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Cohort Profile

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Cohort Profile: The Japanese Population-based Osteoporosis (JPOS) Cohort Study

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Abstract

The Japanese Population-based Osteoporosis (JPOS) Cohort Study was launched in 1996 to produce a reference database of areal bone mineral density (aBMD) by dual energy X-ray absorptiometry (DXA) and bone turnover markers in the Japanese female population and to determine risk factors for osteoporotic fractures. At baseline, 3984 women aged 15 to 79 years were randomly selected to provide representative bone status data and aBMD values for the diagnosis of osteoporosis. Follow-up surveys were conducted in 1999, 2002, 2006 and 2011/12 to determine changes in aBMD and identify incident morphometry-confirmed vertebral fractures and clinical fractures. These outcomes were obtained from 2174 women who participated in at least one follow-up survey. JPOS is a unique resource of individual-level bone health information with radiological and biological archives that include DXA images, and serum, plasma and DNA for future analyses with emerging radiological and biological techniques. The JPOS dataset is not freely available, but new collaborations are encouraged. Potential collaborators are invited to contact the Secretary General (M.I.) at the administrative office of the JPOS Study Group.

Key Messages

- The JPOS cohort study, which is representative of the Japanese female population, suggested that older age, lighter weight and lower intake of Japanese fermented soy beans were associated with greater bone loss in postmenopausal women. Perimenopausal women with higher levels of bone turnover markers at baseline showed greater bone loss over the next 3 or 6 years.
- Older age, lower aBMD, prevalent vertebral deformity, higher levels of bone turnover markers and lower trabecular bone score were associated with an increased risk of morphometry-confirmed incident vertebral fractures in women aged 50 years and older.
- Predicted risk of major osteoporotic fractures by FRAX® at baseline was not significantly different from the observed risk over the next 10 years.

Why was the cohort set up?

Osteoporotic fracture is one of the leading causes of disability for elderly people worldwide.[1,2] Osteoporosis prevention is therefore very important in maintaining quality of life for the elderly[3] and reducing medical expenditures for treatment of fractures and assistance costs for those disabled due to fractures.[4,5] The need for effective fracture-preventive measures and valid management of patients with osteoporosis has grown rapidly.

In the early 1990s, several osteoporosis cohort studies began in Japan[6–8] but were localized to small areas and not sufficiently large for detecting risk factors for fracture. Reference values for bone mineral density (BMD) and biochemical bone turnover markers in the Japanese population were also not yet established, even though areal BMD (aBMD) is an essential element for diagnosing osteoporosis and screening those at elevated risk of fractures.[9]

The Japanese Population-based Osteoporosis (JPOS) Study Group was established in 1995 with financial support from the Japanese Ministry of Agriculture, Forestries and Fisheries and the Dairy Council of Japan. The Study Group conducted a large-scale epidemiological study of Japanese women aged 15 to 79 years randomly selected from seven areas throughout Japan, with the following goals: (i) to establish age-specific aBMD reference values for Japanese women; ii) to establish a criterion aBMD value for the diagnosis of osteoporosis according to World Health Organization[10] and Japanese Society of Bone Mineral Research[11] criteria; and (iii) to form the basis for a prospective cohort study to explore the risk factors for incident osteoporotic fractures and establish a risk assessment model.

Follow-up studies have been conducted by the JPOS Study Group with financial support from the Japanese Society for the Promotion of Science with other funding bodies included in the Funding section.

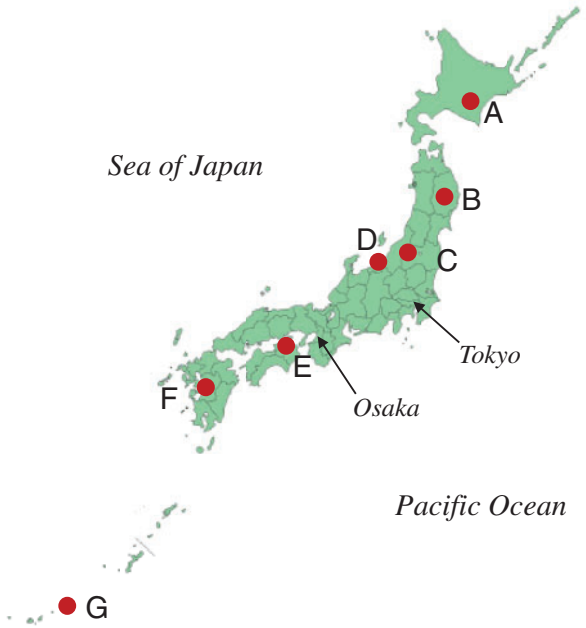

Figure 1. Study areas for the Japanese Population-based Osteoporosis Baseline Study. A: Memuro (town), B: Iwate (town), C: Nishi-Aizu (town), D: Joetsu (city), E: Sanuki (city), F: Kousa (town), G: Miyakojima (city).

