



## Bone Health after Transplant

Celebrating a Second Chance at Life  
Survivorship Symposium

April 17-23, 2021



Joy Wu MD, PhD

Stanford University  
School of Medicine

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**Stanford**  
MEDICINE



@JoyYWu

## Bone Health After Transplant

Joy Wu, MD, PhD  
Associate Professor of Medicine  
Division of Endocrinology

BMT InfoNet Survivorship Symposium  
April 19, 2021

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## Take-home messages

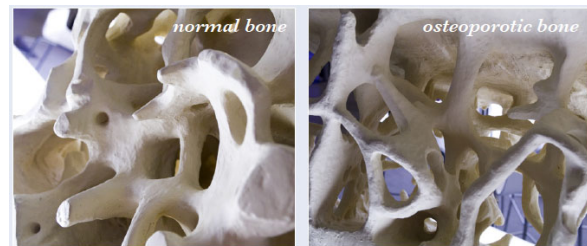
- Bone loss is common after transplant
- Fractures due to osteoporosis are serious but preventable
- Risk of fracture depends on many factors
- Lifestyle changes can slow but not reverse bone loss
- When used properly, osteoporosis medications are safe and effective



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## What is osteoporosis?

- “Porous bone”
- A decrease in bone mass leading to increased fragility and risk of fracture
- 50% of women and 20% of men will suffer a fracture from osteoporosis
- ~300,000 hip fractures per year
  - More than 20% will die within a year
  - Fewer than 50% will walk independently again



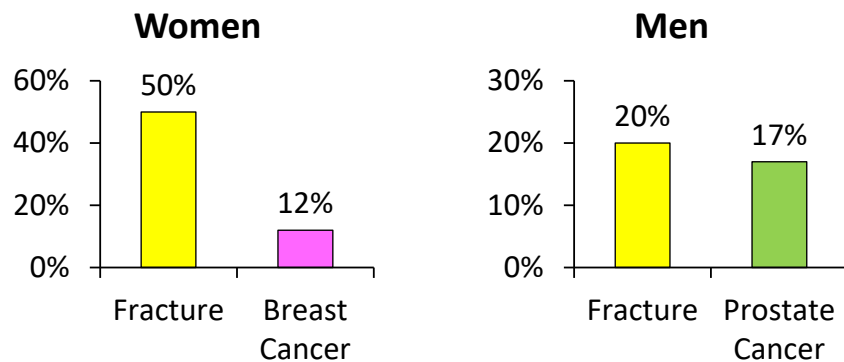
International Osteoporosis Foundation  
World Osteoporosis Day 2012 report



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## Osteoporosis in perspective

Lifetime risk at age 50



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There are 5,500 fractures a day in the US due to osteoporosis...



Photo by J. Wu



[2million2many.org](http://2million2many.org)

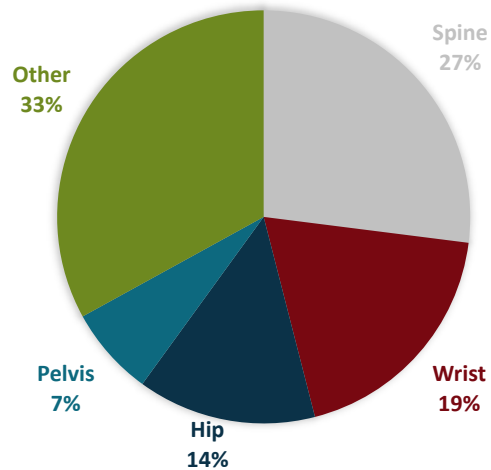
...that's **2 million** fractures a year.



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## Osteoporosis is a serious public health problem

TYPES OF FRACTURES



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## Bone loss after blood and marrow transplant

- Transplant recipients often have low bone mass even before transplant
- Allogeneic transplant recipients can lose 6-9% of bone mass at the spine and 8-17% of bone mass at the hip in the first year after transplant
- Bone loss occurs as early as 3 months after transplant



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## Why are transplant recipients at risk for bone loss?

