Table 3. Association of K/L grade ≥2 knee OA with job title and occupational activity*

	Overall, OR (95% CI)	Men, OR (95% CI)	Women, OR (95% CI)
Job titles (vs. clerical workers/technical experts)			
Agricultural/forestry/fishery workers	1.69 (1.19–2.41)	1.58 (0.98–2.56)	1.90 (1.14–3.20)
Factory/construction workers	1.52 (0.99–2.36)	1.33 (0.72–2.47)	1.64 (0.90–3.06)
Other†	1.18 (0.88–1.60)	1.21 (0.73–2.00)	1.20 (0.82–1.76)
Occupational activities			
Sitting on a chair ≥2 hours/day	0.73 (0.57–0.92)	0.63 (0.44–0.92)	0.80 (0.60–1.09)
Kneeling ≥1 hour/day	1.11 (0.83–1.48)	0.79 (0.49–1.26)	1.36 (0.93–1.97)
Squatting ≥1 hour/day	1.23 (0.94–1.61)	0.89 (0.58–1.35)	1.50 (1.06–2.13)
Standing ≥2 hours/day	1.97 (1.43–2.72)	2.31 (1.32–4.17)	1.78 (1.21–2.63)
Walking ≥3 km/day	1.80 (1.42–2.29)	2.17 (1.49–3.16)	1.59 (1.17–2.16)
Climbing ≥1 hour/day	2.24 (1.65–3.04)	2.43 (1.64–3.60)	1.85 (1.19–2.96)
Lifting weights ≥10 kg at least once a week	1.90 (1.50–2.42)	2.26 (1.52–3.40)	1.68 (1.24–2.26)

* ORs were calculated by a logistic regression analysis after adjustment for age, sex, and BMI in the overall population, and for age and BMI in both sexes. K/L = Kellgren/Lawrence grading system; OA = osteoarthritis; OR = odds ratio; 95% CI = 95% confidence interval; BMI = body mass index.
† Includes all participants except for agricultural/forestry/fishery workers, factory/construction workers, and clerical workers/technical experts.

significant associations of the subpopulation group with lumbar spondylosis and without knee OA compared with the subpopulation group without knee OA or lumbar spondylosis.

DISCUSSION

Using baseline data from the ROAD study, the present investigation evaluated the risk of occupational activity for radiographic knee OA and lumbar spondylosis, and revealed that sitting on a chair was a significant protective factor for both radiographic knee OA and lumbar spondylosis in Japanese subjects. For other occupational activities, kneeling, squatting, standing, walking, climbing, and heavy lifting were significantly associated with radiographic knee OA, whereas there was no significant occupational activity for radiographic lumbar spondylosis in the overall population. To our knowledge, this is the first epidemiologic study using a large-scale population-based cohort to determine the risk of occupational activity for both knee OA and lumbar spondylosis simultaneously in the same population. Information on occupational activities was collected by direct inquiry rather than being inferred from the job title.

In the present study, agricultural, forestry, and fishery workers had a significantly higher prevalence of both radiographic knee OA and lumbar spondylosis compared with clerical workers and technical experts in the overall population. These jobs have historically been among the first to be identified in relation to knee OA in whites (31,32), which is also compatible with our data in this Japanese population. As other authors have hypothesized, the combination of intense exposure to heavy labor of varied nature and repeated local stresses, especially at a young age, could contribute to some systemic mechanism in the development of OA (33). This argument would support the implementation of preventive measures as a priority to reduce the intensity of physical labor in this sector, particularly for young male and female farm workers.

For occupational activities, standing, walking, climbing, and heavy lifting were associated with K/L grade ≥2 knee OA in the overall population, whereas kneeling and squat-

Table 4. Association of K/L grade ≥2 lumber spondylosis with job title and occupational activity*

	Overall, OR (95% CI)	Men, OR (95% CI)	Women, OR (95% CI)
Job titles (vs. clerical workers/technical experts)			
Agricultural/forestry/fishery workers	1.46 (1.02–2.11)	1.49 (0.83–2.68)	1.42 (0.89–2.28)
Factory/construction workers	1.05 (0.68–1.55)	1.52 (0.76–3.22)	0.84 (0.49–1.44)
Other†	1.22 (0.91–1.64)	1.53 (0.87–2.76)	1.11 (0.78–1.58)
Occupational activities			
Sitting on a chair ≥2 hours/day	0.78 (0.62–0.99)	0.48 (0.30–0.76)	0.93 (0.71–1.23)
Kneeling ≥1 hour/day	0.96 (0.72–1.28)	0.95 (0.55–1.70)	0.97 (0.70–1.35)
Squatting ≥1 hour/day	1.05 (0.81–1.38)	0.95 (0.58–1.61)	1.09 (0.80–1.48)
Standing ≥2 hours/day	1.11 (0.81–1.50)	1.14 (0.61–2.04)	1.10 (0.77–1.57)
Walking ≥3 km/day	1.00 (0.79–1.26)	0.89 (0.57–1.40)	1.04 (0.79–1.37)
Climbing ≥1 hour/day	1.02 (0.76–1.38)	1.09 (0.68–1.78)	0.98 (0.67–1.44)
Lifting weights ≥10 kg at least once a week	1.15 (0.91–1.45)	1.09 (0.69–1.72)	1.23 (1.01–1.55)

* ORs were calculated by a logistic regression analysis after adjustment for age, sex, and BMI in the overall population, and for age and BMI in both sexes. See Table 3 for definitions.
† Includes all participants except for agricultural/forestry/fishery workers, factory/construction workers, and clerical workers/technical experts.

