Table 5. Association of KL grade at each intervertebral level with low back pain

	L1/2		L2/3		L3/4		L4/5		L5/S		Severest	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Men												
KL=2	1.30	0.92-1.84	0.94	0.65-1.36	1.43	0.98-2.11	1.24	0.82-1.89	1.12	0.75-1.65	1.15	0.70-1.92
KL≥3	1.30	0.79-2.11	1.25	0.80-1.94	1.49	0.96-2.32	1.42	0.97-2.08	1.22	0.82-1.81	1.44	0.89-2.38
Women												
KL=2	1.20	0.91-1.57	0.99	0.75-1.31	0.96	0.71-1.30	1.25	0.82-1.88	1.07	0.73-1.54	0.99	0.69-1.42
KL≥3	1.66	1.23-2.24*	1.74	1.32-2.30*	2.10	1.62-2.72*	1.88	1.48-2.38*	1.60	1.25-2.06*	1.80	1.38-2.37*

The odds ratio was calculated by logistic regression analysis compared with subjects with KL grade 0 or 1 after adjustment for age and BMI. *$p<0.01$
OR = odds ratio, CI = confidence interval

Supplementary Table 1. Association of KL grade at the severest level with low back pain according to age

	Overall		<70		70-79		80≤	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Men								
KL=2	1.15	0.70-1.92	0.94	0.49-1.86	2.78	0.96-9.38	0.70	0.23-2.37
KL≥3	1.44	0.89-2.38	1.37	0.74-2.62	2.50	0.82-8.71	0.80	0.28-2.53
Women								
KL=2	0.99	0.69-1.42	1.11	0.69-1.79	1.18	0.57-2.39	0.59	0.24-1.36
KL≥3	1.80	1.38-2.37†	1.93	1.34-2.80†	1.82	1.03-3.22*	1.39	0.77-2.57

The odds ratio was calculated by logistic regression analysis compared with subjects with KL grade 0 or 1 after adjustment for BMI. *p<0.05, †p<0.01
OR = odds ratio, CI = confidence interval

Supplementary Table 2. Association of KL grade at the severest level with low back pain according to community

	Overall		Urban		Mountainous		Seacoast	
	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Men								
KL=2	1.15	0.70-1.92	1.96	0.87-4.88	0.54	0.25-1.16	1.75	0.48-8.46
KL≥3	1.44	0.89-2.38	2.49	1.16-6.01*	0.68	0.31-1.48	2.24	0.64-10.53
Women								
KL=2	0.99	0.69-1.42	1.15	0.68-1.93	0.72	0.39-1.31	1.21	0.49-2.88
KL≥3	1.80	1.38-2.37†	1.94	1.32-2.88†	1.52	0.93-2.51	1.80	0.94-3.56

The odds ratio was calculated by logistic regression analysis compared with subjects with KL grade 0 or 1 after adjustment for BMI. *p<0.05, †p<0.01
OR = odds ratio, CI = confidence interval

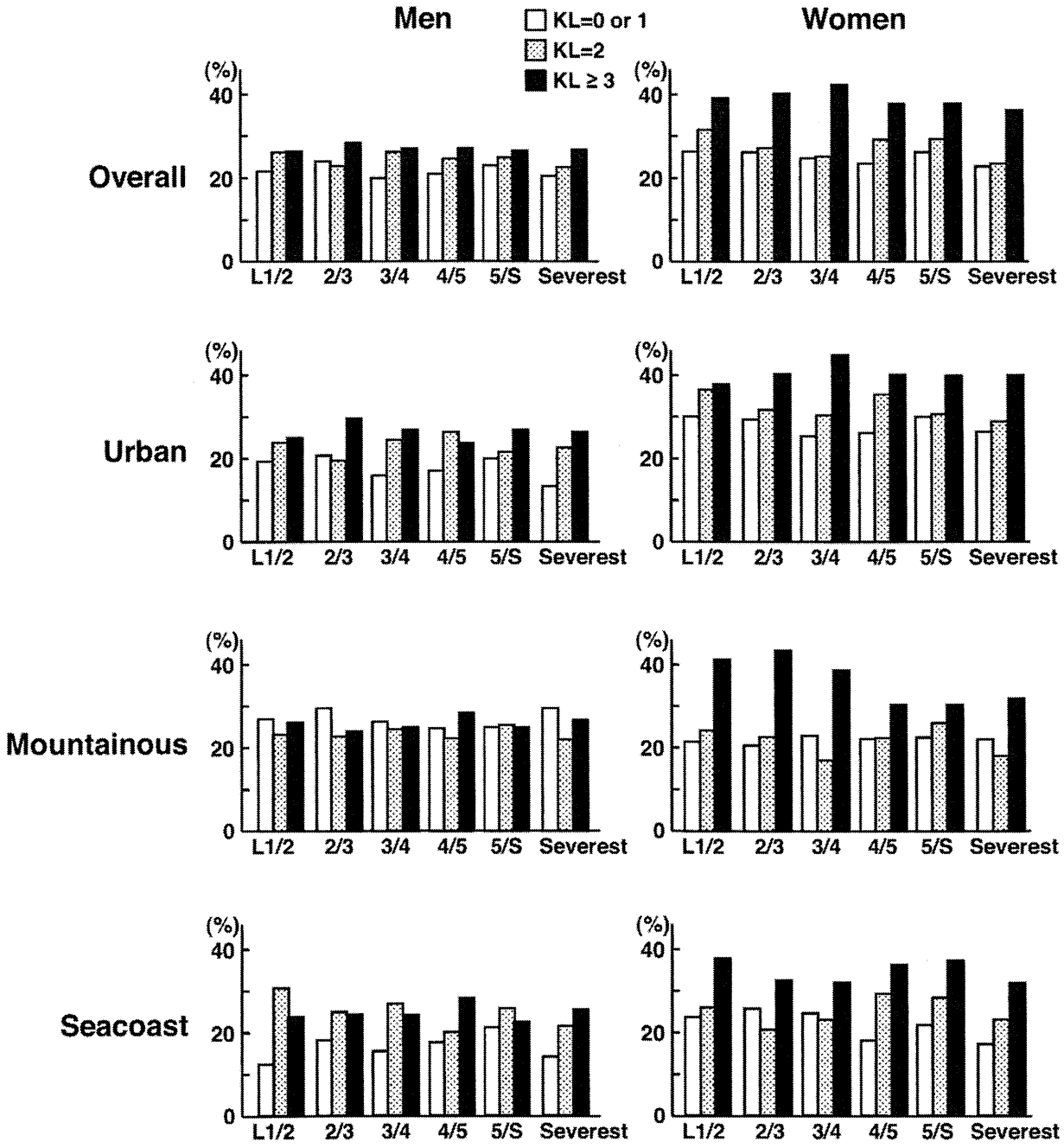

Figure 1

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ORIGINAL ARTICLE

Epidemiology of lumbar osteoporosis and osteoarthritis and their causal relationship—is osteoarthritis a predictor for osteoporosis or vice versa?: The Miyama study

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Abstract
Summary In a 10-year follow-up of a population-based cohort of Japanese subjects, incidences of and causal relationships between osteoporosis (OP) and osteoarthritis (OA) at the lumbar spine were clarified. OP might reduce the risk of subsequent OA at the spine in women, but not in men.
Introduction The aim of this study is to clarify the contribution of osteoarthritis (OA) to osteoporosis (OP) and vice versa.
Methods A population-based, epidemiological study was conducted in a Japanese rural community. From 1,543 participants aged 40–79 years, 200 men and 200 women were selected and followed up for 10 years. Bone mineral density measurements were repeated after 3, 7, and 10 years, and X-rays were repeated after 10 years.
Results The incidence of lumbar OP per 10,000 person-years for persons in their 40s, 50s, 60s, and 70s was 0, 0, 109.5, and 151.1 for men and 124.2, 384.0, 227.3, and 239.5 for women, respectively. The cumulative incidence of lumbar OA over 10 years aged 40–79 years was 25.8% in men and 45.2% in women. Cox's proportional hazards model showed no significant relationship between the presence of lumbar OA at the baseline and incidence of lumbar and femoral neck OP in both genders. A significant relationship was demonstrated between the presence of lumbar OP, not femoral neck OP, at the baseline and cumulative incidence of lumbar OA in women (odds ratio, 0.20; 95% confidence interval, 0.05–0.80; P=0.02).
Conclusion OP in women appears to reduce the future incidence of OA at the lumbar spine.

Keywords Causal relationship · Disc space narrowing · Incidence · Population-based cohort · Prevalence · Risk factors

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Introduction

As the proportion of aging population rapidly increases, the strategy for disease prevention is changing from simply extending life expectancy to extending healthy life expectancy in Japan. Thus, there is an urgent need for the development of methods for preventing musculoskeletal

disorders that impair activities of daily life (ADL) and quality of life (QOL) in the elderly. Osteoporosis (OP) and osteoarthritis (OA) are two major bone and joint health problems among the elderly that cause impairment of ADL and QOL, leading to increased morbidity and mortality. The estimated number of patients with OP in Japan is about 11 million [1], and the prevalence of this disease is the highest among bone metabolic diseases. Hip fracture is the most severe complication of OP, and is ranked third among diseases responsible for bedridden status, according to the National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan [2]. OP also increases mortality rate [3, 4]. The number of patients with OA has rapidly increased, and OA is now ranked second among the causes of disabilities requiring support for ADL in Japan [2].

