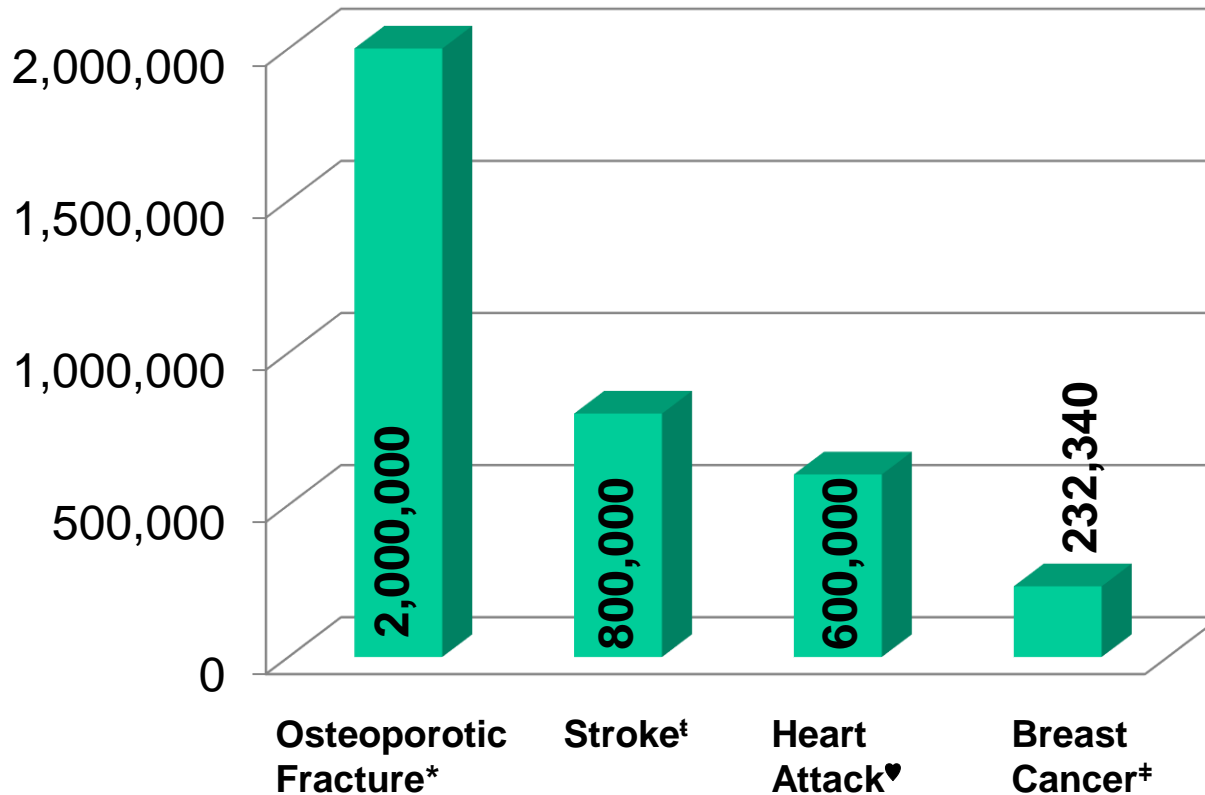


# Minerals in Bone and Heart Health

How much is enough and how much is too much?

Connie M. Weaver, Ph.D.  
Purdue University

# Annual Incidence of Common Diseases



\*National Osteoporosis Foundation (2013)

‡<http://www.cdc.gov/stroke/> (2013)

♥ <http://www.cdc.gov/heartdisease/facts.htm/> (2010)

‡[http://www.breastcancer.org/symptoms/understand\\_bc/statistics](http://www.breastcancer.org/symptoms/understand_bc/statistics) (2013)

# State of Women's Health in Indiana

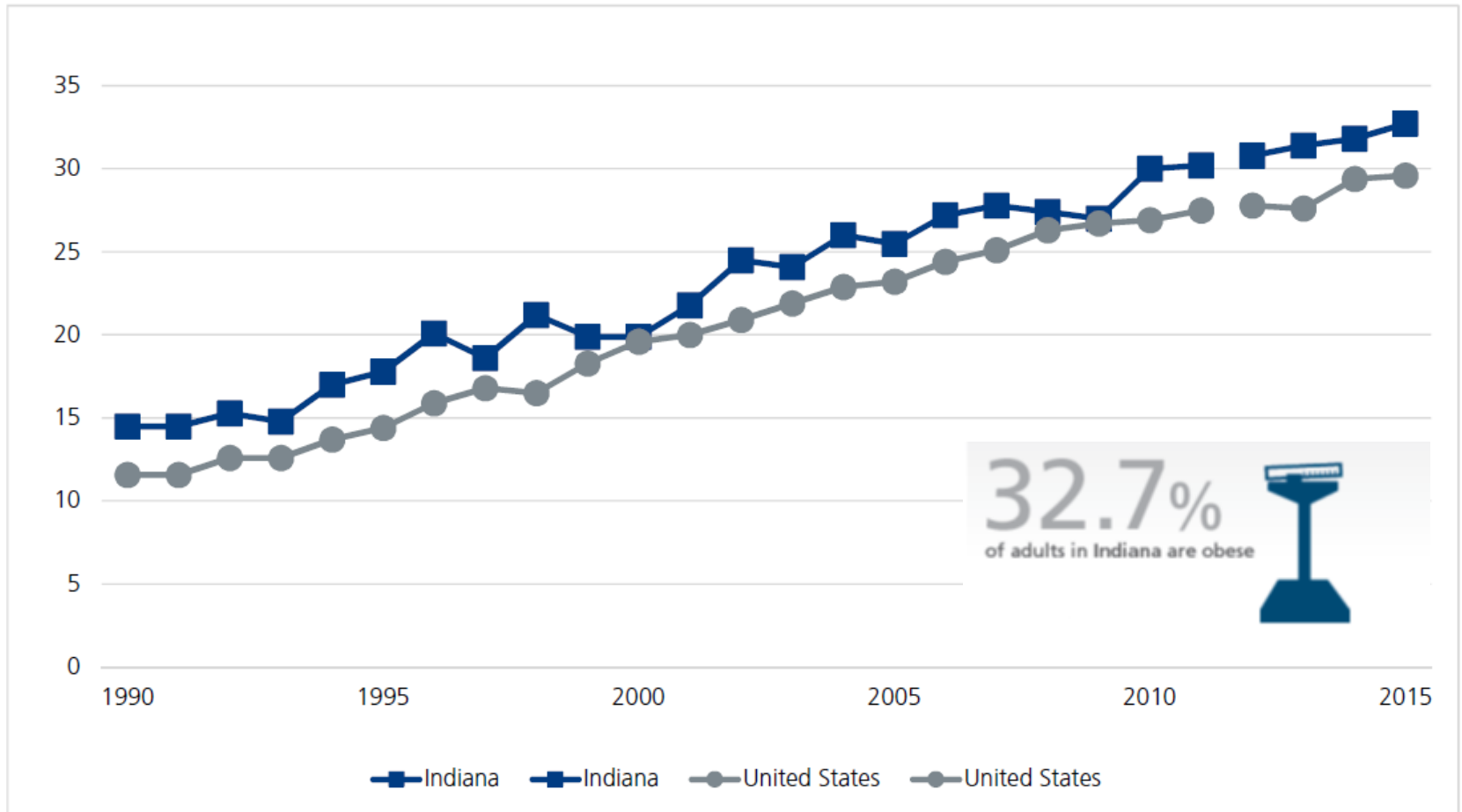
Indiana ranked in the bottom third of the country for the third consecutive year for women's status in categories such as health and well-being, employment and earnings.