Who is in the cohort?

Fifty women were randomly selected from each 5-year age group between 15 and 79 years, based on resident registration in seven municipalities throughout Japan (Figure 1).[12] The number of subjects selected was set at 650 for each study area, for a total of 4550. Study areas covered various regions of Japan to represent different environmental characteristics. Memuro (denoted as A in Figure 1) is located in Hokkaido, a northern island in the subarctic zone, and Miyakojima (G) is in Okinawa, a southern island in the subtropical zone. Iwate (B) is in the northern part of the main island of Honshu, and Nishi-Aizu (C) is located in a

Table 1. Number of participants for each survey and overall participation rates in the Japanese Population-based Osteoporosis Cohort Study

Age at baseline	Number of subjects selected	Number of participants and participation rates								
		Surveys for areas C, E and G				Surveys for areas A C, E and D		All five areas		
		Baseline	1999	2002	2006	Baseline	2011/2012	Baseline	Participants[a]	Rate (%)
15–19	250	98	34	31	22	–	–	–	–	–
20–24	250	113	59	47	43	–	–	–	–	–
25–29	250	128	72	66	64	188	99	223	145	65.0
30–34	250	127	86	88	84	180	132	217	191	88.0
35–39	250	137	125	114	107	179	153	224	209	93.3
40–44	250	137	105	99	101	180	148	224	197	87.9
45–49	250	140	119	132	118	188	168	238	227	95.4
50–54	250	132	129	129	122	191	159	226	213	94.2
55–59	250	126	115	111	108	187	139	219	201	91.8
60–64	250	121	119	108	101	189	129	225	197	87.6
65–69	250	136	120	103	81	177	102	229	177	77.3
70–74	250	130	117	93	56	170	55	215	164	76.3
75–79	250	126	85	52	33	155	10	191	102	53.4
Total	3250	1651	1285	1173	1040	1984	1294	2431	2023	83.2

A, C, D, E and G denote the study areas shown in Figure 1.
[a]Number of women who participated in at least one follow-up survey over 16 years.
JPOS: Japanese Population-based Osteoporosis.

mountain area in the central part and Joetsu (D) faces the Sea of Japan. Sanuki (E) in Shikoku, an island facing the Seto Inland Sea, and Kousa town (F) on the island of Kyushu, represent warm areas with long sunshine hours.

The study protocol was approved by the Ethics Committee of the Kinki University Faculty of Medicine. Written informed consent regarding all study procedures was obtained from each participant in advance.

Of the randomly selected 4550 women, 3985 (87.6%) participated in a baseline study that included aBMD measurements, vertebral fracture assessment (VFA) and other bone health-related assessments. Table 1 shows the number of participants at baseline and for each of the follow-up surveys. Participation rate for the baseline study was sufficiently high, although the rate was lower in younger age groups. With the exception of age, sociodemographic characteristics for non-participants of the baseline study were not available.

How often have they been followed up?

All participants in five areas (A, C, D, E and G) were selected as subjects for the JPOS Cohort Study, with the time line illustrated in Figure 2. Areas B and F were not selected for follow-up since levels of biochemical markers of bone turnover at baseline were not measured for these areas. We conducted four waves of follow-up surveys in 1999, 2002, 2006 and 2011 or 2012 with the same aBMD tests and VFA as at baseline, as well as similar interviews. Baseline participants in Nishi-aizu (C) and Sanuki (E) were invited

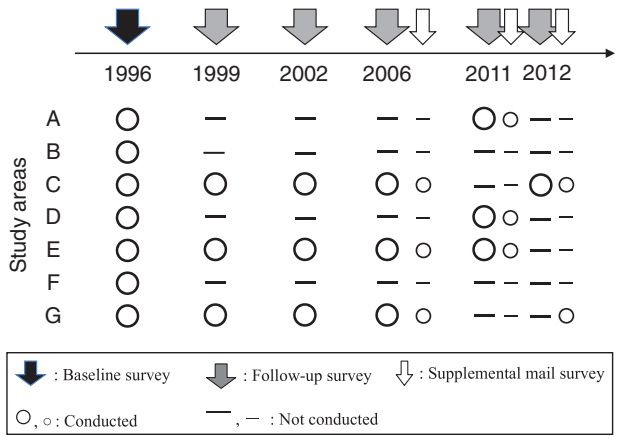

Figure 2. Time line for the Japanese Population-based Osteoporosis Cohort Study.

