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Biomedical Journal

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Original Article

Secular trends in incidence of osteoporosis in Taiwan: A nationwide population-based study

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ARTICLE INFO

Article history:

Received 26 November 2016

Accepted 1 August 2018

Available online 3 November 2018

Keywords:

Hip fracture

Incidence

Osteoporosis

Prevalence

ABSTRACT

Background: The present study aimed to assess the changes in trend of osteoporosis among the Taiwanese population from 2001 to 2011.**Methods:** The National Health Insurance Research Database (NHIRD) of Taiwan, containing records from approximately 23 million insures from 2001 to 2011, was analyzed. Insurees aged ≥ 50 years with osteoporosis were identified either from previously documented osteoporotic diagnosis or osteoporosis-related fractures according to Clinical Modification (ICD-9-CM) diagnostic code.**Results:** The prevalence of osteoporosis increased from 17.4% in 2001 to 25.0% in 2011. The prevalence trend increased from 2001 to 2005 and plateaued thereafter. During 2001–2005, the incidence rate of hip fracture held steady from 277 to 281 per 100,000 person-years, and decreased thereafter from 262 to 247 per 100,000 person-years. The overall incidence of osteoporosis declined among patients younger than 84 years from 2001 to 2011, especially after 2005. As compared with 2005 and before, the incidence rate of osteoporosis was significantly decreased since 2006.**Conclusions:** The secular changes of osteoporosis in Taiwan are quite similar to the trend in western countries. It reveals how osteoporosis awareness and policy interventions can affect the prevalence trend of osteoporosis.

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Peer review under responsibility of Chang Gung University.

<https://doi.org/10.1016/j.bj.2018.08.001>

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At a glance of commentary

Scientific background on the subject

Osteoporosis, as a major threat for public health, is the greatest challenge in the growing aging population. Although Asian population is aging rapidly, osteoporosis awareness has improved last decade. Besides aging factor, updated epidemiological studies may evaluate the efficacy of previous preventive program and also provide information for future policymaking.

What this study adds to the field

Despite an increasing number of annual osteoporosis and hip fractures in people aged 50 years and above from 2001 to 2011 in Taiwan, the annual prevalence of osteoporosis significantly decreased from 2006 to 2011. The policymaking for osteoporosis in Taiwan since 2005 is a watershed for the prevalence of osteoporosis.

Osteoporosis has been recognized as a major threat for public health since it may progress without symptoms and is associated with age-related fractures. As health care improves, longer life expectancy is noted in most regions of the world. According to recent world population surveys, the number of older persons is 841 million in 2013, which is four times higher than the 202 million that lived in 1950 [1]. It can be expected that the greatest challenge to the prevalence of osteoporosis is the growing age of the population.

A recent study for the prevalence of osteoporosis in the United States reveals that assuming osteoporosis and low bone mass prevalence remain unchanged, by 2020, the number of adults over age 50 with osteoporosis or low bone mass will grow from approximately 54 million (2010) to 64.4 million and by 2030, that number will increase to 71.2 million (a 29% increase from 2010); it is anticipated that the number of fractures will also grow proportionally [2]. Although the population of Asia is aging rapidly like the United States, osteoporosis awareness has significantly improved during the last decade. Thus, in addition to the aging factor, updated epidemiological studies are needed to evaluate the efficacy of preventive programs for osteoporosis during this decade.

In Taiwan, the number of adults over age 50 years increased from 4.9 million in 2001 to 7.5 million in 2013. The latest study using bone mineral density (BMD) was conducted by the 2005–2008 National Nutrition and Health Survey in Taiwan (NAHSIT) and reported that 38.3% of women and 23.9% of men older than 50 years of age have osteoporosis [3]. Thus, it was estimated that approximately 1.6 million people in Taiwan, including 950,000 women, suffer from osteoporosis. However, most patients with osteoporosis, including those with fragility fractures, were not diagnosed, evaluated or treated, and the prevalence of osteoporosis appears to be rising since the year 2000 [4]. The study of community-dwelling women aged over 50

years in Taiwan revealed that the prevalence of osteoporosis was 12% in 2001 and 14% in 2006 [5,6]. The increasing incidence of osteoporosis has been translated into the fact that Taiwan has the highest prevalence of hip fracture of any country in Asia, which is also higher than the world average [7]. However, there have been great changes in lifestyle, medical and economic status, as well as awareness of osteoporosis in recent years, the actual incidence of osteoporosis and osteoporotic fractures requires further re-evaluation.