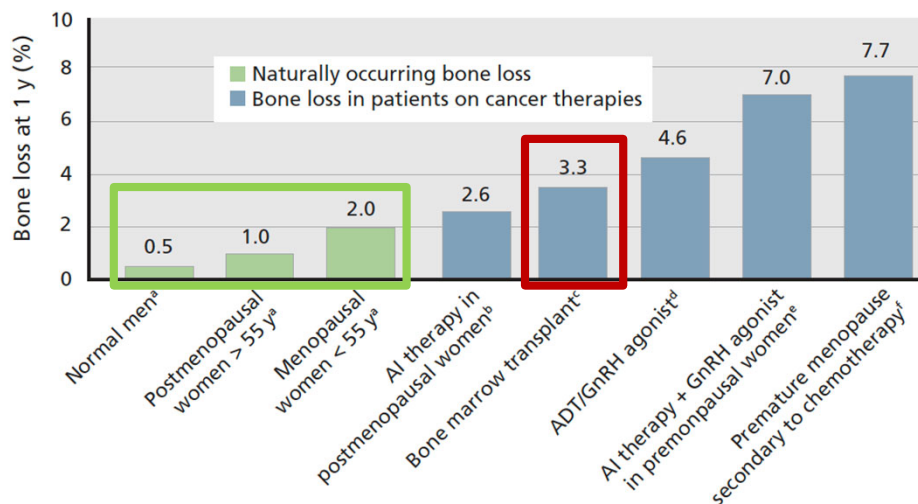
- Underlying disease leading to transplant
- Low estrogen or testosterone
  - Premature menopause after total body irradiation and/or chemotherapy
- Glucocorticoid treatment (for example for GVHD)
- Immunosuppression
- Radiation therapy
- Chemotherapy
- Other causes: heparin, kidney dysfunction, malabsorption, vitamin D deficiency

Weilbaecher, BBMT 2000



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## Rapid bone loss can occur after transplant



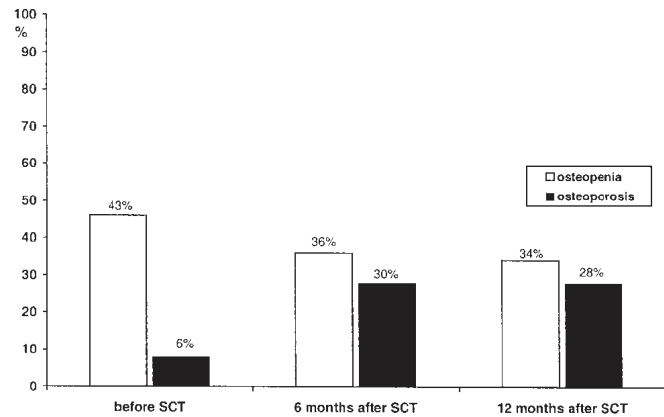
Gralow, JNCCN 2013



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## Bone loss after stem cell transplantation

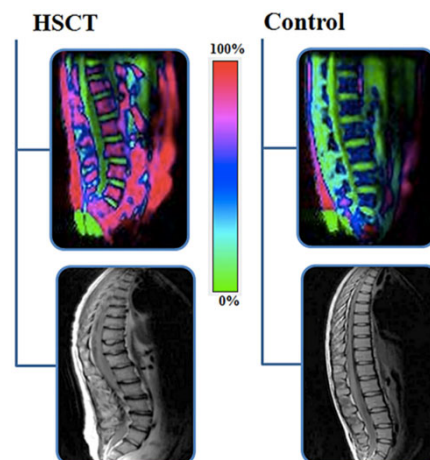
- Massenkeil, Leukemia 2001
  - 67 adults undergoing allogeneic transplant
  - 49% had osteopenia or osteoporosis before transplant
  - 67% had osteopenia or osteoporosis 6 months after transplant



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## Bone loss is common in survivors of pediatric blood and marrow transplantation

- Increased fat tissue in bone marrow
- Spine fractures can be seen at a much younger age than usual



Mostoufi-Moab, JBMR 2015



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## Am I at risk for bone loss?

- Older age
- Lower bone density
- Previous fracture
- Glucocorticoid treatment
- Family history of osteoporosis (especially a parent with a hip fracture)
- Low body weight
- Tobacco use
- Excessive alcohol
- Rheumatoid arthritis
- Secondary causes of osteoporosis



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## Who should have a bone density test?

- General recommendations (American Society for Bone and Mineral Research)
  - Women age 65 and older and men age 70 and older
  - Younger postmenopausal women and men ages 50–69 with clinical risk factors
  - Anyone with a low-trauma fracture after age 50
  - Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids) associated with bone loss



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Biol Blood Marrow Transplant 26 (2020) 1784–1802



## Biology of Blood and Marrow Transplantation

journal homepage: [www.bbmt.org](http://www.bbmt.org)



### Bone Health Management After Hematopoietic Cell Transplantation: An Expert Panel Opinion from the American Society for Transplantation and Cellular Therapy