Some studies have reported an inverse relationship between OP and OA [5–7]. A higher bone mineral density (BMD) in lumbar OA is well documented [8–11]. A decrease in the amount of bone in OP and the formation of bone spurs and increased amounts of bone in OA are evident from BMD measurements; radiography also reveals the opposing features of these two diseases. According to epidemiological studies, risk factors for the two diseases are in opposition. For example, low body weight is a risk factor for OP [12, 13], whereas high body weight represents a risk factor for OA [14, 15].

In contrast to previous opinions, however, recent studies have indicated the association of osteoporotic fractures with lumbar OA. Thus, narrowing of the intervertebral disc space was suggested to increase the risk of osteoporotic vertebral fractures [16, 17]. Although these results imply that lumbar OA should cause osteoporotic fractures, causal relationships between OP itself (not only osteoporotic fractures) and OA at the same site remain obscure. It is uncertain if OA causes OP, OP causes OA, the conditions only coexist, or OP and OA represent concomitant modifications of each other.

To clarify the contribution of OA to OP and vice versa in the general population, a 10-year follow-up study was performed on a cohort established in Miyama village, a rural Japanese community.

Materials and methods

Establishment of baseline cohort

This population-based, epidemiological study was initiated in 1990 in Miyama, a mountain village in Wakayama Prefecture, Japan. As the Miyama cohort has been profiled in detail elsewhere [18, 19], characteristics of the participants are briefly summarized here. A list of all inhabitants born in this village from 1910 to 1949, and therefore aged 40 to 79 years, was compiled from the register of residents as of the end of 1989. A total cohort of 1,543 inhabitants (716 men, 827 women) was identified, and all members of the cohort completed a self-administered, 125-item questionnaire addressing topics such as dietary habits, smoking habits, alcohol consumption, and physical exercise.

A baseline BMD cohort was recruited from the total cohort, consisting of 400 participants divided into four groups each of 50 men and 50 women and stratified into age decades by year of birth (1910–1919, 1920–1929, 1930–1939, and 1940–1949). An interviewer administered a second questionnaire to these 400 participants, covering items of past medical history including questions related to osteoporotic fractures and falls, family history, calcium intake, dietary habits, physical exercise, occupational activities, sun exposure, and, for women, additional questions about reproductive variables. In addition to the baseline questionnaire survey, physical measurements were performed for participants including height (centimeter), body weight (kilogram), arm span (centimeter), bilateral grip strengths (kilogram) and circumstances of both wrists (centimeter), and body mass index (kilogram per square meter). These questionnaire surveys and measurements were repeated on the same 400 participants after 3, 7, and 10 years (1993, 1997, and 2000, respectively).

BMD measurements

The baseline BMD was measured in 1990 by dual energy X-ray absorptiometry (DXA; Lunar DPX, GE Medical Systems, Madison WI, USA), which provided anteroposterior images of lumbar vertebrae (L2–4) and the proximal femur (femoral neck, Ward's triangle, trochanter). These measurements were repeated on the same participants after 3, 7, and 10 years.

To control the precision of DXA, the equipment was checked at every examination in 1990, 1993, 1997, and 2000 using the same phantom. The BMD of the phantom was regulated to 1.270±0.025 g/cm^2 (2%) during all examinations. In addition, the same physician (N.Y.) examined all participants in order to control observer variability. Intra-observer variability of DXA using the Lunar DPX in vitro and in vivo had been measured by the same physician for another study [20], and the coefficient of variance (CV) for L2–4 in vitro was 0.35%. The CV for L2–4, the proximal femur, Ward's triangle, and the trochanter examined in vivo in five male volunteers was 0.61–0.90%, 1.02–2.57%, 1.97–5.45%, and 1.77–4.17%, respectively.

OP was defined based on World Health Organization (WHO) criteria, in which OP was diagnosed mainly by that T-scores of BMD were lower than peak bone mass −2.5 standard deviations (SD) [21]. Mean L2–4 BMD for young adult men and women measured by Lunar DXA in Japan is 1.192 g/cm^2 while the SD is 0.146 g/cm^2 [22]. The present study therefore defined OP at the lumbar spine as L2–4

BMD <0.827 g/cm^2. Mean femoral neck BMD for young adult women measured by Lunar DXA in Japan is reportedly 0.914 g/cm^2 and the SD is 0.119 g/cm^2 [22]. OP at the femoral neck in women was defined as femoral neck BMD <0.617 g/cm^2. We could not define OP at the femoral neck in men because there was no reported mean femoral neck BMD for young adult men measured by Lunar DXA in Japan.

Radiography

The spine of each participant was examined by radiography in 1990. Diagnoses were based on anteroposterior and lateral images of thoracolumbar vertebrae Th5–L5 (initial X-ray survey). Radiography was repeated for individuals who provided consent after 10 years. Lateral images of thoracolumbar vertebrae Th5–L5 were again used for diagnosis (second X-ray survey).

Anteroposterior and lateral radiographs were scored for OA of the lumbar spine in L1–L5 using the Kellgren–Laurence (KL) grade as follows: KL0, normal; KL1, slight osteophytes; KL2, definite osteophytes; KL3, disc space narrowing with large osteophytes; KL4, bone sclerosis, disc space narrowing, and large osteophytes [23]. In the present study, we defined the lumbar spine with disc space narrowing with and without osteophytes as KL3. KL grade was determined at intervertebral spaces from L1/2 to L5/S1, and the highest score among all intervertebral spaces was then identified as the KL grade for that individual. KL scores of all radiographs were determined by a well-experienced orthopedist (S.M.).

Lateral radiographs of the spine were also utilized for the diagnosis of morphometric vertebral fracture (VFx) between Th5 and L5 using the criteria defined by the Japan Bone and Mineral Society as follows: wedged VFx, anterior height/posterior height ≤0.75; biconcave VFx, central height/anterior height or posterior height ≤0.80; compound VFx, anterior/anterior, central/central, and posterior/posterior height of sequential lower or upper vertebra ≤0.80 [24]. Diagnosis of VFx on all radiographs was performed by the same orthopedist (H.K.).

Detection of incidence of OP and OA

Incidence of OP over 10 years was calculated utilizing the results of BMD measurements at the baseline and follow-up studies after 3, 7, and 10 years. It was obtained by the following formula: the total number of incident cases with new OP divided by totaling the person-years of 'population at risk' at baseline. Population at risk refers to a group of participants having the potential of developing OP. Therefore, individuals with OP at the lumbar spine and femoral neck in the initial survey (lumbar spine, 13 men, 63 women; femoral neck, 46 women) were excluded from the numerators and denominators. To calculate the person-years, information on the drop-out (death or movement from the town) of participants was collected every year.

The cumulative incidence of OA over 10 years was calculated utilizing the diagnosis results. Cumulative incidence is simply defined as the ratio of incident cases to the population at risk at the beginning of the observation period. In the present study, we defined incident OA at the lumbar spine as KL grade ≥3 over 10 years in an individual whose KL grade ≤2 at the baseline.

The cumulative incidence of lumbar OA was determined by the following formula: individuals who developed new lumbar OA over 10 years/population at risk at the baseline. Individuals with existing lumbar OA with KL grade ≥3 at the baseline (69 men, 70 women) were excluded from both numerators and denominators.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA Corp., College Station, TX, USA). Differences were tested for significance using ANOVA for comparison among multiple groups and using Scheffe's LSD test for pairs of groups. Significant items were selected, and multiple regression analysis was performed with adjustment of suitable variables.

To clarify the causal relationship of lumbar OA with OP, we applied Cox's proportional hazards model and calculated hazard ratio, in which the incidence of OP was used as an objective factor and lumbar OA at the baseline (1, yes vs. 0, no) was used as an explanatory factor. Next, to clarify the causal relationship of lumbar OA with osteoporotic fractures, we used logistic regression analysis using the cumulative incidence of morphometric VFx over 10 years (1, yes vs. 0, no) as an objective factor and lumbar OA at the baseline (1, yes vs. 0, no) as an explanatory factor, and obtained odds ratio (OR).

Furthermore, logistic regression analysis was used to assess causal relationships of: (a) OP at the lumbar spine and femoral neck with OA; (b) BMD at the lumbar spine L2–4 and femoral neck with OA; and (c) VFx with OA. In the analysis of OP and OA, we calculated the OR using the cumulative incidence of lumbar OA over 10 years (1, yes vs. 0, no) as an objective factor and OP at the baseline (1, yes vs. 0, no) as an explanatory factor. In the analysis of L2–4 and femoral neck BMD and OA, we calculated the OR using the cumulative incidence of lumbar OA over 10 years (1, yes vs. 0, no) as an objective factor and crude BMD values of the L2–4 and femoral neck at the baseline (vs. +1 SD) as an explanatory factor. Finally, in the analysis of VFx and OA, we obtained the OR using the cumulative incidence of lumbar OA over 10 years (1, yes vs. 0, no) as

an objective factor and the presence of VFx at the baseline (1, yes vs. 0, no) as an explanatory factor.

