

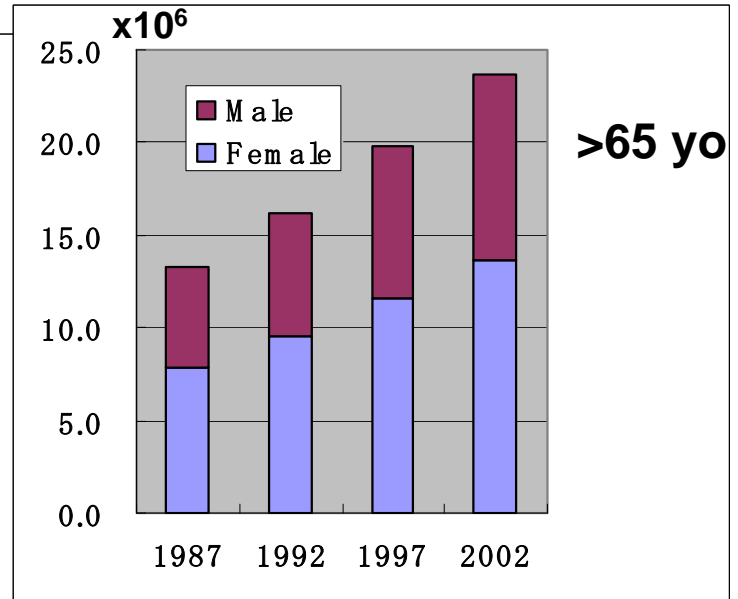
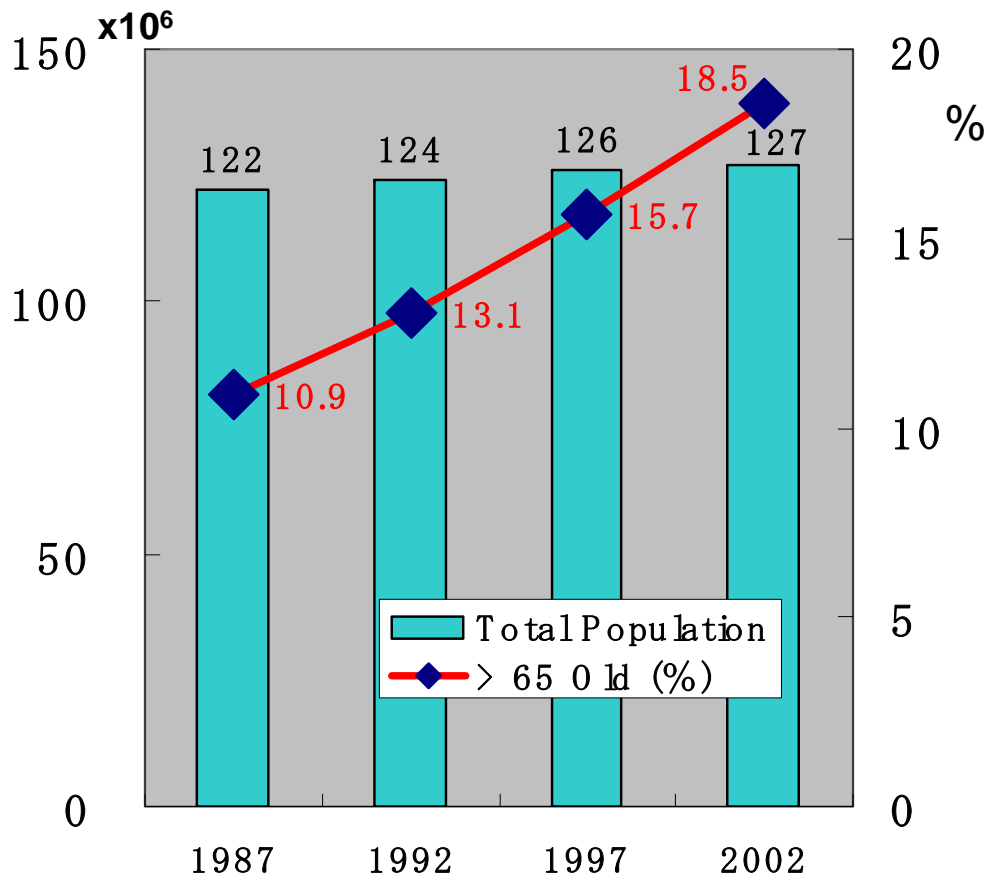
# Osteoporosis Care Around the Globe