Merav Bar<sup>1,2,\*</sup>, Susan M. Ott<sup>2</sup>, E. Michael Lewiecki<sup>3,4</sup>, Kyriakie Sarafoglou<sup>5,6</sup>, Joy Y. Wu<sup>7</sup>,  
Matthew J. Thompson<sup>8</sup>, Jonathan J. Vaux<sup>8</sup>, David R. Dean<sup>9</sup>, Kenneth G. Saag<sup>10</sup>, Shahrukh K. Hashmi<sup>11</sup>,  
Yoshihiro Inamoto<sup>12</sup>, Bhagirathbhai R. Dholaria<sup>13</sup>, Mohamed A. Kharfan-Dabaja<sup>14</sup>, Arnon Nagler<sup>15</sup>,  
Cesar Rodriguez<sup>16</sup>, Betty K. Hamilton<sup>17</sup>, Nina Shah<sup>18</sup>, Mary E.D. Flowers<sup>1,2</sup>, Bipin N. Savani<sup>13</sup>,  
Paul A. Carpenter<sup>1,2</sup>



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## Evaluation of bone health after blood and marrow transplant

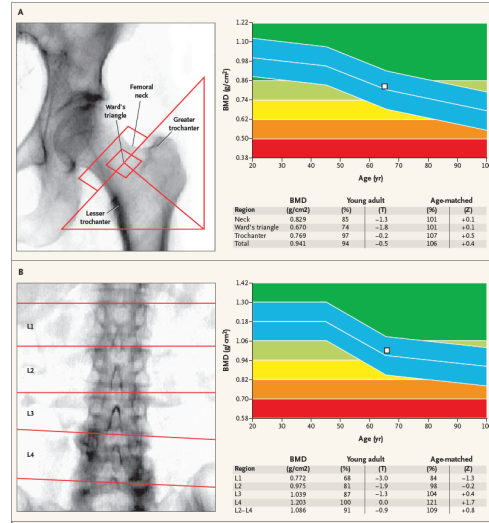
- Bone density (DXA) scan and fracture risk assessment (FRAX):
  - At 3 months, if not done before
  - At 3 months, if early high-dose glucocorticoid treatment was administered
  - After 1 year on treatment and every 1-2 years thereafter



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# What is a bone density scan?



Raisz, NEJM 2005



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**FRAX<sup>®</sup> Fracture Risk Assessment Tool**

Home Calculation Tool Paper Charts FAQ References English

### Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **US (Caucasian)** Name/ID:  [About the risk factors](#)

**Questionnaire:**

1. Age (between 40 and 90 years) or Date of Birth  
 Age:  Y:  M:  D:

2. Sex  Male  Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture  No  Yes

6. Parent Fractured Hip  No  Yes

7. Current Smoking  No  Yes

8. Glucocorticoids  No  Yes

9. Rheumatoid arthritis  No  Yes

10. Secondary osteoporosis  No  Yes

11. Alcohol 3 or more units/day  No  Yes

12. Femoral neck BMD (g/cm<sup>2</sup>)  
 Select BMD

**Weight Conversion**

Pounds   kg

**Height Conversion**

**BMI: 27.4**  
 The ten year probability of fracture (%)

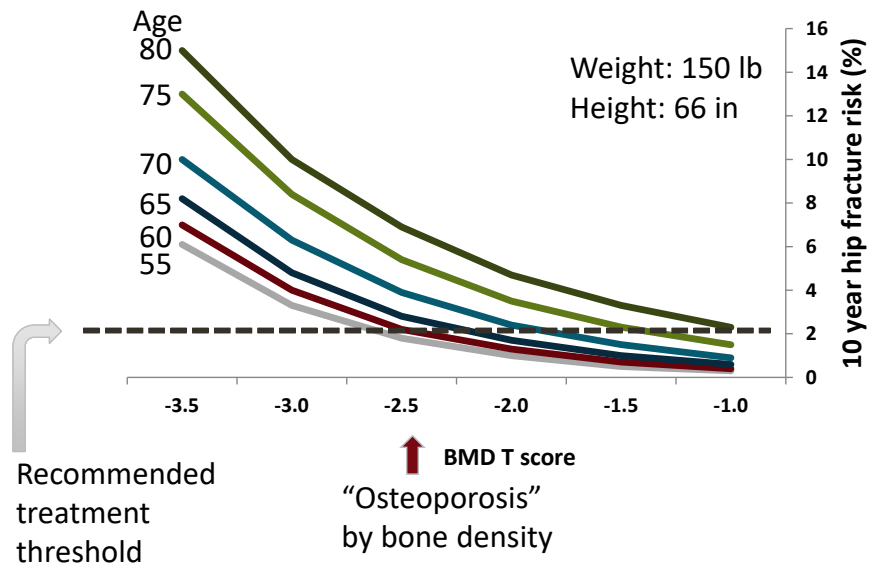
Fracture Type	Probability (%)
Major osteoporotic	18
Hip Fracture	3.3