All data were analyzed in each gender group after adjustment for age and weight at the baseline.

Results

Eligible participants

A baseline BMD cohort comprising 400 participants was selected from the total cohort of 1,543 inhabitants. Characteristics of this baseline BMD cohort including anthropometric factors and BMD are shown in Table 1. Height, weight, and the body mass index (BMI; weight (kg)/(height (m))^2) for persons in their 70s were smaller than those for persons in their 40s and 50s for both men and women. BMD at the lumbar spine was significantly lower in men in their 60s and 70s than in their 40s. BMD at the lumbar spine in women tended to be lower with an increase in age and was significantly lower for women in their 50s, 60s, and 70s than in their 40s.

Of the 400 participants in the initial BMD examination, 390 provided written informed consent to participate in the initial X-ray survey (194 men, 196 women; 97.5%). Figure 1 shows the distribution of KL grades at the baseline for participants according to gender. The prevalence of KL grade ≥2 was 81.3% in men and 62.2% in women, and that of KL grade ≥3 was 35.8% in men and 35.7% in women.

Radiographic surveys after 10 years were performed for 299 (137 men, 162 women; 74.8%) of the 400 inhabitants. Data from 101 participants (63 men, 38 women) were unavailable due to the following reasons: 55 participants died (37 men, 18 women); 16 moved (eight men, eight women); 13 were ill (four men, nine women); eight were busy (eight men); five declined to participate any further (five men); and four were absent from the area during the follow-up study (one man, three women).

A comparison of physical characteristics between completers and non-completers of the study has been described elsewhere [25] and is briefly summarized here. The height, weight, and BMI classified in terms of age group and gender were identical between completers and non-completers. In addition, the mean age of female completers in their 70s was significantly lower than that of female non-completers (mean (SD) of completers vs. mean (SD) of non-completers, 71.7 (1.8) years vs. 75.1 (2.8) years; $P<0.001$).

Prevalence of lumbar OP and OA and changes over 10 years

Table 2 shows the prevalence of lumbar OP and OA at the time of baseline measurements. Prevalence of lumbar OP in 1990 (baseline) and 2000 (over 10 years) were both significantly higher in women than men ($P<0.001$), while no significant difference was seen in the prevalence of lumbar OA in 1990 and 2000 between men and women. Prevalence of lumbar OP gradually increased with age in both men and women ($P<0.01$). However, age was not associated with the prevalence of lumbar OA in either men or women except female prevalence of lumbar OA in 2000 ($P<0.01$).

We then examined the prevalence of lumbar OP in the same age group of men and women in 2000, which was compared with that in 1990. Prevalence of lumbar OP in 1990 in the age group of 50–79 years was 8.7% in men

Table 1 Characteristics of the participants at the baseline measurement

Birth cohort	Age strata	*N*	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	BMD (g/cm^2)
Men							
Total	40–79	200	58.9 (3.1)	160.9 (6.9)	57.6 (9.4)	22.1 (2.7)	1.11 (0.21)
1940–1949	40–49	50	44.2 (3.1)	165.6 (6.8)	63.6 (9.3)	23.1 (2.5)	1.19 (0.17)
1930–1939	50–59	50	54.1 (2.7)[a]	161.4 (5.7)[a]	59.5 (8.4)	22.8 (2.5)	1.15 (0.19)
1920–1929	60–69	50	63.4 (2.7)[a,b]	159.9 (5.5)[a]	56.1 (7.6)[a]	21.9 (2.4)	1.03 (0.18)[a,b]
1910–1919	70–79	50	73.9 (3.0)[a,b,c]	156.9 (6.8)[a,b]	51.0 (7.6)[a,b,c]	20.7 (2.7)[a,b]	1.06 (0.25)[a]
Women							
Total	40–79	200	59.3 (11.0)	148.3 (6.0)	48.8 (8.3)	22.1 (2.9)	0.95 (0.23)
1940–1949	40–49	50	44.7 (3.0)	152.4 (4.7)	53.2 (8.4)	22.8 (2.8)	1.18 (0.16)
1930–1939	50–59	50	54.8 (2.5)[a]	149.8 (5.3)	50.6 (7.4)	22.5 (2.7)	0.99 (0.18)[a]
1920–1929	60–69	50	64.3 (2.7)[a,b]	147.2 (5.0)[a]	47.1 (7.2)[a]	21.7 (3.1)	0.84 (0.19)[a,b]
1910–1919	70–79	50	73.3 (2.9)[a,b,c]	143.9 (5.7)[a,b,c]	44.5 (7.5)[a,b]	21.4 (2.9)[a,b]	0.78 (0.17)[a,b]

Data are means±SD

BMI body mass index, *BMD* bone mineral density

[a] Significantly different from values of the birth cohort group born in 1940–1949

[b] Significantly different from values of the birth cohort group born in 1930–1939

[c] Significantly different from values of the birth cohort group born in 1920–1929

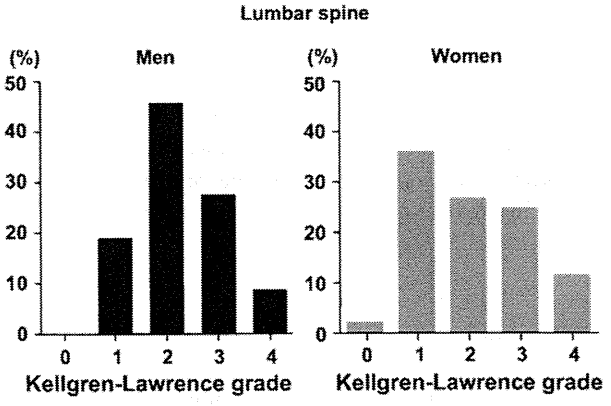

Fig. 1 Distribution of Kellgren–Lawrence grades at the lumbar spine by gender at the baseline in the Miyama population

and 42.0% in women and that in 2000 was 7.8% in men and 37.0% in women. Prevalence of lumbar OP in 2000 in the age group of 50–79 years tended to decrease compared with that in 1990 in both men and women, but no significant differences were identified (men $P=0.81$, women $P=0.39$).

Similarly, the prevalence of lumbar OA between the same age group of men and women in 2000 was compared with that in 1990. Prevalence in the age group of 50–79 years was 34.0% in men and 38.5% in women in 1990 and that in the same age group was 51.0% in men and 48.9% in women in 2000. Prevalence of lumbar OA in 2000 in the age group of 50–79 years increased in men and women compared with that in 1990, with significant differences in men (men $P<0.01$, women $P=0.08$).

Incidence of OP and cumulative incidence of OA at the lumbar spine

Figure 2 shows the incidence of lumbar OP in male and female participants of the cohort over 10 years. Incidence in men and women aged 40–79 years was 55.6 and 231.7 per 10,000 person-years, respectively. This means the annual incidence of lumbar OP among women is more than four times that of men.

The incidence of lumbar OP in men in their 40s, 50s, 60s, and 70s was 0, 0, 109.5, and 151.1 per 10,000 person-years, respectively, with the highest peak in the oldest group. In contrast, the incidence of lumbar OP in women in their 40s, 50s, 60s, and 70s was 124.2, 384.0, 227.3, and 239.5 per 10,000 person-years, respectively, with the highest peak for women in their 50s, the peri- and early postmenopausal periods, and another mild peak in the oldest group (Fig. 2). Incidence of OP at the femoral neck in women in their 40s, 50s, 60s, and 70s was 80.5, 221.9, 205.8, and 338.2 per 10,000 person-years, respectively, with the highest peak in the oldest age group and the second peak in their 50s.

The cumulative incidence of lumbar OA over 10 years aged 40–79 years was 25.8% in men and 45.2% in women. That for persons in their 40s, 50s, 60s, and 70s was 18.5%, 20.0%, 27.6%, and 37.9% for men and 37.1%, 53.6%, 48.4%, and 43.8% for women, respectively (Fig. 3). The cumulative incidence of lumbar OA tended to increase with age in men but not in women. The peak of the cumulative incidence of lumbar OA as well as that of lumbar OP in women was shown in the perimenopausal stratum. The cumulative incidence of lumbar OA was significantly higher in women than in men ($P<0.05$).