to all follow-up surveys, and those in Miyakojima (G) were invited to the first three surveys. Participants in Memuro (A) and Joetsu (D) were invited to the follow-up conducted in 2011. The follow-up survey for Nishi-aizu (C) was planned for 2011 but postponed to 2012 due to the Great East Japan Earthquake and subsequent accident at the Fukushima Daiichi Nuclear Power Plant. Supplemental mail surveys were sent to non-participants of the follow-up studies in 2006 and 2011/2012 to obtain data on the occurrence of clinical fractures. The 20-year follow-up survey is scheduled to begin in 2016. Linkages to morbidity or mortality data sources have not yet been established in the JPOS Study.

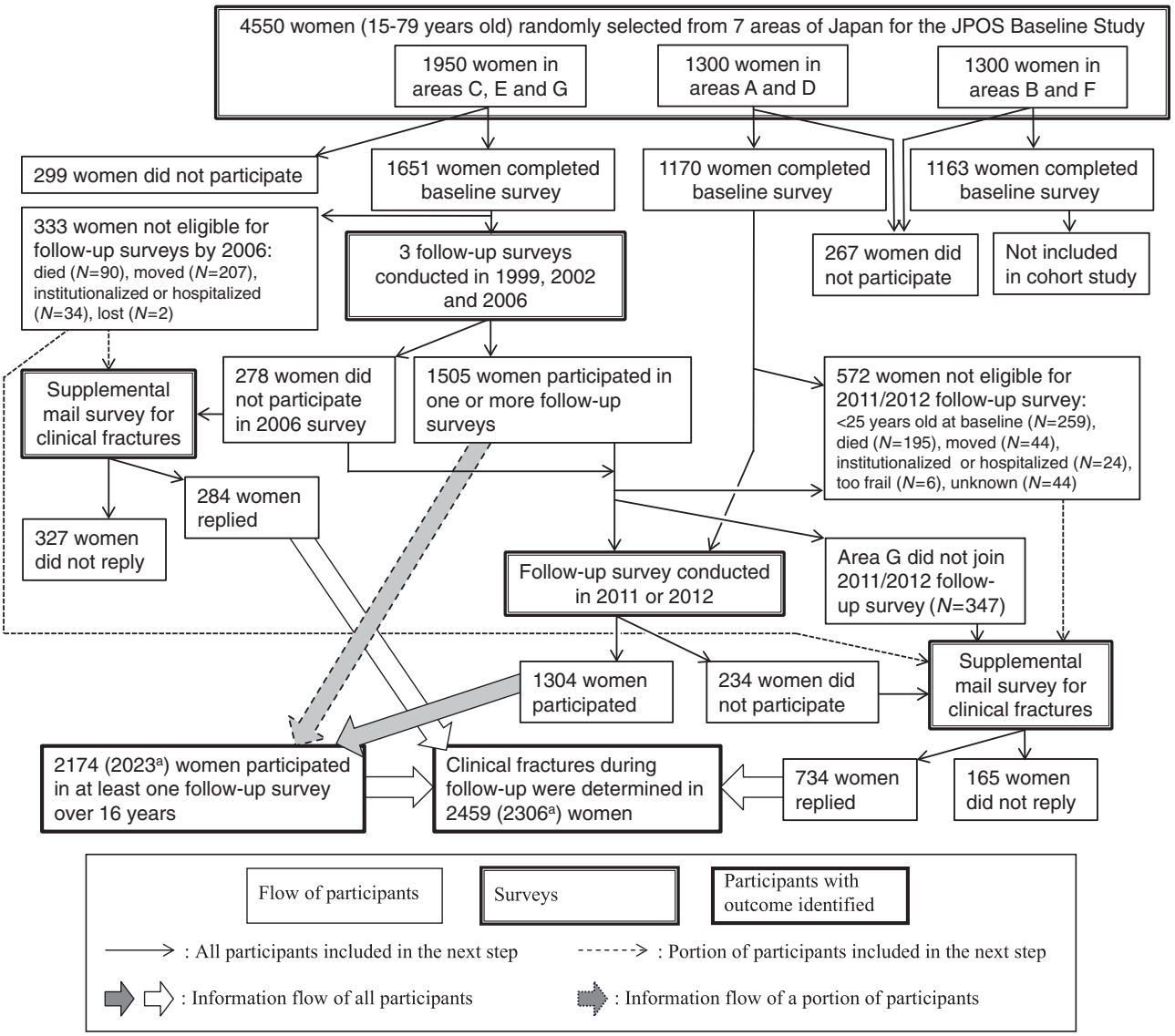

Figure 3. Subject recruitment and follow-up flow diagram for the Japanese Population-based Osteoporosis Cohort Study.
[a]Number of participants aged 25 years and older at baseline.