Japanese perspective

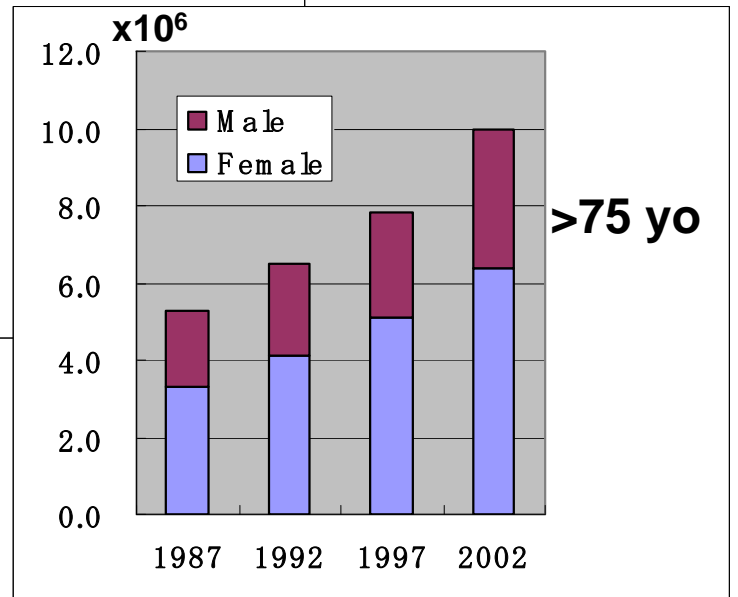
Akira Itabashi, MD

SCBR, Saitama Center for Bone Research  
Saitama, Japan

# Increasing aged population in Japan

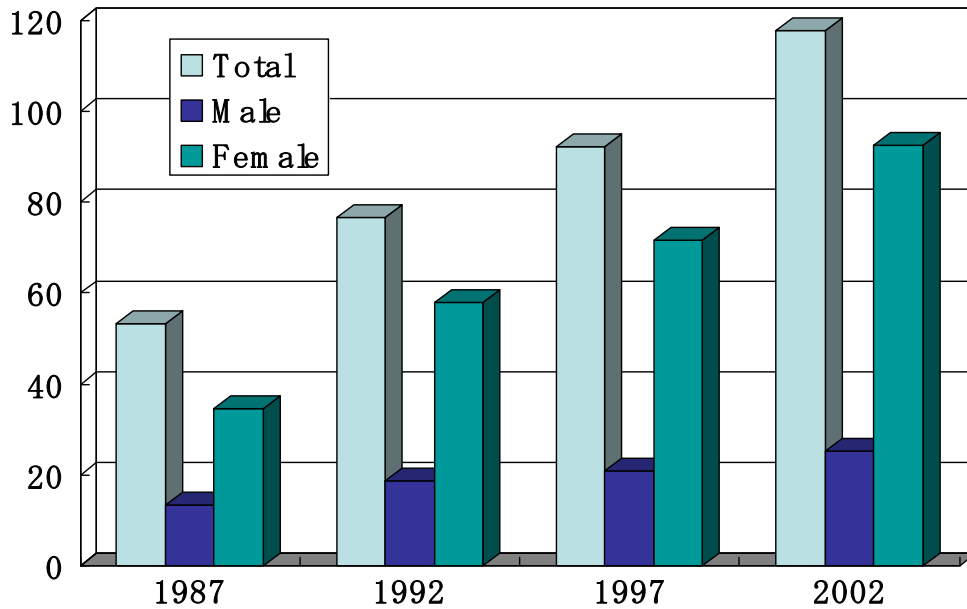


**Aged population in Japan is increasing, both in number and percentage.**



# Epidemiology of osteoporosis in Japan

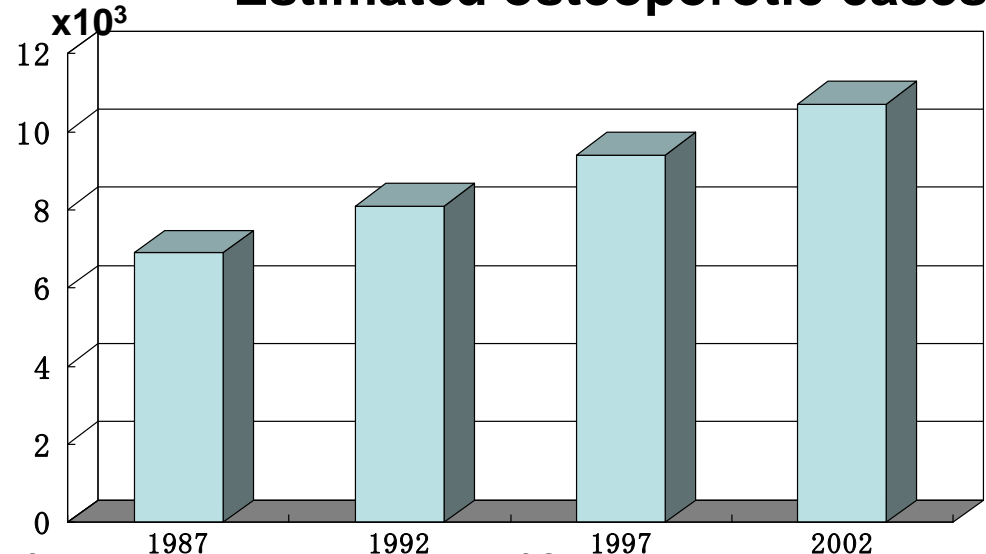
**x10<sup>3</sup> Estimated hip fractures cases**



**Hip fracture cases are still increasing both in females and in males in Japan, nearly 120,00 cases a year.**

**Estimated osteoporotic cases exceed 10 million and increasing.**

**Estimated osteoporotic cases**



Orimo H. et al. : Nihonijishinpo 4180 25-30 (2004)

Japanese Guidelines for the Prevention and Treatment of Osteoporosis (2006 edition)

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# Diagnostic criteria of primary osteoporosis (1995)

- **Cases with vertebral fractures on X-ray film**

**cases with reduced bone mass** (grade I or more severe radiographic osteopenia, or BMD less than **-1.5SD** of young adult mean (YAM)) **and with nontraumatic vertebral fracture** should be diagnosed as having osteoporosis.