Table 2 Change of prevalence of osteoporosis and osteoarthritis at the lumbar spine over 10 years

Birth cohort	Baseline study					Follow-up study over 10 years			
	Age strata (years)	Number of participants (BMD)	Number of participants (X-ray)	Prevalence (%)		Age strata (years)	Number of participants	Prevalence (%)	
				Osteoporosis	Osteoarthritis[a]			Osteoporosis	Osteoarthritis[a]
Men									
Total	40–79	200	194	6.5	35.8	50–89	137	11.7	55.4
1940–1949	40–49	50	47	0.0	41.3	50–59	36	0.0	51.4
1930–1939	50–59	50	48	0.0	23.9	60–69	41	0.0	43.3
1920–1929	60–69	50	50	12.0	39.6	70–79	38	23.7	57.6
1910–1919	70–79	50	49	14.0	38.3	80–89	22	31.8	68.8
Women									
Total	40–79	200	196	31.5	35.7	50–89	162	42.6	54.1
1940–1949	40–49	50	48	0.0	27.1	50–59	49	12.2	35.4
1930–1939	50–59	50	49	18.0	42.9	60–69	46	45.7	50.0
1920–1929	60–69	50	50	48.0	38.0	70–79	40	57.5	64.1
1910–1919	70–79	50	49	60.0	34.7	80–89	27	70.4	83.3

[a] Osteoarthritis at the lumbar spine was defined as the KL grade ≥3

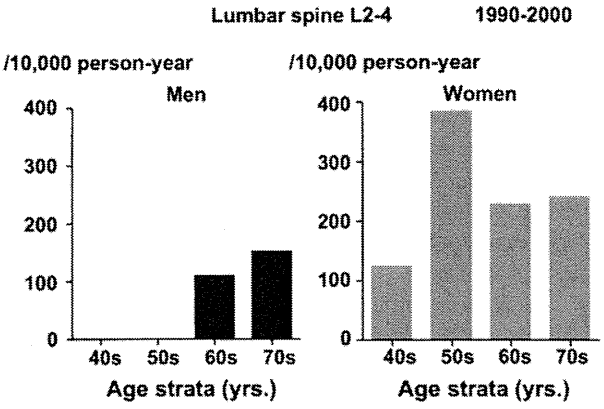

Fig. 2 Incidence of osteoporosis at the lumbar spine over 10 years by age group and gender

Causal relationship between OP and OA

The causal relationships between lumbar OA and OP, BMD, and VFx are summarized in Table 3.

First, the contribution of OA to OP was assessed. Cox's proportional hazard model showed no significant relationship between the presence of lumbar OA at the baseline and incidence of lumbar and femoral neck OP (lumbar OP, men $P=0.71$, women $P=0.79$; femoral neck OP, women $P=0.52$). Then, the association between lumbar OA and the cumulative incidence of VFx was determined by logistic regression analysis. As reported elsewhere, the cumulative incidence of VFx including subjects with previous VFx in their 40s, 50s, 60s, and 70s was 2.1%, 8.3%, 10.0%, and 12.2% for men and 2.1%, 6.1%, 18.0%, and 22.0% for women, respectively [26]. There was no significant relationship between the presence of lumbar OA at the baseline and incidence of VFx in men and women (men $P=0.21$, women $P=0.64$).

Secondly, the contribution of OP to OA was examined (Table 3). A significant relationship existed between the presence of lumbar OP at the baseline and cumulative incidence of lumbar OA in women ($P<0.05$) but not in men ($P=0.07$). Similarly, there was significant association between lumbar BMD at the baseline and the cumulative incidence of lumbar OA in women (vs. +1 SD, $P<0.05$) but not in men ($P=0.25$). No significant association was identified between femoral neck OP and BMD at the baseline and cumulative incidence of lumbar OA in men and women (OP at femoral neck, women $P=0.32$; BMD at femoral neck, vs. +1 SD, men $P=0.23$, women $P=0.77$). These results indicate that the presence of lumbar OP at the baseline would prevent the occurrence of lumbar OA, and conversely, high lumbar BMD would accelerate the progression of lumbar OA in women.

Finally, the association between the presence of VFx at the baseline and cumulative incidence of lumbar OA was assessed. As shown elsewhere, the prevalence of VFx in the present cohort among men in their 40s, 50s, 60s, and 70s was 4.3%, 14.6%, 22.0%, and 24.5% and that among women was 2.1%, 10.2%, 14.0%, and 44.9%, respectively [27]. Logistic regression analysis showed that there was no significant relationship between the presence of previous VFx and the incidence of lumbar OA in men and women (men $P=0.72$, women $P=0.91$; Table 3).

Discussion

The present study is a 10-year follow-up study of a population-based cohort of Japanese middle-aged people and elderly who were assessed for lumbar OP and OA. We clarified the prevalence of lumbar OP and OA and its trend of changes as well as the incidence of lumbar OP and cumulative incidence of lumbar OA. As for causal relationship, the presence of lumbar OA did not increase the risk of lumbar OP in both genders. However, the presence of lumbar OP significantly reduced the risk of lumbar OA, and high lumbar BMD values would accelerate the occurrence of lumbar OA over 10 years in women, while the presence of OP and BMD at the femoral neck did not influence the occurrence of lumbar OA.

The prevalence of lumbar OP in both 1990 and 2000 was significantly higher in women than in men ($P<0.001$) and gradually increased with age. Regarding the trend of changes in the prevalence of lumbar OP between 1990 and 2000 in same-age groups, no significant difference was shown in both men and women. We previously reported that both men and women in later birth cohorts showed higher BMDs in their middle age in this cohort [25]. However, we failed to clarify any significant decrease in the prevalence of lumbar OP in same-age groups of younger birth cohorts in the present study, although the prevalence

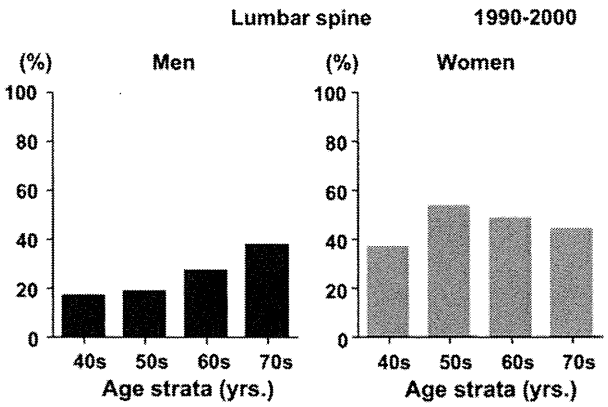

Fig. 3 Cumulative incidence of osteoarthritis at the lumbar spine over 10 years by age group and gender

Table 3 Causal relationship between osteoporosis (OP) and osteoarthritis (OA)

Baseline	Outcome	Reference	Gender	Risk ratio	95% CI	*P* value
Contribution of OA to OP						
OA at lumbar spine	Incidence of OP at lumbar spine	Yes/No	Men	HR 0.76	0.19–3.15	0.71
			Women	HR 0.90	0.40–1.99	0.79
OA at lumbar spine	Incidence of OP at femoral neck	Yes/No	Women	HR 0.74	0.30–1.84	0.52
OA at lumbar spine	Cumulative incidence of VFx	Yes/No	Men	OR 0.41	0.10–1.64	0.21
			Women	OR 1.27	0.46–3.47	0.64
Contribution of OP to OA						
OP at lumbar spine	Cumulative Incidence of OA at lumbar spine	Yes/No	Men	OR 8.68	0.82–92.3	0.07
			Women	OR 0.20	0.05–0.80	0.02
OP at femoral neck	Cumulative Incidence of OA at lumbar spine	Yes/No	Women	OR 0.52	0.14–1.89	0.32
BMD at lumbar spine	Cumulative incidence of OA at lumbar spine	+1 SD	Men	OR 0.80	0.54–1.17	0.25
			Women	OR 1.87	1.16–2.99	0.01
BMD at femoral neck	Cumulative incidence of OA at lumbar spine	+1 SD	Men	OR 0.80	0.56–1.15	0.23
			Women	OR 0.92	0.53–1.60	0.77
VFx	Cumulative incidence of OA at lumbar spine	Yes/No	Men	OR 0.79	0.21–2.95	0.72
			Women	OR 0.91	0.19–4.36	0.91

All analyses were adjusted for age and weight at the baseline
OA at lumbar spine was defined as the KL grade ≥3
BMD bone mineral density, *VFx* vertebral fracture, *SD* standard deviation, *HR* hazard ratio, *OR* odds ratio, *CI* confidence interval

of lumbar OP in 2000 tended to be lower than that in 1990 for all identical age groups in women. This might be explained by the effect of the time gap between the decrease in BMD and occurrence of lumbar OP. Although higher BMD was observed in the middle-aged group, this might not influence epidemiological indices of lumbar OP such as prevalence within only a 10-year span. As participants become old enough to be expected to have lumbar OP, its prevalence is expected to decrease.

Contrary to lumbar OP, the prevalence of lumbar OA was not significantly different between men and women in 1990 and 2000, and age was not associated with the prevalence of lumbar OA except for women in 2000 ($P<0.01$). Regarding the trend of changes in the prevalence of lumbar OA between 1990 and 2000 in same-age groups, the prevalence of lumbar OA in 2000 was higher than that in 1990 in both men and women, with significance in men (men $P<0.01$, women $P=0.08$). Concerning the association between age and lumbar OA, Lawrence found that the radiological prevalence of disc degeneration in the lumbar spine in the age group of 35–45 years increased with age [28]. O'Neill et al. reported that the frequency of vertebral osteophytes increased with age [29]. We previously compared the prevalence of lumbar OA determined by KL grade ≥3 in British and Japanese populations and reported that prevalence was higher in Britain than in Japan [15]. The difference may be partly explained by ethnic variation.