**Treatment recommended:**  
 Major osteoporotic >20%  
 Hip fracture >3%

Individuals with fracture risk assessed since 1st June 2011 NE

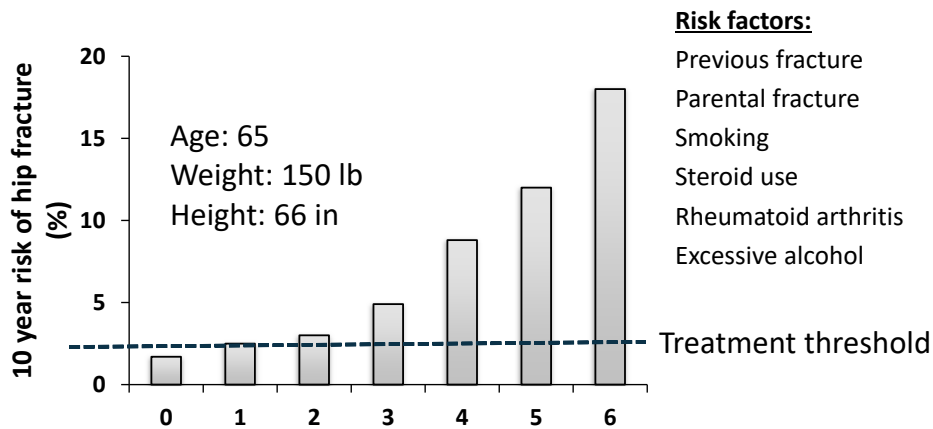
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## Fracture risk depends on BMD and age



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## Fracture risk increases with the number of risk factors



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## How can I improve my bone health?

- Get enough calcium and vitamin D
- Be physically active
- Reduce your risk of falls
- Maintain a healthy weight
- Do not smoke
- Limit alcohol use
- Talk with your doctor about medicines you are taking that could weaken bones

Surgeon General's Report on Bone Health 2019



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## How much calcium?

- Goal 1000-1200 mg daily
- Dietary sources
  - Milk, 1 cup = 302 mg
  - Yogurt, 1 cup = 300 mg
  - Cheddar cheese, 1.5 oz = 306 mg
  - Fortified orange juice, 1 cup = 260 mg
  - Canned salmon, with bones = 181 mg
  - Cottage cheese, 1 cup = 138 mg
  - Broccoli, 1 cup = 90 mg
- Supplements
  - No more than 500 mg at a time
  - If you are taking acid blocking medication, calcium citrate is recommended
  - Otherwise, calcium carbonate is fine



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## How much vitamin D?

- Vitamin D – goal 800-1000 IU a day
  - Vitamin D2 (ergocalciferol) is a plant-based supplement
  - Vitamin D3 (cholecalciferol) is produced in the skin, animal-based



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## Physical activity

- At least 150 minutes of moderate or 75 minutes of vigorous activity a week
- Strength training 2-3 times per week
  - Weights or resistance
- Balance and flexibility are also important
- National Osteoporosis Foundation recommendations:
  - <https://www.nof.org/preventing-fractures/exercise-to-stay-healthy/>



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## Do I need medication for osteoporosis?

- Not on glucocorticoids for GVHD:
  - History of a fragility fracture after age 50
  - Postmenopausal women or men over 50 with osteoporosis on a bone density scan
  - Estimated 10-year risk:
    - Major osteoporotic fracture >20%
    - Hip fracture >3%

Bar, BBMT 2020



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## Do I need medication for osteoporosis?

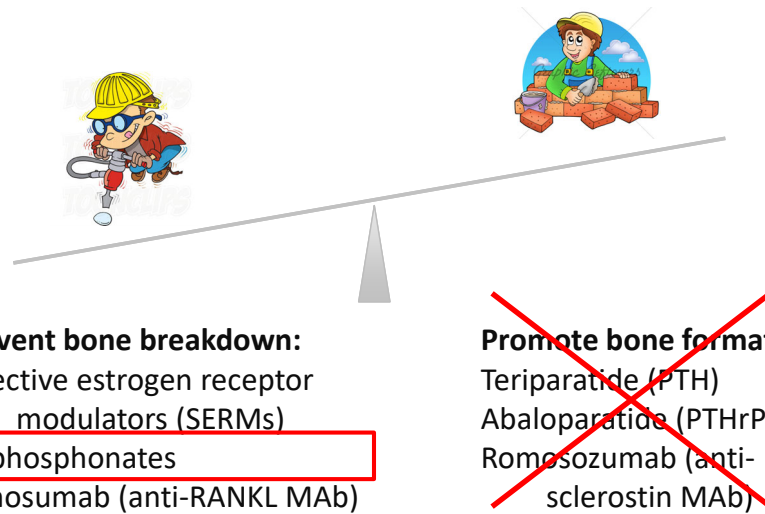
- On glucocorticoids for GVHD:
  - Age over 40
    - History of a fragility fracture after age 50
    - Postmenopausal women or men over 50 with osteoporosis on a bone density scan
    - Estimated 10-year risk:
      - Major osteoporotic fracture >10%
      - Hip fracture >1%
  - Age under 40
    - History of a fragility fracture
    - Severe osteoporosis or rapid bone loss