As shown in Table 1, overall participation rates in follow-up studies decreased over time. However, more than 80% of baseline participants completed at least one follow-up survey over the course of 16 years. A history of clinical fractures over 10 years was also obtained for more than 90% of baseline participants, using interviews in follow-up surveys or the self-reported supplemental mail survey for those who did not attend. Details of participant follow-up are shown in Figure 3.

Table 2 displays differences in demographic characteristics between participants in the follow-up surveys, participants and respondents to the mail surveys and non-participants and non-respondents. The ages of non-participants and non-respondents formed two peaks in their distribution. Very young and very old women tended to drop out of the cohort, and they were significantly lighter in weight and had lower aBMD than participants and respondents.

What has been measured?

Categories for measurements conducted at baseline and follow-up surveys are listed in Table 3. The JPOS Baseline Study covered a wide range of bone health-related indices such as aBMD measurements, VFA for detecting vertebral deformities and biochemical markers of bone turnover. Follow-up surveys were designed to detect outcomes such as change in aBMD, incidence of morphometry-confirmed vertebral fractures and clinical fractures. Levels of biochemical bone turnover markers and other more specific or newly developed markers were determined after baseline using stored serum samples for subgroups of the entire cohort.

Table 2. Difference in baseline characteristics between participants in follow-up surveys and supplemental mail surveys and non-participants in the Japanese Population-based Osteoporosis Cohort Study

Variables	Participants[a]	Participants or respondents[b]	Non-participants and non-respondents[c]	*P* for difference	
				a vs c	b vs c
N	2023	2306	345	–	–
Age (years)	51.4 ± 14.6	52.2 ± 14.9	53.3 ± 19.2	0.0818	0.3129
Height (cm)	152.7 ± 6.5	152.4 ± 6.6	151.9 ± 7.6	0.0865	0.2461
Weight (kg)	54.1 ± 8.3	54.0 ± 8.4	52.9 ± 8.8	0.0145	0.0206
BMI (kg/m^2)	23.2 ± 3.5	23.3 ± 3.5	22.9 ± 3.7	0.0662	0.0387
Current smokers (%)	6.2	5.8	5.8	0.8415	0.9675
Habitual drinkers (%)[d]	6.0	6.6	14.7	<.0001	<.0001
Habitual exercisers (%)[e]	21.2	21.7	24.9	0.1257	0.1813
Dietary intake of calcium (mg/day)	664 ± 266	666 ± 268	635 ± 249	0.0604	0.0410
Spine aBMD (g/cm^2)	0.932 ± 0.171	0.927 ± 0.172	0.904 ± 0.178	0.0059	0.0223
Total hip aBMD (g/cm^2)	0.821 ± 0.132	0.816 ± 0.135	0.787 ± 0.152	0.0001	0.0008
Femoral neck aBMD (g/cm^2)	0.728 ± 0.123	0.724 ± 0.126	0.698 ± 0.139	0.0001	0.0010
1/3 radius aBMD (g/cm^2)	0.667 ± 0.128	0.661 ± 0.130	0.635 ± 0.149	0.0002	0.0022
Serum intact PTH (pg/ml)	36.0 $^{\times}/_{\div}$ 1.54	36.1 $^{\times}/_{\div}$ 1.45	36.5 $^{\times}/_{\div}$ 1.47	0.5638	0.6792
Serum 1,25(OH)$_2$D (pg/ml)	37.6 ± 6.2	37.6 ± 1.4	36.1 ± 1.5	0.0605	0.0581
Serum OC (ng/ml)	6.6 $^{\times}/_{\div}$ 1.54	6.7 $^{\times}/_{\div}$ 1.54	7.0 $^{\times}/_{\div}$ 1.61	0.0245	0.0757
Serum BAP (IU/l)	12.6 ± 6.2	12.7 ± 6.2	13.4 ± 7.6	0.0446	0.0424
Urinary CTX (μg/mmolCr)	240.3 $^{\times}/_{\div}$ 2.00	246.4 $^{\times}/_{\div}$ 2.00	262.0 $^{\times}/_{\div}$ 1.93	0.0322	0.1231
Urinary fDPD (nmol/mmolCr)	5.6 $^{\times}/_{\div}$ 1.39	5.7 $^{\times}/_{\div}$ 1.39	5.6 $^{\times}/_{\div}$ 1.40	0.7926	0.6872
Urinary tDPD (nmol/mmolCr)	10.4 $^{\times}/_{\div}$ 1.52	10.5 $^{\times}/_{\div}$ 1.52	10.9 $^{\times}/_{\div}$ 1.57	0.0588	0.1945
Urinary PYD (nmol/mmolCr)	19.3 $^{\times}/_{\div}$ 1.39	19.5 $^{\times}/_{\div}$ 1.39	20.6 $^{\times}/_{\div}$ 1.45	0.0014	0.0080