To the best of our knowledge, the present study represents the first report on the incidence of lumbar OP in Japan. If the incidence obtained in this study is generalized to the current Japanese population in the age group of 40–79 years, 970,000 new cases of lumbar OP (160,000 men, 810,000 women) are estimated to occur annually. When classified by age, the incidence of lumbar OP in women was the highest in their 50s, followed by those in their 70s. We previously reported that the rate of change in lumbar spine BMD in women in the present population was the highest in their 50s [12, 25] and is related to the decrease in female hormones [30]. The present finding that the incidence of lumbar OP was the highest among women in their 50s suggests that the incidence of lumbar OP is closely related to the menstrual status, particularly menopause, and rate of change in lumbar spine BMD. Since more than 2.2% of women are estimated to develop lumbar OP annually in their 60s and 70s (ages at which the effects of menopause are thought to be attenuated), measures for preventing lumbar OP among the elderly as well as women during perimenopause are urgently required. The annual incidence of lumbar OP among men in their 60s and 70s was more than 1.0%. Although this incidence is lower than that among women, it is estimated that 160,000 male cases occur annually as previously mentioned, which nevertheless should not be ignored. Predictors for finding early and/or potential lumbar OP in both women and elderly men need to be established immediately.

In addition, we determined the cumulative incidence of lumbar OA with disc space narrowing for the first time in Japan. The 10-year cumulative incidence of lumbar OA with KL grade ≥3 tended to increase with age in men, but not in women, and it was higher in women than in men. Few reports have described the incidence of lumbar OA in

population-based cohorts. Hassett et al. showed that the progression rates for anterior osteophytes and disc space narrowing were 4% and 3% per year, respectively, among female participants in the Chingford study [31], which was approximately similar to the results of the present study. However, since epidemiological indices such as prevalence and incidence are highly dependent on the definition of OA, we cannot compare our results directly with those of other studies. For example, we defined lumbar OA as KL grade ≥3, which shows disc space narrowing with or without osteophytes, while the Chingford study determined lumbar OA based on the grading system of osteophytes and disc space narrowing reported by Lane et al. [32]. Since few reports have investigated the incidence of lumbar OA in the general population, further studies are needed to verify ethnic and geographical differences in the incidence of lumbar OA. When classified by age, the cumulative incidence of lumbar OA and OP was highest in women in their 50s during the early postmenopausal period. Therefore, it might be suggested that endogenous sex steroids play a role in the occurrence or progression of lumbar OA in women.

In some population-based prospective studies, OA of extremities was reported to increase the risk of osteoporotic fractures. In the Rotterdam study, knee OA increased the risk of vertebral and non-vertebral fractures [33]. Arden et al. reported that patients with knee OA and knee pain have an increased risk of hip and other non-vertebral fractures, which was not explained by the increased risk of falls [34]. Intervertebral disc space narrowing was found to increase the risk of VFx in the OFELY study [16, 17]. These findings suggest that OA is involved in the onset of fractures resulting from OP. Conversely, Roux et al. reported that intervertebral disc space narrowing and osteophytes decreased the prevalence of VFx in postmenopausal women with OP [35]. In the present study, there was no significant association between the presence of lumbar OA and future occurrence of lumbar OP and VFx. Lumbar OP is diagnosed by lumbar BMD (the value of which is easily affected by osteophytes and sclerosis of vertebrae and facets and the calcification of abdominal aorta [36]), which can artifactually increase BMD. Therefore, lumbar BMD might not be a good surrogate index of OP. As this is the first report about the causal relationship of lumbar OA and OP in the Japanese population, the difference might be partly due to the ethnic variation between Western and Oriental populations. Further studies are necessary to confirm the causal relationship of OA and OP in Japan and other countries.

Regarding the contribution of OP to OA, we elucidated that OP at the lumbar spine reduced the risk for the progression of lumbar OA in women while high BMD at the lumbar spine accelerated this progression. Zhang et al. found that higher BMD at the hip was associated with prevalent and incident knee OA in older women in the Framingham study [37]. They also found that increased BMD over the follow-up period indicated a high risk of incident knee OA [37]. Hart et al. confirmed that, for women that developed incident knee OA, BMD was higher in the Chingford study [38]. Although these studies reported findings on the BMD and OA at extremities, not the spinal OP and OA, our results were almost similar to those of the above-mentioned cohort studies. Further prospective cohort studies with a larger sample size and longer observational periods are required to conclude the causal relationship of OP and OA.

Contrary to lumbar OP, no causal relationship was observed between OP or BMD at the femoral neck and cumulative incidence of lumbar OA. This might be because OP was diagnosed at different sites, which might have diluted the influence of OA occurrence. This hypothesis will be clarified in a study of the association between OP at the femoral neck and hip OA.

The presence of VFx at baseline showed no association with occurrence of lumbar OA. The prevalence of VFx includes various causes, and not all VFx were caused by OP. The geographic area in which the present cohort was established is mountainous, and a significant number of male subjects worked in the forestry industry and had experienced falls from trees or down slopes accidentally. In addition, most participants with previous VFx at the baseline were old and did not complete the 10-year follow-up. This survival bias might have influenced the evaluation of the influences of VFx on occurrence of OA.

The inverse causal relationship between lumbar OP and OA was only observed in women, not in men. These gender differences might be explained partly by differences in the incidence of lumbar OP. The incidence in men in the present study might be insufficient to detect the causal relationship. Alternatively, differences in gender-dependent factors such as endogenous sex steroids could influence the association of OP and OA.

There are several limitations in this study. The primary limitation is that the cohort comprised a relatively small number of participants. We were able to follow male and female residents with confirmed regional representativeness for 10 years with a high participation rate of 74.8%. However, 101 participants were lost in the follow-up study during the 10 years. The main reason for them dropping out of the study was death. The mean age of women completers of the age group 70-79 was significantly younger than that of drop-outs. Therefore, the prevalence of lumbar OP and cumulative incidence of lumbar OA in this age group might be underestimated due to the effects of survival bias. A secondary limitation is related to the definition of lumbar OA. Cumulative incidence as used in the present study was

detected by dividing the number of individuals who developed new lumbar OA by the number of participants in the follow-up study. Individuals with previous lumbar OA were excluded from both the numerators and denominators. In this formula, we excluded 69 male and 70 female participants with lumbar OA at the baseline to obtain the incidence of the first lumbar OA, which might reduce the total number of population at risk and cause a decrease in statistical power. Our result regarding lumbar OA incidence in the present study might need to be confirmed in larger population-based cohorts.

With the goal of elucidating the environmental and genetic background of bone and joint diseases represented by OA and OP, we established larger scale cohorts based on the present cohort, called Research on Osteoarthritis/Osteoporosis Against Disability (ROAD), and have already started the follow-up study [39]. This enlarged population-based cohort study may confirm the consistency of epidemiological trends for OP and OA and clarify the causal relationship between these two major bone and joint diseases.

Conclusion

Based on observations from a population-based cohort over a 10-year period, the estimated incidence of OP at the L2–4 level of the lumbar spine per 10,000 person-years for men in their 40s, 50s, 60s, and 70s was 0, 0, 109.5, and 151.1 and that for women was 124.2, 384.0, 227.3, and 239.5, respectively. The cumulative incidence of lumbar OA over 10 years for men in their 40s, 50s, 60s, and 70s was 18.5%, 20.0%, 27.6%, and 37.9% for men and 37.1%, 53.6%, 48.4%, and 43.8% for women, respectively. Cox's proportional hazards model showed no significant relationship between the presence of lumbar OA at the baseline and future incidence of lumbar and femoral neck OP. A significant relationship existed between the presence of lumbar OP at the baseline and future incidence of lumbar OA in women (odds ratio 0.20, 95% confidence interval 0.05–0.80, $P<0.05$). It may be suggested that the presence of OA does not increase the risk of incident OP in both genders and that the presence of OP reduces the risk of incident OA at the spine in women.

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Conflicts of interest None.

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ORIGINAL ARTICLE

Prevalence of knee osteoarthritis, lumbar spondylosis, and osteoporosis in Japanese men and women: the research on osteoarthritis/osteoporosis against disability study

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Abstract Musculoskeletal diseases, especially osteoarthritis (OA) and osteoporosis (OP), impair activities of daily life (ADL) and quality of life (QOL) in the elderly. Although preventive strategies for these diseases are urgently required in an aging society, epidemiological data on these diseases are scant. To clarify the prevalence of knee osteoarthritis (KOA), lumbar spondylosis (LS), and osteoporosis (OP) in Japan, and estimate the number of people with these diseases, we started a large-scale population-based cohort study entitled research on osteoarthritis/osteoporosis against disability (ROAD) in 2005. This study involved the collection of clinical information from three cohorts composed of participants located in urban, mountainous, and coastal areas. KOA and LS were radiographically defined as a grade of ≥2 by the Kellgren–Lawrence scale; OP was defined by the criteria of the Japanese Society for Bone and Mineral Research. The 3,040 participants in total were divided into six groups based on their age: ≤39, 40–49, 50–59, 60–69, 70–79, and ≥80 years. The prevalence of KOA in the age groups ≤39, 40–49, 50–59, 60–69, 70–79, and ≥80 years 0, 9.1, 24.3, 35.2, 48.2, and 51.6%, respectively, in men, and the prevalence in women of the same age groups was 3.2, 11.4, 30.3, 57.1, 71.9, and 80.7%, respectively. With respect to the age groups, the prevalence of LS was 14.3, 45.5, 72.9, 74.6, 85.3, and 90.1% in men, and 9.7, 28.6, 41.7, 55.4, 75.1, and 78.2% in women, respectively. Data of the prevalence of OP at the lumbar spine and femoral neck were also obtained. The estimated number of patients with KOA, LS, and L2–L4 and femoral neck OP in Japan was approximately 25, 38, 6.4, and 11 million, respectively. In summary, we estimated the prevalence of OA and OP, and the number of people affected with these diseases in Japan. The ROAD study will elucidate epidemiological evidence concerning determinants of bone and joint disease.

