1 FREE CPEU

Exclusive Webinar Presentation

Overview of the Nutritional & Health Attributes of Soy

Learning Library
TODAY'S DIETITIAN

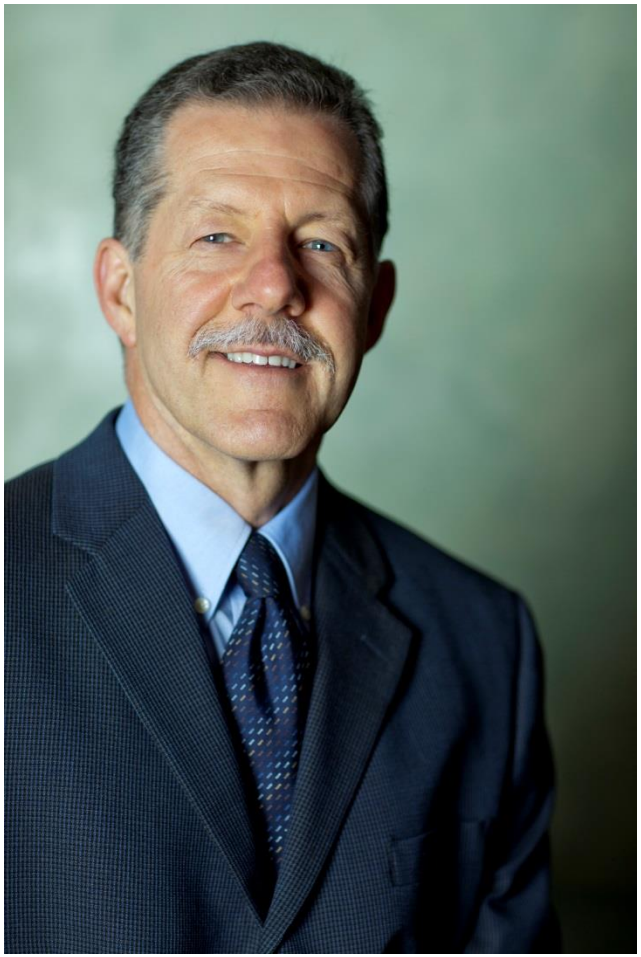
Presented by Mark Messina, PhD, on **Wednesday, August 24, 2-3 pm EDT**

Learning Objectives

After completing this continuing education course, nutrition professionals should be able to:

1. State the ways in which soybean isoflavones are different from the hormone estrogen
2. Make appropriate recommendations about consumption of soyfoods for women who are at high risk of developing breast cancer or who have breast cancer
3. Identify health advantages of soyfoods for men
4. Describe the results of clinical studies on isoflavones and male feminization
5. Make intake recommendations for individuals of all ages and regardless of health status

Mark Messina, PhD



Dr. Messina reports the following relevant disclosure:

He serves as a consultant to United Soybean Board, Pharmavite and Vitasoy. He has certified that no conflict of interest exists for this program.

Overview of the Nutritional and Health Attributes of Soyfoods

Outline

- Macronutrient composition
- Coronary heart disease
- Isoflavones
- Breast cancer
- Hot flashes
- Bone health
- Misunderstandings

Is tofu bad for you?

What is good soy and what is bad soy?