This study was therefore designed to estimate the trend in the prevalence and incidence of osteoporosis from 2001 to 2011 in Taiwan, based on data from the Taiwan National Health Insurance Research Database (NHIRD).

Material and methods

Ethics

This study was approved by the Ethical Medicine Committee of Chang Gung Memorial Hospital and supported by the Clinical Monitoring Research Program (CMRP) of Chang Gung Memorial Hospital at Keelung. The study protocol was also reviewed by the National Health Research Institute (NHRI), who consented to the planned analysis of the National Health Insurance Research Database (NHIRD) data.

Data source

The National Health Insurance Research Database (NHIRD) of Taiwan contains records for approximately 23 million insureds, accumulated between January 1996 and December 2011. At the end of 2007, NHIRD included more than 99% of the population enrolled in this insurance program, which is contracted with 97% of clinics and hospitals in Taiwan. Information available in the NHIRD covers all medical services received by each enrollee from 1996 to 2011, as well as the characteristics of the patients, hospitals, and physicians. For administrative use and research, the National Health Research Institute (NHRI), Department of Health, provided the research database, which are de-identified and encrypted before being released for medical research. Osteoporosis, osteoporotic vertebral fractures, hip fractures, and humero-radio-ulnar fractures from the whole population were identified in NHIRD.

Definition of variables

This study searched among the whole population for those aged 50 years and above who were diagnosed with osteoporosis and fractures during the period January 1, 2001 to December 31, 2011. Patients were identified from the database through the presence of the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic code for osteoporosis (733.0, 733.00, 733.01, 733.02, 733.03, 733.09) or for osteoporotic fractures, including vertebral fractures (805.2–805.9), hip fractures (820.x), humeral (812.x), and radio-ulnar fractures (813.x) on their outpatient records or hospitalization discharge records from January 1, 2001 to December 31, 2011. Traumatized patients suffering from traffic accidents were excluded.

Statistical analysis

Prevalence of osteoporosis was defined as the proportion osteoporotic patients (osteoporosis, spine fracture, hip fracture, or humero-radio-ulnar fracture) divided by mid-year population. Incidence rate (per 100,000 person-years) was defined as numbers of occurrence of osteoporosis divided by age-specific mid-year population at-risk (subtracting previous osteoporosis population). To estimate the impact of policy interventions, we defined period 1 as 2001 to 2005 calendar year whereas period 2 2006–2012 calendar year. Next, we conducted multivariate analysis using the Poisson regression modeling to investigate the impact of age, sex, and the calendar year on incidence rate of osteoporosis. The quasi-Poisson method was used to estimate the dispersion parameter. In order to overcome the problem with overdispersion (underestimation of the variance) in Poisson regression, we conducted robust sandwich covariance matrix estimator to estimated standard errors and corresponding p-values. All reported confidence intervals (CIs) and tests were 2-sided with a 5% significance level. All analyses were performed with R software (R Foundation for Statistical Computing, Vienna, Austria). Robust sandwich covariance matrix estimator was analyzed used the distributed package “sandwich”.