Keywords Epidemiology · Prevalence · Establishment of population-based cohort · Osteoarthritis · Osteoporosis

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Introduction

Osteoarthritis (OA) and osteoporosis (OP) are major public health problems in the elderly that affect their

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activities of daily life (ADL) and quality of life (QOL), leading to increased morbidity and mortality. The number of patients with OA increases with the age of the population. According to the recent National Livelihood Survey of the Ministry of Health, Labour and Welfare in Japan, OA is ranked fourth, and falls and osteoporotic fractures are ranked fifth, among the diseases causing disabilities that subsequently require support for activities related to daily living [1]. The authors of the present study as well as other authors have reported increased mortality following osteoporotic fractures at the hip and other sites [2, 3].

Because of the increasing proportion of the aging population in Japan, there is an urgent need for a comprehensive and evidence-based prevention strategy for musculoskeletal diseases, including OA and OP. However, few prospective longitudinal studies have been undertaken, and little information is available regarding the prevalence and incidence of OA and lumbar spondylosis (LS), as well as pain and disability, in the Japanese population [4–7]. Only the estimated number of patients with knee osteoarthritis (KOA) and LS is not known.

More population-based prospective studies have been performed for OP than for OA [8–12]. Japanese guidelines for the prevention and treatment of OP, on the basis of evidence obtained from studies conducted with Japanese subjects, were published in 2006 [13]; however, many epidemiological indices of OP still remain to be clarified. For instance, there is insufficient evidence regarding the risks relating to the incidence of OP, osteoporotic vertebral fractures, and bone loss. Further, data on the number of patients with OP were last reported in 1999 [14], thus necessitating an analysis based on the current prevalence of OP. It is difficult to design rational clinical and public health approaches for the diagnosis, evaluation, and prevention of OA and OP without such epidemiological data.

The research on osteoarthritis/osteoporosis against disability (ROAD) study is a prospective cohort study that aims to elucidate the environmental and genetic background for bone and joint diseases, especially OA and OP; it is designed to examine the extent to which risk factors for these diseases are related to clinical features, laboratory and radiographic findings, bone mass and bone geometry, lifestyle, nutritional factors, anthropometric and neuromuscular measures, and fall propensity, as well as to determine how these diseases affect ADL and QOL in Japanese men and women.

Here, the prevalence of KOA, LS, and OP is clarified, and the number of patients with these diseases in Japan is estimated by analyzing the baseline data of the ROAD study.

Participants and methods

Study population

A complete baseline database was established that included the clinical and genomic information of 3,040 inhabitants (1,061 men and 1,979 women) with a mean age of 70.3 [standard deviation (SD), 11.0] years, 71.0 (SD, 10.7) years in men and 69.9 (SD, 11.2) years in women. These subjects were recruited from listings of resident registrations in three communities with different characteristics: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in Taiji, Wakayama (Fig. 1).

Itabashi Ward, an urban community located in the eastern Tokyo (area, 32 km^2) has a population of 529,400, and the proportion of aged people in this region, defined as the number of residents who were 65 years old or older ($\geq$65) divided by the total population, is 19.1%. The percentage of the population having jobs in primary industries (agriculture, forestry, fishing, or mining), secondary industries (manufacturing and construction), and in tertiary industries (service industries) is 0.1, 25, and 75%, respectively [15]. Hidakagawa Town, a rural mountainous community located in the center of Wakayama (area, 330 km^2), has a population of 11,300 and 30.5% of the inhabitants are $\geq$65 years old. The percentages of workers with jobs in the primary, secondary, and tertiary industries are 29, 24 and 47%, respectively [15]. Taiji Town, a rural coastal community located south of Wakayama (area, 6 km^2), has a population of 3,500, with 34.9% of inhabitants $\geq$65 years old; the percentages of workers with jobs in primary, secondary, and tertiary industries are 13, 18, and 69%, respectively [15].

Residents of these three urban, mountainous, and coastal regions were recruited from the resident-registration lists of the relevant regions. Participants in the urban region, aged $\geq$60 years, were recruited from among those of a randomly selected cohort study from the previously established Itabashi Ward resident registration database [16]. The

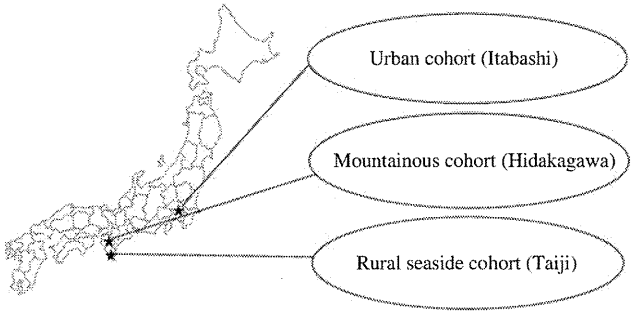

Fig. 1 Location of the three cohorts with different characteristics in Japan

response rate was 75.6%. Participants in the mountainous and coastal regions, aged ≥40 years, were recruited from listings of resident registration. However, those inhabitants aged <60 years in the urban area and <40 years in the mountainous and coastal areas who were interested in participating in the study were invited to be examined.

In addition to residence in the communities as outlined above, the inclusion criteria were as follows: the patient had to (1) be able to walk to the clinic at which the survey was performed, (2) provide self-reported data, and (3) understand and sign an informed consent form. No other exclusion criteria were used.

Participants were enrolled and the initial baseline examinations were completed over a 1.5-year period from October 2005 through March 2007. All participants provided written informed consent. The study was conducted with the approval of the ethics committees of the University of Tokyo (nos. 1264 and 1326) and the Tokyo Metropolitan Institute of Gerontology (no. 5). Careful consideration was given to ensure a safe experience for participants during their examinations and any other study procedures.

Radiographic assessment

Plain radiographs of the lumbar spine in the anteroposterior and lateral views and bilateral knees in the anteroposterior view with weight-bearing and foot map positioning were obtained. The severity of radiographic OA was determined according to Kellgren–Lawrence (KL) grading as follows [17]: KL0, normal; KL1, slight osteophytes; KL2, definite osteophytes; KL3, joint or intervertebral space narrowing with large osteophytes; KL4, bone sclerosis, joint or intervertebral space narrowing, and large osteophytes. In the ROAD study, participants were classified into KL3 if they had joint or intervertebral space narrowing without large osteophytes. Radiographs at each site, i.e., the knees, hips, and vertebrae, were examined by a single, experienced orthopaedic surgeon (S.M.), who was masked regarding participants' clinical status. If at least one knee joint was graded as KL2 or higher, the participant was diagnosed with radiographic KOA. Similarly, if at least one intervertebral level of the lumbar spine was graded as KL2 or higher, the participant was diagnosed with radiographic LS.

Bone mineral density measurement

In the mountainous and coastal areas, bone mineral density (BMD) was measured at the lumbar spine (L2–L4) and the proximal femur using dual-energy X-ray absorptiometry (DXA) (Hologic Discovery; Hologic, Waltham, MA, USA) at baseline.

To control quality, the same DXA equipment was used and the same spine phantom was scanned daily to monitor the machine's performance in study populations at different regions. The BMD of the phantom was adjusted to 1.032 ± 0.016 g/cm^2 (±1.5%) during all examinations. In addition, the same physician (N.Y.) examined all participants to prevent observer variability. Intraobserver variability using the Lunar DPX in vitro and in vivo had been measured by the same physician (N.Y.) for another study [18]. Coefficient of variance (CV) for L2–L4 in vitro was 0.35%, and CVs for L2–L4, the proximal femur, Ward's triangle, and the trochanter examined in vivo in five male volunteers were 0.61–0.90, 1.02–2.57, 1.97–5.45, and 1.77–4.17%, respectively.

OP was defined as a BMD of less than 70% of peak bone mass according to the criteria of the Japanese Society for Bone and Mineral Research [19]. OP was defined by BMD < 0.708 g/cm^2 at the lumbar spine in the case of both men and women, and by BMD < 0.604 g/cm^2 at the femoral neck for men and <0.551 g/cm^2 for women, respectively.

Statistical analysis

All statistical analyses were performed using STATA statistical software (STATA, College Station, TX, USA). Differences in proportion were compared by the chi-square test. Differences of continuous values were tested for significance using analysis of variance (ANOVA) for comparisons among multiple groups and Scheffe's least significant difference (LSD) test for pairs of groups. Significant items were selected, and multiple regression and logistic regression analyses were performed by adjusting suitable variables.

Results

Table 1 shows selected characteristics of the participants in the three regions including age, height, weight, body mass index (BMI), and BMD. The percentage of participants >60 years of age was 99.8, 84.3, and 54.7% in the urban, mountainous, and seacoast regions, respectively. Two-thirds of the 3,040 participants were women, and the mean age of female participants was 1 year less than that of the male participants.