# INDIANA HEALTH STATISTICS

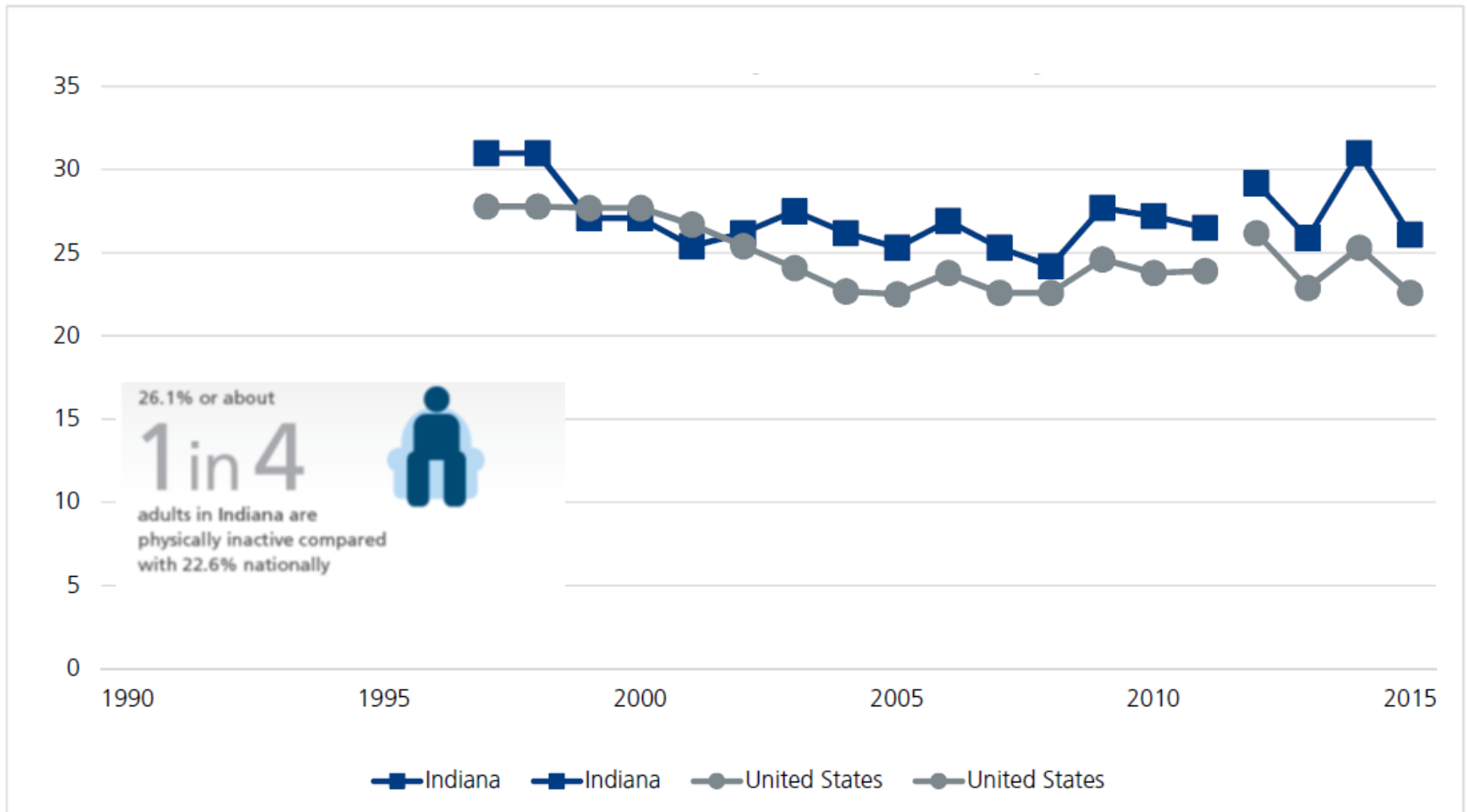
## Incidence in Adults

Obesity	32.7%
Diabetes	10.7%
Hypertension	33.5%
Low bone density	13.4%

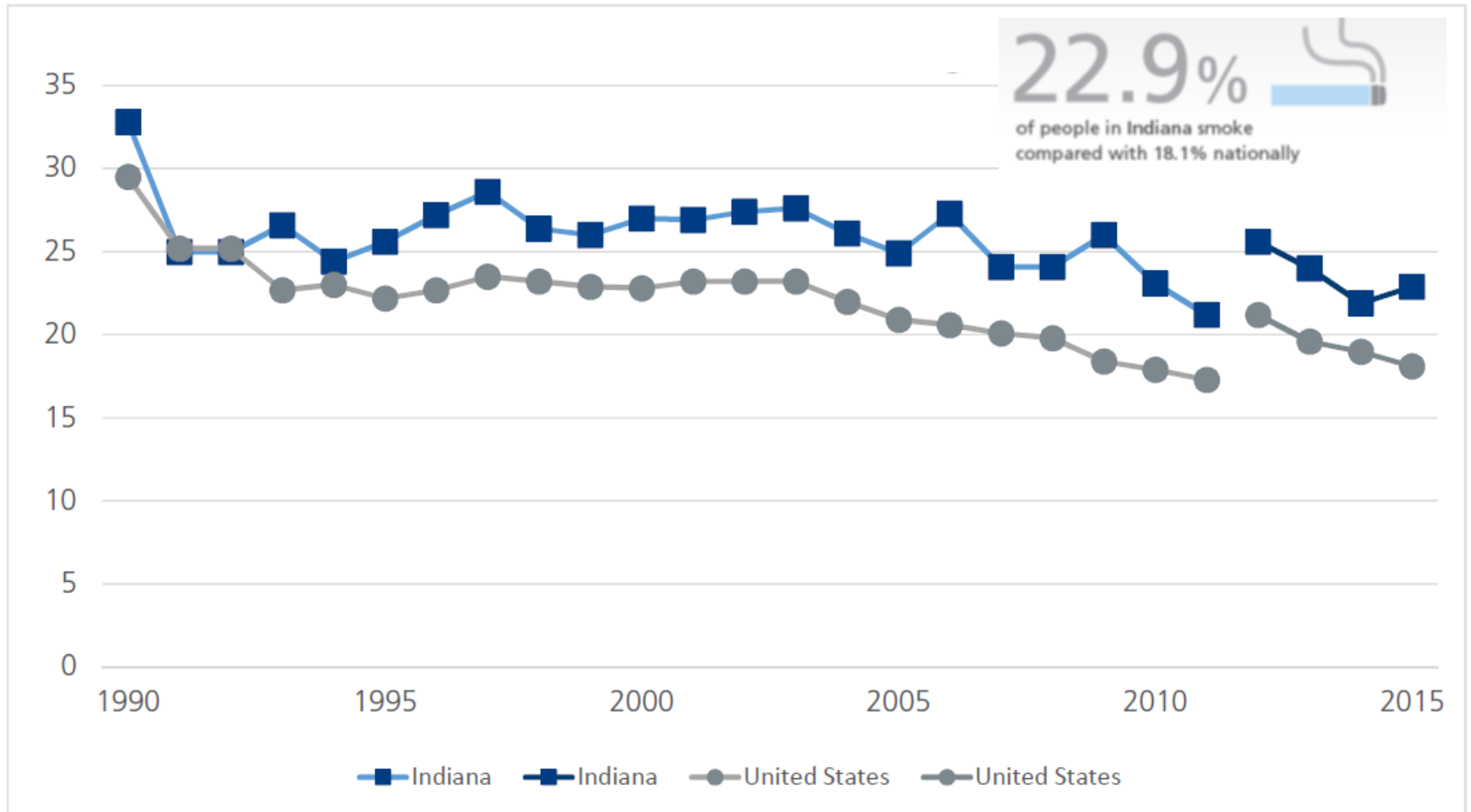
# Prevalence of Obesity



# Prevalence of Physical Inactivity



# Prevalence of Smoking



# Women's Global Health Institute at Purdue



<http://www.purdue.edu/discoverypark/WGHI/>

*"Discovery with Delivery for Women's Health Research"*



# Vision

To improve the health and quality of women worldwide through:

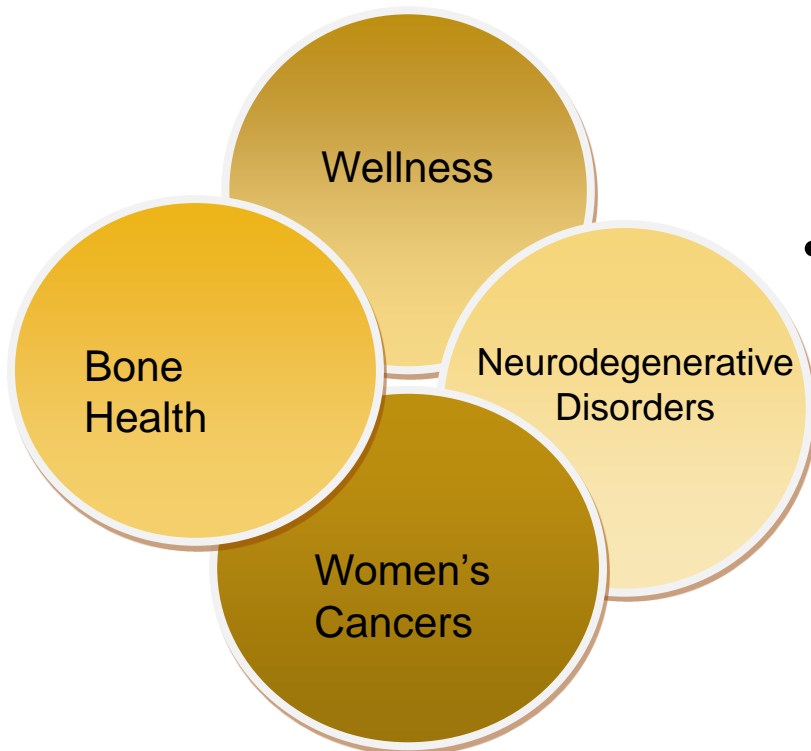
- Research
- Training future investigators





Women's Global Health Institute

- Focus on Wellness and disease **Prevention, early detection and effective interventions**



- Combine strong technology, engineering, natural and social sciences – a hub for interdisciplinary research
- Four research platforms
  - Bone Health
  - Women's Cancers
  - Neurodegenerative Disorders
  - Wellness



Women's Global Health Institute

# Bone Health



- **1 in 3 women over 50 will experience bone fractures**
- **Affects 200 million women worldwide**
- **80% of fractures are in women**
- **Nearly 25% increase in hip fracture worldwide between 1990 and 2000**
- **Mortality increases up to 25% in the first year after fracture**

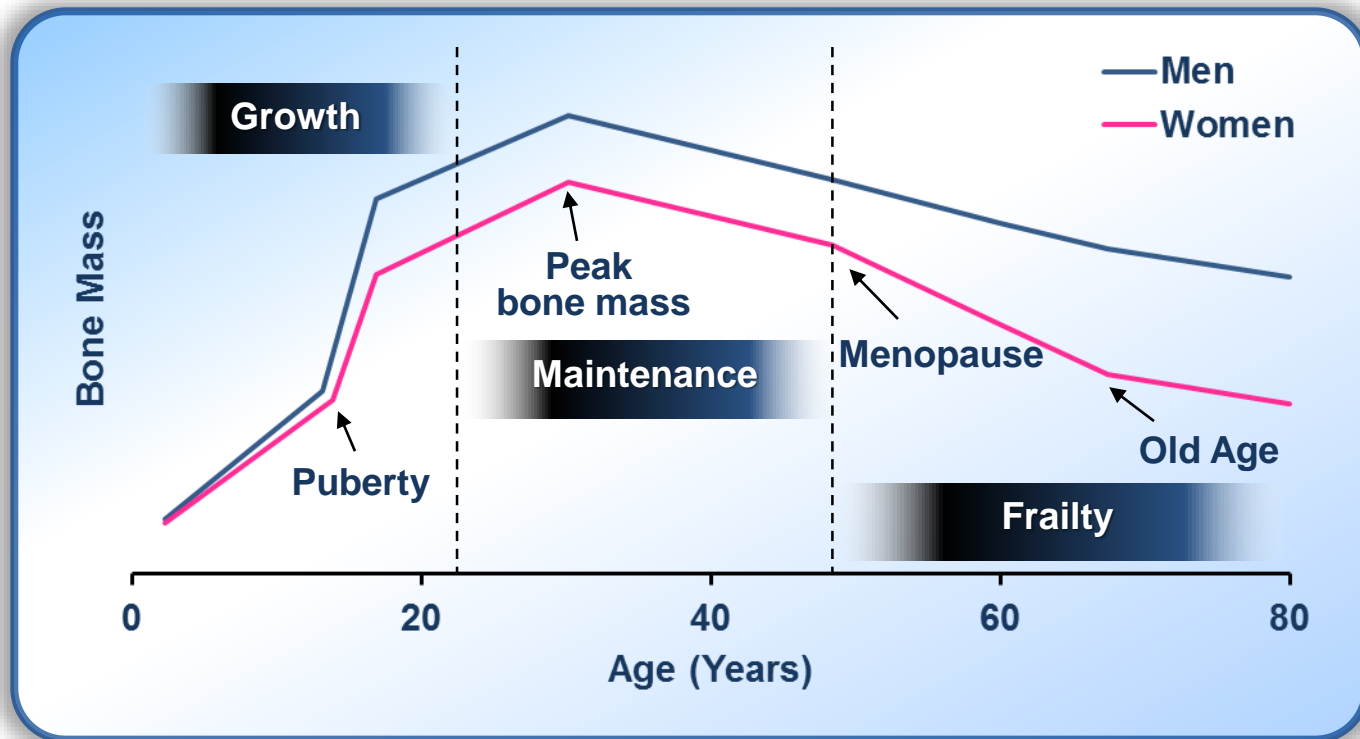
**World wide cost of hip fracture - \$131 billion.**