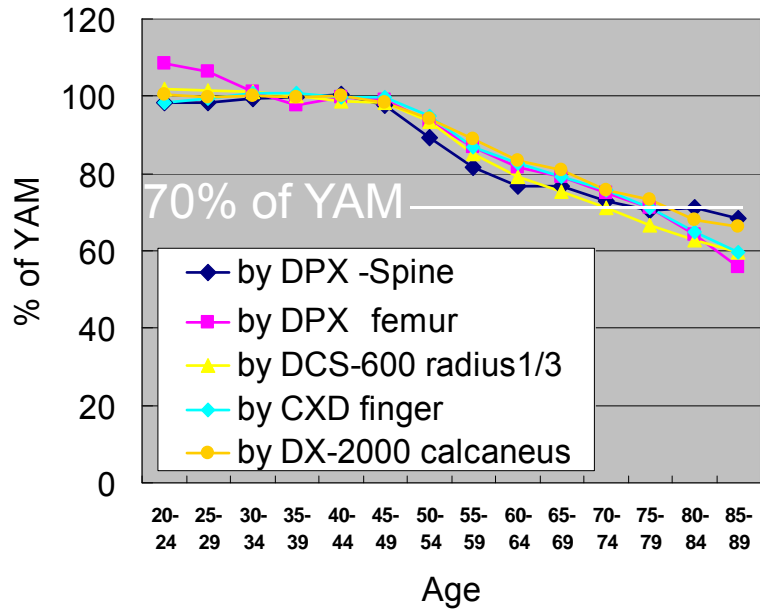
- **Cases without vertebral fractures on X-ray film**

	X-ray film of spine	Lumbar BMD
Normal	No radiographic osteopenia	
Osteopenia	Grade I radiographic osteopenia	Less than -1.5SD of YAM
Osteoporosis	Grade II or more severe radiographic osteopenia	Less than <b>-2.5SD</b> of YAM

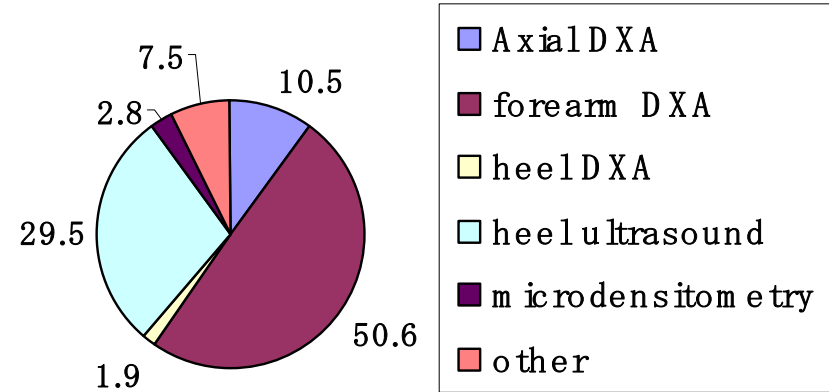
YAM, young adult mean (20-44 years old)

# Using percent of YAM instead of T-score in Japan

## Speed of Bone Loss with Age (% of YAM)



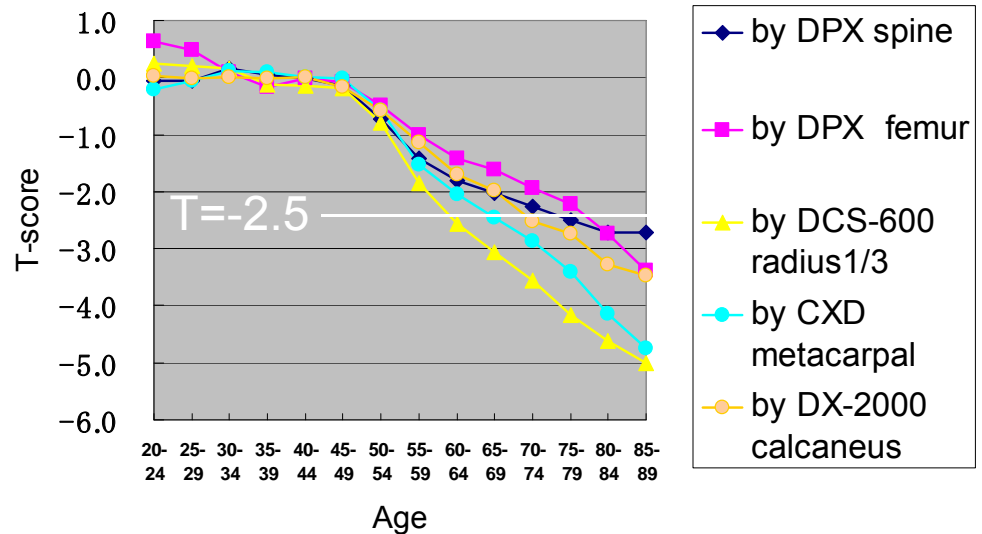
## Bone densitometer sales in Japan as 2005