[a]Women who participated in at least one follow-up survey and were aged 25 years or older at baseline.
[b]Women who participated in at least one follow-up survey or responded to mail surveys and were aged 25 years or older at baseline.
[c]Women who did not participate in any follow-up surveys, did not respond to mail surveys and were aged 25 years or older at baseline.
[d]Women who drank alcohol 5 times/week or more.
[e]Women who exercised 2 times/week or more.
BMI: body mass index, aBMD: areal bone mineral density, PTH: parathyroid hormone, 1,25(OH)$_2$D: 1,25 dihydroxy vitamin D.
OC: osteocalcin, BAP: bone-specific alkaline phosphatase, CTX: type I collagen C-terminal telopeptide, fDPD: free deoxypyridinoline.
tDPD: total deoxypyridinoline, PYD: pyridinoline.
Values connected by $\times/\div$ denote geometric mean and SD.

Assessment of outcomes

Vertebral fractures

Thoracolumbar vertebrae were imaged by X-ray absorptiometry at baseline (T7 through L4) and each of the follow-up (T4 through L4) surveys by certified radiological technologists using a single scanner (QDR4500A, Hologic Inc., Bedford, MA, USA) installed in a mobile test room. VFA was performed with these images as previously described.[13]

An incident vertebral fracture during follow-up was diagnosed morphometrically when a vertebra met the following criteria: (i) the vertebra had anterior, central or posterior heights reduced by 20% or greater on a follow-up image compared with baseline height; and (ii) the vertebra satisfied McCloskey–Kanis criteria[14] or grade 2 or 3 fracture criteria from Genant's method[15] on a follow-up image.

Clinical fractures

Interviews at each follow-up survey obtained the time of a fracture event, the skeletal site of fracture, the situation in which the fracture occurred and use of radiographs for forming the diagnosis of fracture by a physician. Supplemental mail surveys were conducted just after the follow-up surveys in 2006 and 2011/12 to obtain the same information from non-participants. Fragility fracture was defined as a fracture that occurred without strong external force, caused pain and was diagnosed by a physician with radiographic examination.

Assessment of predictors for fractures

Prevalent vertebral deformity

Vertebral deformities were diagnosed at baseline according to McCloskey–Kanis criteria[14] and visually confirmed using Genant's semiquantitative assessment method.[15]

Bone mineral density measurements

L1 to L4 vertebrae and the proximal femur were scanned in posteroanterior projection, with the same

Table 3. Measurement categories in each phase of the Japanese Population-based Osteoporosis Cohort Study

Phase	Measurements
Baseline survey in 1996	Anthropometric measurements: weight, height and grip strength
	Self-reported histories for fractures, major diseases and treatments
	Self-reported major **behaioural** risk factors for bone loss and fractures
	aBMD measured at the spine, hip and forearm by DXA
	VFA based on digital images of the spine taken by X-ray absorptiometry
	Hip structure analysis of DXA images of the proximal femur
	Trabecular bone score calculation from DXA images of the spine
	Serum samples taken for proteins, lipids, creatinine and liver enzymes assayed and serum aliquots stored at −80°C
	First-void urine samples taken to measure calcium excretion
	For subgroups:
	Markers of bone formation assayed (serum OC and BAP, $N = 3093$; P1NP, $N = 1060$)
	Markers of bone resorption assayed (urinary CTX, total and free forms of DPD and free PyD, $N = 3077$; serum CTX, $N = 1060$)
	Hormones for mineral metabolism assayed (intact PTH, 1,25 $(OH)_2$ D, $N = 3093$)
	Additional bone-related markers assayed (serum pentosidine and hsCRP, plasma homocysteine, $N = 873$)
	DNA extracted and plasma aliquots stored at −80°C, $N = 1600$
Follow-up surveys in 1999, 2002, 2006 and 2011/2012	Same aBMD measurements, VFA and anthropometric measurements as baseline study
	Similar questionnaire on clinical fractures and major diseases that occurred during follow-up period
	Physical performance tests in 2011/2012
	Supplemental mail surveys on occurrence of clinical fractures for women who did not participate in the follow-up surveys in 2006 and 2011/2012
Ongoing	20-year follow-up surveys in 2016 and 2017 with examinations similar to previous follow-up surveys are being planned