Table 5. Comparison of characteristics of epidemiologic studies

Author, ref.	Ethnicity/country	Age, years	Total no.	Men:women
Muraki et al, current study	Japan	≥50	1,471	531:940
Yoshimura et al, 34	Japan	≥45	202	0:202
Lau et al, 35	Chinese		1,316	332:984
Anderson and Felson, 19	Blacks and whites/US	55–64	1,250	606:644
Felson et al, 20	Whites/US	≥63	1,376	569:807
Cooper et al, 21	UK	≥55	327	90:237
Coggon et al, 22	UK	≥47	1,036	410:626
Sandmark et al, 23	Sweden	≥55	1,173	589:584
Manninen et al, 24	Finland	≥55	805	195:610

ting were not, which was similar to previous studies in Japan and China (34,35). Comparison of characteristics and ORs for knee OA associated with occupational activity among epidemiologic studies is shown in Tables 5 and 6. The present study showed different results from other previously published studies (Table 6). Because each study defined knee OA and cases somewhat differently (in some studies, a case was defined as a subject with K/L grade ≥3 OA with knee pain, while it was defined as a subject with K/L grade ≥2 or K/L grade ≥3 OA in the present study), our results are not directly comparable with those of other studies. Even so, studies of whites have suggested that occupational activities of kneeling and squatting and job titles that required kneeling and squatting were associated with knee OA (19–24), whereas these activities were not associated with K/L grade ≥2 OA in this study. The discrepancies between white and Japanese subjects may be partly explained by the Japanese traditional lifestyle, which includes sitting on the heels on a mat and using the Japanese-style lavatory, where subjects have to take a deep squatting position. These positions may cause mechanical stress to the knee joint and possibly lead to the acceleration of knee OA. Among elderly Japanese subjects, kneeling and squatting are common postures in daily life, which could obscure the association between knee OA and occupational activities of kneeling and squatting.

The direction of the association of kneeling and squatting with knee OA was also different between sexes in the present study, although these differences were not signif-

Table 6. Comparison of odds ratios for knee osteoarthritis associated with occupational activity among epidemiologic studies*

	Muraki et al (current study)		Yoshimura et al (34), K/L ≥3 with knee pain	Lau et al (35), K/L ≥3	Anderson and Felson (19), K/L ≥2	Felson et al (20)		Cooper et al (21), K/L ≥3 with knee pain	Coggon et al (22), listed for knee surgery	Sandmark et al (23), TKA	Manninen et al (24), TKA
	K/L ≥2	K/L ≥3				K/L ≥2	K/L ≥3				
Sitting on a chair	0.7†	0.8	–					1.2		–	
Men	0.6†	0.8	–					–		0.7	
Women	0.8	0.8	0.4†					–		0.9	
Kneeling	1.1	1.4†	–	–				3.4†	1.8†	–	1.7‡
Men	0.8	0.9	–	1.4				–	1.7†	2.1†	1.7
Women	1.4	1.7†	1.0	0.9				–	2.0†	1.5	1.8†
Squatting	1.2	1.3†	–	–	–	–	–	6.9†	2.3†	–	1.7‡
Men	0.9	1.0	–	1.2	2.5†	2.2†	2.0	–	2.2†	2.9†	1.7
Women	1.5†	1.5†	1.1	1.1	3.5†	0.4	0.7	–	2.8†	1.1	1.8†
Standing	2.0†	1.4	–					0.8		–	0.6†
Men	2.3†	1.1	–					–		1.7†	0.4†
Women	1.8†	1.5	1.2					–		1.6†	0.7
Walking	1.8†	1.1	–	–				0.9	1.9†		1.1
Men	2.2†	0.9	–	2.2†				–	1.7		1.5
Women	1.6†	1.1	0.9	1.4†				–	2.1†		1.1
Climbing	2.2†	1.3	–	–				2.7†	1.5†	–	1.6
Men	2.4†	1.0	–	4.1†				–	2.3†	1.2	2.8
Women	1.9†	1.5	0.9	6.1†				–	0.7	1.4	1.5
Lifting weights	1.9†	1.6†	–	–				1.4	1.7†	–	1.0
Men	2.3†	1.3	–	1.7				–	1.9†	3.0†	0.9
Women	1.7†	1.7†	1.0	1.5†				–	1.5†	1.7†	1.1

* K/L = Kellgren/Lawrence grading system; TKA = total knee arthroplasty.
† $P < 0.05$.
‡ $P < 0.05$. Kneeling or squatting.

icant, except for squatting in women. Because men are known to have greater muscle strength than women of all ages and muscle strength has a protective effect on knee OA (36–38), it might be that the greater muscle strength obscures the harmful effects of kneeling and squatting on knee OA in men, resulting in lower ORs for knee OA than in women.

For K/L grade ≥2 lumbar spondylosis, there were no occupational activities associated with the increased prevalence except for heavy lifting in women. Few studies have focused on risk factors for lumbar spondylosis associated with occupational activity (25–28), and no increased risk of lumbar osteophytes due to physical activities has been reported (25,39,40).

In the present study, the occupational activity of sitting on a chair was inversely associated with both K/L grade ≥2 knee OA and lumbar spondylosis. For knee OA, our previous small-scale study showed that prolonged sitting on a chair at work was associated with a reduced prevalence of knee OA (34) (Table 5). Regarding the relationship between sedentary work and OA, the results of studies investigating the influence of sedentary work on knee OA are controversial (21,22). Although sitting on a chair clearly involves reduced load on many joints compared with other working activities, no other studies have reported a relationship between sedentary activity and knee OA. Sitting on a chair as a physical activity in the work place appears to represent a characteristic protective factor for OA in Japan.