## Prevalence of osteoporosis in women more than 50 years old as diagnosed by WHO criteria

Site	Method	Prevalence(%)
Lumbar spine	DXA	24.4
Hip	DXA	10.9
Radius, one-third	DXA	52.2
Calcaneus	SXA	34.1
Metacarpal	CXD	36.9

## Speed of Bone Loss with Age (T-score)



Orimo, H, et al: J Bone Miner Metab (1998) 16:139-150

Osteoporosis care around the globe Japanese perspective

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Diagnostic criteria of primary osteoporosis (revised in 1996)

- **Cases with vertebral fractures on X-ray film**

**cases with reduced bone mass** (grade I or more severe radiographic osteopenia, or BMD less than 80% of young adult mean (YAM)) **and with nontraumatic vertebral fracture** should be diagnosed as having osteoporosis.

- **Cases without vertebral fractures on X-ray film**

	X-ray film of spine	Lumbar BMD
Normal	No radiographic osteopenia	
Osteopenia	Grade I radiographic osteopenia	70%-80% of YAM
<b>Osteoporosis</b>	Grade II or more severe radiographic osteopenia	<b>Less than 70% of YAM</b>

YAM, young adult mean (20-40 years old)

Note: In principle, BMD means bone mineral density of lumbar spine, but if lumbar BMD is difficult to assess, that of radius, second metacarpal bone, femoral neck, or calcaneus may be used

Orimo, H, et al: J Bone Miner Metab (1998) 16:139–150

# Presence of fragility fracture, or BMD less than 70% of YAM even without prevalent fracture

## Diagnostic criteria for primary osteoporosis (2000 revision)

If the results of bone evaluation meet the following conditions and other diseases characterized by low bone mass or secondary osteoporosis are not recognized, it is diagnosed as primary osteoporosis.

I With fragility fracture <sup>1</sup>			
II Without fragility fracture			
	BMD <sup>2</sup>	Radiographic osteopenia of the spine <sup>3</sup>	Conventional bone atrophy standard
Normal	80% of YAM or higher	Absent	No
Decreased bone mass	70-80% of YAM	Possible	Grade I
Osteoporosis	Less than 70% of YAM	Present	Grade II or more severe

**1** Fragility fracture is a nontraumatic bone fracture that is caused by slight external force to a bone with low BMD (BMD less than 80% of YAM). Sites of fracture include the spine, femoral neck, and the distal end of the radius.

**2** BMD usually refers to lumbar BMD. However, when the measurement is inappropriate for reasons such as spinal deformity, the femoral neck BMD should be used. When measurement at that site is difficult, BMD of the radius, second metacarpal bone, or calcaneus will be used.

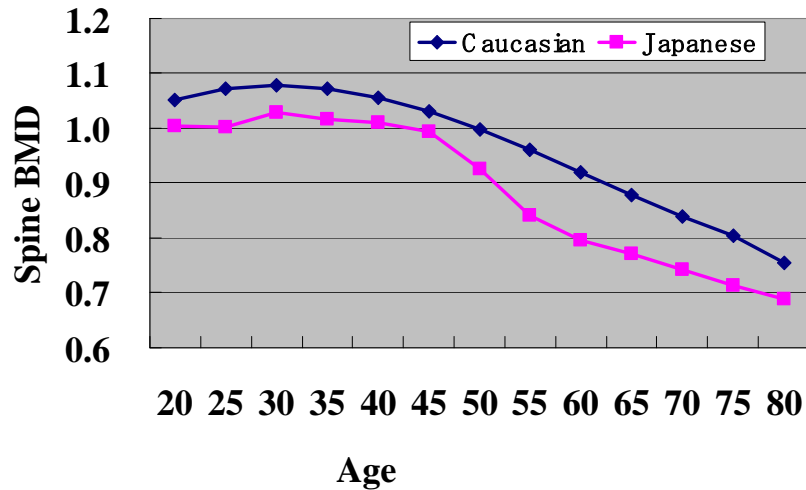
**3** Assessment of radiographic osteopenia of the spine is performed according to the conventional bone atrophy standard.

YAM: young adult mean

From Orimo H, et al. J Bone Miner Metab 2001; 18: 76-82.