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# Bone Health: A Lifelong Concern

- Peak skeletal mass achieved by ages 20-30
- Adult skeleton remodeled and replaced every 10 years



Strategies to prevent fracture are to build peak bone mass early in life and to reduce bone loss later in life



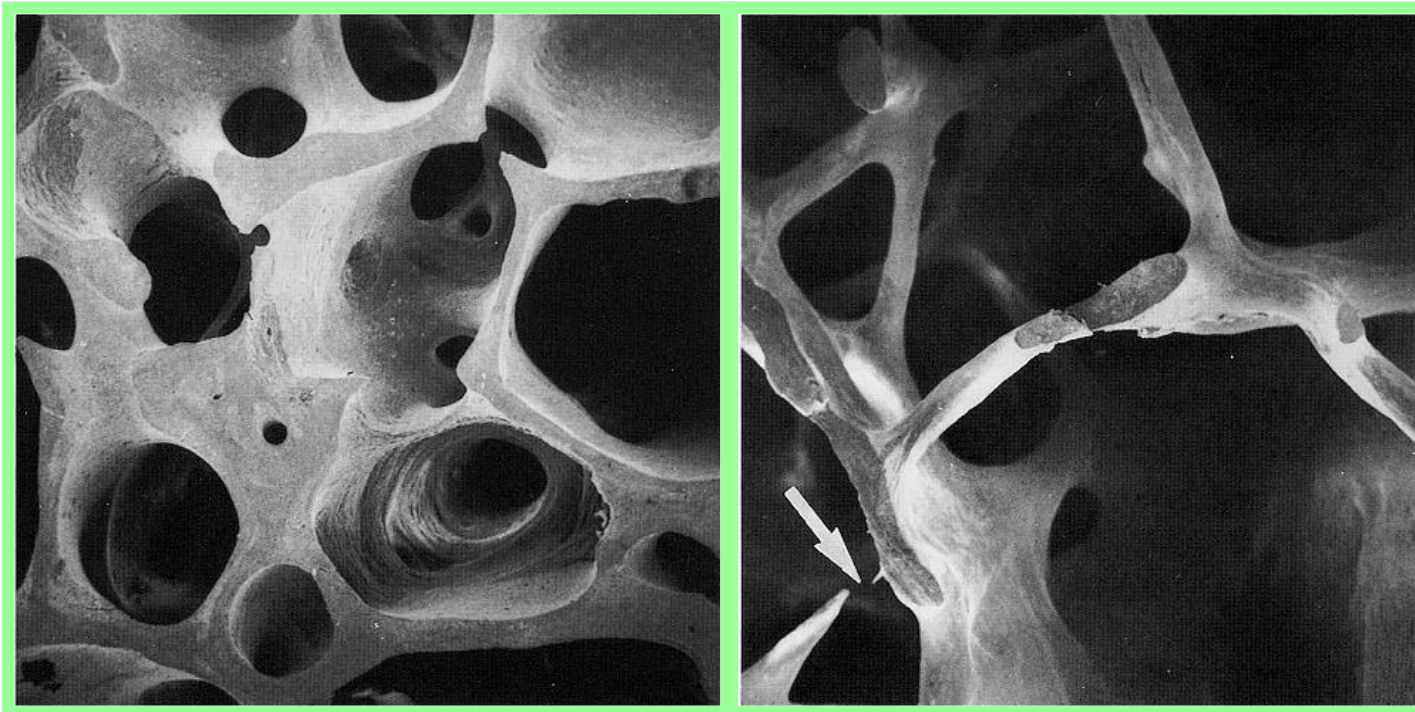


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# What is Osteoporosis?

**Normal Bone**

**Osteoporotic Bone**



Reproduced from *J Bone Miner Res.* 1986;1:15-21  
with permission of the American Society for Bone and Mineral Research

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## Call to Action to Address the Crisis in the Treatment of Osteoporosis

---

- **American Society for Bone and Mineral Research**
- American Academy of Orthopaedic Surgeons
- American Academy of Physician Assistants
- American Association of Clinical Endocrinologists
- American Bone Health
- American College of Rheumatology
- American Medical Society for Sports Medicine
- American Orthopaedic Association
- American Osteopathic Academy of Orthopedics
- American Society for Surgery of the Hand
- Australia New Zealand Bone and Mineral Society
- Bulgarian Society of Osteoporosis and Osteoarthritis
- Czech Society for Metabolic Bone Diseases
- Dutch Society of Cancer and Bone Metabolism
- European Calcified Tissue Society
- European Union Geriatric Medicine Society
- Finnish Osteoporosis Association

- Hellenic Osteoporosis Foundation
- International Geriatric Fracture Society, Inc.
- International Osteoporosis Foundation
- International Society for Clinical Densitometry
- Michigan Consortium for Osteoporosis
- National Bone Health Alliance
- **National Osteoporosis Foundation**
- Northern California Institute for Bone Health, Inc.
- Orthopaedic Research and Education Foundation
- Orthopedic Research Society
- Osteoporosis Australia
- Osteoporosis New Zealand
- Syrian National Osteoporosis Society
- University of Rochester Department of Orthopaedics and Rehabilitation
- U.S. Bone and Joint Initiative
- 4BoneHealth

- New evidence that the 30-year downward trend in hip fractures in the U.S. has hit a plateau over the past few years
- Fewer high risk individuals are being treated

*ASBMR Sept. 2016  
Lewiecki et al. 2016 JBMR 31 (Supp 1)*



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# Current Treatment Options



- **Non-pharmacologic**
  - Calcium and Vitamin D
  - Weight-bearing exercise
- **Pharmacologic**
  - Anti-Catabolic Drugs
    - bisphosphonates
    - RANKL inhibitor
    - estrogen
    - SERMS
  - Anabolic Drugs
    - teriperitide



**FORTEO**  
teriparatide injection  
(rDNA origin)



# Dietary Guidelines for Americans

## Nutrients of Public Health Concern

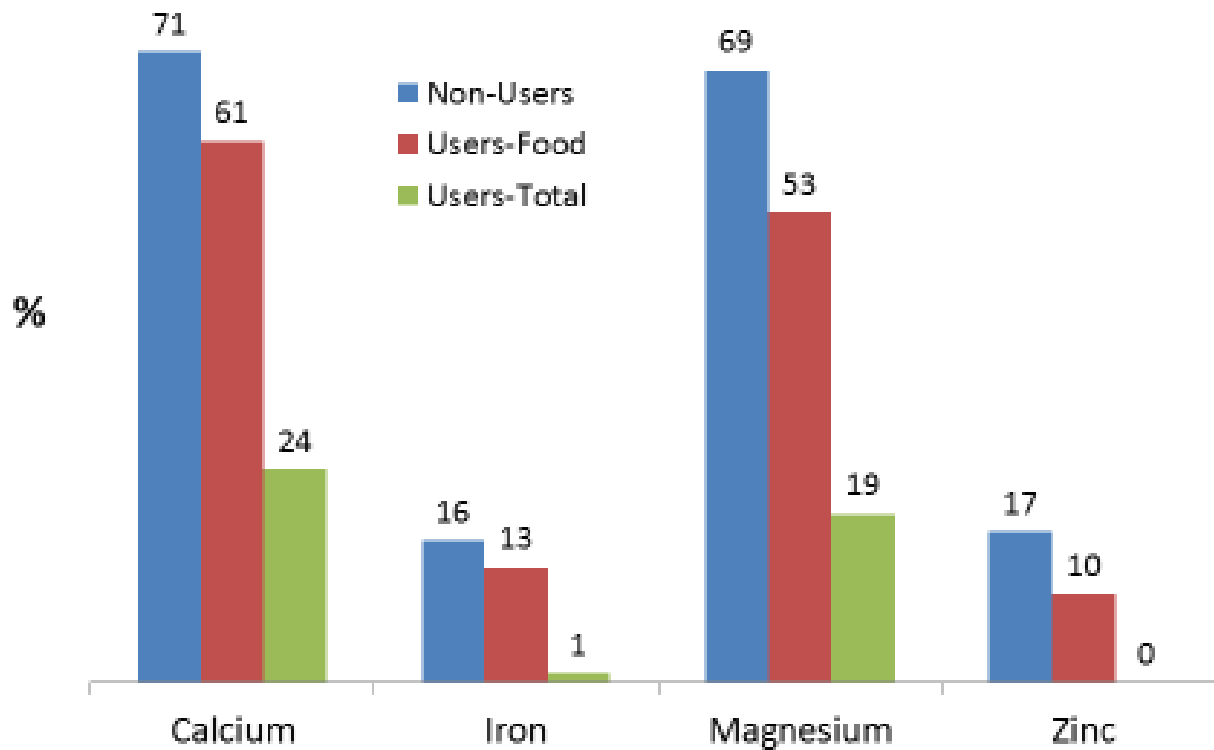
- **Potassium** - The Adequate Intake (AI) for potassium for adults is 4,700 mg per day.
- **Calcium** -The RDA ranges from 1000-1300 mg/d for > age 4y.
- **Magnesium** -The RDA ranges from 240 to 420 mg/d for those >age 9y.





