# Osteoporosis Prevention and Treatment in Chinese

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# Disclosures

Dr. Huey has been a speaker for the following Pharmaceutical Companies in the last 10 years:

Glaxo Smith Kline

Novo Nordisk

Roche

Sanofi Aventis

# Theme

- Living to 100 years and beyond!
- Osteoporosis
- Prevention is the Key!

# Osteoporosis

- Definition:

- A skeletal disease characterized by compromised bone strength predisposing a person to an increased risk of fracture

# Osteoporosis & Osteopenia

- Incidence

- In USA approximately 44 Million adults
- About 55% of Population >50 y/o

## Diagnostic categories for osteopenia and osteoporosis based upon bone mineral density measurement by DXA

| Category | Bone mass |
|---|---|
| Normal | A value for bone mineral density (BMD) within one standard deviation of the young adult female reference mean (T-score greater than or equal to -1 SD). |
| Low bone mass (osteopenia) | A value for BMD more than one but less than 2.5 standard deviations below the young adult female reference mean (T-score less than -1 and greater than -2.5 SD). |
| Osteoporosis | A value for BMD 2.5 or more standard deviations below the young adult female reference mean (T-score less than or equal to -2.5). |
| Severe (established) osteoporosis | A value for BMD more than 2.5 standard deviations below the young adult female reference mean in the presence of one or more fragility fractures. |

*Data from The World Health Organization Assessment of osteoporosis at the primary health care level. Summary report of a WHO Scientific Group. 2007; WHO, Geneva*

**Osteoporosis screening recommendations**

| | |
|---|---|
| National Osteoporosis Foundation (NOF) and International Society for Clinical Densitometry (ISCD) | The NOF and ISCD recommend measurement of BMD (DXA of the hip and spine) in[1-3]: |
| | • All women 65 years and older and men 70 and older regardless of risk factors. |
| | • Postmenopausal women and men 50 to 70 years when risk factors are present. |
| | • Adults who have a fracture after age 50. |
| | • Adults with a condition or taking a medication associated with low bone mass or bone loss. |
| | • Anyone being considered for pharmacologic therapy for osteoporosis. |
| | • Anyone being treated for osteoporosis to monitor response to therapy. |
| | • Anyone not receiving therapy when evidence of bone loss would lead to treatment. |
| | • Women in the menopausal transition if there is a specific risk factor associated with increased fracture, such as low body weight, prior low-trauma fracture, or high risk medication. |
| | • Postmenopausal women discontinuing estrogen should be considered for bone density testing. |
| | • The 33 percent forearm (1/3 radius) site is recommended in the following cases: |
| | - If hip and/or spine cannot be measured or interpreted. |
| | - Hyperparathyroidism. |
| | - Severe obesity (over the weight limit of DXA table). |
| Association of Clinical Endocrinologists (AACE) | AACE recommends measurement of BMD (DXA) in[4]: |
| | • All women 65 years and older. |
| | • Any adult with a history of fracture not caused by severe trauma. |
| | • Younger postmenopausal women with clinical risk factors for fracture. |
| | • The lumbar spine (PA) and proximal femur are recommended sites of measurement. |
| United States Preventive Services Task Force (USPSTF) | USPSTF recommends measurements of BMD in[5]: |
| | • All women ages 65 and older. |
| | • In addition, they recommend screening in younger women whose fracture risk is equal to or greater than that of a 65-year old white woman who has no additional risk factors. |
| | • The best site to screen is not mentioned, although the report agrees that DXA of the hip is the best predictor of hip fracture. |
| American Academy of Family Physicians | The American Academy of Family Physicians recommends measurement of BMD in[6]: |
| | • Women ages 65 and older. |
| | • Women 60 and older at increased risk for osteoporotic fracture. |
| National Institutes of Health | The NIH recommends[7]: |
| | • BMD measurements for individuals at high risk for osteoporosis. They do not recommend universal screening. |
| Royal College of Physicians | The Royal College of Physicians does not recommend population screening at this time. They are in favor of performing BMD measurements for high risk individuals only, including those with radiologic evidence of osteopenia or vertebral fracture, height loss, previous fracture, chronic corticosteroid use, early menopause (<age 45), secondary amenorrhea of greater than one year's duration, primary hypogonadism, maternal history of hip fracture and low BMI[8]. |
| United Kingdom National Screening Committee | Population screening is not recommended at this time[9]. |