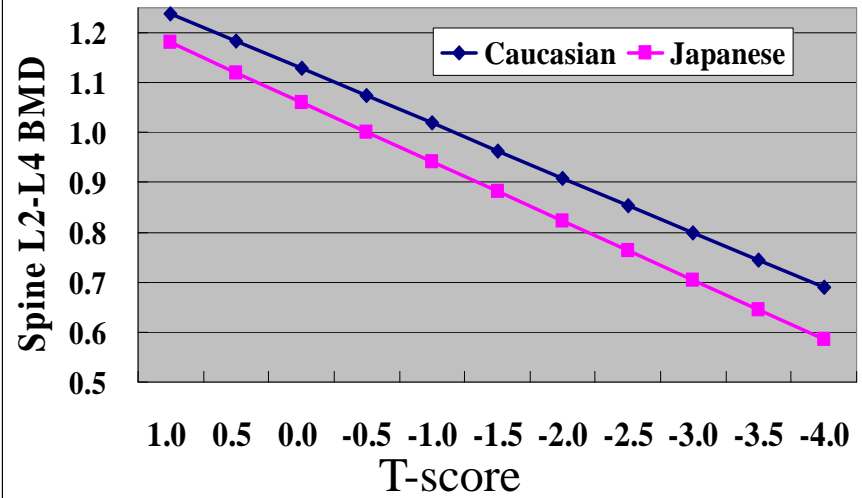
# BMD difference Caucasian vs Japanese

## Spine L2-L4 BMD decline curve

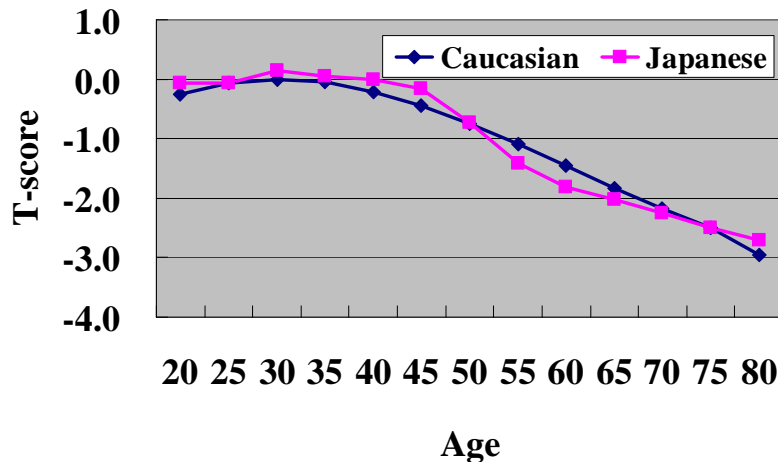


(Hologic QDR series)