Contrary to K/L grade ≥2 knee OA, occupational activities of kneeling and squatting were significantly associated with K/L grade ≥3 knee OA, whereas those of standing, walking, and climbing were not. Considering the definition of the K/L grade, this may suggest distinct risk factors between osteophytosis and joint space narrowing. In this population-based cohort study, the prevalence of K/L grade ≥2 knee OA was 45.6% in men and 61.2% in women, which was higher than that in whites, whereas that of K/L grade ≥3 was 16.8% and 26.5%, which is comparable with that in whites (41), suggesting that the Japanese lifestyle may be associated with osteophytosis rather than joint space narrowing. Therefore, regarding K/L grade ≥2 knee OA, the Japanese lifestyle could obscure the association between knee OA and occupational activities of kneeling and squatting as mentioned above. Furthermore, the discrepancy between risk factors for K/L grade ≥2 and K/L grade ≥3 knee OA may also be due to differences between the mechanism of osteophytosis and joint space narrowing. There is accumulating evidence that osteophytosis and joint space narrowing have distinct etiologic mechanisms (25,42–47). A previous prospective study using a large-scale OA cohort reported that there was no association between the 2 representative features of knee OA (44). A recent cross-sectional study also showed that osteophytosis was unrelated not only to joint space narrowing on plain radiographs, but also to cartilage loss measured by quantitative magnetic resonance imaging (45). Furthermore, our study on an experimental mouse model for OA has identified a cartilage-specific molecule, carminerin, which regulates osteophytosis without affecting joint cartilage destruction during OA progression (46,47). Further clinical and basic research will disclose the distinct backgrounds of these 2 features of OA.

There are several limitations in the present study. First, this is a cross-sectional study on factors associated with knee OA and lumbar spondylosis, so a causal association with occupational activity could not be determined. However, information collected included a lifetime occupational history and details of specific work place physical activities; therefore, ample evidence on the background of knee OA and lumbar spondylosis could be obtained. Second, information regarding past occupational exposures was obtained by self-report and there is a possibility that both self-selection bias and recall bias may have occurred. People with painful conditions may choose work that allows them to avoid aggravation of their conditions, so the impact of job titles and occupational activities on knee OA and lumbar spondylosis may be underestimated in the present study. Conversely, people with painful knee and lumbar conditions are likely to look for and assign a cause when asked about past work exposures. To determine the impact of working conditions on knee OA and lumbar spondylosis independently of the presence of pain at the examination, we analyzed the association of knee OA and lumbar spondylosis with job titles and occupational activities according to the presence of knee pain and low back pain at the baseline examination. The direction of association was similar regardless of the presence of pain, and the results between the overall population and the subpopulation without knee pain or low back pain were not different, suggesting that pain at the examination may not affect the results of the overall population very much in this study.

In conclusion, the present cross-sectional study using a large-scale population from the ROAD study revealed distinct risk factors of occupational activities for radiographic knee OA and lumbar spondylosis in Japanese subjects. Sitting on a chair was a significant protective factor for both radiographic knee OA and lumbar spondylosis. Other occupational activities of kneeling, squatting, standing, walking, climbing, and heavy lifting were risk factors for radiographic knee OA, but not for radiographic lumbar spondylosis. Further studies, along with longitudinal data in the ROAD study, will elucidate the environmental backgrounds of OA and spondylosis and clarify clinical evidence for the development of disease-modifying treatments.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Muraki had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Prevalence of radiographic lumbar spondylosis and its association with low back pain in elderly subjects of population-based cohorts: the ROAD study

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ABSTRACT

Objectives: Although lumbar spondylosis is a major cause of low back pain and disability in elderly people, few epidemiological studies have been performed. The prevalence of radiographic lumbar spondylosis was investigated in a large-scale population study and the association with low back pain was examined.

Methods: From a nationwide cohort study (Research on Osteoarthritis Against Disability; ROAD), 2288 participants aged ≥60 years (818 men and 1470 women) living in urban, mountainous and coastal communities were analysed. The radiographic severity at lumbar intervertebral levels from L1/2 to L5/S was determined by Kellgren/Lawrence (KL) grading.

Results: In the overall population the prevalence of radiographic spondylosis with KL≥2 and ≥3 at the severest intervertebral level was 75.8% and 50.4%, respectively, and that of low back pain was 28.8%. Although KL≥2 spondylosis was more prevalent in men, KL≥3 spondylosis and low back pain were more prevalent in women. Age and body mass index were risk factors for both KL ≥2 and KL≥3 spondylosis. Although KL = 2 spondylosis was not significantly associated with low back pain compared with KL = 0 or 1, KL≥3 spondylosis was related to the pain only in women.

Conclusions: This cross-sectional study in a large population revealed a high prevalence of radiographic lumbar spondylosis in elderly subjects. Gender seems to be distinctly associated with KL≥2 and KL≥3 lumbar spondylosis, and disc space narrowing with or without osteophytosis in women may be a risk factor for low back pain.

Lumbar spondylosis is considered a major public health issue causing chronic disability of elderly people in most developed countries.[1 2] Despite the urgent need for strategies for the prevention and treatment of this condition, epidemiological data on lumbar spondylosis such as its prevalence and association with symptoms are sparse. With the goal of establishing epidemiological indices to evaluate clinical evidence for the development of disease-modifying treatment, we set up a large-scale nationwide cohort study for bone and joint disease called ROAD (Research on Osteoarthritis Against Disability) in 2005. We have to date created a baseline database with detailed clinical and genetic information on three population-based cohorts in urban, mountainous and coastal communities of Japan.

Lumbar spondylosis is characterised by disc degeneration and osteophytosis.[2 3] Although this disorder has been widely studied in a clinical setting, few population-based radiological studies have been attempted.[4–11] The reported prevalence of radiographic lumbar spondylosis differs greatly in these reports from about 40% to 85%. This may be due to limitation of the sample size and variability in age. The present study therefore initially investigated the prevalence and distribution of this disorder according to age, gender and community using cohorts of 2288 participants aged ≥60 years in the baseline survey of the ROAD study.