*References:*

1. *Fulton JP. New guidelines for the prevention and treatment of osteoporosis. National Osteoporosis Foundation. Med Health R I 1999; 82:110.*
2. *NOF's New Clinician's Guide to Prevention and Treatment of Osteoporosis. http://www.nof.org/sites/default/files/pdfs/NOF_ClinicianGuide2009_v7.pdf (Accessed on January 10, 2011).*
3. *The Internationals Society for Clinical Densitometry Official Positions. www.iscd.org/Visitors/positions/OfficialPositionsText.cfm (Accessed on January 10, 2011).*
4. *American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Postmenopausal Osteoporosis. http://www.aace.com/pub/pdf/guidelines/OsteoGuidelines2010.pdf (Accessed on January 10, 2011).*
5. *U.S. Preventive Services Task Force. Screening for Osteoporosis Recommendation Statement. http://www.uspreventiveservicestaskforce.org/uspstf10/osteoporosis/osteors.htm (Accessed on February 10, 2011).*
6. *American Academy of Family Physicians. Recommendations for clinical preventative services. http://www.aafp.org/exam.xml. (Accessed on January 10, 2011).*
7. *www.consensus.nih.gov (Accessed on January 10, 2011).*
8. *Royal College of Physicians. Osteoporosis - Clinical guidelines for prevention and treatment. http://www.rcplondon.ac.uk/pubs/wp/wp_osteo_update.htm (Accessed on January 10, 2011).*
9. *National Screening Committee policy - osteoporosis screening. http://www.library.nhs.uk/screening/viewResource.aspx?catID=5534&resID=61088 (Accessed on January 10, 2011).*

# Osteoporosis Prevention

- Why?

- Major cause of Morbidity and Mortality
- As BMD decreases there is an increased fracture risk as a continuum.
- There is **NO Fracture Threshold!**

# Osteoporosis Prevention

- Often a Fracture is the beginning of the END!

- A large percentage of pts die within 1 year of a fracture.
- These pts "dwindle " away
- They survive the surgery but lose all their vitality. Anorexia then portends poor survival

# Osteoporosis Prevention

- -1SD BMD Hip= Increases Fx risk 2.6 Fold

- Loss of BMD results in micro architectural changes (Bone Loss) which are largely **IRREVERSIBLE!**
- Treatment may stabilize or increase BMD & decrease Fx risk but does **not** fully restore losses