Soy increases cancer risk

Soy lowers blood pressure

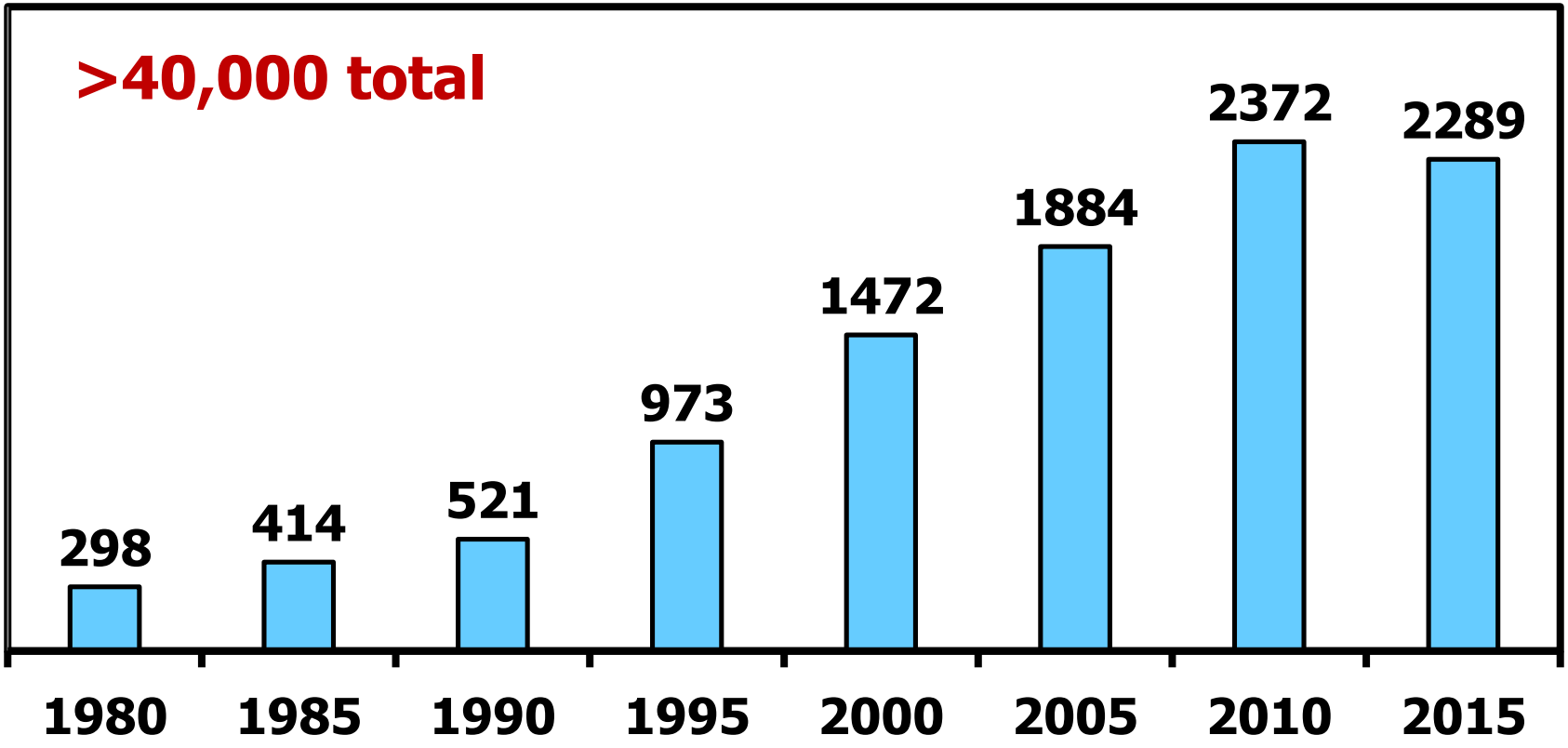
10 Reasons to Never Ever drink soy milk

Soy can regulate cholesterol

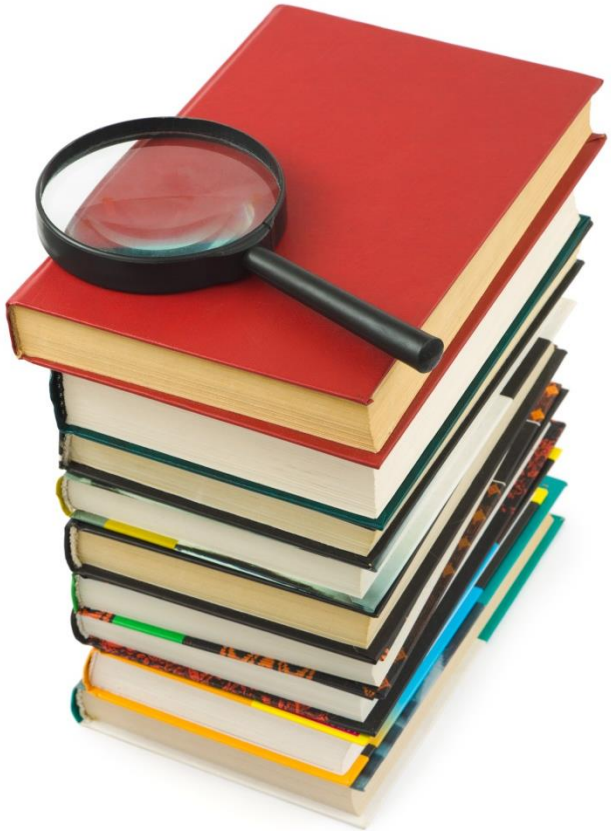
Soy is harmful to kids

Cherry-pick: To choose in a highly selective manner

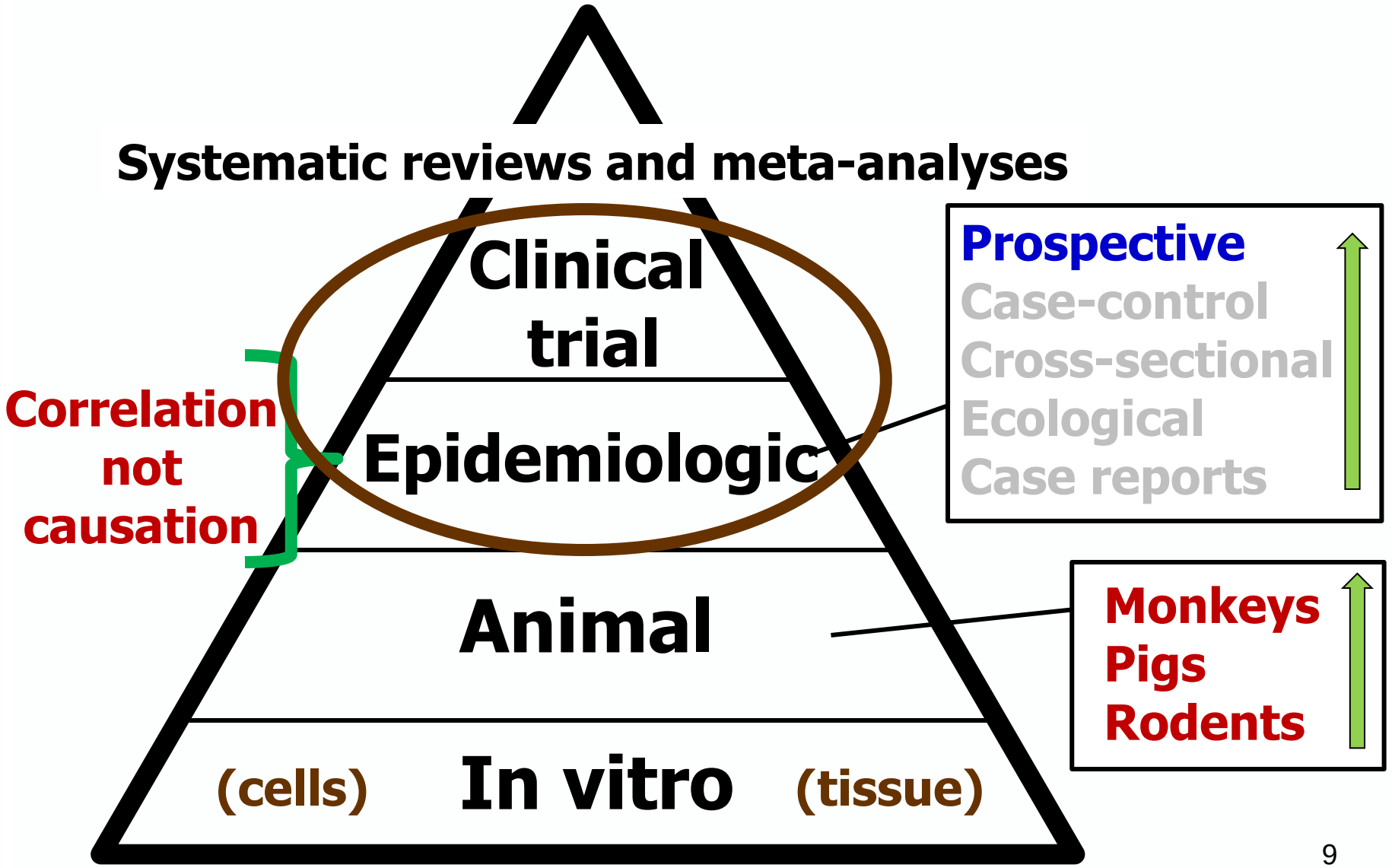
Annual Number of Soy-Related Peer-Reviewed Publications