The most popular grading system for the radiographic severity of osteoarthritis is the Kellgren/Lawrence (KL) system with classification into five grade scales (0–4) where KL≥2 is the conventional standard of the diagnosis.[12] For lumbar spondylosis, KL grade 2 is defined as osteophyte formation and grade 3 as disc space narrowing in addition to osteophyte formation,[12] although few epidemiological studies have applied the KL system to evaluate the lumbar spine.[5 6 9] Hence, to assess osteophyte formation alone and disc space narrowing with or without osteophytosis separately, this study examined not only the prevalence of KL≥2 spondylosis but also that of KL≥3 spondylosis.

Although low back pain is believed to be the principal clinical symptom of lumbar spondylosis, its association with the radiographic severity remains unclear. The correlation was not as strong as one would expect, and there is often a disconnection between them.[7 8] In previous reports radiographic spondylosis was determined at the severest intervertebral level, but it is possible that other levels with milder spondylotic change might give rise to low back pain. This study therefore assessed the radiographic severity at all intervertebral levels of the lumbar spine by the KL system, and examined the association between radiographic severity and low back pain.

METHODS

Participants

The ROAD study is a nationwide prospective cohort study for bone and joint diseases consisting of population-based cohorts established in several communities in Japan. To date we have created a baseline database which includes clinical and genomic information of 3040 inhabitants (1061 men, 1979 women) in the age range 23–95 years (mean 70.6) in three communities: an urban region in Itabashi, Tokyo; a mountainous region in Hidakagawa, Wakayama; and a coastal region in

Taiji, Wakayama. Participants in the urban region were recruited from those of a cohort study[13] in which the participants were randomly drawn from the register database of Itabashi ward residents, with a response rate in the age group ≥60 years of 75.6%. Participants in the mountainous and coastal regions were recruited from resident registration lists, with response rates in the groups aged ≥60 years of 68.4% and 29.3%, respectively.

Participants completed an interviewer-administered questionnaire of 400 items which included lifestyle information such as smoking habits, alcohol consumption, family history, past history, physical activity, reproductive variables and health-related quality of life. Anthropometric measurements included height, weight, arm span, bilateral grip strength and body mass index (BMI, kg/m^2). Medical information was taken by experienced orthopaedic surgeons (SM and HO) on systemic, local and mental status including information on low back, knee and hip pain, swelling and range of motion of the joints, and patellar and achilles tendon reflex. All participants were interviewed regarding low back pain by asking: "In the past month, have you had pain on most days lasting?", and those who answered yes were defined as having low back pain. Blood and urine samples were collected for biochemical and genetic examinations. Plain radiographs of the lumbar spine, knee and hip were taken for all participants. Participants were confirmed to be comparable to the Japanese general population according to the national nutrition survey by the Ministry of Health, Labour and Welfare (Japan). The height of the men and women in the ROAD study was 162.5 cm and 149.7 cm, respectively, compared with 162.6 cm and 149.9 cm in the Japanese general population. Weight was 61.3 kg and 51.8 kg, respectively, compared with 61.6 kg and 53.8 kg. The percentage of the men and women in the study population with a smoking habit was 26.4% and 3.2%, respectively, compared with 29.4% and 4.0% in the general population. From the baseline data of the overall participants, the present study analysed 2288 subjects (818 men and 1470 women) aged ≥60 years.

Radiographic assessment

Plain radiographs of the lumbar spine were taken in the anteroposterior and lateral positions and the images were downloaded into Digital Imaging and Communication in Medicine (DICOM) format files to assess radiographic spondylosis. Contrast-adjusted images were used to detect osteophytes and intervertebral spaces when the original images were obscure. Osteophytes were analysed at endplates. The severity of lumbar spondylosis was determined according to the KL grading[12] at each intervertebral level from L1/2 to L5/S by a single experienced orthopaedic surgeon (SM) who was blind to the background of the patients. To evaluate the intra-observer variability of the KL grading, 100 randomly selected radiographs of the lumbar spine were scored by the same observer more than 1 month after the first reading. Furthermore, 100 other radiographs were scored by two experienced orthopaedic surgeons (SM and HO) using the same radiographic atlas for inter-observer variability. The intra- and inter-observer variabilities were evaluated by kappa analysis. The variability in KL grading of the lumbar radiographs was found to be sufficient for assessment (0.84 and 0.76, respectively).

Statistical analysis

The non-paired *t* test was used to examine the difference in age and BMI between men and women. To compare the percentage of patients with radiographic spondylosis (KL≥2 or ≥3 at the severest level) and low back pain between men and women, logistic regression analysis was performed after adjustment for age and BMI. The differences in prevalence among the age groups were determined using one-way analysis of covariance and Scheffe's test after adjustment for BMI. The association of the variables such as age, BMI, gender and community with radiographic spondylosis and low back pain was evaluated by multivariate logistic regression analysis. The association of radiographic spondylosis at each intervertebral level with low back pain was determined by logistic regression analysis after adjustment for age and BMI. The association of the number of intervertebral level with KL≥3 with low back pain was determined by multiple regression analysis after adjustment for age and BMI. Data analyses were performed using SAS Version 9.0 (SAS Institute, North Carolina, USA).

RESULTS

Table 1 shows the overall characteristics of the 2288 participants aged ≥60 years in the three cohorts of the ROAD study. Although the men were significantly older than the women in the overall population and in some communities, BMI was comparable between them.