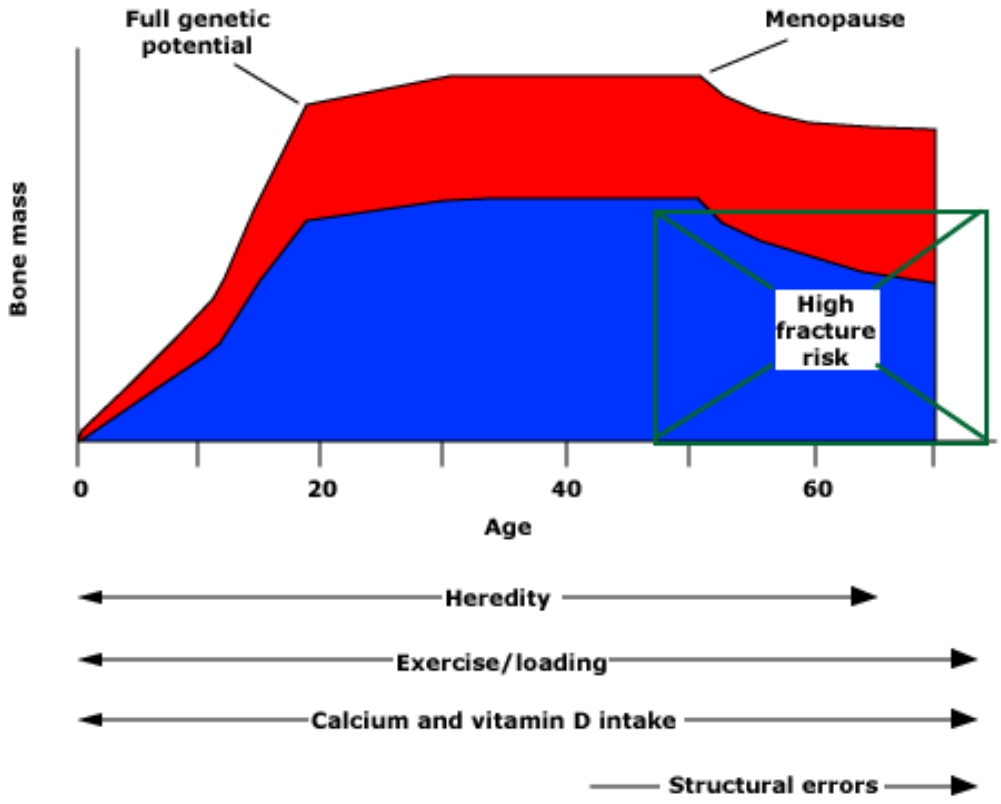
# Osteoporosis Prevention

- Ultimate goal:

- Maximize bone mass
- Minimize bone loss
- Maintain Bone Strength

- Thus preventing Fractures

## Diagrammatic representation of the bone mass life-line in individuals who achieve their full genetic potential for skeletal mass and in those who do not




(The magnitude of the difference between curves is not intended to be to scale). Along the bottom of the graph are several factors known to be of particular importance.

*Data from Robert P. Heaney, 1999.*

# Osteoporosis Prevention

- Risk Factors:

- Low body weight (Low BMI)
- Late menarche >15 y/o
- Physical inactivity especially as adolescents and teenagers
- Cigarette smoking and excessive Etoh use
- Caucasian or Asian Ethnicity