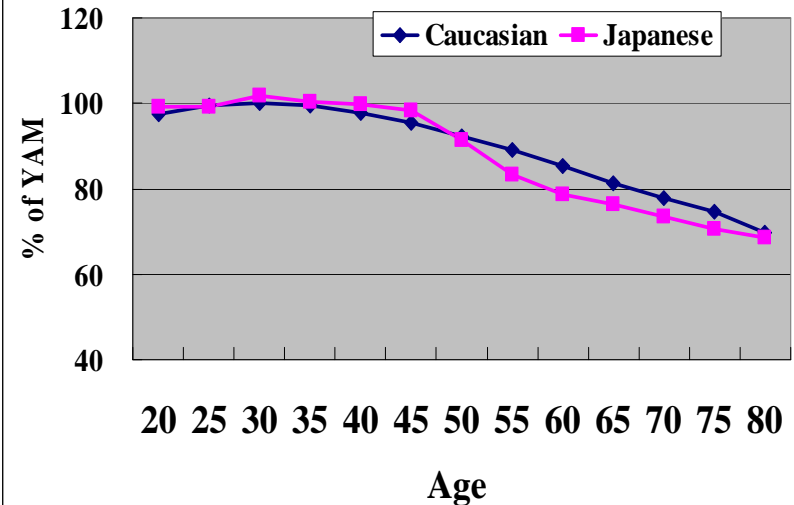
## Spine L2-L4 BMD vs T-score



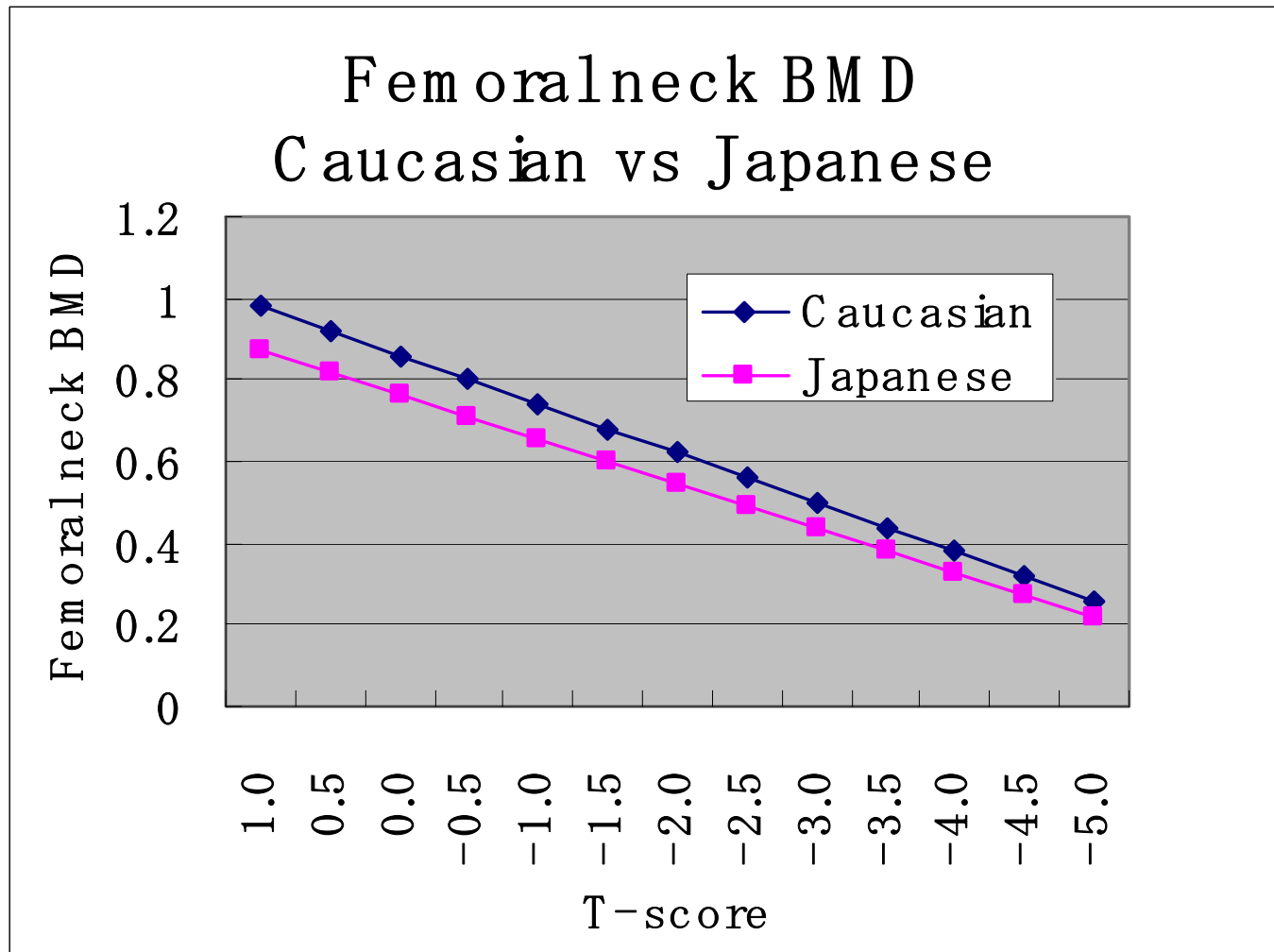
## Spine BMD T-score decline curve



## Percent of YAM decline curve



# BMD difference Caucasian vs Japanese



**Caucasian : Mean 0.86 SD 0.12 -2.5SD 0.56**  
**Japanese : Mean 0.76 SD 0.11 -2.5SD 0.49**  
**(Hologic QDR series)**

# Bone metabolism markers: valid means for predicting osteoporotic fracture risk

	Markers	Reference range	Cutoff level	Abnormally high level
Bone resorption	Urine DPD	2.8-7.6* <sup>1</sup> nmol/mmol · Cr	7.6	>13.1
	Urine NTX	9.3-54.3* <sup>1</sup> nmolBCE/mmol · Cr	54.3	>89.0
	Urine CTX	40.3-301.4* <sup>1</sup> µg/mmol · Cr	301.4	>564.8
	Serum NTX	7.5-16.5* <sup>2</sup> nmolBCE/L	16.5	>24.0
Bone formation	Serum BAP	7.9-29.0* <sup>1</sup> U/L	29.0	>75.7

\* 1 : Premenopausal women aged between 30 to 44

\* 2 : Premenopausal women aged between 40 to 44

- Cutoff levels are equivalent to the mean (for premenopausal women) + 1.96 SD.
- When abnormally high levels are detected, diseases other than primary osteoporosis should be considered.
- Currently data on serum CTX are insufficient.

DPD=free deoxypyridinoline  
 NTX=N-telopeptide  
 CTX=C-telopeptide  
 BAP=bone-specific alkaline phosphatase

Adapted from Committee on the Guidelines for the Use of Biochemical Markers of Bone Turnover in Osteoporosis; Japan Osteoporosis Society. J Bone Miner Metab 2005; 23: 97-104.

Japanese Guidelines for the Prevention and Treatment of Osteoporosis (2006 edition)

## Diagnosis of osteoporosis

## Reimbursement

Almost all the Japanese population are generally covered with medical insurances. (However, uninsured population is increasing.)