Table 2 shows the prevalence of radiographic lumbar spondylosis and low back pain in the overall population and subgroups classified by gender and age strata. In the overall population the prevalence of radiographic spondylosis with KL≥2 and ≥3 at the severest intervertebral level was 75.8% and 50.4%, respectively, and that of low back pain was 28.8%. The prevalence of osteoporotic fracture at the lumbar spine was 10.7%. Logistic regression analysis after adjustment for age and BMI showed that the prevalence of radiographic spondylosis with KL≥2 was higher in men than in women, while the prevalence of KL≥3 radiographic spondylosis and low back pain was higher in women than in men. When the prevalence was

Table 1 Characteristics of study participants

	Men				Women			
	Overall	Urban	Mountainous	Coastal	Overall	Urban	Mountainous	Coastal
No of subjects	818	397	266	155	1470	742	434	294
Age (years)	74.7 (6.1)	77.3 (4.1)	72.1 (6.2)	72.7 (7.4)	74.0 (6.4)*	76.4 (4.8)*	72.1 (7.1)	70.9 (6.8)*
Height (cm)	161.3 (6.3)	161.2 (5.9)	160.3 (6.6)	163.0 (6.1)	148.6 (6.2)	148.6 (5.8)	146.8 (6.4)	151.2 (5.9)
Weight (kg)	60.1 (9.9)	59.8 (8.3)	59.3 (11.4)	62.2 (10.6)	50.9 (9.0)	50.7 (8.4)	49.8 (9.8)	53.1 (8.8)
BMI (kg/m^2)	23.0 (3.2)	23.0 (2.7)	23.0 (3.8)	23.3 (3.3)	23.0 (3.7)	22.9 (3.4)	23.1 (4.2)	23.2 (3.5)
Current smoker (%)	24.6	25.2	26.3	20.0	3.1*	3.1*	4.4*	1.0*
Current drinker (%)	61.2	60.0	67.0	54.8	20.2*	21.0*	22.1*	15.3*

Data are mean (SD).
*$p<0.05$ vs men in the corresponding group by the non-paired *t* test.
BMI, body mass index.

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Table 2 Number (%) of participants with radiographic lumbar spondylosis and low back pain according to gender and age

		Radiographic lumbar spondylosis		
		KL≥2	KL≥3	Low back pain
Overall	2288	1728 (75.8)	1149 (50.4)	659 (28.8)
Men	818	688 (84.1)	383 (46.8)	201 (24.6)
<70	154	114 (74.0)	51 (33.1)	35 (22.7)
70–79	491	419 (85.3)*	232 (47.3)*	119 (24.2)
≥80	173	155 (89.6)*	100 (57.8)*	47 (27.2)
Women	1470	1040 (70.7)†	766 (52.1)†	458 (31.2)†
<70	356	196 (55.1)	128 (36.0)	80 (22.5)
70–79	818	612 (74.8)*	456 (55.7)*	273 (33.4)*
≥80	296	232 (78.3)*	182 (61.5)*	105 (35.5)*

Radiographic spondylosis was determined at the severest level among L1/2–L5/S1.
*p<0.05 vs subjects aged <70 years by Scheffe's test after adjustment for body mass index.
There was no significant difference between ages 70–79 and ≤80 in both genders.
†p<0.05 vs men by logistic regression analysis after adjustment for age and body mass index.
K/L, Kellgren/Lawrence grading.

compared among the generations, radiographic spondylosis (KL≥2 and ≥3) and low back pain tended to increase with age. Interestingly, the difference was greater between ages <70 and 70–79 years than between 70–79 and ≥80 years.

To identify risk factors for the radiographic spondylosis and low back pain, we further performed the logistic regression analysis to estimate odds ratios and confidence intervals (table 3). Age and BMI were significantly associated with radiographic spondylosis. Male sex was confirmed to be a risk factor for KL≥2 spondylosis while female sex was a risk factor for KL≥3 and low back pain. Among the communities, residents of the mountainous area had a lower risk for KL≥3 spondylosis than urban residents.

We then examined the association between radiographic spondylosis and low back pain. Considering that intervertebral levels other than the severest level of radiographic spondylosis might possibly cause low back pain, spondylosis at all intervertebral levels from L1/2 to L5/S was evaluated: KL≥2 spondylosis was found to be comparably prevalent at L2/3, L3/4 and L4/5 while KL≥3 spondylosis was remarkably prevalent at L4/5 in both men and women (table 4). In fact, among the five levels L4/5 was most frequently determined to be the severest level in both genders (men: L1/2 49.4%, L2/3 59.5%, L3/4 58.0%, L4/5 64.5%, L5/S 48.3%; women: L1/2 49.5%, L2/3 58.0%, L3/4 58.6%, L4/5 65.5%, L5/S 44.3%). We then looked at the percentage of subjects with low back pain in three groups: KL = 0 or 1, KL = 2, and KL≥3, at each intervertebral level and the severest level in the overall population and the three communities (fig 1). When odds ratios of KL = 2 and KL≥3 spondylosis compared with KL = 0 or 1 for pain were estimated by logistic regression analysis after adjustment for age and BMI, KL = 2 spondylosis was not significantly associated with pain in either gender at any intervertebral level (table 5). However, KL≥3 spondylosis was related at all levels in women while in none of the levels in men. Furthermore, the number of intervertebral levels with KL≥3 spondylosis was significantly associated with low back pain in women (p<0.01) but not in men by multiple regression analysis after adjustment for age and BMI. The association between KL≥3 spondylosis at the severest level and low back pain in women was evident at younger ages (<70 and 70–79 years; see table 1 in online supplement) and in the urban community (see table 2 in online supplement).

DISCUSSION

This study showed that the prevalence of radiographic lumbar spondylosis with KL≥2 and KL≥3 in elderly people (≥60 years) was 75.8% and 50.4%, respectively, and that of low back pain was 28.8% in the overall population. Although KL≥2 spondylosis was more prevalent in men (84.1%) than in women (70.7%), KL≥3 spondylosis and low back pain were more prevalent in women. This study also showed that KL = 2 spondylosis was not significantly associated with low back pain compared with KL = 0 or 1, while KL≥3 spondylosis was related to the pain only in women.