Results

Disease burden of osteoporosis in Taiwan

From 2001 to 2011, the population distribution aged 50 years or older increased from 4,708,800 to 6,990,347, an estimated increase from 22.0% to 31.8%. Among this population, the number of females increased from 2,321,799 (22.3%) in 2001 to 3,589,618 (32.8%) in 2011, while the number of males increased from 2,387,001 (21.7%) in 2001 to 3,400,729 (31.7%) in 2011. According to the NHIRD, the estimated number of osteoporotic patients in those aged 50 years or older was 818,033 in 2001 and 1,746,049 in 2011. As seen in Fig. 1A, the prevalence of osteoporosis increased from 17.4% in 2001 to 25.0% in 2011. Compared to the steadily increasing pattern of people aged 50 years or over, the prevalence of osteoporosis increased from 2001 to 2005; however, the trend plateaued thereafter. In women aged 50 years or older, the number of estimated osteoporotic patients increased from 653,072 in 2001 to 1,293,759 in 2011. However, the prevalence of osteoporosis in women markedly increased from 28.1% in 2001 to 36.2% in 2005 but plateaued and even slightly decreased from 36.5% in 2006 to 36.0% in 2011. In men aged 50 years or over, the estimated osteoporotic patients increased from 164,961 in 2001 to

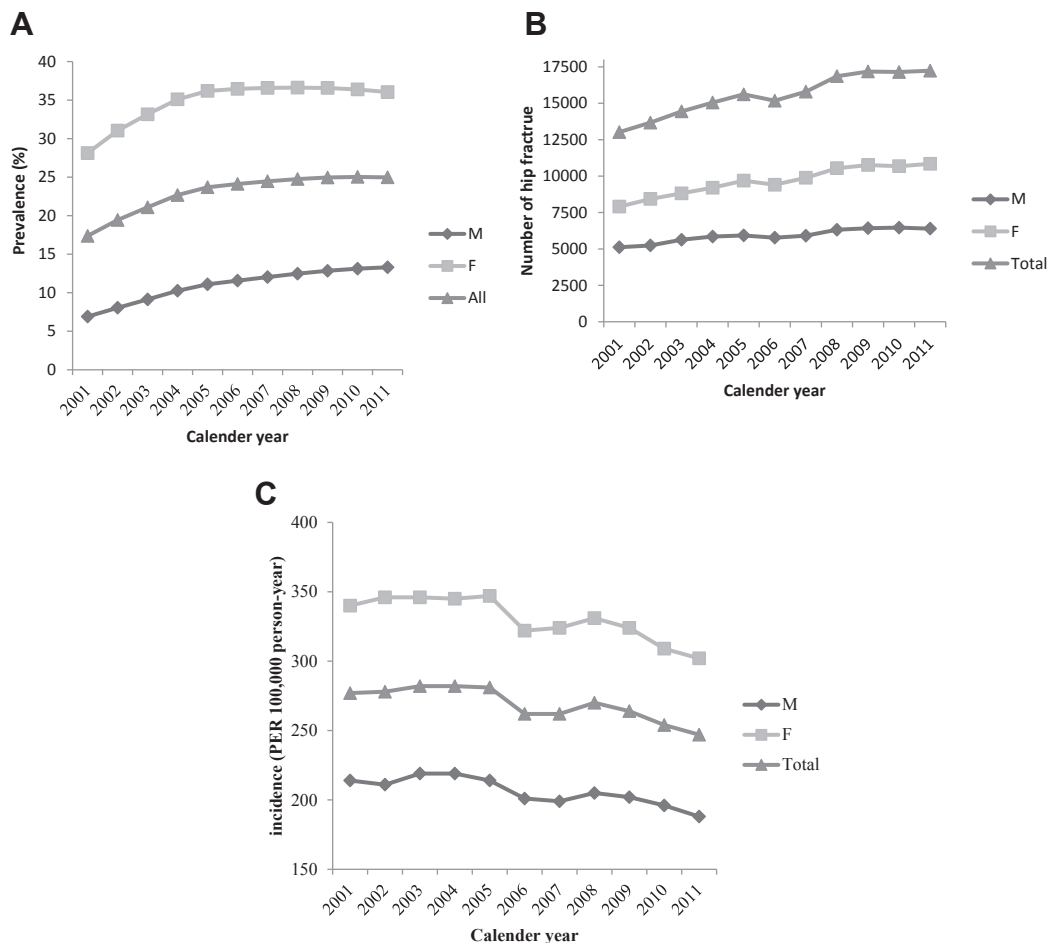


Fig. 1 The prevalence rate of osteoporosis (A) and number (B) and incidence rate (C) of hip fractures based on the Taiwan National Health Insurance Research Database, 2001–2011.