# Osteoporosis Prevention

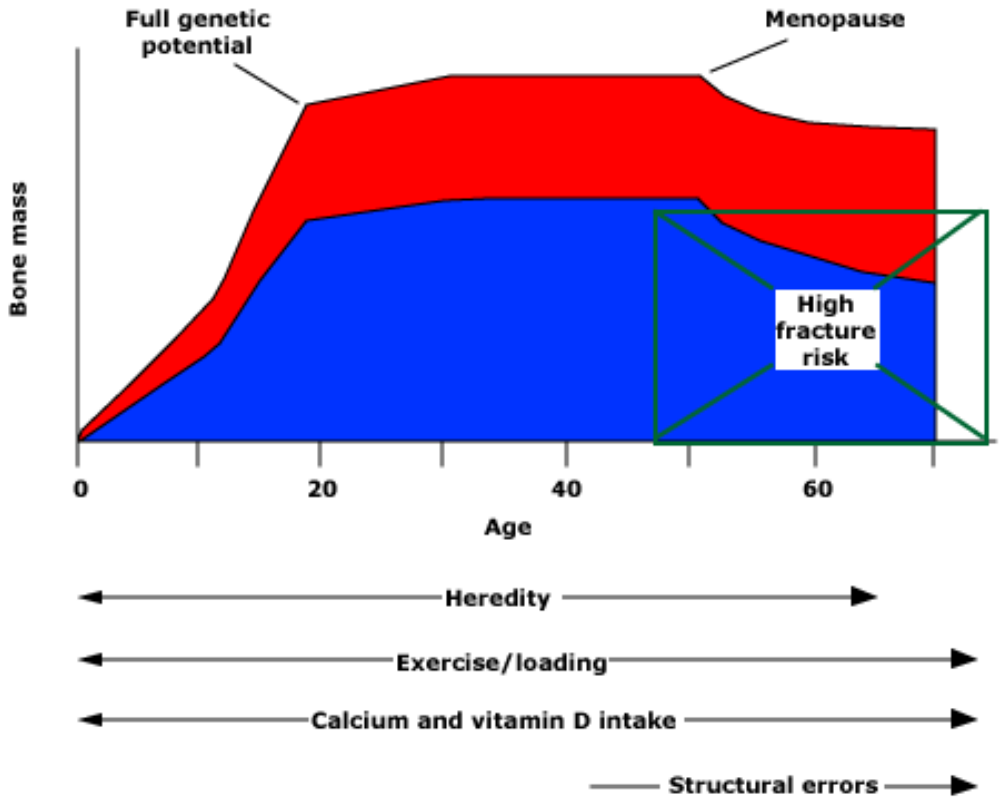
- Professor Charles Dent

"Senile Osteoporosis is a Pediatric Disease"

# Osteoporosis Prevention

- Although Peak Bone Mass (PBM) is 60-70% genetic (twin studies)
- 30-40% is environmental (Diet, exercise, habits, activity, diseases, & medications)

## Diagrammatic representation of the bone mass life-line in individuals who achieve their full genetic potential for skeletal mass and in those who do not

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*Data from Robert P. Heaney, 1999.*

# Osteoporosis Prevention

- The Problem
- Asians: High risk population now living in the USA
- Increased risk over our native land due to
  - Inactivity: game boy, computers, TV, schools with no Gym, Grandparents caring for children
  - Diet: high fat, CHO, Sugar with no Calcium/Vit D

## Foods and drinks with calcium

| Food | Calcium, milligrams |
|---|---|
| Milk (skim, 2 percent, or whole, 8 oz) | 300 |
| Yogurt (6 oz) | 250 |
| Orange juice (with calcium, 8 oz) | 300 |
| Tofu with calcium (1/2 cup) | 435 |
| Cheese (1 oz) | 195-335 (hard cheese = higher calcium) |
| Cottage cheese (1/2 cup) | 130 |
| Ice cream or frozen yogurt (1/2 cup) | 100 |
| Soy milk (1 cup) | 100 |
| Beans (1/2 cup cooked) | 60-80 |
| Dark, leafy green vegetables (1/2 cup cooked) | 50-135 |
| Almonds (24 whole) | 70 |
| Orange (1 medium) | 60 |

**Comparison of sources of absorbable calcium with milk**

| Food | Serving size*, g | Calcium content•, mg | Fractional absorptionΔ, percent | Estimated absorbable calcium◇, mg | Servings needed to equal 240 mL milk, n |
|---|---|---|---|---|---|
| Milk | 240 | 300 | 32.1 | 96.3 | 1.0 |
| Beans | | | | | |
| Pinto | 86 | 44.7 | 26.7 | 11.9 | 8.1 |
| Red | 172 | 40.5 | 24.4 | 9.9 | 9.7 |
| White | 110 | 113 | 21.8 | 24.7 | 3.9 |
| Bok choy | 85 | 79 | 53.8 | 42.5 | 2.3 |
| Broccoli | 71 | 35 | 61.3 | 21.5 | 4.5 |
| Cheddar cheese | 42 | 303 | 32.1 | 97.2 | 1.0 |
| Cheese food | 42 | 241 | 32.1 | 77.4 | 1.2 |
| Chinese cabbage flower leaves | 85 | 239 | 39.6 | 94.7 | 1.0 |
| Chinese mustard greens | 85 | 212 | 40.2 | 85.3 | 1.1 |
| Fruit punch with calcium citrate malate | 240 | 300 | 52.0 | 156 | 0.62 |
| Kale | 85 | 61 | 49.3 | 30.1 | 3.2 |
| Spinach | 85 | 115 | 5.1 | 5.9 | 16.3 |
| Sweet potatoes | 164 | 44 | 22.2 | 9.8 | 9.8 |
| Rhubarb | 120 | 174 | 8.54 | 10.1 | 9.5 |
| Tofu with calcium | 126 | 258 | 31.0 | 80.0 | 1.2 |
| Yogurt | 240 | 300 | 32.1 | 96.3 | 1.0 |