Most previous epidemiological studies on lumbar spondylosis focused on middle-aged or younger populations, reporting the prevalence to be 46.5–83.7%.[4 6–8 10 11] Our previous small-scale study on a younger population reported the prevalence to be 76.3% and 37.4%.[9] Interestingly, the subjects were living in a mountainous area in Japan, which was shown to have a lower risk for spondylosis in the present study. The variability may therefore be due to the differences in age, community, the sample size and ethnic variation. In fact, a study on elderly people (≥65 years) showed that the prevalence of KL≥2 spondylosis was 84.8% and 70.6%, similar to the present results, although in a relatively small number of subjects.[5] We have reported a different prevalence of lumbar spondylosis in Japan and the UK in a small-scale comparative study,[9] which may in part relate to ethnic variation. It should be noted that this is the first population-based study to investigate the age-related prevalence of lumbar spondylosis in elderly people. Although KL≥2 and KL≥3 spondylosis tended to increase with age, a significant difference was detected between the 60s and the 70s, but not thereafter. However, this cross-sectional

Table 3 Association of gender and community with radiographic lumbar spondylosis and low back pain

	Radiographic lumbar spondylosis		
	KL≥2	KL≥3	Low back pain
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (years)	1.07 (1.06 to 1.09)†	1.05 (1.04 to 1.07)†	1.02 (1.00 to 1.04)*
BMI (kg/m^2)	1.06 (1.03 to 1.09)†	1.04 (1.01 to 1.06)†	1.02 (0.99 to 1.05)
Women (vs men)	0.68 (0.61 to 0.76)†	1.13 (1.03 to 1.23)†	1.19 (1.08 to 1.31)†
Community (vs urban)			
Mountainous	0.82 (0.65 to 1.04)	0.56 (0.45 to 0.69)†	0.87 (0.69 to 1.08)
Coastal	1.24 (0.93 to 1.66)	1.06 (0.84 to 1.34)	0.86 (0.66 to 1.11)

Radiographic spondylosis was determined at the severest level among L1/2–L5/S1.
The odds ratios were calculated by logistic regression analysis after adjustment for all other variables.
*p<0.05; †p<0.01.
BMI, body mass index; KL, Kellgren/Lawrence grading; OR, odds ratio; CI, confidence interval.

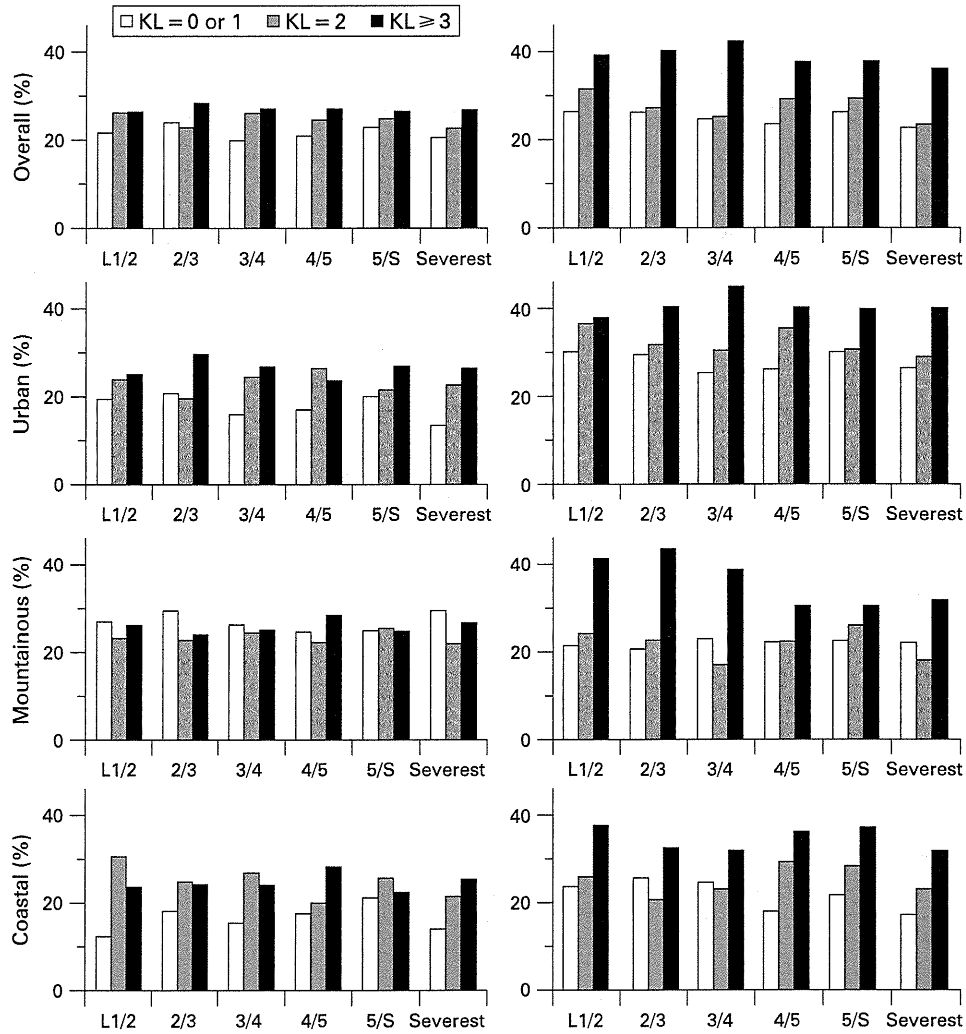

Figure 1 Percentage of subjects with low back pain according to the Kellgren/Lawrence (KL) grade in the overall population and in urban, mountainous and coastal communities.

analysis does not, of course, lead to the conclusion that individual lumbar spondylosis hardly progresses after 80 years. Since the ROAD study is a prospective cohort study of >10 years, the follow-up data will clarify the progression with ageing. Furthermore, there was a difference in prevalence between urban and mountainous communities. Considering that lumbar spondylosis is a common disease whose progression is governed by environmental and genetic factors, the regional difference is inevitable, as previously reported.[6] Although age and obesity are known to be representative risk factors for lumbar spondylosis,[2] the difference between communities in the present study was significant even after adjustment for age and BMI, indicating the involvement of other factors. Here again, a further longitudinal survey of the ROAD database including detailed environmental and genomic information will elucidate the underlying backgrounds.