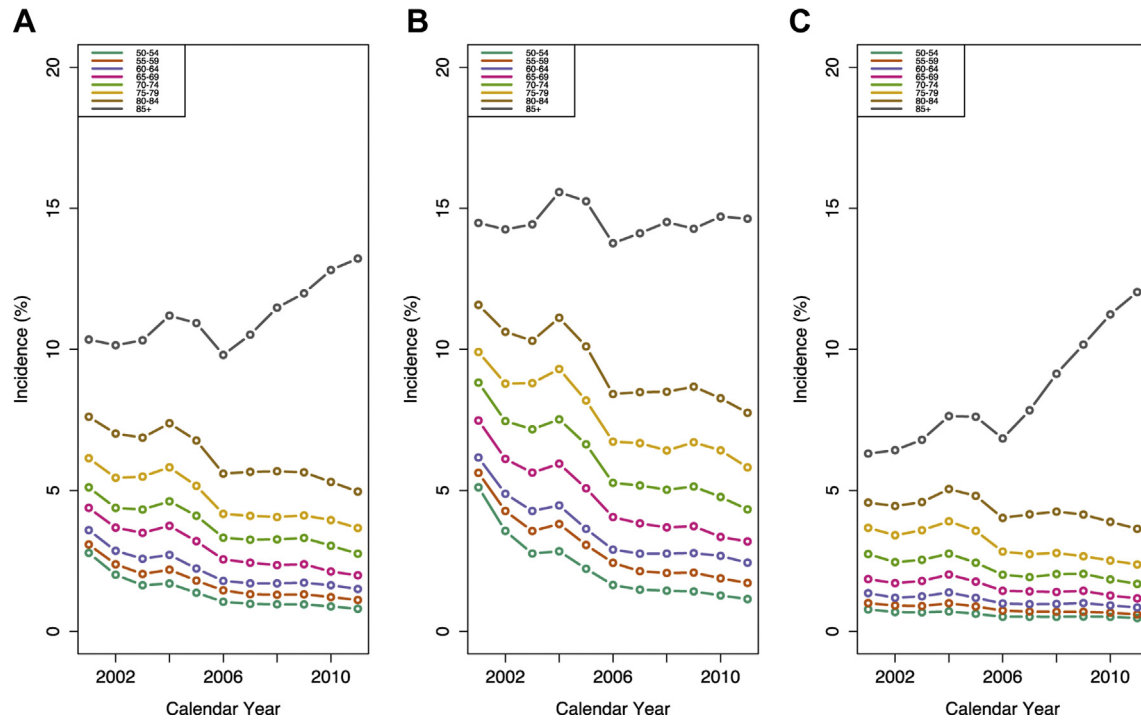


Fig. 2 Annual incidence rate of osteoporosis stratified by age in (A) overall population, (B) females, and (C) males. Adapted from the Taiwan National Health Insurance Research Database, 2001–2011.

452,290 in 2011. Although the prevalence osteoporosis in men still increased from 6.9% in 2001 to 13.3% in 2011, the increasing slope became smooth since 2009.

Although the number of hip fractures increased from 13,021 in 2001 to 17,236 in 2011 (Fig. 1B), the incidence rate of

hip fracture held steady from 277 to 281 per 100,000 person-years during 2001–2005, and decreased thereafter from 262 to 247 per 100,000 person-years during 2006–2011 (Fig. 1C).

Fig. 2 demonstrates the annual incidence of osteoporosis stratified by age. Annual incidence of osteoporosis increased prominently with increasing age. The overall incidence of osteoporosis declined among patients younger than 84 years from 2001 to 2011, especially after 2005 (Fig. 2A). A similar condition was noted in women; furthermore, the incidence plateaued in women aged 85 years or older (Fig. 2B). In contrast, the incidence of osteoporosis still increased in men aged 85 years or older, especially since 2006 (Fig. 2C).