* Based on half-cup serving size (~85 g for green leafy vegetables) except for milk and fruit punch (1 cup or 240 mL) and cheese (1.5 ounces).
• From references 4 and 5 (averaged for beans and broccoli processed in different ways) except for the Chinese vegetables, which were analyzed in our laboratory.
Δ Adjusted for load by using the equation for milk (fractional absorption = 0.889-0.0964 in load (6)) then adjusted for the ratio of calcium absorption of the test food relative to milk tested at the same load, the absorptive index. The absorptive index was taken from the literature for beans (7), bok choy (8), broccoli (8), Chinese vegetables (9), fruit punch with calcium citrate mulate (10), kale (8), sweet potatoes (9), rhubarb (9), tofu (11), and dairy products (12).
◇ Calculated as calcium content x fractional absorption.

# Osteoporosis Prevention

- Typical Adolescent Chinese diet has between 300 to 600 mg Calcium/day
- Dietary Calcium needs typically >1000 mg/day
- Chinese typically do not eat yogurt, milk, cheese (dairy) therefore inadequate Ca & Vit D

# Osteoporosis Prevention

**Estimated energy requirements (low activity) and Dietary Reference Intakes of selected nutrients for infants, children, and adolescents**

| Age, years | Energy (females) kcal/day | Energy (males) kcal/day | Protein g/day | Total fat g/day | Iron mg/day | Calcium mg/day | Zinc mg/day |
|---|---|---|---|---|---|---|---|
| 1-3 | 750-1250 | 850-1300 | 13 | 30-40 | 7 | 700 | 3 |
| 4-8 | 1300-1600 | 1400-1700 | 19 | 25-35 | 10 | 1000 | 5 |
| 9-13 | 1700-2000 | 1800-2300 | 34 | 25-35 | 8 | 1300 | 8 |
| 14-18, boys | -- | 2500-2800 | 52 | 25-35 | 11 | 1300 | 11 |
| 14-18, girls | 2000 | -- | 46 | 25-35 | 15 | 1300 | 9 |

*Adapted from:*


1. *The Dietary Reference Intakes, National Academy of Sciences, Washington, DC, 2002.*
2. *National Academies Press. Dietary Reference Intakes for Calcium and Vitamin D (2010). Available at http://books.nap.edu/openbook.php?record_id=13050&page=291. Accessed on December 13, 2010.*

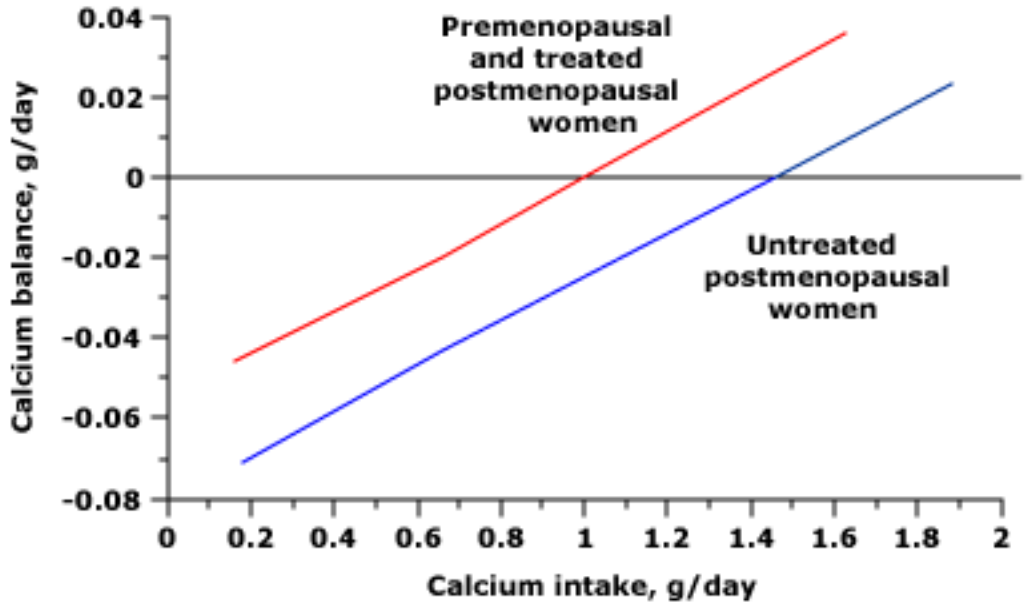
**Assessment of calcium intake and risks for suboptimal bone health in infants, children, and adolescents**