Interestingly, KL≥2 spondylosis was more prevalent in men than in women, while KL≥3 spondylosis was more prevalent in women. We and others also have reported that osteophytosis of the lumbar spine is more common in men than in women,[8 9] while disc space narrowing is more prevalent in women.[9] Based on the definition of the KL grading,[12] the discrepancy may be due to distinct aetiological mechanisms between osteophyte formation and disc space narrowing. A cross-sectional study which investigated the extent, prevalence and distribution of spinal spondylosis in women also showed that osteophytosis and disc space narrowing were significantly correlated, but each predicted only 19% of the variation in the other .[11] A previous prospective study in knee joints in the Chingford Study cohort found no association between osteophyte formation and joint space narrowing.[14] A recent study using quantitative magnetic resonance imaging (MRI) in knee joints also reported that osteophyte formation was unrelated to cartilage loss.[15] Furthermore, in an experimental mouse knee osteoarthritis model, we have identified a cartilage-specific molecule, carminerin, that induces only osteophyte formation without affecting cartilage degeneration during the progression of osteoarthritis.[16 17] Further clinical and basic research will disclose the distinct backgrounds of these two representative features of osteoarthritis.

Table 4 Number (%) of subjects with radiographic lumbar spondylosis at each intervertebral level in all cohorts

	KL≥2		KL≥3	
	Men	Women	Men	Women
L1/2	474 (57.9)	609 (41.4)	116 (14.2)	254 (17.3)
L2/3	541 (66.1)	749 (51.0)	164 (20.1)	355 (24.2)
L3/4	554 (67.7)	735 (50.0)	194 (23.7)	419 (28.5)
L4/5	523 (63.9)	736 (50.1)	306 (37.5)	605 (41.2)
L5/S	400 (48.9)	576 (39.2)	197 (24.2)	413 (28.1)

KL, Kellgren/Lawrence grading.

Table 5 Association of Kellgren/Lawrence (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 to 1.84)	0.94 (0.65 to 1.36)	1.43 (0.98 to 2.11)	1.24 (0.82 to 1.89)	1.12 (0.75 to 1.65)	1.15 (0.70 to 1.92)
KL≥3	1.30 (0.79 to 2.11)	1.25 (0.80 to 1.94)	1.49 (0.96 to 2.32)	1.42 (0.97 to 2.08)	1.22 (0.82 to 1.81)	1.44 (0.89 to 2.38)
Women						
KL = 2	1.20 (0.91 to 1.57)	0.99 (0.75 to 1.31)	0.96 (0.71 to 1.30)	1.25 (0.82 to 1.88)	1.07 (0.73 to 1.54)	0.99 (0.69 to 1.42)
KL≥3	1.66 (1.23 to 2.24)*	1.74 (1.32 to 2.30)*	2.10 (1.62 to 2.72)*	1.88 (1.48 to 2.38)*	1.60 (1.25 to 2.06)*	1.80 (1.38 to 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 body mass index.
*$p<0.01$.
OR, odds ratio; CI, confidence interval.

Symptomatic low back pain was associated with KL≥3 spondylosis in women but not in men, but not with KL≥2 spondylosis in either gender. Considering the definition of KL grading, this may suggest that disc space narrowing but not osteophytosis of the lumbar spine contributes to low back pain, which is consistent with previous reports.[18] Differences in the association between genders might be dependent on muscle strength to compensate for spinal instability due to disc space narrowing, since men are known to have greater muscle strength than women at all ages.[19] However, approximately 30% of participants without definite radiographic lumbar spondylosis (KL = 0 or 1) had low back pain, and the odds ratio of KL≥3 spondylosis for pain was 1.44 in men and 1.80 in women, which is much lower than the previously reported odds ratio of 8.5 for KL≥3 osteoarthritis in the knee joint for knee pain.[20] This may be because low back pain arises from a number of disorders other than disc space narrowing such as nociceptive stimuli, inflammation, muscle weakness and abnormal load on muscle, ligament or capsular tissues.[21] Indeed, disc degeneration was detected by MRI in at least one lumbar level in all but one asymptomatic volunteers aged 60–80 years.[22] Furthermore, pain is also influenced by psychological factors such as depression, since a significant association between low back pain and depression has been confirmed in many longitudinal studies.[23–25] A recent psychophysical study has shown that anxiety was linked to self-reported and induced low back pain in men but not in women.[26] This might be an alternative reason for the lower association between radiographic spondylosis and low back pain in men.

This study has several limitations. First, prevalence figures using a large-scale population-based sample of elderly people may be generalisable to the Japanese population. However, this study investigated elderly participants who lived independently rather than those who lived in institutional settings, so the calculated prevalence may be underestimated. Second, the definition of low back pain in the present study did not determine the severity. The association of lumbar spondylosis with the severity of low back pain could not be examined in this study. Third, the analyses did not include facet joint osteoarthritis or vertebral fracture, which would probably be associated with low back pain. This is the next factor to be investigated in the ROAD study. Fourth, since the KL system emphasises osteophytosis, it is unclear how to handle lumbar spondylosis with disc space narrowing but no osteophytosis. Since quantitative MRI is still too laborious and expensive to perform in general clinical practice, we are now developing a computer-aided diagnostic program which enables the fully automatic measurement of major features of lumbar spondylosis including disc space narrowing and osteophytosis on plain radiographs.

In conclusion, this cross-sectional study using a large-scale population from the ROAD study revealed a high prevalence of radiographic lumbar spondylosis in elderly people. The prevalence differed to some extent by age, gender and community. Gender seems to be distinctly associated with KL≥2 and KL≥3 lumbar spondylosis, and disc space narrowing with or without osteophytosis in women may be a risk factor for low back pain. Further progress, along with continued longitudinal survey in the ROAD study, will elucidate the environmental and genetic backgrounds of lumbar spondylosis and its relation with low back pain.