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## % of Female Adults with Mineral Intakes < Estimated Average Requirements



Bailey RL, Fulgoni VL, Keast DR, Dwyer J. *American Journal of Clinical Nutrition*, 2011;94:1376–81.



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# Bone Building Nutrient – Calcium

- Constant uptake and release = bone turnover
- Only 10 – 30% of calcium is actually absorbed
- Absorption is best in <500 mg doses

## Estimated Average Requirement

- 4-8 year olds – 800 mg/day
- 9-18 year olds – 1100 mg/day
- Adults <51 – 800 mg/day
- Males 51-70 – 800 mg/day
- Females 51-70 – 1,000 mg/day
- All adults >70 – 1,000 mg/day

## Sources

- Dairy products
- Fortified foods
- Broccoli, kale





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# Bone Building Nutrient – Vitamin D

- Cholecalciferol (D3) & ergocalciferol (D2) are both bioactive
- Enhances absorption of calcium and phosphorous
- Found naturally in very few foods
  - Fortified foods provide ~70% of Vit D in the diet

## Estimated Average Requirement

- All ages – 400 IU/day

## Sources

- Fortified dairy products
- Fortified cereal and juice
- Fatty fish

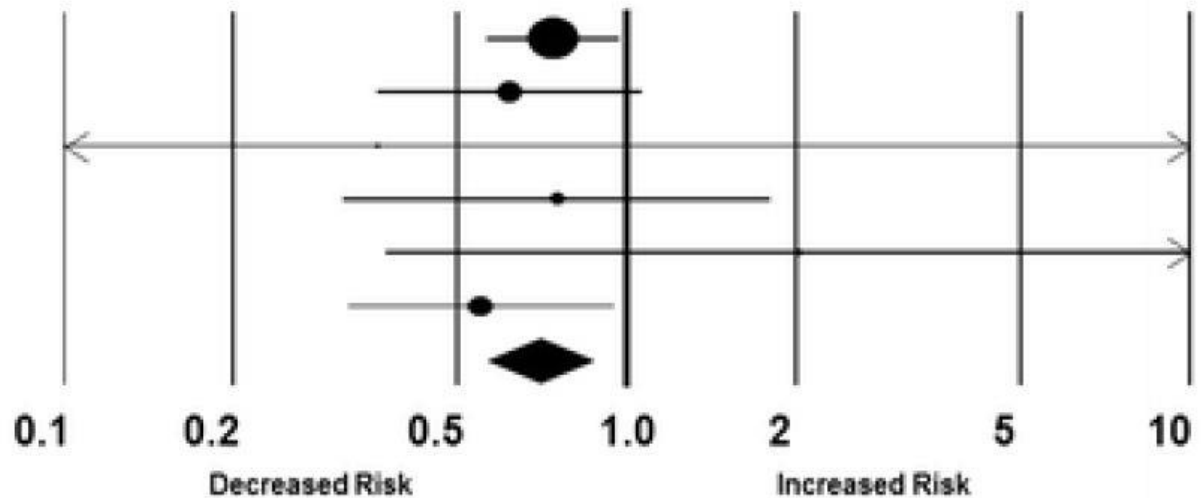


# Meta analysis shows Calcium plus vitamin D reduces risk of hip fractures by 30%

**a** Study Name

Rate Ratio and 95% CI

Chapuy, 1992 [20]  
Chapuy, 2002 [21]  
Dawson-Hughes, 1997 [22]  
Porthouse, 2005 [23]  
Salovaara, 2010 [24]  
Prentice, 2013 [10]<sup>a</sup>  
SRRE = 0.70 (0.56–0.87)  
*P*-heterogeneity = 0.74  
*I*<sup>2</sup> = 0.00



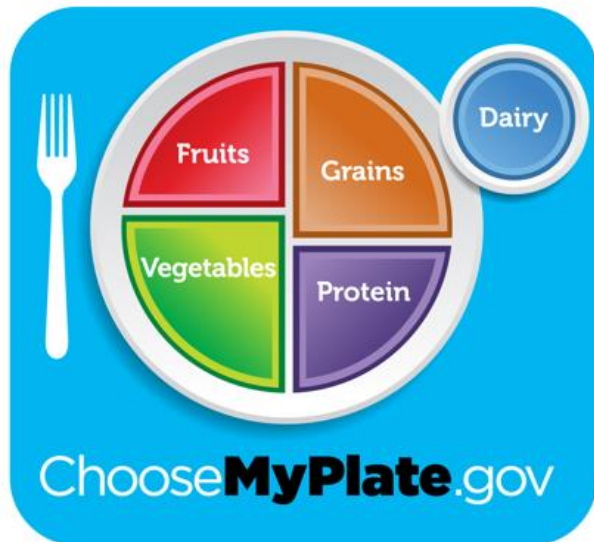
# Dietary Patterns for Bone Health

- **2015 Dietary Guidelines for Americans**
  - For adults, dietary patterns ...
    - higher in vegetables, fruits, grains, nuts, and dairy products
    - lower in meats and saturated fat
- ...Are associated with more favorable bone health outcomes
- Grade of evidence: “limited”



# Prudent Recommendations

- 3 cups of low-fat dairy product equivalents/day



- 300mg calcium supplement for each serving missed

## Percent calcium in common salts

	<u>%</u>
Calcium carbonate	40
Tricalcium phosphate	38
Dicalcium phosphate, dihydrate	36
Bone meal	31
Oyster shell	28
Dolomite	22
Calcium citrate	21
Calcium citrate malate	13
Calcium lactate	13
Gluconate	9
Glubionate	6.5

*Weaver, C.M. and Heaney, R.P. Ch. 9 Food Sources, Supplements and Bioavailability. In: Calcium in Human Health. Weaver, C.M. and Heaney, R.P., eds. Humana Press. 129-142, 2006.*

# Safety of High Doses of Calcium

BMJ

RESEARCH

Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis

Mark J Bolland, senior research fellow,<sup>1</sup> Alison Avenell, clinical senior lecturer,<sup>2</sup> John A Baron, professor,<sup>3</sup> Andrew Grey, associate professor,<sup>1</sup> Graeme S MacLennan, senior research fellow,<sup>2</sup> Greg D Gamble, research fellow,<sup>1</sup> Ian R Reid, professor<sup>1</sup>



 CBS EVENING NEWS  
with SCOTT PELLEY

[FULL EPISODES](#) [ON THE ROAD](#) [THE TEAM](#) [ABOUT US](#)

July 29, 2010 8:56 PM

PRINT  TEXT 

## Calcium Supplements Linked to Heart Attacks



# Ossabaw Pig

## Model for Soft Tissue Calcification?



**Connie Weaver**  
Nutrition Science



**Alyssa Phillips**  
Graduate Student



**George Jackson**  
AMS/Physics



**J. Scott Radcliffe**  
Animal Science



**Sean Newcomer**  
Health and Kinesiology



**Meryl Wastney**  
Kinetic Modeling

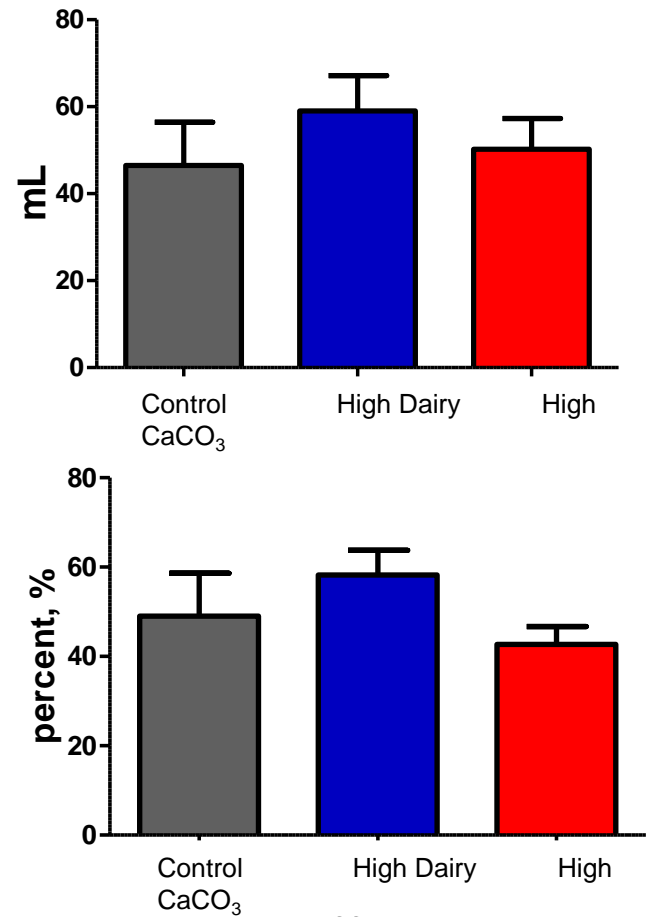


**Bill Van Alstine**  
Veterinary Medicine



**Mike Sturek**  
IU School Medicine

# Imaging: PET-CT to assess cardiovascular function



- Stroke Volume and Ejection Fraction did not differ among groups

# CONCLUSIONS

6-month feeding of high calcium from calcium carbonate or dairy did not alter cardiovascular function, coronary artery disease burden or coronary artery calcification in Ossabaw miniature swine.

# Combined Effort to Elucidate Role of Calcium in Cardiovascular Disease

Calcium intake and CV disease risk:  
Updated systematic review  
and meta-analysis  
Tufts University

Position statement :  
National Osteoporosis Foundation (NOF) and  
American Society for Preventive Cardiology (ASPC)

# Why is peak bone mass important?

- 30 to 50% of children have at least one fracture by the end of teenage years
- a 5–10% difference in PBM may result in a 25–50% difference in hip fracture rate later in life
- (Estimated annual costs exceed \$131 billion for hip fractures worldwide.)