aBMD: areal bone mineral density, DXA: dual energy X-ray absorptiometry, VFA: vertebral fracture assessment, OC: osteocalcin, BAP: bone-specific alkaline phosphatase, P1NP: type I collagen N-terminal propeptide, CTX: type 1 collagen C-terminal telopeptide, DPD: deoxypyridinoline, PyD: pyridinoline, hsCRP: high sensitivity C-reactive protein, PTH: parathyroid hormone, 1,25 $(OH)_2$ D: 1,25 dihydroxy vitamin D, JPOS: Japanese Population-based Osteoporosis.

scanner used for spine imaging. aBMD of the spine was calculated for the L1 to L4 vertebrae, and aBMD of the femoral neck, trochanteric, intertrochanteric and Ward's triangle regions were obtained from proximal femur scans. aBMD of the one-third radius and an ultradistal site on the forearm were determined on the non-dominant side with a DXA scanner (pDXA, Norland/Stratec, USA/Germany).[12]

Speed of sound and broadband ultrasonic attenuation of the calcaneus were measured using a quantitative ultrasound bone densitometer (SAHARA, Hologic Inc.).[16]

Bone architecture assessment

DXA images of the proximal femur archived at baseline were assessed with a hip structure analysis (HSA) program (APEX software, Version 2.3, Hologic Inc.) to evaluate structural strength. The program yielded a set of indices such as cross-sectional area (cm^2), subperiosteal diameter (cm), section modulus (cm^3) and buckling ratio at three regions of interest defined as the narrow neck, intertrochanter and femoral shaft.[17]

Spine DXA images archived at baseline were further analysed by TBS iNsight software (Version 1.9.2, MedImaps, Bordeaux, France) to obtain the trabecular bone score (TBS). TBS is a texture measurement that quantifies local variations in grey level distribution of DXA images.[18] TBS is not a direct physical measurement of bone microarchitecture, but is correlated to its three-dimensional parameters.[19,20]

Bone metabolism assessment

In the JPOS baseline study, venous blood samples were drawn from all participants on their visits from 09:00 to 14:00 h without controlling meals. The serum samples were stored at −80°C prior to assay tests.[21] First-void urine samples were obtained after an overnight fast and stored at −20°C prior to assay tests.[21]

Serum osteocalcin (OC) and bone-specific alkaline phosphatase were measured as markers of bone formation, and

urinary type I collagen C-terminal telopeptide (CTX), free (fDPD) and total (tDPD) forms of deoxypyridinoline and free pyridinolines as markers of bone resorption in 3093 participants from the five study areas.[21] Markers available only after the baseline survey, such as serum type I procollagen N-terminal propeptide and serum CTX, were assessed using stored serum samples from 1060 participants aged 40 years and older at baseline who completed at least one follow-up survey during the first 10 years or responded to the supplemental mail survey in 2006.

Other bone-related measurements

For a subgroup of baseline participants, serum pentosidine, plasma homocysteine and serum high-sensitivity C-reactive protein levels were measured to analyse their associations with risk of fracture during follow-up surveys.

What has it found? Key findings and publications

A complete list of publications from the JPOS Study can be found at (http://www.med.kindai.ac.jp/pubheal/jpos/Publications.html).

Reference values of bone-related indices

Age-specific aBMD reference values of the spine, hip and forearm for the Japanese female population were obtained from 3465 participants in the baseline study with no current record or history of any disease or drugs that affected bone metabolism detectable by baseline interviews or laboratory tests.[12] T-scores of aBMD at various skeletal sites are shown in Figure 4 as a function of age. Age-related changes in aBMD appeared to vary at different skeletal sites. Criterion aBMD values for the diagnosis of osteoporosis in Japanese women were provided from the young adult subgroup of the cohort.

Reference values for HSA indices[22] and biochemical markers of bone turnover[21] were provided from subgroups of the entire cohort.