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ARD

Prevalence of radiographic lumbar spondylosis and its association with low back pain in elderly subjects of population-based cohorts: the ROAD study

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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 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 (≥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 ≥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 ≥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 ≥60 years, were recruited from among those of a randomly selected cohort study from the previously established Itabashi Ward resident registration database [16]. The

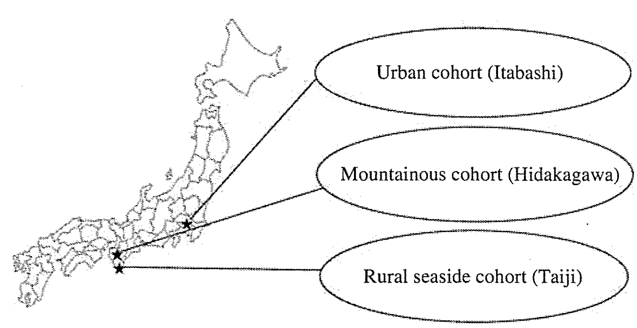

Fig. 1 Location of the three cohorts with different characteristics in Japan

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 threefold 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

KOA was higher in the mountainous area than in the seacoast area, whereas the prevalence of LS was higher in the seacoast area than in the mountainous area. The difference in the presence of KOA and LS based on gender difference may in part relate to the etiological differences of these two diseases, including genetic factors; the differences based on regional differences could be affected by environmental factors. Further investigation of the ROAD study will elucidate the genetic and environmental background underlying these diseases, although these could not be determined by the present study. Regarding OP, a high prevalence of OP among the ROAD study participants was confirmed; female sex and advanced age were associated with the presence of OP; and it was confirmed that BMI was associated with BMD at any site. The ROAD study participants will be followed up for at least 10 years to clarify the relationships between musculoskeletal diseases and risk factors for the early prevention of the disabilities caused by them.

There are several limitations in the present study. First, although the ROAD study includes a large number of participants (>3,000), these participants do not truly represent the general population as they have been recruited from only three areas. To confirm whether the participants of the ROAD study are representative of the Japanese population, we compared anthropometric measurements and frequency of smoking and alcohol drinking between the participants and the general Japanese population. The values for the general population were obtained from the report on the 2005 National Health and Nutrition Survey conducted by the Ministry of Health, Labour and Welfare, Japan [25]. The mean BMI (standard deviation in parentheses) of men in the age groups of 40, 50, 60, 70–74, 75–79, and 80 years or older as reported in the National Health and Nutrition Survey was 23.99 (3.27), 23.74 (3.07), 23.75 (2.94), 23.68 (3.18), 23.31 (3.04), and 22.27 (2.64), respectively, and that of women was 22.44 (3.49), 23.06 (3.37), 23.54 (3.66), 23.16 (3.42), 23.42 (3.53), and 22.50 (3.97), respectively. In the ROAD study, the mean BMI for men in identical age strata was 24.50 (4.36), 23.58 (2.90), 23.78 (3.16), 23.08 (2.82), 22.81 (2.86), and 22.62 (2.90), and for women it was 21.92 (4.08), 23.04 (3.29), 23.31 (3.21), 23.44 (3.46), 22.96 (3.66), and 22.21 (3.16), respectively. No significant differences were identified between our participants and the total Japanese population, except that the male participants aged 70–74 years in the ROAD study were significantly smaller in terms of body structure than the overall Japanese population ($P < 0.05$). This difference should be taken into consideration when evaluating the potential risk factors in men aged 70–74 years; factors such as body build, particularly heavy weight, are known to be associated with the occurrence of KOA [26]. Thus, our results might represent an underestimation. Conversely, a small body build is frequently associated with occurrence of OP [27]; therefore, in this case, our results might represent an overestimation.

Although care should always be taken when generalizing results obtained from the ROAD study for all similarly aged men and women, the overall BMI of the participants was basically comparable to that of the broader Japanese population. In addition, the proportion of current smokers and current drinkers (those who regularly smoked or drank more than one drink/month) in the general Japanese population was compared with that in the study population. Both proportions were significantly higher in the general Japanese population than in the study population (smokers: men, 34.8% in Japanese population, 25.3% in ROAD subjects, $P < 0.001$; women, 8.8% in Japanese population, 3.4% in ROAD subjects, $P < 0.001$; drinkers: men, 69.8% in Japanese population, 64.4% in ROAD subjects, $P < 0.01$; women, 30.8% in Japanese population, 25.5% in ROAD subjects, $P < 0.001$), suggesting that participants of the ROAD study had healthier lifestyles than the general Japanese population. This "healthy" selection bias should be taken into consideration when generalizing the results obtained from the ROAD study. Second, the age distributions of the participants among the three cohorts were different. In the urban, mountainous, and coastal areas, 99.8, 84.3, and 54.7% of the participants, respectively, were more than 60 years old. This selection bias should be considered in the analysis of regional differences of frequencies and risk factors. Third, BMD values were not collected from the participants in Itabashi Ward because of lack of available apparatus. So, our estimation of the number of patients with osteoporosis was based on the data collected in the countryside. This selection bias should always be taken into consideration when generalizing the study data to the Japanese population.

In conclusion, the prevalence of KOA, LS, and OP was clarified, and the number of people affected with these diseases in Japan was estimated, using the baseline data of the ROAD study. This study will provide the information required to develop clinical algorithms for the early identification of potential high-risk populations, as well as essential information for the development of policies for the detection and prevention of OA, OP, or osteoporotic fractures. Furthermore, establishment of the cohort will also facilitate the expansion of other studies in related areas of investigation. The knowledge gained from the ROAD study will have major implications for the understanding and management of several additional common problems of aging.

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