# Camp Calcium

**11 Controlled Feeding Studies 1990-2010**

**What are calcium requirements  
in adolescents?**

*Funded by NIH*



# Tribute to Main Team



**Munro Peacock, M.D.**  
Clinical Researcher



**George McCabe, Ph.D.**  
Statistics Genius



**Linda McCabe, M.S.**  
Statistician



**Meryl Wastney, Ph.D.**  
Kinetic Modeler



**Berdine Martin, Ph.D.**  
Research Associate





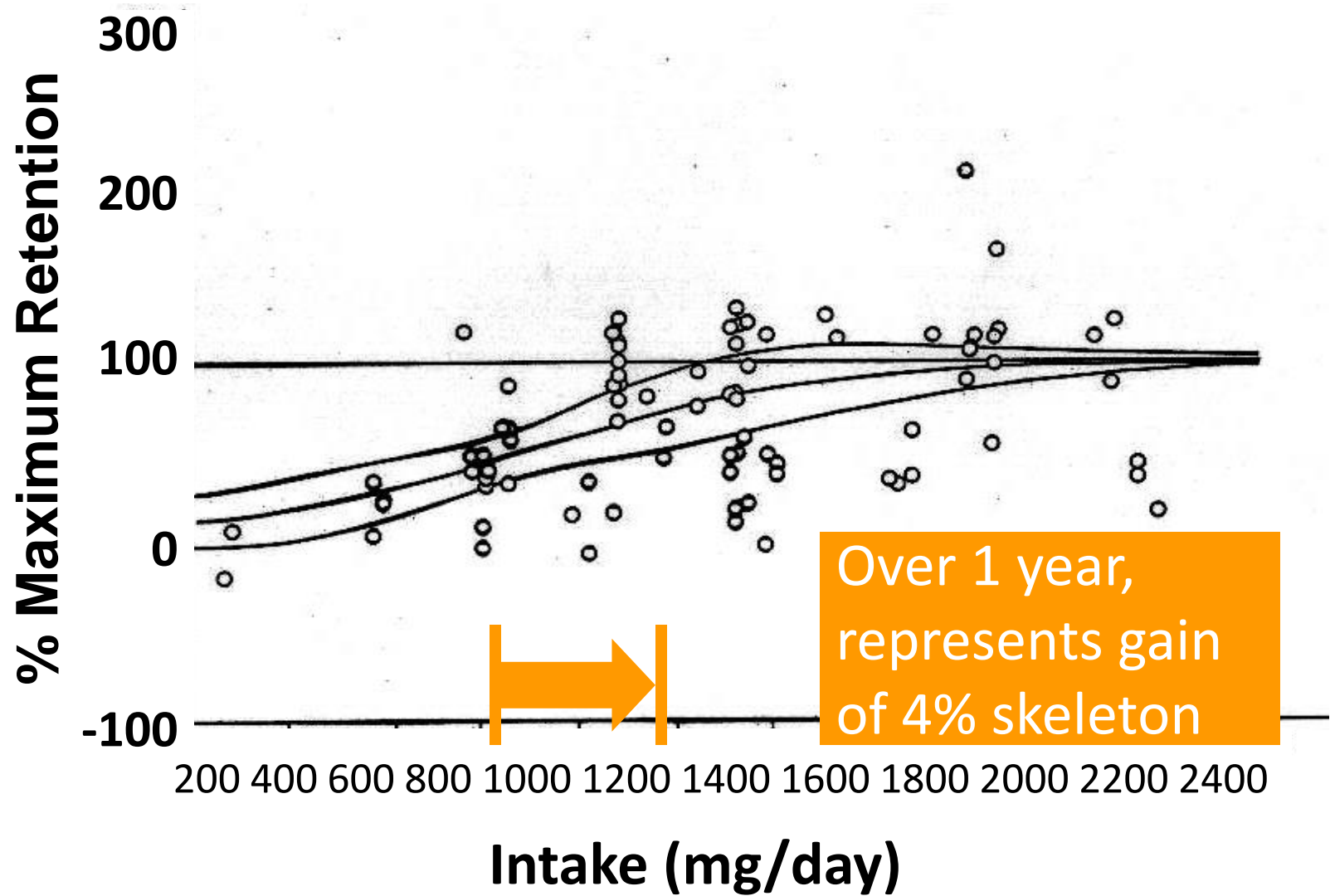
**We LOVE the fountain!**





# **Summer Research Camp = Controlled Feeding Studies**

# Maximal Calcium Retention as a Function of Intake



Over 1 year,  
represents gain  
of 4% skeleton

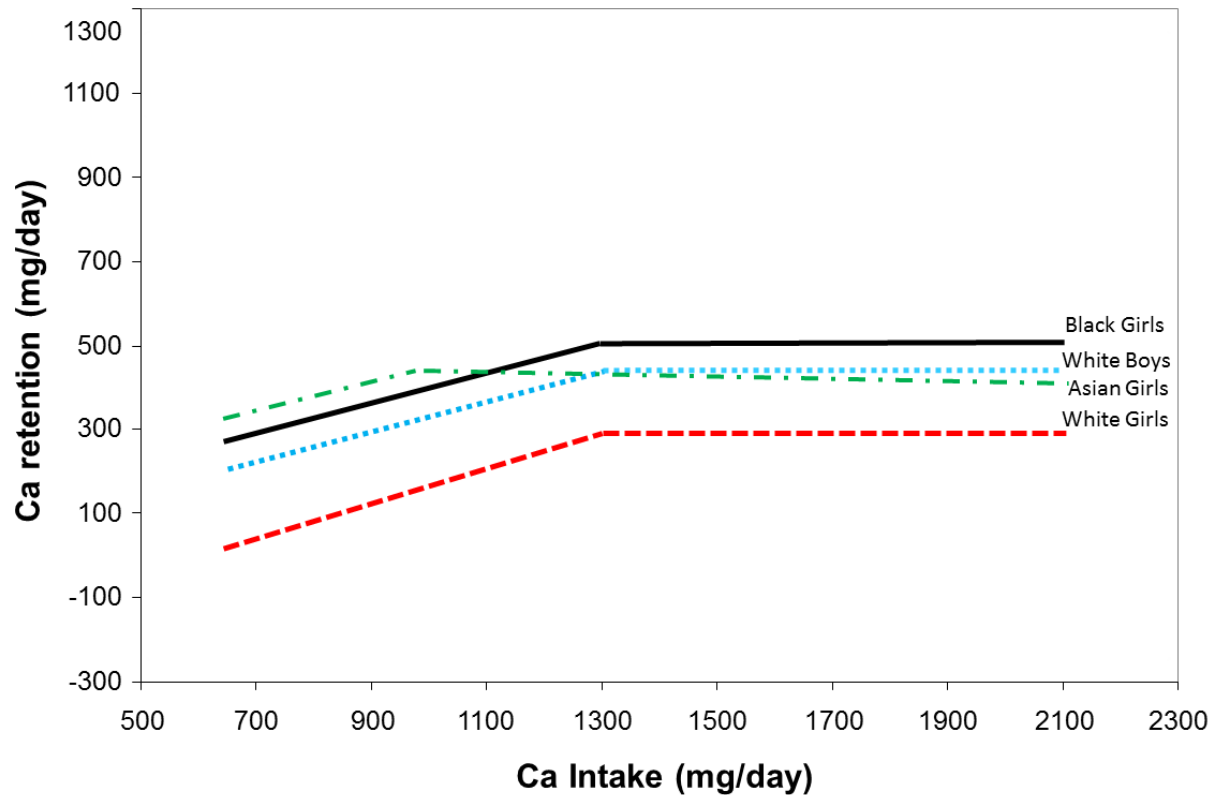
- Optimal calcium intake for maximal skeletal calcium retention is 1300 mg/d (RDA for adolescents)

# Estimated bone gain from our model

increasing Ca intake from 800 → 1300 mg/d:

10 % increase in peak bone mass This could delay onset of *osteoporosis* by 13 years and decrease risk of *fracture* in postmenopausal women by 50 %

# Calcium retention varies by sex and race



- Optimal Ca intake is 1300 mg/d (RDA)
- Blacks acquires more bone mass than whites and boys more than girls
- Chinese girls require less calcium than white girls

# Public Impact

Data determined the calcium requirements for adolescents for North America – 1997