Risk factors for bone loss

We explored baseline risk factors for subsequent bone loss and found that higher levels of biochemical bone turnover markers, especially serum OC and urinary CTX, were associated with greater bone loss in perimenopausal or early postmenopausal women but not in late postmenopausal women.[23] Higher serum OC and urinary tDPD levels were associated with increased risk of progression from osteopenia to osteoporosis in postmenopausal women, with the area under the receiver operating characteristic curve (AUC) at 0.716.[24] Smoking habits were associated with low aBMD in premenopausal women,[25] and a lower

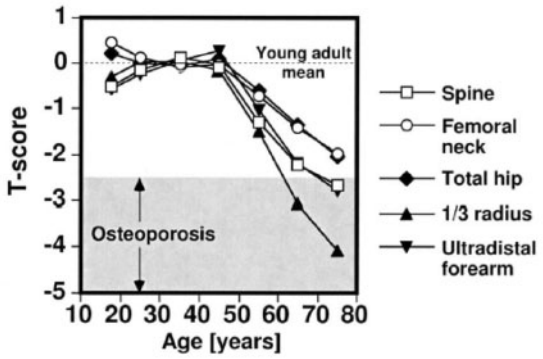

Figure 4. T-score of aBMD at various skeletal sites in 10-year age groupings adapted from Iki *et al.*[12] with permission.

intake of fermented soy beans (*natto*) correlated to greater bone loss at the hip or femoral neck in postmenopausal women independently of age, body weight and dairy food intake.[26]

Genetic predispositions for low aBMD and bone loss were evaluated for vitamin D receptor[27,28] and peroxisome proliferator-activated receptor gamma (PPARγ)[29] gene polymorphisms. The overall effect of these polymorphisms was small, but premenopausal women with the CT/TT genotype of PPARγ showed significantly lower aBMD than those with the CC genotype, suggesting that PPARγ may affect peak bone mass.

Determinants of the change in HSA indices were also explored, with weight maintenance possibly beneficial in preserving aBMD and structural hip strength.[30]

Risk factors for fractures

Prevalent vertebral deformity has been known to increase the risk of incident vertebral fractures.[31,32] This increase may be overestimated, however, since the risk factors that caused prevalent deformity may increase the risk of incident fracture. We adjusted the risk of incident vertebral fracture by introducing a propensity score for prevalent vertebral deformity. The rate ratio of incident vertebral fractures for prevalent vertebral deformity was greater than 4.0, but the risk was reduced to 2.96 when adjusted using the propensity score.[13]

BMD accounts for more than 70% of the variance in bone strength but alone is not sufficiently accurate for fracture risk assessment in clinical settings. FRAX® was developed to improve prediction accuracy for major osteoporotic fractures by using 11 clinical risk factors.[33] We evaluated the validity of FRAX® using 10-year follow-up data from the JPOS cohort. Predicted risk of major osteoporotic fractures by FRAX® was not significantly different from observed risk, but its validity was not significantly better than a simple model incorporating only age, weight

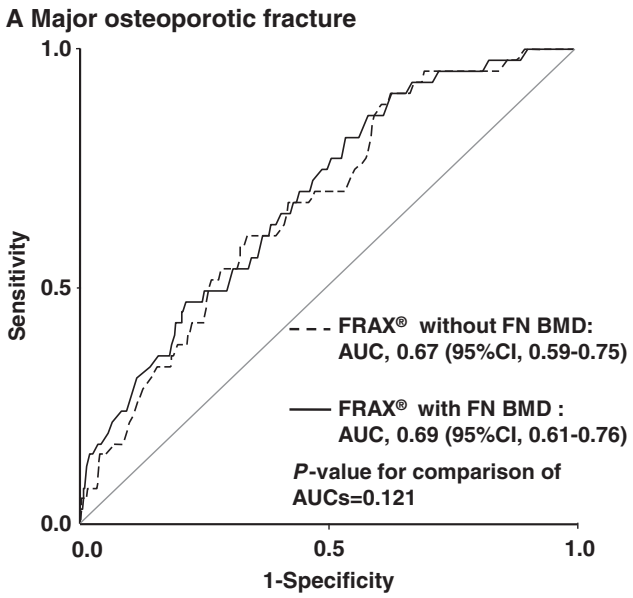

Figure 5. Validity of FRAX model with and without aBMD for prediction of major osteoporotic fractures over the next 10 years (adapted from Tamaki *et al.*[34] with permission). Major osteoporotic fractures include hip, clinical spine, distal forearm and proximal humerus fractures. FN BMD: areal bone mineral density at the femoral neck, AUC: area under receiver operating characteristic curve, 95% CI: 95% confidence interval.