- **Totality of the evidence**
- **Study type and quality**



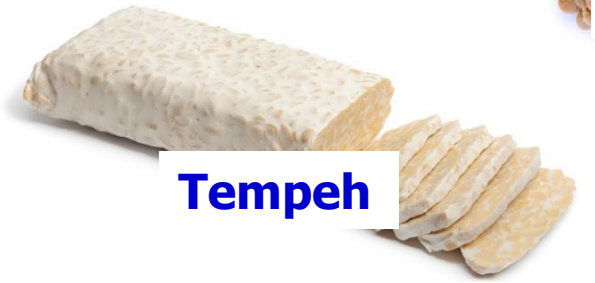
Hierarchy of Evidence



Traditional Asian Soyfoods

Unfermented

Fermented



Asian Soyfood Consumption[1]

Location	Servings per day[2]	Type of soyfood
Shanghai	1 – 2	Unfermented
Singapore	½ – ¾	Unfermented
Hong Kong	½	Unfermented
China	½	Unfermented
Japan	1 – 2	50% fermented
Korea	½ – 1	30% fermented

[1]Among older adults [2]Servings: 240 ml milk, 85-100 g tofu

Macronutrient Composition




vs.



Macronutrient (% calories) Composition of Soybeans in Comparison to Common Beans

Macronutrient	Soybeans	Common beans
Carbohydrate	27*	70
Protein	33	27
Fat	40	3

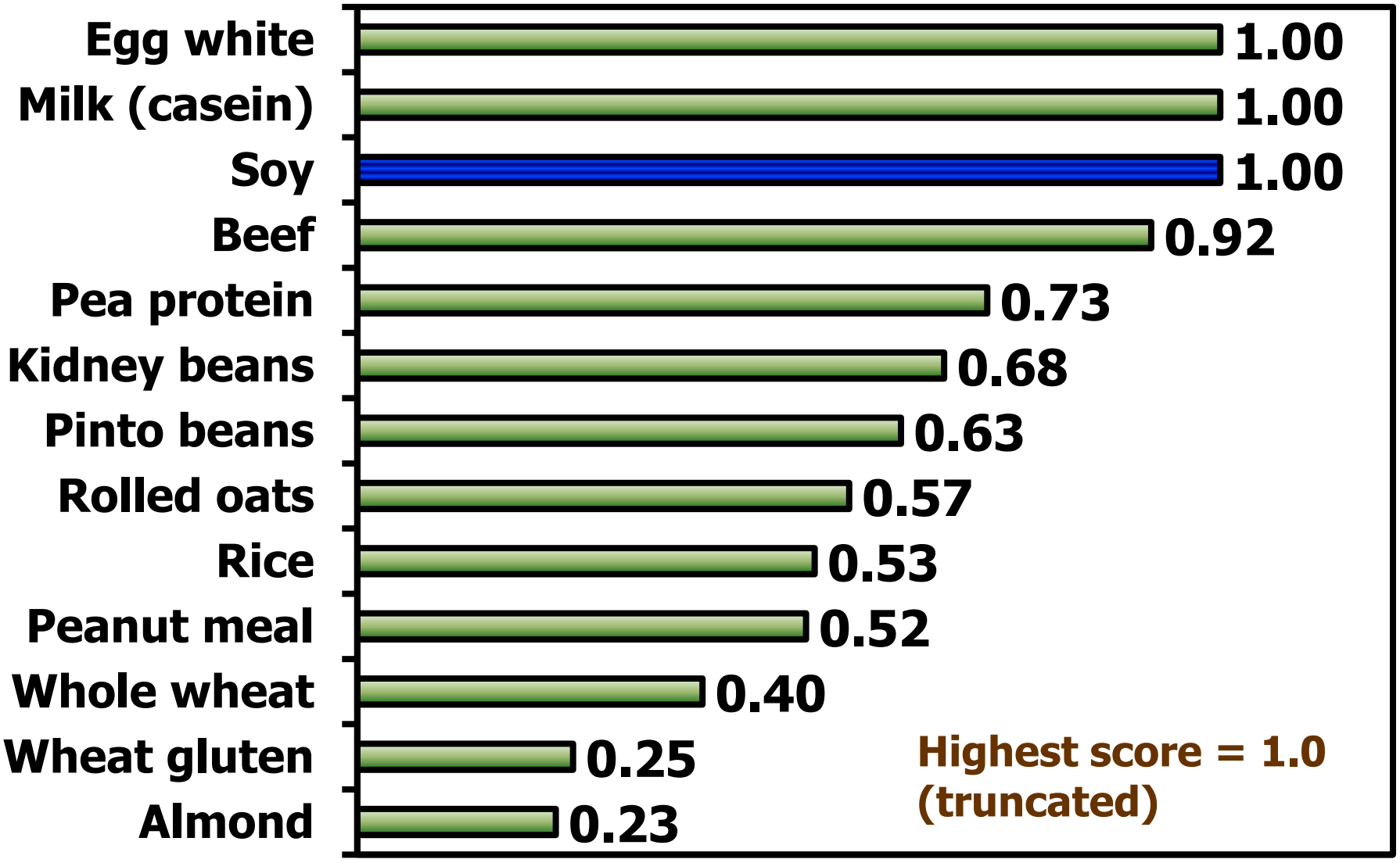
*Mostly oligosaccharides (indigestible)
Capable of functioning as prebiotics