Used for 2004 Surgeon General's Report on Bone Health

Used for 2005 Dietary Guidelines



**THE**  
**heart**  
**TRUTH**<sup>®</sup>

# CARDIOVASCULAR DISEASE



**U.S. Department of Health and Human Services**  
National Institutes of Health



**National Heart  
Lung and Blood Institute**  
People Science Health

**womenshealth.gov**

The Federal Government Source for Women's Health Information

# Women Receive Fewer Interventions to Prevent and Treat Heart Disease

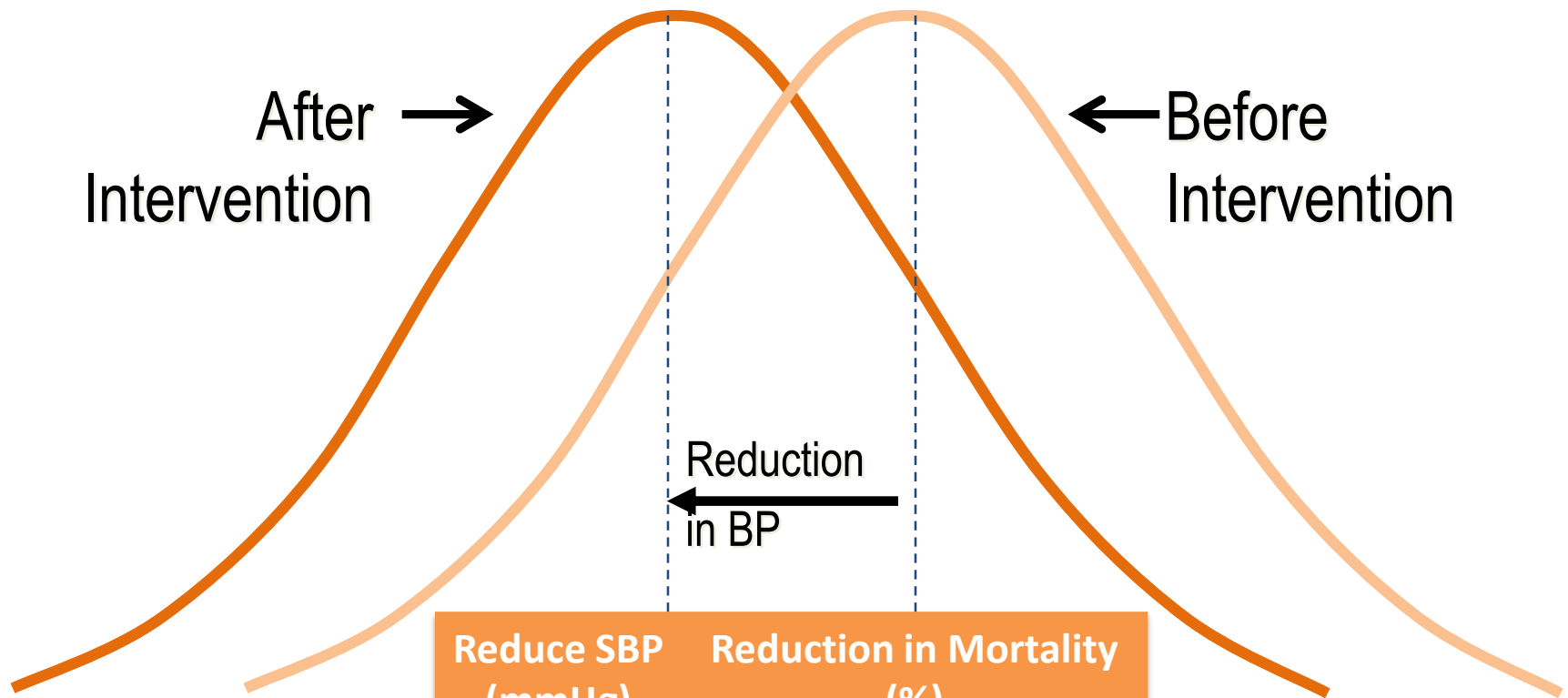
- Less cholesterol screening
- Fewer lipid-lowering therapies
- Less use of heparin, beta-blockers and aspirin during myocardial infarction
- Less antiplatelet therapy for secondary prevention
- Fewer referrals to cardiac rehabilitation
- Fewer implantable cardioverter-defibrillators compared to men with the same recognized indications



- 79% said they would call 9-1-1 if someone else was having a heart attack
- Only 53% of women said they would call 9-1-1 if experiencing the symptoms of a heart attack
  - For themselves, 46% of women would do something other than call 9-1-1—such as take an aspirin, go to the hospital, or call the doctor



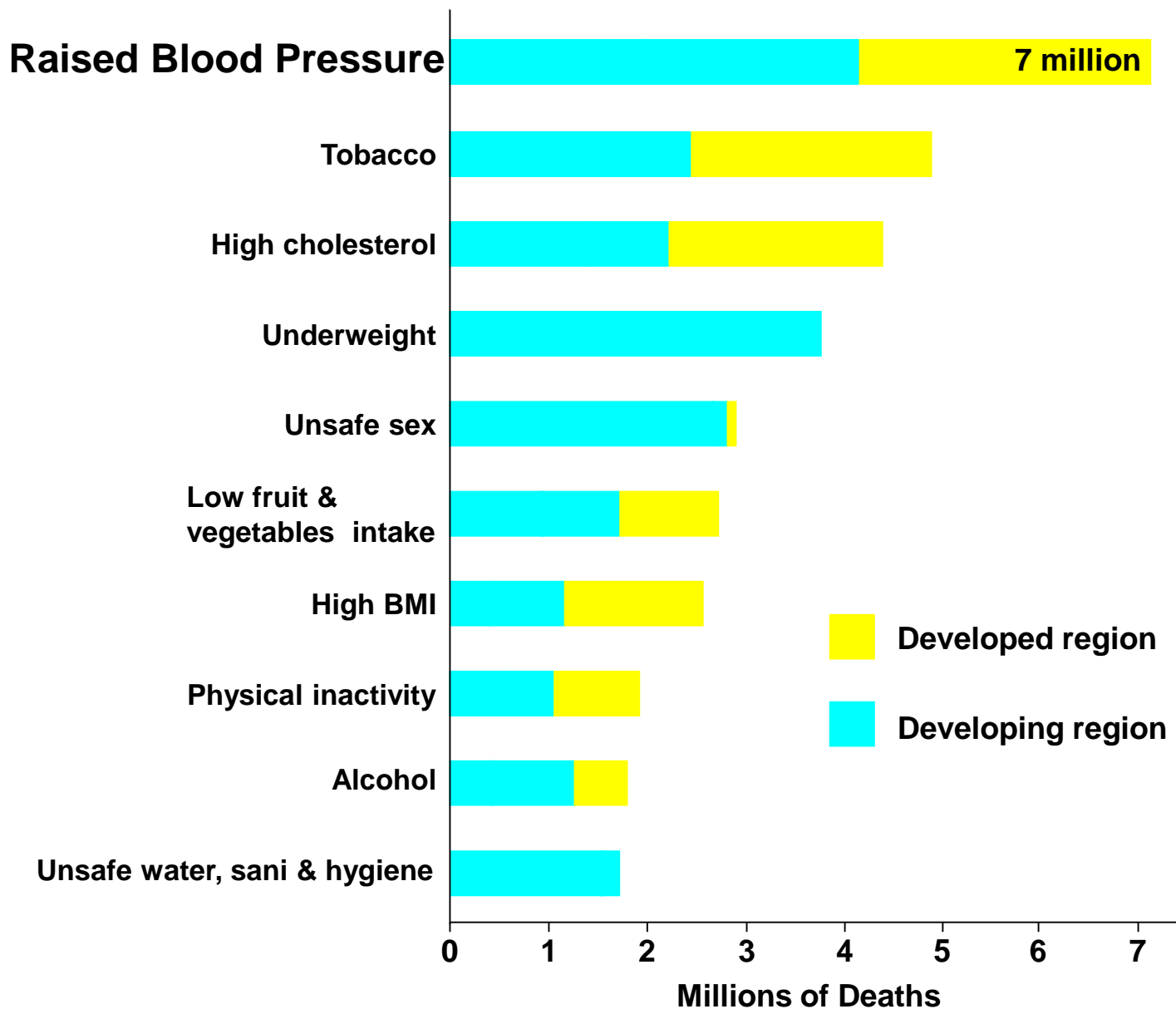
# Effects of Population-Based BP Reduction (Shifting SBP Distribution Downward)



Reduce SBP (mmHg)	Reduction in Mortality (%)		
	Stroke	CHD	TOTAL
2	-6	-4	-3
3	-8	-5	-4
5	-14	-9	-7

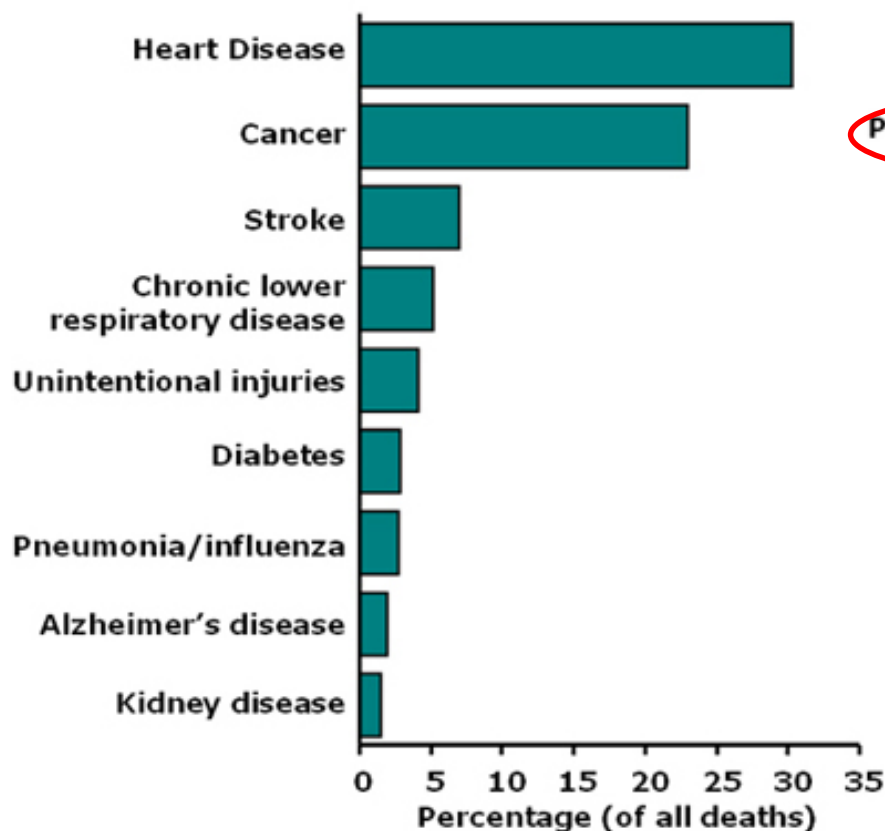
Source: Stamler  
R. Hypertension  
1991

# Major Underlying Factors causing Death - Worldwide

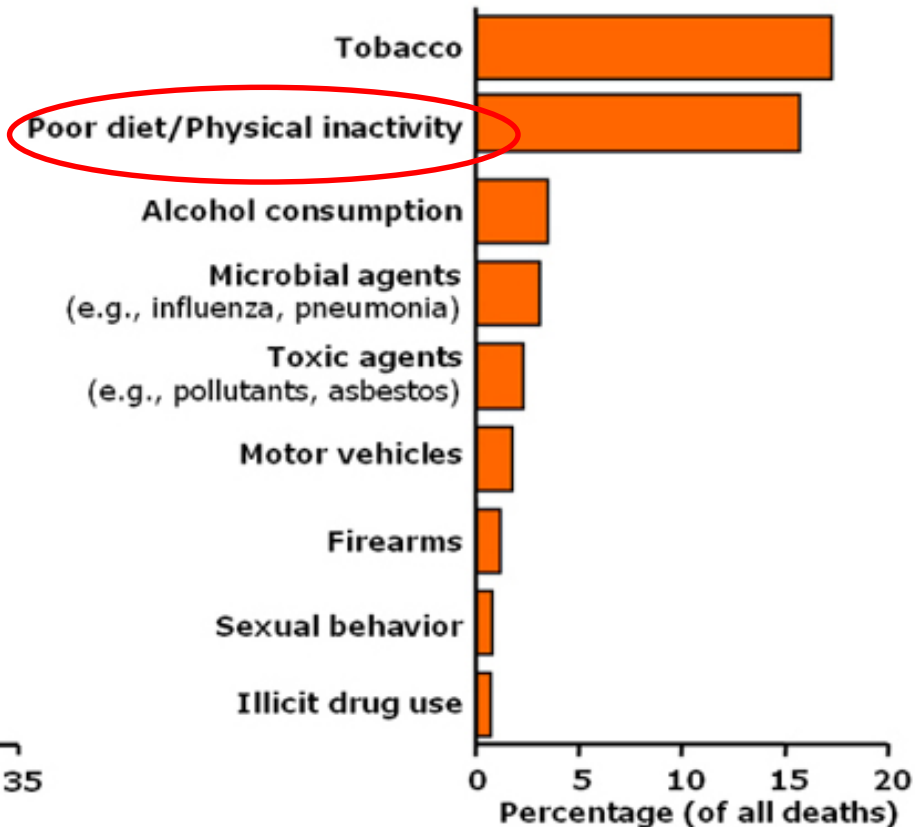


Source: Ezzati et al. Lancet 2002;360:1347-60.