Regarding the gender differences in the anthropometric measurements, height and weight were significantly lower in women than in men, but no significant difference in BMI was noted between the genders. All values of BMD at L2–L4, femoral neck, and total hip were significantly higher in men than in women ($P < 0.001$).

Table 1 Age–sex distribution and mean values (standard deviation) of selected characteristics of the participants

Age strata (years)	Men				Women			
	Total	Urban	Mountainous	Seacoast	Total	Urban	Mountainous	Seacoast
–39	14	0	2	12	31	0	7	24
40–49	44	0	7	37	105	0	17	88
50–59	107	0	36	71	211	2	67	142
60–69	168	11	93	64	385	60	183	142
70–79	535	315	150	70	913	594	196	123
80–	193	139	31	23	334	229	75	30
Total	1,061	465	319	277	1,979	885	545	549
Age (years)	71.0 (10.7)	77.2 (4.3)	69.5 (9.1)	62.6 (13.2)	69.9 (11.2)	76.3 (5.0)	68.6 (10.4)	60.8 (12.5)
Height (cm)	162.5 (6.7)	161.3 (5.9)	161.4 (6.9)	165.8 (6.8)	149.8 (6.5)	148.5 (5.6)	148.2 (6.7)	153.2 (6.2)
Weight (kg)	61.3 (10.0)	60.0 (8.5)	60.0 (10.2)	64.8 (11.0)	51.5 (8,6)	50.8 (8.3)	50.5 (8.6)	53.5 (8.8)
BMI (kg/m^2)	23.1 (3.0)	23.0 (2.8)	23.0 (3.0)	23.5 (3.4)	22.9 (3.5)	23.0 (3.4)	23.0 (3.4)	22.8 (3.6)
BMD (g/cm^2)								
L2–L4	1.05 (0.20)	–	1.04 (0.20)	1.06 (0.21)	0.87 (0.18)	–	0.83 (0.18)	0.91 (0.18)
Femoral neck	0.74 (0.13)	–	0.73 (0.13)	0.76 (0.13)	0.63 (0.12)	–	0.60 (0.12)	0.66 (0.13)
Total hip	0.88 (0.14)	–	0.87 (0.14)	0.90 (0.14)	0.74 (0.14)	–	0.72 (0.13)	0.76 (0.14)

BMI body mass index, *BMD* bone mineral density

Table 2 shows the age-sex distribution for prevalence of radiographic KOA and LS determined by a KL grade ≥2, classified by region. In the overall population, prevalence of radiographic KOA and LS was 54.6% (42.0% in men and 61.5% in women) and 70.2% (80.6% in men and 64.6% in women), respectively, indicating that the prevalence of LS was higher than that of KOA in the overall population, as well as in the respective genders. When the prevalence was compared among the age strata, radiographic KOA and LS tended to be higher with age in both genders (Table 2). Prevalence of radiographic KOA was 0% in men and 3.2% in women in the <40-year age group and 42.6% in men and 62.4% in women in the ≥40-year age group, and the differences were significant ($P < 0.001$). According to gender, the prevalence was significantly higher in women than in men in the overall population ($P < 0.001$). OA in both knees was observed in 43.1% (31.5% in men and 49.4% in women) of all participants. The overall prevalence of radiographic LS across all ages was 80.6% in men and 64.6% in women, which was considerably higher than that of KOA. In contrast to radiographic KOA, the prevalence of this condition was significantly higher in men than in women ($P < 0.001$). Similar to KOA, the prevalence of LS was lower in the <40-year age group than in the ≥40-year age group, with significant differences in both genders ($P < 0.001$). Among all the participants, 42.3% (37.1% in men and 45.1% in women) had both KOA and LS.

The prevalence of KOA and LS classified by region is also shown in Table 2. Regarding the regional differences, the prevalence of KOA was the highest in the mountainous area, followed by the urban area and the seacoast area in both men and women. By contrast, the prevalence of LS was the highest in the urban area, followed by the mountainous area and the seacoast area.

Logistic regression analysis was performed to determine the effect of region, gender, age, and body build on the prevalence of OA in participants ≥60 years of age, using the presence of KOA as an objective variable, and region (seacoast: 0, mountainous: 1), gender (men: 0, women: 1), age, and BMI as explanatory factors. The analysis revealed that the risk for KOA was significantly higher in the mountainous area [odds ratio (OR), 2.7; 95% confidence interval (CI), 2.1–3.6, $P < 0.001$], in women (OR, 3.4; 95% CI, 2.79–4.06; $P < 0.001$), in advanced age (+1 year: OR, 1.09; 95% CI, 1.07–1.11, $P < 0.001$), and in larger body build (+1 BMI: OR, 1.16; 95% CI, 1.13–1.20; $P < 0.001$). By contrast, the risk of LS was reduced in the mountainous area (OR, 0.63; 95% CI, 0.48–0.83; $P < 0.01$) and in women (OR, 0.47; 95% CI, 0.38–0.58; $P < 0.001$). Advanced age and higher BMI were associated with the presence of LS as well as KOA (+1 year: OR, 1.08; 95% CI, 1.06–1.10; $P < 0.001$; +1 BMI: OR, 1.09; 95% CI, 1.05–1.12; $P < 0.001$, respectively).

Table 3 shows the mean values of BMD among residents of mountainous and coastal regions in the ROAD study. Although the mean BMD values of the lumbar spine were no different between men and women in the age group of <40 years, those of the femoral neck and proximal total hip in the same age group were significantly

Table 2 Prevalence (%) of knee osteoarthritis and lumbar spondylosis classified by age, gender, and region

Age strata (years)	Knee osteoarthritis				Lumbar spondylosis			
	Total	Urban	Mountainous	Seacoast	Total	Urban	Mountainous	Seacoast
Men								
–39	0.0	–	0.0	0.0	14.3	–	0.0	16.7
40–49	9.1	–	42.9	2.7	45.5	–	28.6	48.7
50–59	24.3	–	55.6	8.5	72.9	–	75.0	71.8
60–69	35.2	37.5	44.1	21.9	74.6	75.0	69.9	81.3
70–79	48.2	41.3	63.5	45.7	85.3	83.8	85.3	91.4
80–	51.6	45.6	74.2	56.5	90.1	89.9	90.3	91.3
Total	42.0	42.5	57.1	23.8	80.6	85.5	78.4	75.1
Women								
–39	3.2	–	0.0	4.2	9.7	–	0.0	12.5
40–49	11.4	–	29.4	8.0	28.6	–	29.4	28.4
50–59	30.3	50.0	46.3	22.5	41.7	100.0	29.9	46.5
60–69	57.1	49.1	68.3	45.8	55.4	64.3	50.3	58.5
70–79	71.9	69.3	83.2	66.1	75.1	76.1	70.4	32.0
80–	80.7	77.3	91.9	76.9	78.2	79.6	69.3	90.0
Total	61.5***	70.0***	72.1***	37.8***	64.6***	76.3***	56.3***	54.6***

*** Significantly different ($P < 0.001$) from prevalence in men of the same region

higher in men than in women ($P < 0.001$). When the BMD values were compared among age strata, the prevalence of OP tended to be higher with age in both genders; however, the tendency was much greater in women than in men. Multiple regression analysis was performed to determine the effect of region, gender, age, and body build on BMD in the overall population of the mountainous and seacoast areas, using each value of BMD at lumbar spine, femoral neck, and total hip as an objective variable, and region (seacoast: 0, mountainous: 1), gender (men: 0, women: 1), age, and BMI as explanatory factors. The analysis revealed there was no regional difference in the BMD values at L2–L4, femoral neck, and total hip, whereas there were significant differences in gender (beta at L2–L4, femoral neck, and total hip, −0.41, −0.41, and −0.47, respectively, all $P < 0.001$), age (beta at L2–L4, femoral neck, and total hip, −0.28, −0.43, and −0.42, respectively, all $P < 0.001$), and BMI (beta at L2–L4, femoral neck, and total hip, 0.29, 0.33, and 0.37, respectively, all $P < 0.001$).

Table 4 reveals the prevalence of OP at the lumbar spine, the femoral neck, and the total hip among residents of mountainous and coastal regions in the ROAD study. The prevalence of OP in women was six, two, and three-fold higher, respectively, than in men, with a significant difference ($P < 0.001$). Although the prevalence of OP at the lumbar spine was higher for persons in the seacoast area than in the mountainous area, the prevalence at the femoral neck and total hip were higher in the mountainous area than in the seacoast area. In women, the prevalence of OP at the lumbar spine, femoral neck, and total hip were all higher in the mountainous area than in the seacoast area.

Logistic regression analysis was performed to determine the effect of region, gender, age, and body build on the prevalence of OP, using the presence of OP at L2–L4 as an objective variable, and region (seacoast: 0, mountainous: 1), gender (men: 0, women: 1), age, and BMI as explanatory factors. The analysis revealed that the risk for OP at L2–L4 was significantly higher in women (OR, 10.2; 95% CI, 6.07–17.1; $P < 0.001$), in advanced age (+1 year: OR, 1.10; 95% CI, 1.08–1.12; $P < 0.001$), whereas it was significantly lower in larger body build (+1 BMI: OR, 0.74; 95% CI, 0.69–0.79; $P < 0.001$). There was no significant difference in the prevalence of OP at L2–L4 between the mountainous and seacoast area. A similar tendency was shown in the prevalence of OP at the femoral neck and total hip (femoral neck: women versus men, OR, 3.82; 95% CI, 2.77–5.27; $P < 0.001$; +1 year: OR, 1.11; 95% CI, 1.09–1.13; $P < 0.001$; +1 BMI: OR, 0.75; 95% CI, 0.72–0.79; $P < 0.001$; total hip: women versus men, OR, 4.39; 95% CI, 2.88–6.70; $P < 0.001$; +1 year: OR, 1.11; 95% CI, 1.09–1.14; $P < 0.001$; +1 BMI: OR, 0.70; 95% CI, 0.65–0.75; $P < 0.001$).