| Calcium intake questions | Approximate calcium content* |
|---|---|
| How many times a day do you (or does your child) drink white or flavored milk? | 1 cup whole milk: 246 mg |
| | 1 cup 1% milk: 264 mg |
| | 1 cup nonfat milk: 223 mg |
| | 1 cup calcium fortified soy milk: 200 to 500 mg |
| How often do you (or does your child) eat cheese, yogurt, yogurt drinks, or other dairy products? | 1 oz cheese: 202 mg |
| | 3/4 oz processed cheese: 144 mg |
| | 1/2 cup part skim ricotta: 337 mg |
| | 6 oz nonfat yogurt: 258 mg |
| | 1/2 cup frozen vanilla yogurt: 103 mg |
| Do you (or does your child) drink calcium-fortified juices? | 1 cup: 300 mg |
| Do you (or does your child) eat any calcium-fortified foods such as cereals or breads? | 3/4 to 1 cup breakfast cereal: 100 mg |
| | 1/2 cup fortified instant oatmeal (made with water): 65 mg |
| | 1 calcium enriched English muffin: 99 mg |
| Do you (or does your child) eat any of the following: broccoli, beans, cooked greens, tofu? | 1 cup cooked, chopped broccoli: 62 mg |
| | 1 cup cooked white beans: 161 mg |
| | 1 cup canned baked beans mg: 127 mg |
| | 1 cup cooked, chopped greens: 266 mg |
| | 1/2 cup tofu: 204 mg |
| Do you (or does your child) take calcium supplements including those containing vitamins? | Varies depending upon the supplement |
| **Bone health questions** | |
| How often do you (or does your child) drink sweetened drinks (soft drinks, fruit drinks, etc)? | |
| How many time a week do you (or does your child) participate in vigorous weight-bearing physical activity? | |
| Have you (or has your child) had any bone fractures? | |
| Is there a family history of osteoporosis? | |
| Were you (or was your child) born prematurely? | |

* Source: U.S. Department of Agriculture, Agriculture Research Service. U.S. Department of Agriculture NutrientData Laboratory.

*Adapted with permission from Greer, FR, Krebs, NF. Optimizing bone health and calcium intakes of infants, children, and adolescents. Pediatrics 2006; 117:578.*

## Relation between calcium intake and calcium balance




Plot of the regression lines relating calcium balance to calcium intake in premenopausal or estrogen-treated postmenopausal women (top line) and untreated postmenopausal women (bottom line). Positive calcium balance was achieved with calcium intakes above 1000 mg/day in the former group and 1500 mg/day in the latter group.