### Leading Causes of Death\* United States, 2000

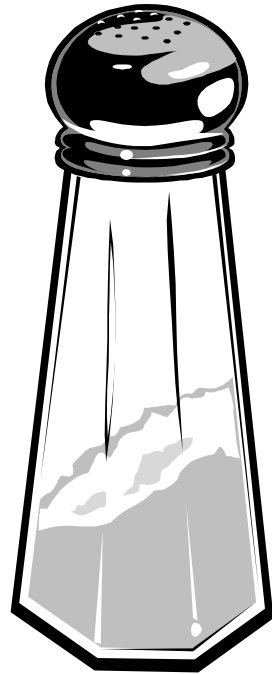


### Actual Causes of Death† United States, 2000



\* Miniño AM, Arias E, Kochanek KD, Murphy SL, Smith BL. Deaths: final data for 2000. National Vital Statistics Reports 2002; 50(15):1-120.  
 † Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. JAMA. 2004;291(10):1238-1246.

# Role of Salt



# Sodium Retention in Black and White Female Adolescents in Response to Salt Intake



# Effect of Dietary Salt on Mineral Retention

- Metabolic balance study
  - Randomized order high/low salt
- Adolescent black and white subjects matched for size and sexual maturity



**Low Na diet → 1.3 g/d**  
**High Na diet → 4 g/d**

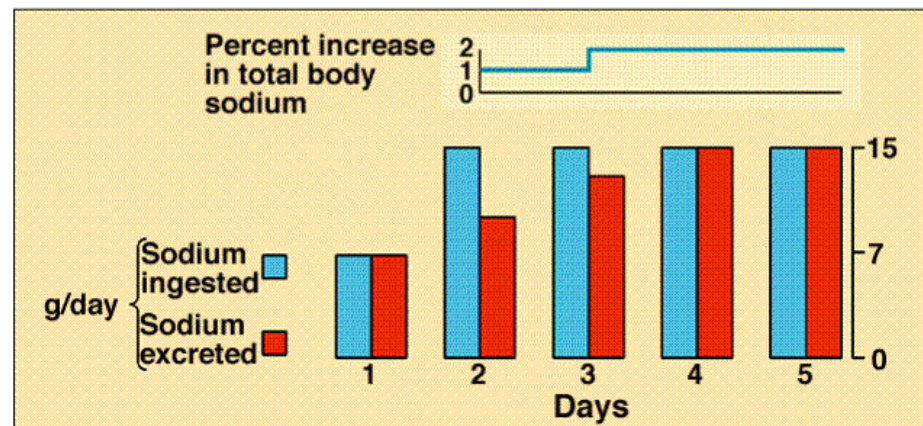


# Traditional Theory

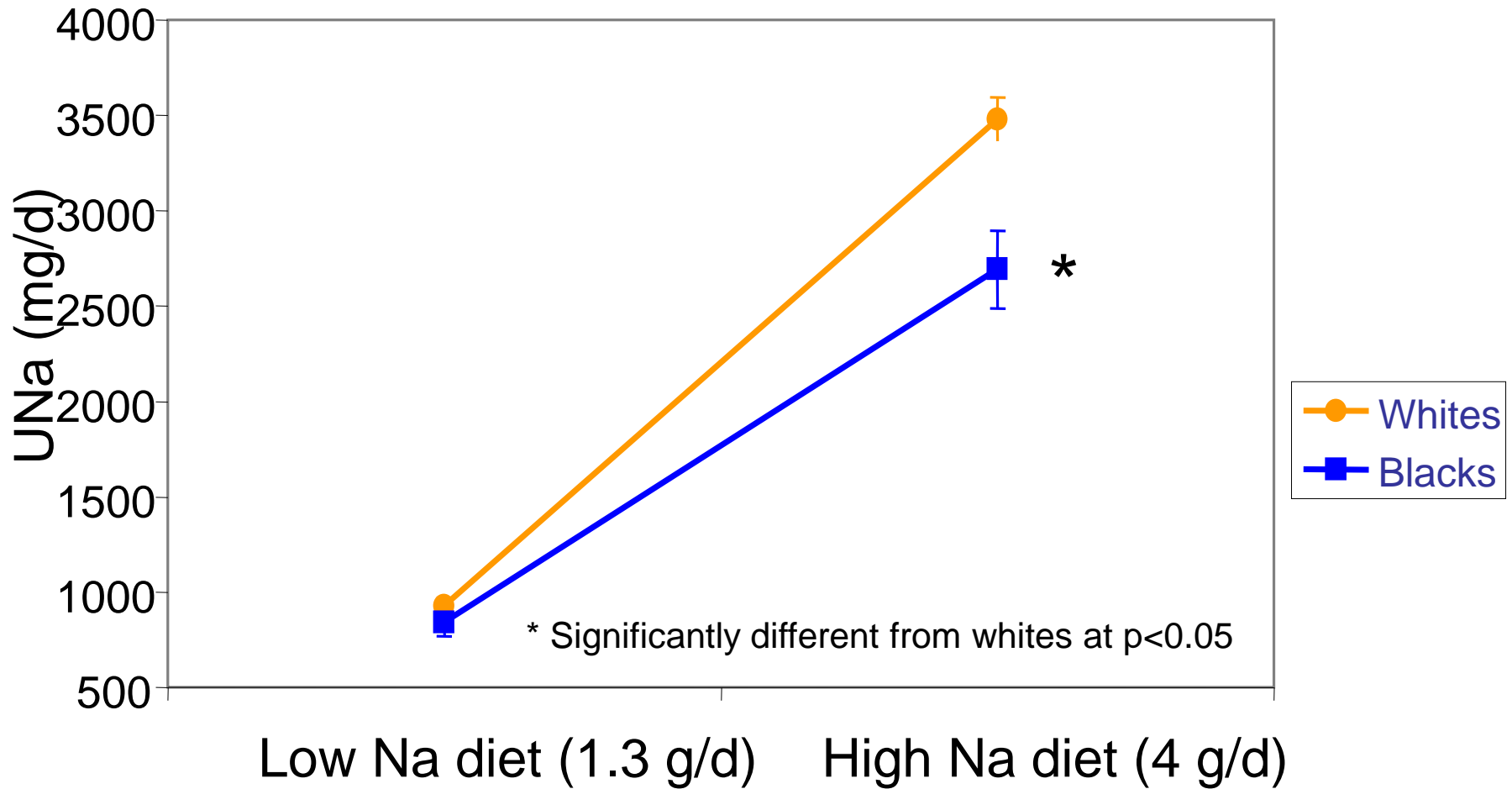
- Sodium intake and excretion are in balance within one day after drastic shifts
- Total body  $\text{Na}^+$  content is maintained constant within narrow limits

Vander/ Sherman/ Luciano *Human Physiology*, 7th edition. Copyright © 1998 McGraw-Hill Companies, Inc. All Rights Reserved.

## Sodium Balance



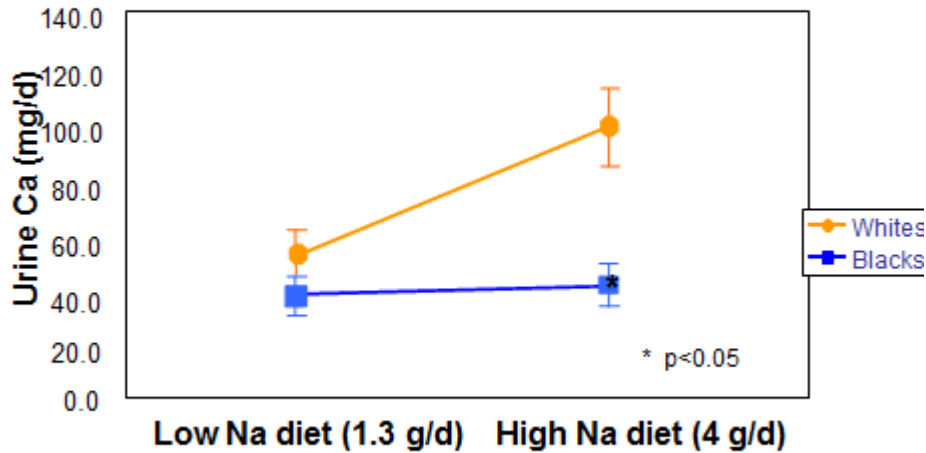
# Urinary sodium excretion (Mean $\pm$ SEM)





# Effects of Salt intake on Calcium Excretion and Balance in Black and White Adolescents

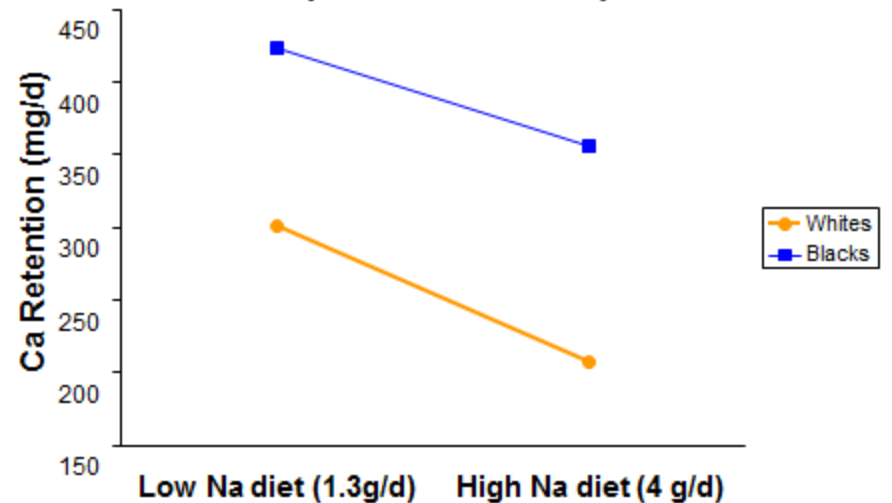
## Urinary calcium excretion (Mean $\pm$ SEM)



Palacios, et al. JCEM 89(4):1858-1863, 2004 .