### Examination fee:

#### Bone Densitometry

central DXA	3,600JPY	340USD
peripheral DXA	1,400JPY	130USD
heel ultrasound	800JPY	75USD

(Insurance covers when the patients are diagnosed or suspected for osteoporosis, every 4 months)

#### Bone metabolic markers

Urinary NTx	1,600JPY	150USD
Serum NTx	1,600JPY	150USD
Urinary CTx	1,600JPY	150USD
Urinary DPD	1,600JPY	150USD

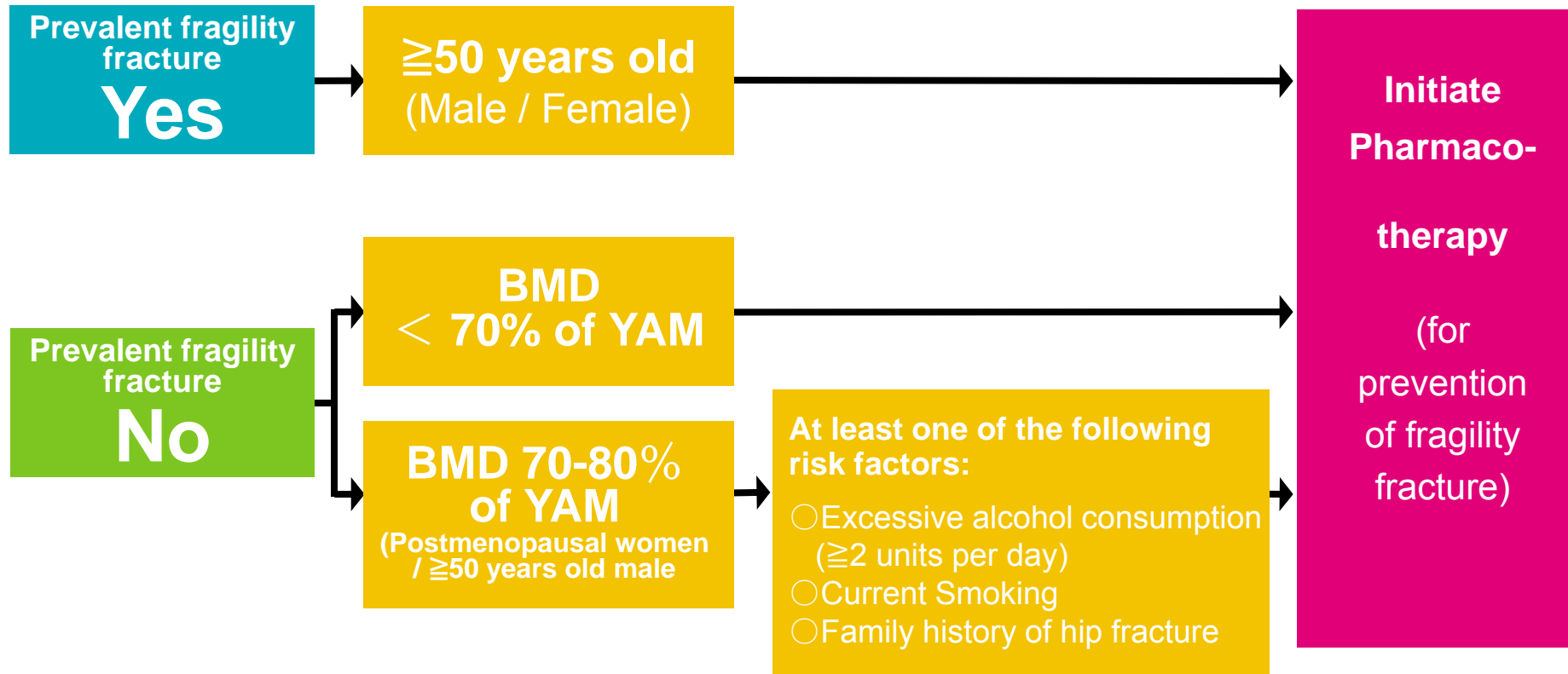
(Insurance covers when the patients are diagnosed for osteoporosis, before and within 6 ms of treatment )

Serum Bone Specific Alkaline Phosphatase (BAP)	1,700JPY	160USD
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# Treatment osteoporosis in Japan

**Purpose of treatment: to control fracture risks and to maintain or improve QOL**

## Criteria for initiation of pharmacotherapy for prevent fragility fractures



Japanese Guidelines for the Prevention and Treatment of Osteoporosis (2006 edition)