Multivariate analysis of Poisson regression model

Results of multivariate Poisson regression model revealed that age, female gender, and the calendar year are statistically significant with associated incidence rate of osteoporosis (Table 1). It reveals that the annual incidence of osteoporosis increased prominently with increasing age and dominantly in females. In addition, as compared with the incidence of osteoporosis in 2005, significant improvement of the incidence rates was noted since 2006.

The trend of estimated incidence of osteoporosis and the utility of dual-energy x-ray absorptiometry (DXA) in Taiwan (Fig. 3)

The utility of DXA was calculated from the NHIRD. Therefore, it did not include the data of self-paid DXA evaluations. From 2001 to 2011, the average utility of DXA per year for those aged 50 years and above was only 43,419. A surge in utility of DXA

Table 1 Multivariate Poisson regression model stratified by age, calendar year, and sex.

Variable	Rate ratio	95% CI	p-value
Age			
50–54 years	Reference		
55–59 years	1.248446527	1.240109894 1.256713525	<0.0001
60–64 years	1.645262589	1.634276175 1.656322859	<0.0001
65–69 years	2.219540073	2.205159849 2.234014073	<0.0001
70–74 years	2.841408841	2.822999579 2.859938154	<0.0001
75–79 years	3.466342488	3.442507052 3.489993941	<0.0001
> = 80 years	4.91553206	4.882219832 4.949071583	<0.0001
Calendar year			
Year 2005	Reference		
Year 2000	2.043164844	2.02729015 2.059163845	<0.0001
Year 2001	1.443831003	1.431753619 1.455864671	<0.0001
Year 2002	1.180927327	1.170580758 1.191365347	<0.0001
Year 2003	1.108048101	1.098230227 1.117953744	<0.0001
Year 2004	1.199734161	1.189222818 1.210217384	<0.0001
Year 2006	0.743341289	0.736018518 0.750661846	<0.0001
Year 2007	0.702436692	0.69544733 0.709496298	<0.0001
Year 2008	0.692671097	0.685847486 0.699562597	<0.0001
Year 2009	0.712838779	0.705957671 0.719858942	<0.0001
Year 2010	0.643264041	0.636863457 0.649728952	<0.0001
Year 2011	0.564734257	0.558947348 0.57063814	<0.0001
Sex			
Male	Reference		
Female	4.057633817	4.040627493 4.074711717	<0.0001

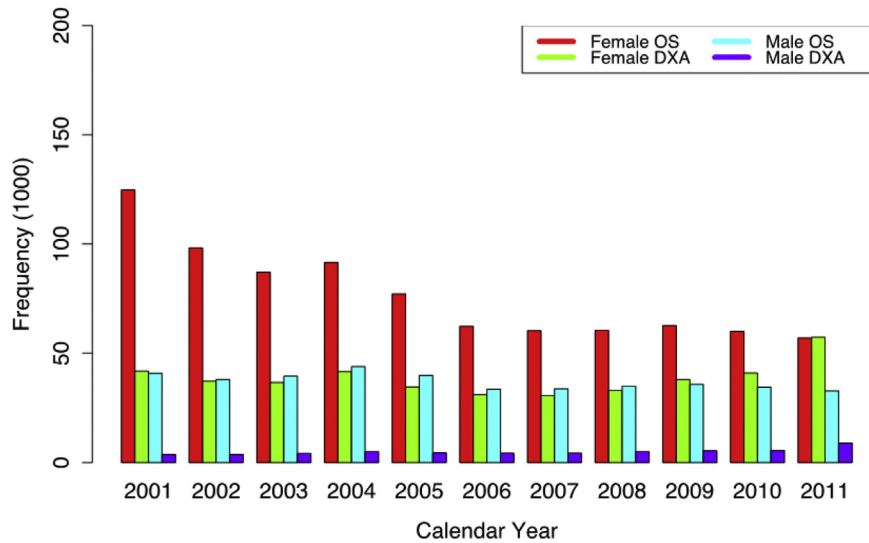


Fig. 3 The trend and comparison of number of osteoporosis and utility of DXA for BMD examination between both genders. Adapted from the Taiwan National Health Insurance Research Database, 2001–2011.

occurred in 2011 (66,319 cases). The utility of DXA in women was greater than those in men. However, as compared to the incidence of osteoporosis, the utility of DXA was lower, especially in men.