AJCN 70: 439S, 1999

Attributes of Soy Protein

- **High quality (PDCAAS, 0.9-1.0)**
  Similar to animal protein
- **Lowers LDL-cholesterol (4-5%)**
- **May lower blood pressure (~2 mmHg)**
- **May favorably affect kidneys**

Protein Quality Scores*



*Protein Digestibility Corrected Amino Acid Score (PDCAAS)

Attributes of Soy Protein

- **High quality (PDCAAS, 0.9-1.0)**
  Similar to animal protein
- **Lowers LDL-cholesterol (4-5%)**
  Health claims in >10 countries
- **May lower blood pressure (~2 mmHg)**
- **May favorably affect kidneys**

Food and Drug Administration

"25 grams of soy protein per day … may reduce risk of heart disease"

Countries with approved health claims

- United States (1999)
- Indonesia
- Japan
- Korea
- Chile
- Turkey
- Malaysia
- Philippines
- Brazil
- Columbia
- South Africa
- Canada (2014)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
December 6, 2007

Health Claims and Qualified Health Claims:

Dietary Lipids and Cancer, Soy Protein and Coronary Heart Disease, Antioxidant Vitamins and Certain Cancers, and Selenium and Certain Cancers; Reevaluation;

Opportunity for Public Comment

"The FDA is announcing … its intent to reevaluate the scientific evidence for the soy protein … health claim."

Decrease in LDLC (%) in Response to Soy Protein: Meta-Analysis Results

Author	Studies	(N)	↓ LDLC
Anderson	20	1946	5.5
Jenkins	22	757	4.3
Harland	10	2913	6.0
Reynolds	36	1387	4.0
Zhan	33	1749	5.0

Anderson; J Am College Nutr 30: 79, 2011; Jenkins J Nutr 140: 2302S, 2010; Harland, Atherosclerosis 200: 13, 2008; Reynolds, Am J Cardiol 98: 633, 2006; Zhan, AJCN 81: 397, 2005

A Dietary Portfolio Approach to Cholesterol Reduction: Combined Effects

David J.A. Jenkins, Cyril W.C. Kendall, Dorothea Faulkner, Edward Vidgen, Elke A. Trautwein, Tina L. Parker, Augustine Marchie, George Koumbridis, Karen G. Lapsley, Robert G. Josse, Lawrence A. Leiter, and Philip W. Connelly

Abstract

Plant sterols, soy proteins, and viscous fibers are advised for cholesterol reduction but their combined effect has never been tested. We therefore assessed their combined effect on blood lipids in hyperlipidemic subjects who were already consuming a low--saturated fat, low-cholesterol diet before starting the study. The test (combination) diet was 1 month in duration and was very low in saturated fat and high in plant sterols (1 g/1,000 kcal), soy protein (23 g/1,000 kcal), and viscous fibers (9 g/1,000 kcal) obtained from foods available in supermarkets and health food stores. One subject also completed 2 further diet periods: a low-fat control diet and

Metabolism, 51: 1596, 2002

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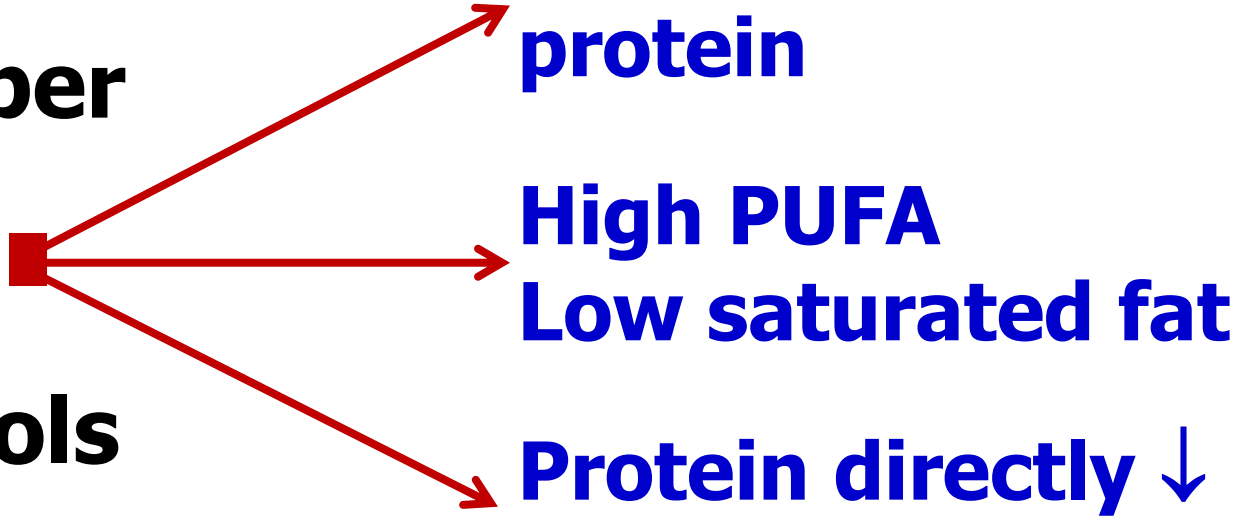
Portfolio diet is a comprehensive dietary approach shown to lower LDL-cholesterol by 30%

Metabolism, 51: 1596, 2002

Components of the Portfolio Diet

- Almonds
- Low saturated fat
- Soluble fiber
- Soyfoods
- Phytosterols
- Fruits/vegetables



Attributes of Soy Protein

- **High quality (PDCAAS, 0.9-1.0)**
  Similar to animal protein
- **Lowers LDL-cholesterol (4-5%)**
  Health claims in >10 countries
- **May lower blood pressure (~2 mmHg)**
  All 4 meta-analysis show reductions
- **May favorably affect kidneys**
  Possibly multiple benefits