## Treatment of osteoporosis

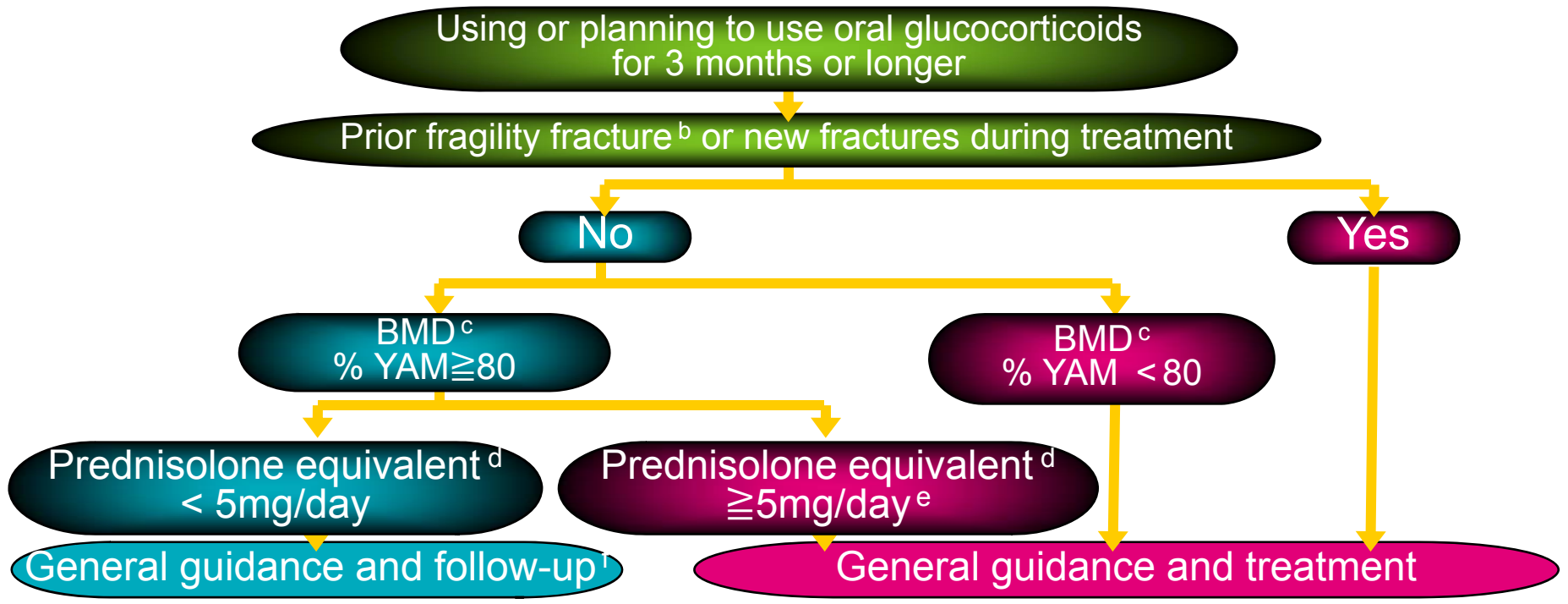
# Detailed and comprehensive recommendations on each drugs based on all available evidences

Therapeutic agent	BMD (Grade)	Veretbral fracture (Grade)	Non-vertebral fracture (Grade)	Overall evaluation (Grade)
Calcium	C	C	C	C
Estrogen	A	A	A	C
Active Vitamin D3	B	B	B	B
Viamin K2	B	B	B	B
Etidronate	A	B	B	B
Alendronate	A	A	A	A
Risedronate	A	A	A	A
SERM: Raloxifene	A	A	B	A
Calcitonin※	B	B	C	B
Ipriflavone	C	C	C	C
Anabolic steroid	C	C	C	C

※Calcitonin: “analgetic, and reducing pain (Grade A)”

Japanese Guidelines for the Prevention and Treatment of Osteoporosis (2006 edition)

# Guidelines on the management and treatment of corticosteroid-induced osteoporosis (2004 edition)<sup>a</sup>



**General guidance:**  
 Lifestyle guidance, nutritional guidance, and exercise therapy are based on those for primary osteoporosis.  
**Follow-up observation:**  
 Bone mineral density measurements and thoracic and lumbar vertebra X-rays are performed on a regular basis (even 6 months or 1 year).  
**Drug treatment:**  
 1. Bisphosphonates are first-line drugs.  
 2. Active vitamin D<sub>3</sub> and vitamin K<sub>2</sub> are second-line drugs.

YAM: young adult mean (20-44 years old) BMD: bone mineral density  
 a These guidelines cover patients 18 years of age and older.  
 b Definition of fragility fractures is the same as that for primary osteoporosis.  
 c BMD measurements are based on those for primary osteoporosis (2000 revised edition).  
 d Mean daily dose.  
 e Patients administered 10mg or more per day are at risk of fractures even when BMD is high (cut-off value, %YAM90).  
 f Risk of fractures is higher in the elderly.

From Nawata H, et al. J Bone Miner Metab 2005; 23: 105-9

Japanese Guidelines for the Prevention and Treatment of Osteoporosis (2006 edition)

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# **Future directions in osteoporosis care in Japan**

**How to deal with the delay of the development of the new drug?**

**Parathyroid hormone, strontium ranelate, ibandronate are currently being evaluated and have not been approved for treatment of osteoporosis.**

**Alendronate, risedronate and raloxifene were approved several years after US or EU approval. Weekly alendronate and risedronate were recently approved.**

**Therefore, concurrent development is necessary, such as joining the global trial.**

**How to evaluate the bone strength change in the clinical setting?**

**Introduction of central DXA to more sites where only the peripheral measurements are available.**

**More precise DXA measurement and evaluation--- need for training.**

**Introduction of CT measurement for bone strength study.**

**Evaluation of bone metabolic markers and newer ones such as pentocidin, under-carboxylated osteocalcin, etc.**

**Encouraging controlled clinical studies and bigger epidemiological studies.**