Discussion

Little epidemiological information is available for musculoskeletal diseases such as OA and OP in Japan. The

Table 3 Mean values (standard deviation) of bone mineral density of participants classified by age, gender, and region

Age strata (years)	L2–L4 (g/cm^2)			Femoral neck (g/cm^2)			Total hip (g/cm^2)		
	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast
Men									
–39	1.05 (0.13)	0.97 (0.03)	1.06 (0.13)	0.83 (0.13)	0.72 (0.02)	0.84 (0.14)	0.96 (0.15)	0.87 (0.12)	0.98 (0.15)
40–49	1.06 (0.15)	1.08 (0.15)	1.06 (0.15)	0.82 (0.13)	0.77 (0.09)	0.83 (0.14)	0.96 (0.14)	0.94 (0.08)	0.96 (0.15)
50–59	1.05 (0.20)	1.03 (0.20)	1.06 (0.19)	0.80 (0.15)	0.81 (0.17)	0.79 (0.14)	0.93 (0.15)	0.93 (0.17)	0.93 (0.14)
60–69	1.04 (0.17)	1.05 (0.16)	1.03 (0.18)	0.75 (0.10)	0.76 (0.10)	0.75 (0.12)b	0.90 (0.12)	0.90 (0.11)	0.89 (0.14)
70–79	1.05 (0.23)	1.03 (0.22)	1.08 (0.25)	0.71 (0.12)abcd	0.70 (0.13)cd	0.73 (0.12)b	0.85 (0.14)bc	0.85 (0.14)	0.86 (0.12)b
80–	1.04 (0.26)	1.05 (0.25)	1.01 (0.30)	0.68 (0.12)abcd	0.69 (0.13)c	0.68 (0.12)abcd	0.80 (0.15)abcd	0.81 (0.13)c	0.78 (0.16)abc
Total	1.05 (0.20)	1.04 (0.20)	1.06 (0.21)	0.74 (0.13)	0.73 (0.13)	0.76 (0.13)	0.88 (0.14)	0.87 (0.14)	0.90 (0.14)
Women									
–39	1.08 (0.12)	1.11 (0.15)	1.07 (0.12)	0.78 (0.13)	0.76 (0.16)	0.78 (0.12)	0.86 (0.13)*	0.86 (0.13)	0.86 (0.13)*
40–49	1.04 (0.13)	1.06 (0.10)	1.04 (0.14)	0.74 (0.12)***	0.75 (0.09)	0.74 (0.12)***	0.85 (0.13)***	0.86 (0.10)	0.84 (0.13)***
50–59	0.94 (0.16)ab***	0.94 (0.16)**	0.94 (0.16)ab***	0.71 (0.11)a***	0.70 (0.10)***	0.71 (0.12)***	0.81 (0.12)***	0.83 (0.12)***	0.80 (0.12)***
60–69	0.85 (0.15)abc***	0.85 (0.15)abc***	0.86 (0.16)abc***	0.63 (0.09)abc***	0.62 (0.10)abc***	0.63 (0.09)abc***	0.75 (0.11)abc***	0.75 (0.11)bc***	0.74 (0.11)abc***
70–79	0.80 (0.17)abcd***	0.79 (0.17)abcd***	0.82 (0.17)abc***	0.57 (0.10)abcd***	0.56 (0.10)abcd***	0.59 (0.10)abcd***	0.68 (0.11)abcd***	0.67 (0.11)abcd***	0.69 (0.11)abcd***
80–	0.76 (0.16)abcd***	0.84 (0.16)abcd***	0.78 (0.16)abc***	0.52 (0.08)abcde***	0.52 (0.08)abcd***	0.52 (0.09)abcd***	0.60 (0.10)abcde***	0.61 (0.10)abcde***	0.59 (0.10)abcde***
Total	0.87 (0.18)***	0.83 (0.18)***	0.91 (0.18)***	0.63 (0.12)***	0.60 (0.11)***	0.66 (0.13)***	0.74 (0.13)***	0.72 (0.13)***	0.76 (0.14)***

[a] Significantly different ($P < 0.05$) from values of the age group in their thirties

[b] Significantly different ($P < 0.05$) from values of the age group in their forties

[c] Significantly different ($P < 0.05$) from values of the age group in their fifties

[d] Significantly different ($P < 0.05$) from values of the age group in their sixties

[e] Significantly different ($P < 0.05$) from values of the age group in their seventies

*, **, *** Significantly different (* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$) from values in men of the same age-strata and the same region

Table 4 Prevalence (%) of osteoporosis according to the JSBMR criteria, classified by age, gender, and region

Age strata (years)	L2–L4			Femoral neck			Total hip		
	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast	Total	Mountainous	Seacoast
Men									
–39	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
40–49	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
50–59	2.8	5.6	1.4	6.5	8.3	5.6	2.8	2.8	2.8
60–69	2.6	0.0	6.3	7.0	4.3	10.9	3.2	1.1	6.3
70–79	3.6	3.3	4.3	22.3	23.3	20.0	8.2	10.0	4.3
80–	7.4	6.5	8.7	13.0	16.1	8.7	18.5	16.1	21.7
Total	3.4	2.8	3.6	12.4	14.7	9.8	6.1	6.9	5.1
Women									
–39	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
40–49	1.9	0.0	2.3	2.9	0.0	3.4	3.8	0.0	4.6
50–59	5.3	3.0	6.3	4.8	1.5	6.4	3.9	1.5	5.0
60–69	13.5	15.3	11.4	22.2	23.0	21.3	10.8	10.9	10.6
70–79	29.8	31.8	26.0	42.9	44.6	40.2	25.9	25.6	26.2
80–	43.8	47.3	36.7	65.1	64.4	66.7	46.6	43.8	53.3
Total	19.2***	23.4***	12.8***	26.5***	32.7***	20.3***	16.3***	19.0***	13.6***

JSBMR Japanese Society for Bone and Mineral Research

*** Significantly different ($P < 0.001$) from prevalence in men of the same region

ROAD study is the first large observational study that was conducted in the Japanese population, and it was designed to supply essential information mainly regarding OA and OP. Among the large-scale population-based epidemiological studies aimed at preventing OA, the present ROAD study, which includes 3,040 participants, ranks at the same level as the Framingham study with 1,805 participants [20] and the Chingford study with 1,353 participants [21].

The present study clarified the age-sex distribution of the prevalence of KOA and LS as radiographically diagnosed in Japanese populations. If the results obtained from the ROAD study were applicable to the total age-sex distribution derived from the Japanese census in 2005 [15], it would be assumed that 25,300,000 people (8,600,000 men and 16,700,000 women) aged 40 years and older would be affected by radiographic KOA and 37,900,000 people (18,900,000 men and 19,000,000 women) aged 40 years and older would be affected by radiographic LS. This estimation would include asymptomatic OA. However, because one-quarter of men with radiographic OA and one-third of women with radiographic OA were reported to have pain, which is considered symptomatic OA [22, 23], it was determined that approximately 7,800,000 people (2,200,000 men and 5,600,000 women) aged 40 years and older would be affected by symptomatic KOA. Further, 11,000,000 people (4,700,000 men and 6,300,000 women) would be affected by symptomatic LS, based on the same assumption of the proportions of symptomatic and asymptomatic OA.

In this study, the Japanese criteria were used to clarify the prevalence of OP at the lumbar spine and hip. If the results obtained from the ROAD study were again applied to the entire Japanese age–sex distribution, 6,400,000 people (800,000 men and 5,600,000 women) aged 40 years and older would be affected by OP at the lumbar spine, and 10,700,000 people (2,600,000 men and 8,100,000 women) and 6,600,000 people (1,300,000 men and 5,300,000 women) would be affected by OP at the femoral and total hip, respectively. Because there are huge estimated numbers of patients with KOA, LS, and OP in Japan, these bone and joint diseases may be called national diseases. The Japanese Orthopaedic Association has proposed that the term "locomotive syndrome" be adopted to designate the condition evident in the high-risk group with musculoskeletal disorders who are highly likely to need nursing care [24]. The present study estimated that a total of 47,000,000 people (21,000,000 men and 26,000,000 women) aged 40 years and older would be affected by either OA or OP and are candidates for developing locomotive syndrome. Considering that the population of Japan is aging very rapidly and that more than 20% of the population is aged 65 years and over, there is an urgent need to develop preventive strategies for addressing these diseases that cause disability in the elderly.

In addition, the various associated factors for KOA and LS were identified in this research. The prevalence of KOA was higher in women than in men, whereas that of LS was higher in men than in women. Further, the prevalence of