AJCN 88:38, 2008; BJN 106:317, 2011; Nutr Metab CVC 22: 463, 2012; J Hypertens. 28: 1971, 2010; World J Nephrol 5: 233, 2016

Macronutrient (% calories) Composition of Soybeans in Comparison to Common Beans

Macronutrient	Soybeans	Common beans
Carbohydrate	27*	70
Protein	33	27
Fat	**40**	**3**

***Mostly oligosaccharides (indigestible)**
Capable of functioning as prebiotics

AJCN 70: 439S, 1999

Fatty Acid Composition of Soybean Oil

Fatty acid	Percent
Saturated	12
Monounsaturated	29
Omega-6 PUFA (LA)*	53
Omega-3 PUFA (ALA)*	6

*Essential fatty acids: LA, linoleic acid; ALA, α-linolenic acid

J. Agric. Food Chem. 2004 52, 5322; 57: 11174, 2009

Saturated fat intake should be limited to less than 10% of calories per day

The Controversy over Dietary Fat & Coronary Heart Disease

Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease

A Prospective Cohort Study

Yanping Li, PHD,* Adela Hruby, PHD, MPH,* Adam M. Bernstein, MD, SCD,y Sylvia H. Ley, PHD,* Dong D. Wang, MD,* Stephanie E. Chiuve, SCD,*z Laura Sampson, RD,* Kathryn M. Rexrode, MD, MPH,z Eric B. Rimm, SCD,*xk Walter C. Willett, MD, DRPH,*xk Frank B. Hu, MD, PHD*xk

BACKGROUND: The associations between dietary saturated fats and the risk of coronary heart disease (CHD) remain controversial, but few studies have compared saturated with unsaturated fats and sources of carbohydrates in relation to CHD risk. OBJECTIVES: This study sought to investigate associations of saturated fats compared with unsaturated fats and different sources of carbohydrates in relation to CHD risk. METHODS: We followed

J Am Coll Cardiol, 66, 1538, 2015

Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease

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"… the macronutrient substituted for SFAs is critically important."

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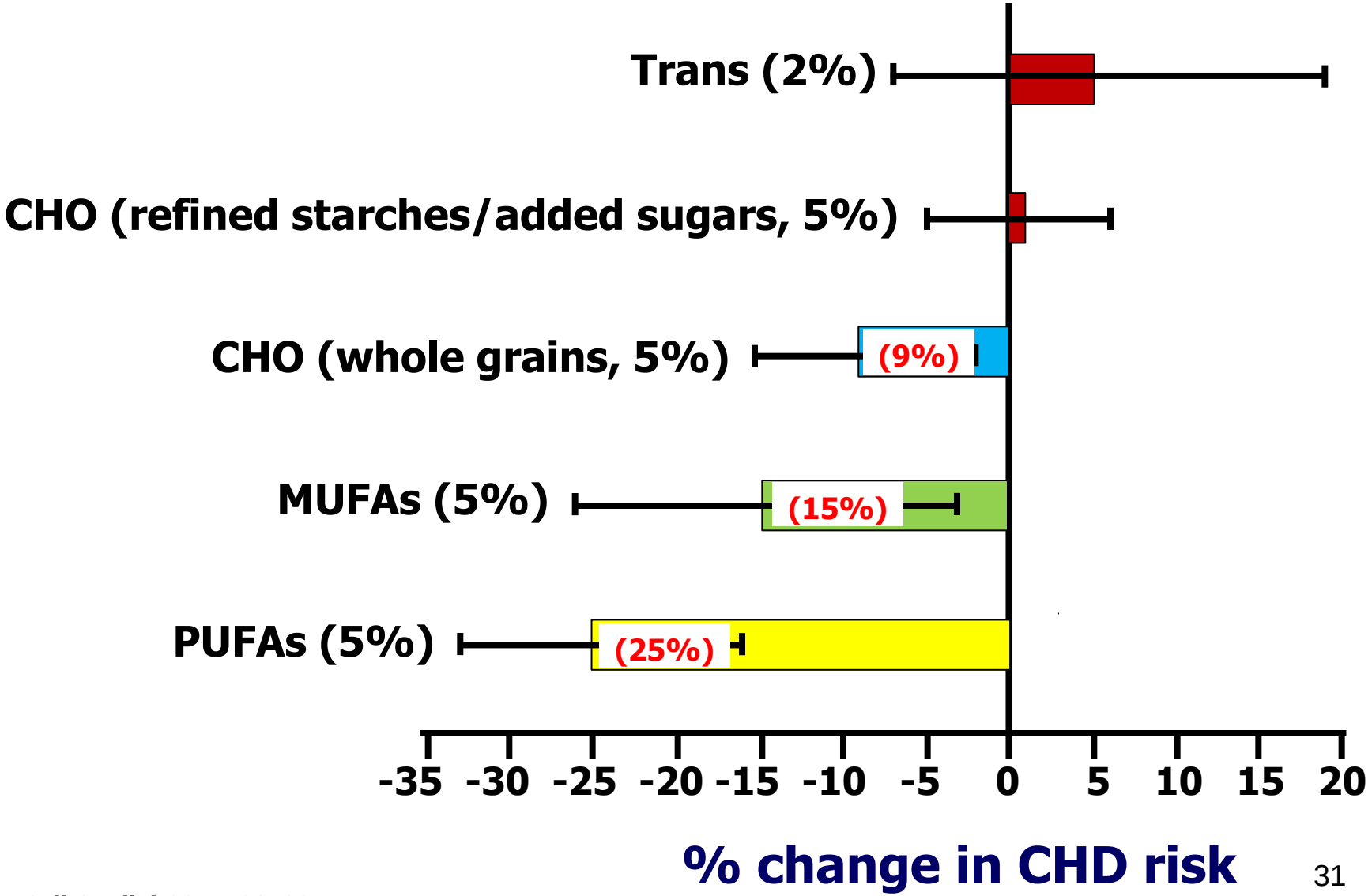
J Am Coll Cardiol, 66, 1538, 2015

Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease

A Prospective Cohort Study

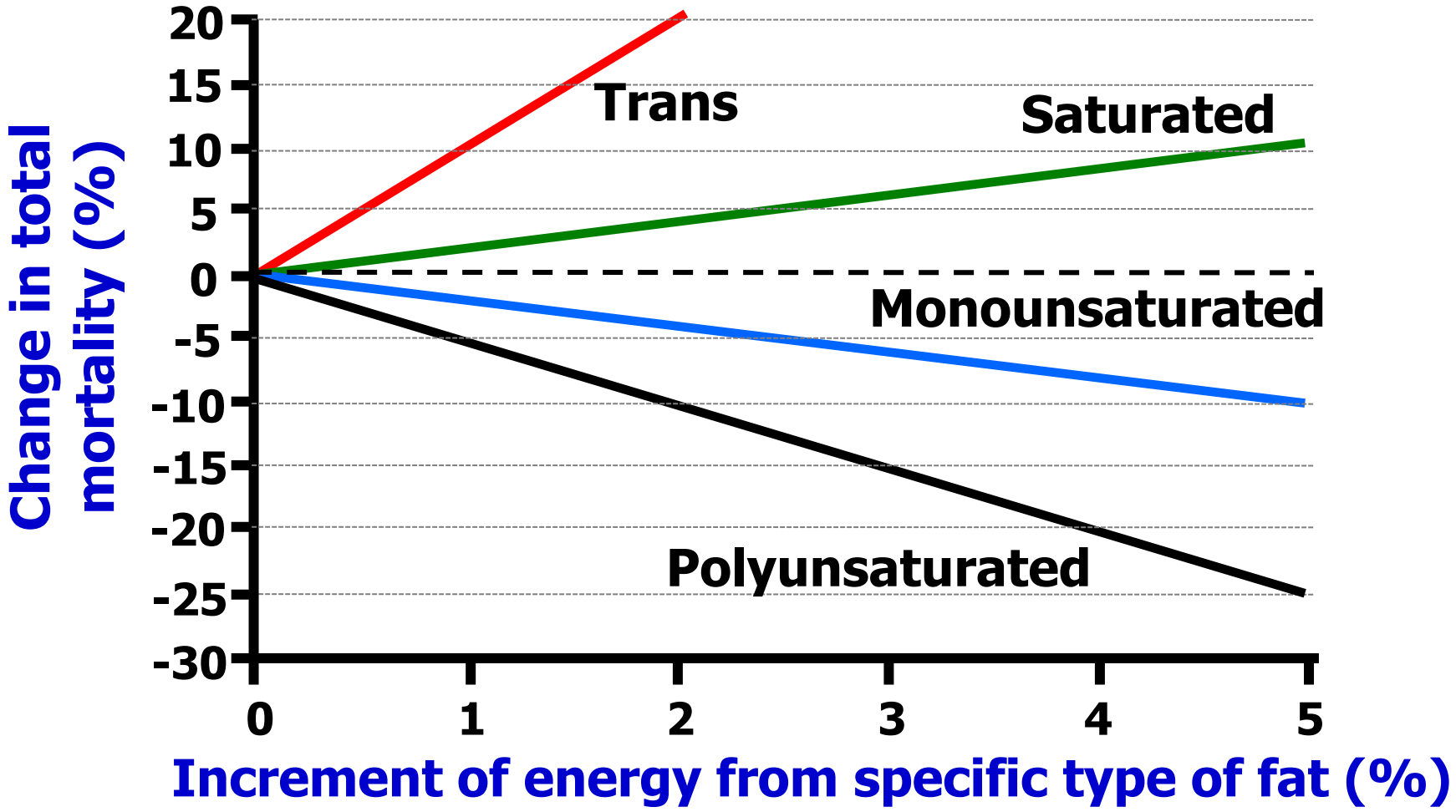
- **Nurses' Health Study (N=84,628 women)**
- **Health Professionals Follow-up Study (N=42,908 men)**
- **24 to 30 years of follow-up**
- **7,667 incident cases of CHD**

Isocaloric substitution of SFAs from:



J Am Coll Cardiol 66: 1538, 2015

Change in Total Mortality associated with an ↑ in the % Kcal from Specific Types of Fat*



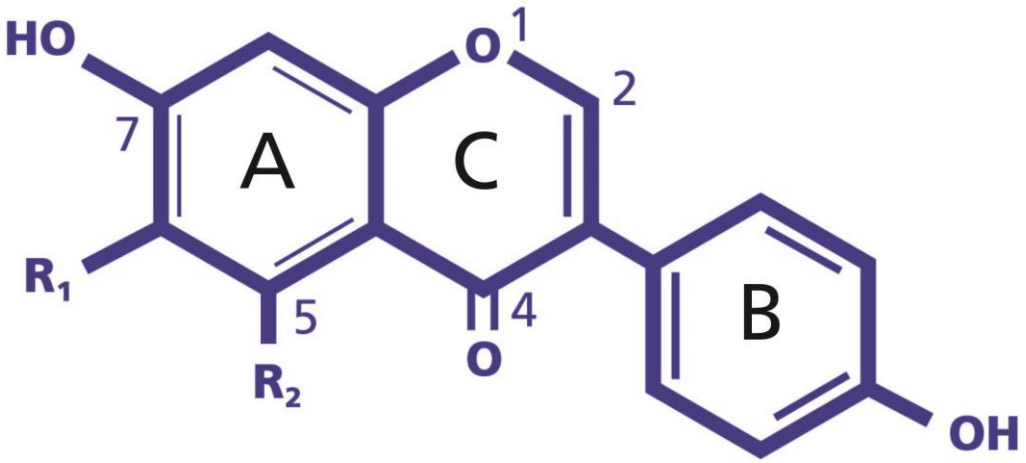
*Replacing CHO. Results adjusted for age, race, marital status, BMI, PA, smoking, ROH, vitamin use, Vit. E, aspirin, family history MI, diabetes, BP, cancer, cholesterol; Kcal, cholesterol, protein, menopausal status, hormone use, fatty acid intake. **Wang et al. JAMA Internal Med July 5, 2016**

