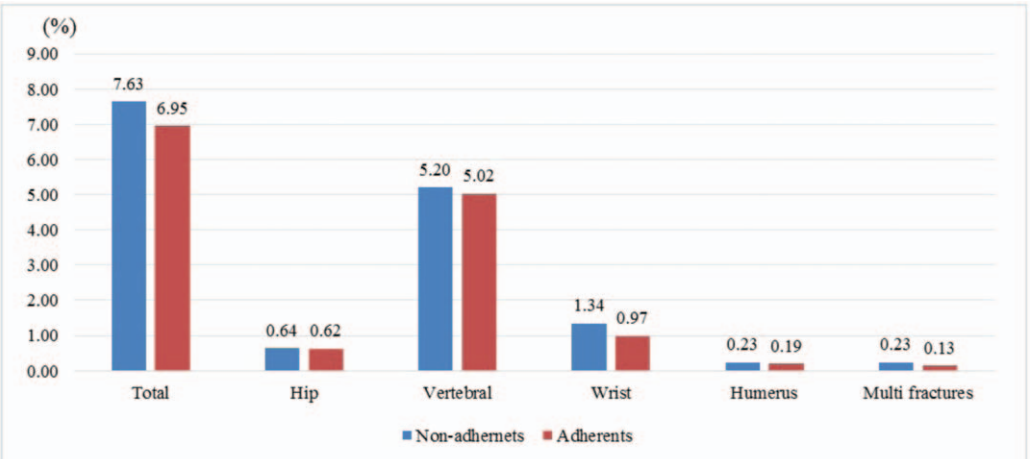

Figure 2. Proportion of fractures among osteoporosis patients between adherents and non-adherents.

Table 2

Difference in osteoporosis-related health care costs between fracture and non-fracture.

			Total	Non-fracture	Fracture	*P*	Difference in osteoporosis-related costs
Total		Number of patients	438,845	406,017	32,828		
		Mean costs (±SD)	861 (1344)	714 (1174)	2675 (1883)	<.001	1961
Gender	Men	Number of patients	39,726	35,638	28,740	<.001	
		Mean costs (±SD)	1068 (1563)	874 (1390)	2662 (1877)		1788
	Women	Number of patients	399,119	370,379	4088		
		Mean costs (±SD)	840 (1319)	699 (1150)	2768 (1923)		2069
Age, y	50–64	Number of patients	145,032	139,480	5552	<.001	
		Mean costs (±SD)	699 (1087)	631 (998)	2415 (1669)		1784
	65–74	Number of patients	179,634	167,793	11,841		
		Mean costs (±SD)	875 (1393)	753 (1270)	2605 (1834)		1851
	≥75	Number of patients	114,179	98,744	15,435		
		Mean costs (±SD)	1043 (1,526)	765 (1228)	2822 (1977)		2058

SD = standard deviation.

in non-adherents was 1.04 times that in adherents. The proportion of the wrist and the humerus in non-adherents was 1.4 and 1.2 times, respectively, that in adherents. The proportion of multi-fractures was lowest but that in non-adherents was approximately 1.8 times that in adherents.

Table 2 describes the difference in osteoporosis-related health care costs between patients with fractures and those without fractures. Medical care costs per patient was $ 2675 for those with fractures and $ 714 for those without fractures, with a difference of $ 1961 ($P < .001$). The difference in mean medical care costs between fractures and non-fractures was $ 1788 and $ 2069 for men and women, respectively, with a greater difference for women ($P < .001$). The difference in mean medical care costs between fractures and non-fractures was $ 1784 for 50 to 64 years, $ 1851 for 65 to 74 years, and $ 2058 for 75 years and older, with differences increasing with older age ($P < .001$).

Inpatient costs accounted for 82.8% of costs for patients with fractures and 47.12% of costs for patients without fractures (Table 3). Outpatients and pharmacy costs comprised greater proportion of total health care costs for patients without fractures (29.1% and 23.8%) than patients with fractures (11.6% and 5.6%, respectively). Mean pharmacy costs per patient were higher for patients without fractures and those with fractures ($ 161 vs $ 141).

The GLM showed that osteoporotic fractures were the most influential factor for osteoporosis-related health care costs (Table 4). Especially, coefficients for hip and multiple fractures were greater than other fracture sites ($P < .001$). Older age was more strongly associated with increases in costs: patients aged 65 years and older years incurred significantly more costs than those aged 50 to 64 years ($P < .001$). Men paid more costs than women and residents in small to medium-sized cities and rural areas paid more costs than those in large cities ($P < .001$). Osteoporosis-related health care costs were higher for beneficiaries of medical aid than those of health insurance ($P < .001$). Patients incurred higher health care costs at general hospitals and hospital than at clinics, and public health centers ($P < .001$). A history of fractures, as compared with an established one, increased osteoporosis-related health care costs ($P < .001$). Bisphosphonate and SERMs decreased costs, compared to calcitonin ($P < .001$). Osteoporosis-related health care costs among adherents were higher than costs among non-adherents ($P < .001$). Finally, the presence of comorbidities increased costs ($P < .001$).