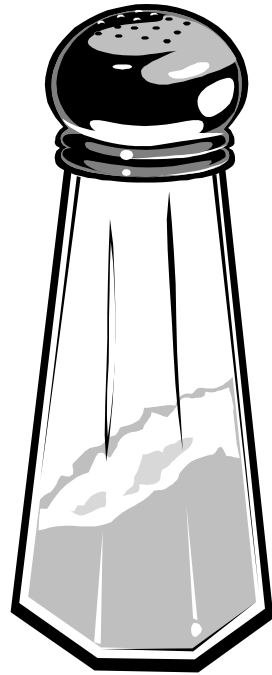
Na and Ca share same transporters in kidney.

## Calcium retention (Mean $\pm$ SEM)



\*  $p < 0.05$  for diet and race

# Role of Salt

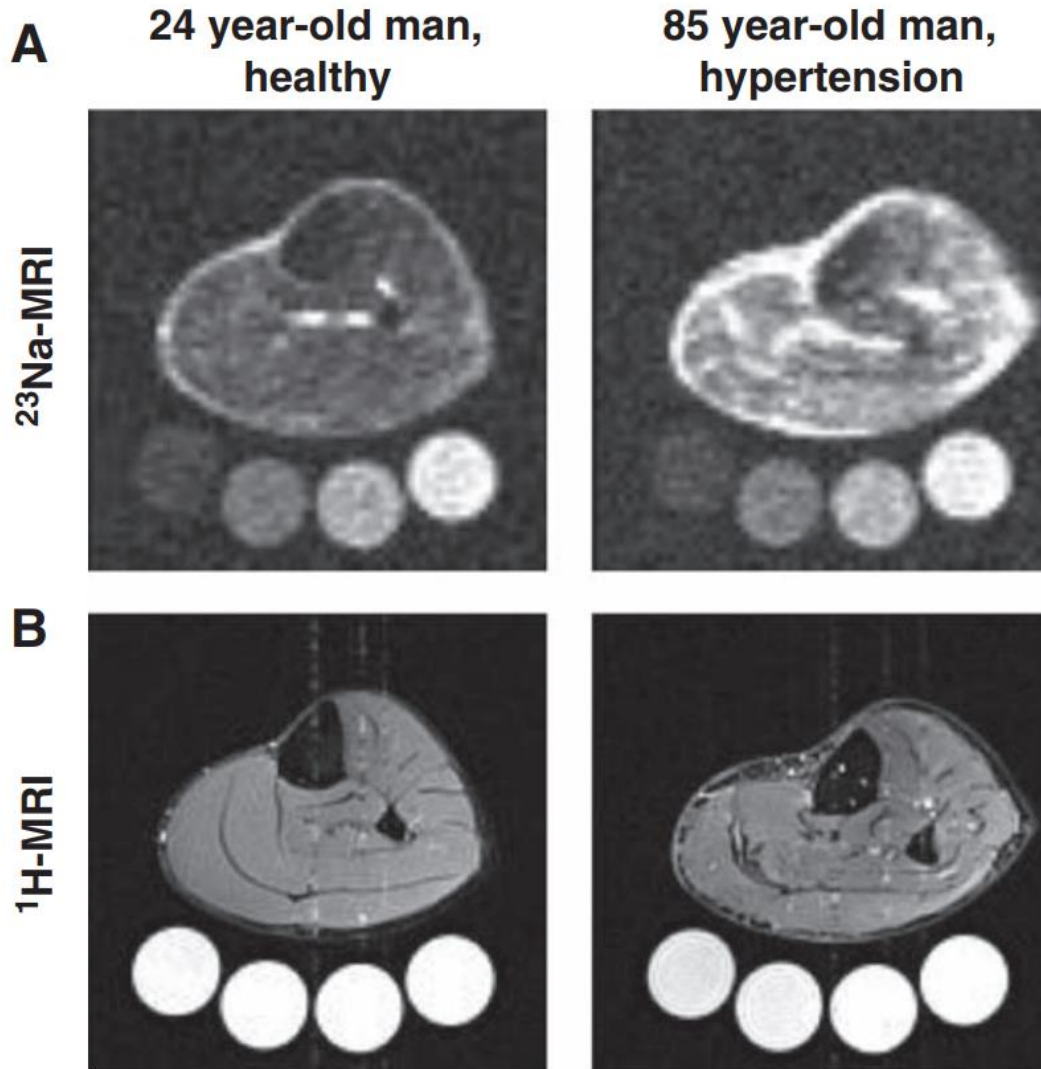


Salt bad for bones-worse in whites  
Salt is bad for heart-worse in blacks

Determining sodium distribution in the body in response to salt intakes is important to understand mechanisms

- Soft Tissue MRI-NA-23 Coil , Ulrike Dydak
- Bone NAA, Linda Nie

# $^{23}\text{Na}$ MRI Leg Tissue $\text{Na}^+$ Tubes with $\text{NaCl}$ Solutions used to Calibrate



# Mineral Intakes and BP in US Adults

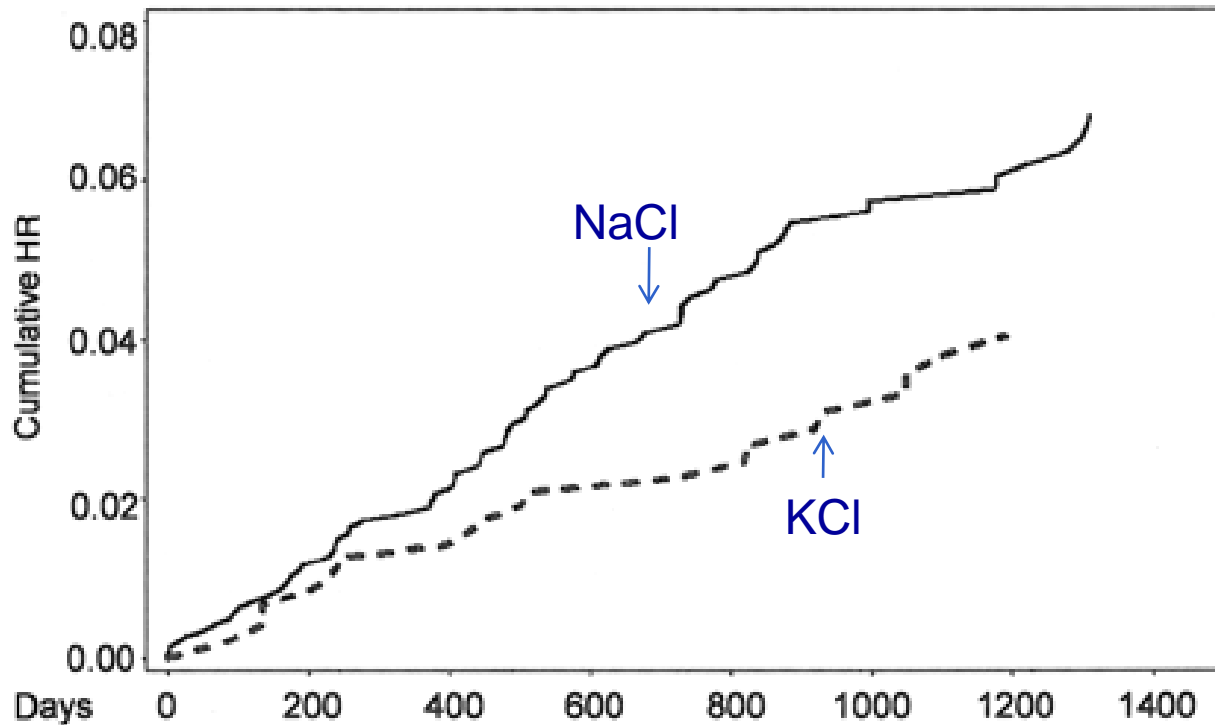
## The Data



n = 4382 women and 4395 men

Na:K intake predicted  
( $P < 0.01$ ) SBP in  
females and males  
but not Na or K alone

# K and CVD-Related Deaths RCT in 1981 in elderly men



**59% reduction in CVD mortality**



# DASH Diet

Emphasizes:

Fruits, Vegetables, Low-fat Dairy Foods

Includes:

Whole Grains, Nuts, Poultry, Fish

Reduced in:

Fats, Red Meat, Sweets, and Sugar-containing Beverages



# Diet in American Children Falls Short of Guidelines

DASH Accordance Scores in 9793 US aged 8-18y  
from NHANES 2003-2012

Score range 0-9

Range mean scores 1.48-2.14

Total fat  
Saturated fat  
Protein  
Cholesterol  
Fiber  
Calcium  
Magnesium  
Potassium  
Sodium

**All Low!**

# Preventable Disease Burden and national health Spending

**>75%** of national health spending is attributable to chronic diseases that are largely preventable

- 80% of cardiovascular disease
- 80% of diabetes
- 60% of lung diseases
- 40% of cancers

**<3%** of national health spending is allocated to public health and prevention

**A Call to Arms!**