Overview of the Nutritional and Health Attributes of Soyfoods

Outline

- Macronutrient composition
- Coronary heart disease
- **Isoflavones**
- **Breast cancer**
- Hot flashes
- Bone health
- Misunderstandings

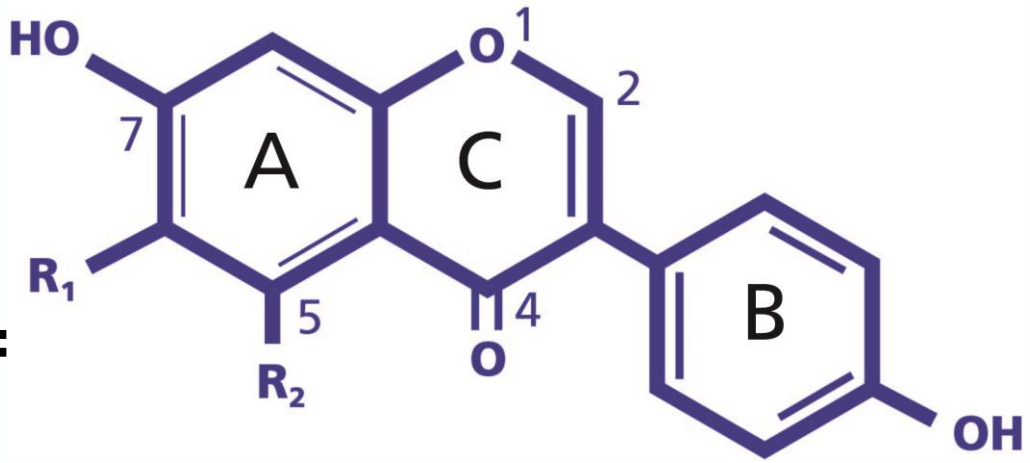
Isoflavones



Naturally-occurring plant chemicals

>20,000 peer-reviewed publications

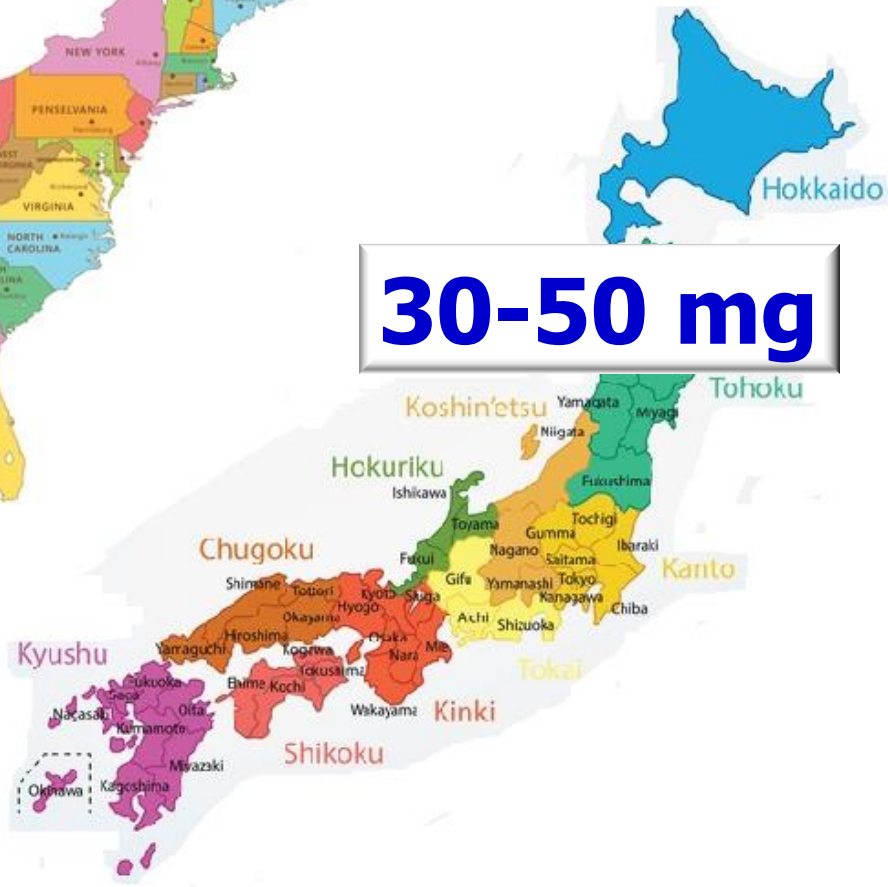
Isoflavones