Table 5 presents the economic effects of fracture prevention through improving medication adherence among osteoporosis patients when other covariates were adjusted for. The estimated number of excess fractures in non-adherents was 2342, consisting of 46 in the hip, 596 in vertebral, 1231 in the wrist, 131 in the humerus, and 338 in multiple fractures. We estimated that national health insurance expenses could be saved by $ 5,025,050 if all non-adherents become adherents.

4. Discussion

The study compared osteoporosis-related health care costs of osteoporosis between patients with fractures and those without fractures by using population-based health insurance claims data.

Table 3

Osteoporosis-related health care costs by fracture site.

		Hospitalization		Outpatient		Pharmacy		Total	
Fracture site	Number of patients	Mean (±SD)	%	Mean (±SD)	%	Mean (±SD)	%	Mean (±SD)	%
Hip	2788	5137 (1661)	93.61	210 (238)	3.83	141 (163)	2.57	5488 (1676)	100.00
Vertebral	22,640	1954 (1520)	82.02	277 (315)	11.63	151 (155)	6.36	2382 (1580)	100.00
Wrist	5508	1444 (1543)	70.01	474 (313)	23.00	144 (143)	6.99	2062 (1556)	100.00
Humerus	964	2279 (1901)	79.96	419 (418)	14.69	152 (163)	5.35	2850 (1921)	100.00
Multi fracture	928	4333 (2316)	89.71	361 (322)	7.47	136 (142)	2.82	4830 (2269)	100.00
Fracture	32,828	2215 (1866)	82.81	311 (323)	11.62	149 (154)	5.57	2675 (1883)	100.00
Non-Fracture	406,017	336 (1140)	47.12	208 (249)	29.10	170 (159)	23.78	714 (1174)	100.00

SD = standard deviation.

Table 4

Predictors of osteoporosis-related health care costs.

Characteristic		Exponential estimate (Cost ratio)	Pr > χ^2
Fracture site	Hip	6.8895	<.001
	Vertebral	3.0892	<.001
	Wrist	2.9350	<.001
	Humerus	3.7199	<.001
	Multiple fractures	6.3458	<.001
	None	Reference	
Age, y	50–64	Reference	
	65–74	1.2151	<.001
	≥75	1.1990	<.001
Gender	Men	reference	
	Women	0.8360	<.001
Area of residence	Metropolis	reference	
	Small to medium cities	1.0206	<.001
	Rural areas	1.1300	<.001
Type of health coverage	Health insurance	0.8748	<.001
	Medical Aid	Reference	
Medical institution	General hospital	1.3406	<.001
	Hospital	1.6680	<.001
	Clinic/public medical center	Reference	
Fracture history	Yes	1.3551	<.001
	No	Reference	
Anti-osteoporosis drugs	Bisphosphonate	0.7535	<.001
	SERM	0.8720	<.001
	Calcitonin	Reference	
MPR	<80%	Reference	
	≥80%	1.3485	<.001
CCI	0	Reference	
	1	1.1370	<.001
	2	1.2109	<.001
	3+	1.3101	<.001

CCI = Charlson comorbidity index, MPR = medication possession ratio, SERM = selective estrogen receptor modulator.

Moreover, this study sought to identify the predictors of osteoporosis-related health care costs and to analyze the economic effects of improved medication adherence. We showed that there was a difference in the proportion of osteoporotic fractures according to medication adherence. Similarly, previous studies on the association between medication adherence of anti-osteoporosis drugs and fracture incidence showed a higher risk of fractures in non-adherents (MPR < 50%) than in adherents (MPR ≥ 80%).[22,39]

Osteoporosis-related health care costs among patients with fractures were 3.8 times the costs among those without fractures. This was because health care costs for osteoporosis patients with fractures predominantly comprised of hospitalization cost among 3 components of costs that also included outpatient and pharmacy costs.[40,41]

This study also found predictor variables by using the GLM. Predictors of osteoporosis-related health care costs were fracture site, age, gender, area of residence, type of health coverage, medical institution, fracture history, anti-osteoporosis drugs, medication adherence, and CCI, Previous studies reported that medical care costs were higher for men than for women and increased with older age, higher CCI.[10,13,21,35] Health care costs of osteoporosis patients with fracture were higher than those without fracture. Ha et al[40] reported that from 2008 to 2011, health care costs per patient with osteoporotic fractures were 1.8 time costs per patient without fractures. Indeed, health care costs are much higher in hip fracture. When hip fracture occurred, health care costs increase three times in the United States.[27] Mean health care costs per male patients with osteoporosis were 1.5 times higher than the costs per female patients in previous study.[40] Health care costs for beneficiaries of medical aid were higher than those for beneficiaries of national health insurance. Medical aid patients might have low economic burden because of lower out-of-pocket money. Jung et al[42] reported medical aid patients had received more pharmacotherapies than health insurer, and another study found out that mean health care costs of medical aid patients were higher than those of health insurer.[40]