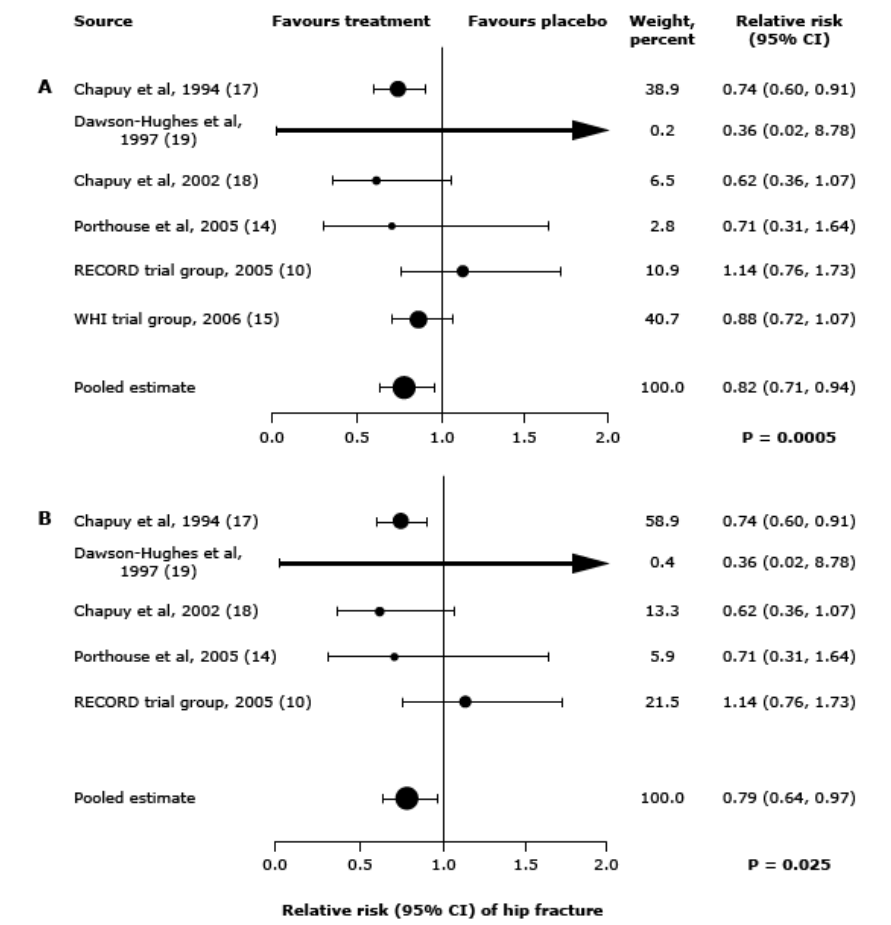
*Data from Heaney, RP, Recker, RR, Saville, PD, J Lab Clin Med 1978; 92:953.*

# Osteoporosis Prevention

- Calcium Vs Vitamin D

- Many studies document benefits of Ca supplementation alone but not Vit D alone
- However many studies have shown the added benefit of Ca plus Vit D supplementation

## Risk of hip fracture: Vitamin D plus calcium versus placebo




(A) Forest plot comparing the risk of hip fracture between vitamin D and calcium and placebo/no-treatment groups. The analysis includes the WHI trial.
(B) Forest plot comparing the risk of hip fracture between vitamin D and calcium and placebo/no-treatment groups. The exploratory analysis excludes the WHI trial.

CI: confidence interval; RECORD: Randomised Evaluation of Calcium Or vitamin D; WHI: Women's Health Initiative.

# Osteoporosis Prevention

- Vitamin D How much?

- Infants typically 400 iu/day but can be up to 800 iu in winter months. (Note Breast milk is low in Vit D)
- Children age 1 – 18 years 600 iu/day (IOM)
- Adults 19 –70 years 600 iu/day (max 4000 iu/day)
- Adults > 70 years 800 iu/day (max 4000 iu/day)

# Osteoporosis Prevention

- Typical Chinese diet falls far short of the 400 - 800 iu Vit D needed.
- Lack of physical activity and sun exposure (they don't go outside)
- Remember milk/OJ with Ca/D fortified to have 400 iu Vit D per quart (100 iu/ 8 oz)
- Without supplementation these children have **lifelong deficiency of Ca & Vit D**