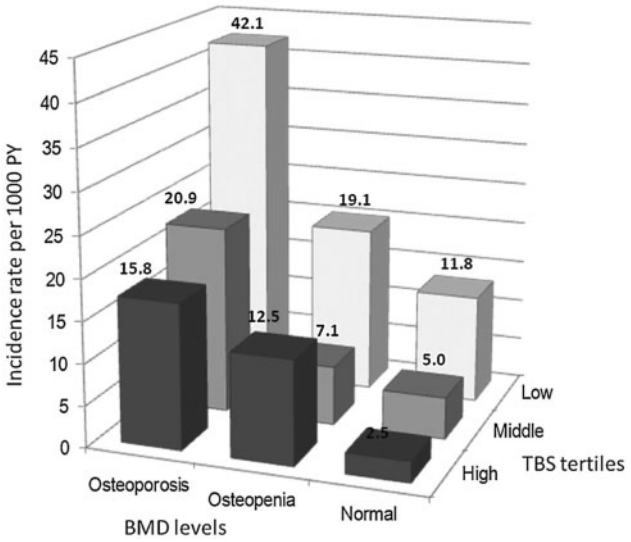

Figure 6. Incidence rates of vertebral fractures in TBS tertile groups within normal, osteopenic and osteoporotic aBMD strata (adapted from Iki *et al.*[37] with permission). PY: person-years, aBMD: areal bone mineral density at the spine, TBS: trabecular bone score.

and aBMD.[34] The accuracy of FRAX® should thus be improved further. However, a FRAX® model without aBMD, including only clinical risk factors which can be obtained by interviews, showed similar validity to a FRAX® model with aBMD (Figure 5), and thus may be used as a screening tool in community medicine for people at increased risk of fractures.

Several attempts to improve fracture risk assessment have been conducted in the JPOS cohort. One of the determinants of bone strength is biochemical bone turnover markers. We found that elevated urinary fDPD levels at baseline were associated with an increased risk of vertebral fractures over 10 subsequent years independently of age, weight and aBMD in postmenopausal women.[35] Serum pentosidine levels further improved the prediction accuracy for vertebral fractures and achieved an AUC exceeding 0.7.[36]

Another determinant of bone strength is bone microarchitecture. This can be assessed non-invasively by high resolution computed tomography and magnetic resonance imaging but may not be practical for routine osteoporosis screening or management. The TBS obtained from the JPOS baseline study was significantly associated with incident vertebral fracture risk over the next 10 years independently of aBMD, as shown in Figure 6. The odds ratio of vertebral fractures for a one standard deviation decrease in TBS was calculated to be 1.52 (95% CI: 1.16, 2.00) after adjusting for age, aBMD and vertebral deformity prevalent at baseline.[37] Thus, TBS could effectively improve fracture risk assessment achieved by aBMD and conventional predictors in clinical settings.

What are the main strengths and weaknesses?

Strengths of the present study include an adequate sample size for an acceptable sampling error, study areas distributed throughout Japan to reduce the effects of regional differences in aBMD and other bone indices, randomly selected subjects from each study area, inclusion of a wide range of ages, an acceptable participation rate, well-controlled and precise bone mass measurements and lack of inter-machine variation for bone measurements. Indeed, the bone indices from this study are the most accurate reference values for Japanese women to date.

JPOS has some limitations worth noting. Study areas were distributed throughout Japan, but they were not randomly selected from all municipalities and may have better health and welfare services compared with the average municipality. Also, aBMD measurements are highly instrument-dependent, and the present findings cannot be utilized by users with densitometers other than Hologic instruments. Blood specimens were taken from participants without strict control over sampling time or meals. VFA based on X-ray absorptiometry was used instead of conventional radiographs to diagnose vertebral fractures or deformities. Since VFA determines mostly vertebral shapes, vertebral fractures such as concave type or endplate

fractures may have been missed.[38] Finally, we did not confirm self-reported fracture events with data from medical records, although previous studies indicated that self-reported data are relatively accurate for forearm, vertebral and hip fractures.[39,40]

Can I get hold of the data? Where can I find out more?

JPOS is the only cohort study representative of the Japanese female population and provides a unique resource with a wide range and depth of individual-level information on bone and bone metabolism of cohort members. The study also includes biomaterial archives with serum, plasma and DNA for future analyses of emerging biomarkers or genes for bone metabolism. The JPOS dataset is not freely available, but the Study Group has collaborated with several other groups to share study data and encourages new collaborations. Potential collaborators are invited to contact the Secretary General (M.I.) at the administrative office of the JPOS Study Group at the Department of Public Health, Kinki University Faculty of Medicine, Osaka-Sayama, Japan.

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