We showed that medication adherence was more strongly associated with increases in costs. These finding are similar to those of previous studies.[13,43] However, better adherence may increase medical care costs due to treatment and prevention costs associated with osteoporosis medication but the occurrence of fractures can lead to greater health care costs. As a result, improved adherence can save osteoporosis-related health care costs. Our study estimated that if non-adherents become adherents, health care expenditure can be saved by $5 million. Similarly, Olsen et al[22] estimated that non-adherents incurred excess costs of $ 2.5 million due to fractures, compared to adherents (MPR ≥ 80%). Sokol et al[44] found that although pharmacy costs are related to increasing costs, improved medication adherents can reduce total health care costs among patients with some chronic diseases, diabetes, hypertension, hypercholesterolemia, and congestive heart failure.

Using national health insurance claims data, this study identified the disease burden of all patients who were diagnosed

Table 5

Economic effects of increased medication adherence among osteoporosis patients.

Fracture site	Non-adherents (n = 341,376)		Adherents (n = 97,469)		Number of excess fractures in non-adherents	Osteoporosis treatment costs	Amount that can be saved
	Number of fracture incidents	%	Number of fracture incidents	%			
Hip	2179	0.64	609	0.62	46	4882	224,728
Vertebral	17,744	5.20	4896	5.02	596	1732	1,032,452
Wrist	4558	1.34	950	0.97	1231	1604	1,973,895
Humerus	779	0.23	185	0.19	131	2254	295,460
Multiple fractures	797	0.23	131	0.13	338	4431	1,498,515
Total	26,057	7.63	6771	6.95	2,342	14,903	5,025,050

Adjusted for age, gender, area of residence, type of health coverage, medical institution, fracture history, osteoporosis medication, medication possession ratio (MPR), and Charlson comorbidity index (CCI).

with osteoporosis and treated in Korea. We further estimated osteoporosis-related health care costs that could be saved by increasing medication adherence. Although a number of studies investigated health care costs paid by Korean patients with fractures, a few went as far to estimate how much money could be saved by preventing fractures as this present study did.[19,45,46] The findings of this study may inspire osteoporosis patients to initiate and maintain active medical treatment to prevent fractures.

Despite the strengths, however, the current study has various limitations. First, we may have overestimated the values of the MPR since they were based on the prescriptions but not whether patients actually took their prescribed medicines. Nevertheless, the MPR method is the best available tool to measure medication adherence using health insurance claim data.[25,47] Second, this study included only direct medical costs from the payer's perspective. We did not evaluate non-medical costs, including physical therapy, rehabilitation, orthotic treatments for fracture patients, herbal medicines, and caregiver costs, as well as indirect costs, such as work loss costs. This may have led to an underestimation of health care costs of osteoporosis patients.[34,48] A previous study in Korea reported that social costs of osteoporotic fractures including out-of-pocket payment, long-term care cost, and non-medical costs are more than twice the total national health insurance payment due to osteoporotic fractures between 2007 and 2011.[19] Third, the KNHICD contains electronic medical use records and prescription data for over 99% of the entire population but does not include non-reimbursable services such as medical checkups. For that reason, expensive non-reimbursable services might have been excluded from the analysis, underestimating health care costs. We also did not examine potential covariates such as family history of osteoporotic fractures, bone mineral density, and patient's health behaviors (smoking and alcohol use). Lastly, we demonstrated that medication adherence lowered the occurrence of fractures by 1.3%, since we could not assess long term medication adherence. A previous study showed that long-term therapy of anti-osteoporosis drugs for more than 5 years reduced the chance of experiencing a fracture by 35%.[49,50] A future study based on a longer study period may demonstrate larger savings of health care expenditures due to a greater difference in fracture probability according to medication adherence.

Despite these limitations, the findings of this study has policy implications on saving health care costs and improving quality of care of patients with osteoporosis. Improved osteoporosis medication adherence can prevent osteoporotic fractures and therefore reduce health care costs associated with osteoporotic fractures. Cost savings can be bigger if osteoporosis patients expand to the whole. Our findings highlight the need for self-care of patients, engagement of pharmacists, and education on the importance of improving medication adherence for the prevention of fractures to reduce overall health care burden.

In conclusion, this study identified the presence of fractures, age, and medication adherence as the factors affecting osteoporosis-related health care costs. Moreover, this study estimated that improved medication adherence could save nearly $ 5 million of osteoporosis-related health care costs annually. Persistent pharmacotherapy is recommended to prevent osteoporotic fractures and reduce health care costs in patients with osteoporosis.

Author contributions

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