# Factors that accelerate bone loss

- Endocrine Disorders
  - Hyperthyroidism
  - Hypopituitarism
  - Hypogonadism
  - Cushings Disease
  - Primary Hyperparathyroidism
- Gastrointestinal Disorders
  - Celiac disease
  - Short Bowel Disease
  - Inflammatory Bowel Disease
- Hematologic Disorders
  - Multiple myeloma
  - Systemic Mastocytosis

AACE Postmenopausal Guidelines 2010

# Factors that accelerate bone loss

- Renal Disorders
  - Chronic Renal Failure
  - Idiopathic Hypercalciuria
- Neuromuscular Disorders
  - Muscular Dystrophy
  - Paraplegia, Quadraplegia
  - Proximal Myopathy

AACE Postmenopausal Guidelines 2010

# Factors that accelerate bone loss

- Medications
  - Corticosteroids
  - Proton Pump inhibitors
  - Anticonvulsants
  - Medroxyprogesterone (Depo-Provera)
  - Selective Serotonin reuptake inhibitors (SSRI's)
  - Thiazolidinediones (TZD's)

AACE Postmenopausal Guidelines 2010

# Factors that accelerate bone loss

- *Rheumatologic* problems- Rheumatoid *Arthritis and other inflammatory problems*
- *Renal Disease*
- *Cardiac problems*
- *Any medical problems that lead to inactivity or nutritional deficiency*

## Clinical risk factors for fracture

| |
|---|
| Advancing age |
| Previous fracture |
| Glucocorticoid therapy |
| Parental history of hip fracture |
| Low body weight |
| Current cigarette smoking |
| Excessive alcohol consumption |
| Rheumatoid arthritis |
| Secondary osteoporosis (eg, hypogonadism or premature menopause, malabsorption, chronic liver disease, inflammatory bowel disease) |

*Data from: Kanis, JA, Borgstrom, F, De Laet. C, et al. Assessment of fracture risk. Osteoporosis International 2005; 16:581.*

# Osteoporosis Prevention

- Premenopausal Women

- Pregnancy may be a risk factor for fracture.
  - Minimal Bone loss from pregnancy but may increase with multiparity
  - Lactation can cause 3 - 10% bone loss at spine and hip related to duration of lactation & amenorrhea
  - Bone loss partly reversible with weaning and takes up to 18 mos or longer and may never completely reverse

# Osteoporosis Prevention

- Pregnancy associated Osteoporosis
  - Vertebral Fx in 3rd Trimester or early post partum
    - Abnl bone changes vs. pre-existing skeletal fragility
  - Transient Osteoporosis of Hip- rare, 3rd Trim unilateral or bilat. Hip pain can develop Fx
  - Idiopathic Fx- occurring during pregnancy etiologies can include Decreased IGF-1 or E2, Increased bone turnover, abnl osteoblastic function

# Pharmacologic Therapies

- Bisphosphonates: alendronate, risedronate, Ibandronate, Zolendronate
- Calcitonin: parenteral vs. intranasal
- SERMS: (used post menopausal primarily) Raloxifene
- Human PTH- stimulates osteoclastic & indirectly osteoblastic activity
- Denosumab: inactivates RANKL (TNF superligand shuts down osteoclastic activity)

# Summary

- Osteoporosis is a major health issue leading to significant morbidity and mortality
- It starts in the pediatric age with poor quality bone in Asians
- Multifactorial lifestyle problems interfere with bone health in the adolescent and teenage years
- The Chinese diet and culture lead to lifelong deficiencies in Ca and Vit D

# Summary

- This sets the stage for poor quality bone and low BMD in adulthood.
- Further worsened in women by pregnancy and lactation
- Adult Chinese diet and lifestyle do not provide adequate Ca and Vit D either
- Poor Bone Health occurs before menopause when accelerated bone losses occur.

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