Discussion

The results of this study demonstrates that despite an increasing total number of annual osteoporosis and hip fractures in people aged 50 years and above from 2001 to 2011 in Taiwan, there was a significant reduction in the incidence of osteoporosis and hip fracture. When the prevalence of osteoporosis was compared to the demographic changes in the entire Taiwanese population, the annual prevalence of osteoporosis significantly decreased from 2006 to 2011. A similar trend was also noted in the incidence rate of hip fracture. It revealed that in Taiwan, the increase in the total annual number of hip fracture is attributable to the demographic changes in the population, i.e. increased proportion of aged people. However, the improvement in the incidence of osteoporosis plays an important role in the reduction of hip fracture incidence. The aetiologies affecting this trend should be considered for future policymaking to further improve osteoporosis prevention and treatment. To our knowledge, this is the most updated report regarding the epidemiology of osteoporosis, which is affected by socioeconomic changes in Asian countries.

It is well established that osteoporosis is strongly related to advancing age and is more common in women. Thus, when estimating the annual prevalence or incidence of osteoporosis in a population, the population distribution equal to and above 50 years old is the most representational. The present study also reveals that the annual incidence of osteoporosis increased among the geriatric population (≥ 85 years) and the slope increased prominently along with increasing age. In addition, many studies have reported that the prevalence of

osteoporosis was relatively higher in women than in men [8,9]. In the present study, the prevalence and incidence of osteoporosis was 2- to 4-fold higher in women than in men in Taiwan. As the proportion of aged people increases over time, it is inevitable that the total number of people with osteoporosis should increase. In the present study, when the population of people aged 50 years and older in Taiwan increased from 4,708,800 in 2001 to 6,990,347 in 2011, the number of people with osteoporosis was 818,033 in 2001 and progressively increased to 1,746,049 in 2011. In addition, the number of hip fractures also increased from 13,021 in 2001 to 17,236 in 2011.

It seems that this increasing trend cannot be overcome. However, the present study demonstrates that the incidence rate of osteoporosis significantly decreased since 2006, especially in women. A similar condition was also noted in the hip fracture rate trend in the present study. This demonstrates how osteoporosis and fractures are affected mainly by aging but can be controlled. It has been documented that the earliest decreases of hip fracture rate were noted in the United Kingdom starting in the late 1970s and in North America starting in the mid-1980s, followed by Scandinavia where rates started to decline in the early 1990s for Norway and Sweden, and the late 1990s for Denmark and Finland [10]. The present finding reveals that the incidence rate of hip fracture in Taiwan remained constant between 2001 and 2005 and significantly decreased since 2006. Besides being a decade or so behind these Western countries, Taiwan's improving trend is quite similar to theirs. In Asia, most countries, such as China [11], Japan [12], South Korea [13], and Singapore [14], show a continuous increase of hip fracture rate this decade. However, similar findings regarding hip fracture rate as the present study was also reported but only in Hong Kong [15]. The aetiologies of these secular patterns in the aforementioned countries have not been completely clarified. Declared factors include urbanization, birth cohort effects, changes in bone mineral density and body mass index (BMI), osteoporosis medication use, and/or lifestyle interventions, such as

smoking cessation, improvement in nutritional status, and fall prevention [10,15]. We do believe that most of the aforementioned factors are associated to the osteoporosis trend in Taiwan.