Bar, BBMT 2020



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## Medications for treating osteoporosis



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## Osteoporosis medications used in transplant recipients

Class	How it's given	Pros	Cons
Oral bisphosphonates: • <b>Alendronate</b> (Fosamax) • <b>Risedronate</b> (Actonel) • Ibandronate (Boniva)	• Weekly tablets (except Boniva which is monthly)	• Safe and effective	• Heartburn • Cannot be used with kidney disease • Boniva has not been shown to reduce all fracture types
IV bisphosphonate: • <b>Zoledronic acid</b> (Reclast)	• Intravenous infusion once a year	• Convenient	• Cannot be used with kidney disease • Mild flu-like reaction can occur
Anti-RANKL monoclonal antibody: • <b>Denosumab</b> (Prolia)	• Injection every 6 months	• Marked increase in BMD • Can be used with kidney disease	• No safety or efficacy data in HCT • Trial is ongoing



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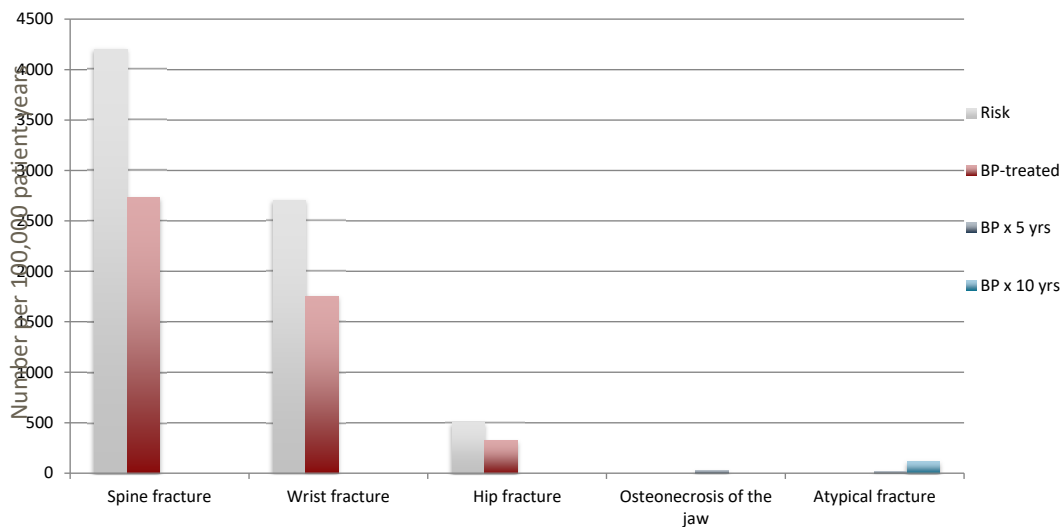
## Common concerns about medications

- “I prefer natural remedies to taking medication.”
- “I am very sensitive to medications.”
- “I’ve read that osteoporosis medications can be dangerous.”
- “I have a mother/sister/aunt/friend that took this medication and had an unpleasant side effect.”



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## What are the benefits vs. risks of treatment?



Modified from Adler, JBMR 2016



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## What are the benefits vs. risks of treatment?

Over 10,000 patient-years

Number of preventable fractures:



Number of cases of:



Osteonecrosis of the jaw



Atypical fractures (5 years)



Atypical fractures (10 years)



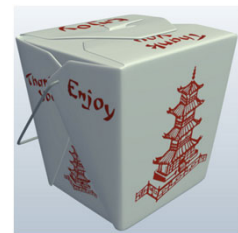
In the appropriate patients, the benefits of 5 years of bisphosphonate treatment far outweighs the risk.



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## Take-home messages

- Bone loss is common after transplant
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- Lifestyle changes can slow but not reverse bone loss
- When used properly, osteoporosis medications are safe and effective



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# Questions?



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