From the analysis of the osteoporosis prevalence rate and incidence of osteoporosis and hip fractures in the past decade in Taiwan, policymaking and social efforts seem to have stabilized and even improved the increasing gradient due to the aging population. Taiwan's National Health Insurance (NHI) has provided comprehensive service since 1995 and more than 97% of the population has benefited from the health care coverage [16,17], including anti-osteoporosis medication which has been covered since November 1998. From 1999 to 2010, the total anti-osteoporosis medication expenditure increased 7.2-fold from US\$8.1 million to US\$58.9 million [18]. It should be considered as a factor contributing to the declining incidence of osteoporosis in Taiwan. In 2005, osteoporosis was declared as a government mandated national health priority (NHP) in Taiwan. Since then, programs for osteoporosis prevention and public awareness have been promoted through media and various groups. The efficacy can be proved by research from the National Nutrition and Health Survey in Taiwan (NAHSIT), in which cohort studies demonstrated an increase in calcium intake from food [19], increase in calcium and vitamin D supplement consumption [20], and obesity prevalence [21] when comparing 2005–2008 with 1993–1996. In addition, the survey from the Bureau of Health Promotion, Taiwan, reported a decline in smoking prevalence from 2004 to 2010 [22]. The Taiwanese Osteoporosis Association published the “Clinical practice guidelines for the prevention and treatment of osteoporosis in Taiwan” in 2007 and with support from the Health Promotion Administration, Ministry of Health and Welfare, it was completely revised and published in Chinese in 2011 and in English in 2012 [23]. All of these actions resulted in more physicians being involved in the care of osteoporosis. The present study demonstrates that when compared to the steadily increasing pattern of people aged 50 years and over, the prevalence of osteoporosis also increased from 2001 to 2005, and reached a plateau during 2006–2011. The policymaking for osteoporosis in Taiwan since 2005 is a watershed for the prevalence of osteoporosis. These facts can be confirmed by the significant reduction of hip fracture rates since 2006, as compared with the previous trend from 2001 to 2005.

Dual-energy x-ray absorptiometry (DXA) is used to diagnose osteoporosis in Taiwan. However, reimbursement for DXA use is limited in Taiwan and the data from self-paid DXA evaluations was not included in the present study. Thus, the annual utility of DXA was markedly low in the present study. The progressive decrease in osteoporosis incidence found in this study is encouraging. However, as compared with the utilization of DXA, whether the incidence of osteoporosis may be under-estimated or not should be considered. The DXA testing rate was 7–10 times greater in females than in males. It has been reported that an increase in BMD testing and use of bone-sparing medications have resulted in decreased fracture rates [24]. Although there hasn't been a significant increase of DXA use in both males and females from 2001 to 2010, a much lower frequency in males should be considered as the factor contributing to why the slope reduction of the osteoporosis incidence rate, as well as hip fracture, was not as prominent

as compared with females. A sudden increase in DXA utilization in 2011 was due to a new NHI reimbursement policy, which standardized a requirement of DXA evaluation prior to osteoporosis medication coverage and use for those with one fragility fracture plus a T-score ≤ -2.5 or ≥ 2 fragility fractures plus a T-score ≤ -1 . Although the utilization of DXA has increased since 2011, medication cost also dropped roughly 15% with the reimbursement policy changes. The effects from this policy change should be monitored.

The strength of this study is that NHIRD included more than 99% of the population enrolled in this insurance program. Thus, this population-based study spanning 11 years is representative of the Taiwanese population without selection bias. The limitation of this study is that the data only includes those who have been diagnosed with osteoporosis. However, it does not permit the direct identification of osteoporotic patients, according to the official definition set forth by the WHO, nor those with fractures.

In conclusion, the present study indicates that the incidence rate of osteoporosis and hip fractures has significantly reduced in the Taiwanese population aged 50 years and over. Analyzing the ever-changing attitudes regarding osteoporosis from both policymakers and various associations, it has revealed how both the awareness of osteoporosis and policy interventions affect the efficacy of osteoporosis prevention. The secular trend has primarily been driven by a decrease in the osteoporosis incidence of women. It revealed that additional emphasis should be placed on the osteoporosis problem in Taiwanese males. Since Taiwan is still a high-risk country for osteoporosis, it is imperative for policymakers to further their efforts in implementing public health strategies to prevent osteoporosis and fractures.

Conflicts of interest

The authors declare that they have no conflict of interest.

Acknowledgments

This study was supported by the Medical Research Center (Chang Gung Memorial Hospital, Keelung) and a research grant from the Clinical Monitoring Research Program (CMRPG2D0361, CMRPG2D0362, CMRPG2D0363) of Chang Gung Memorial Hospital, Keelung.

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