- **Found primarily in soybeans**

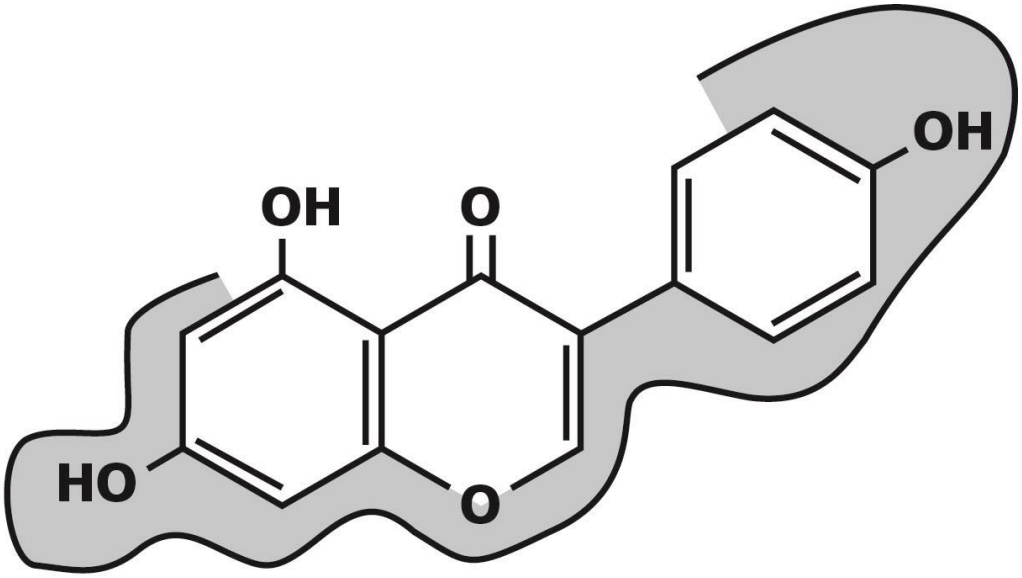
Mean Daily Isoflavone Intake

Int J Food Sci Nutr 65: 9, 2014

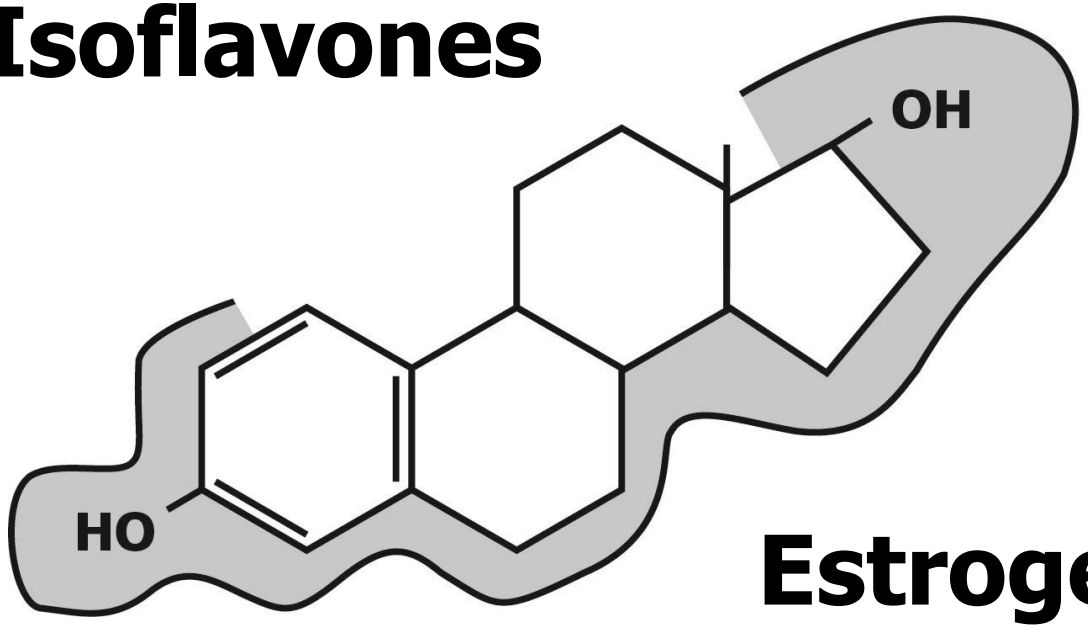


Nutr Cancer 55:1, 2006

Traditional soyfoods:
3-4 mg/g protein
One serving ~25 mg

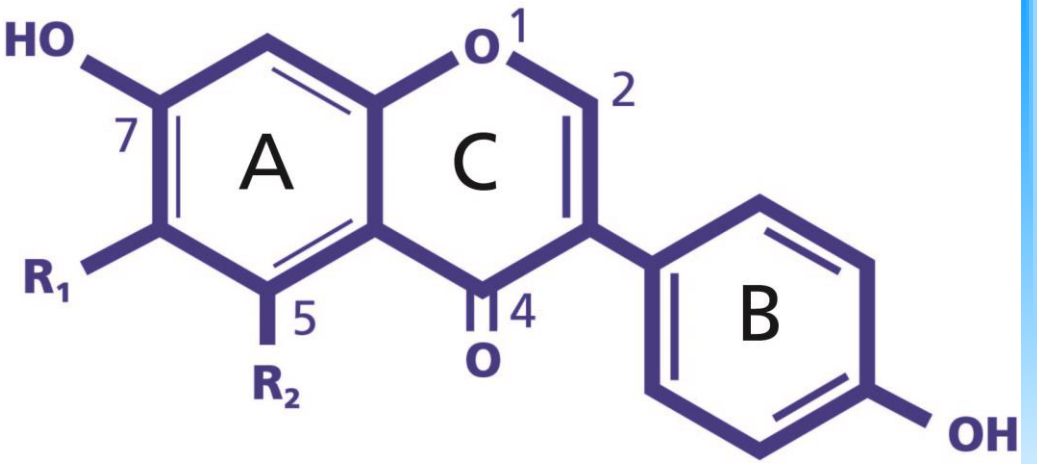


Isoflavones



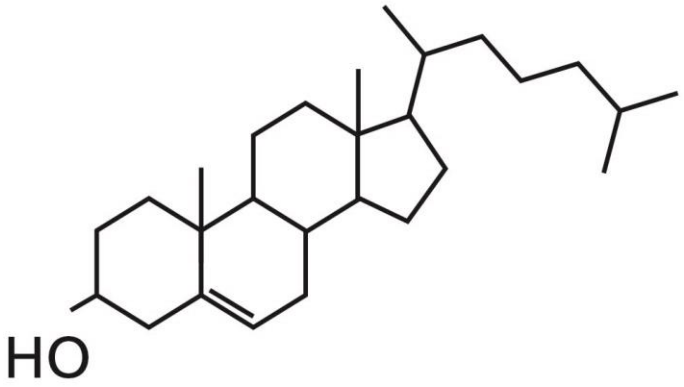
Estrogen

Isoflavones

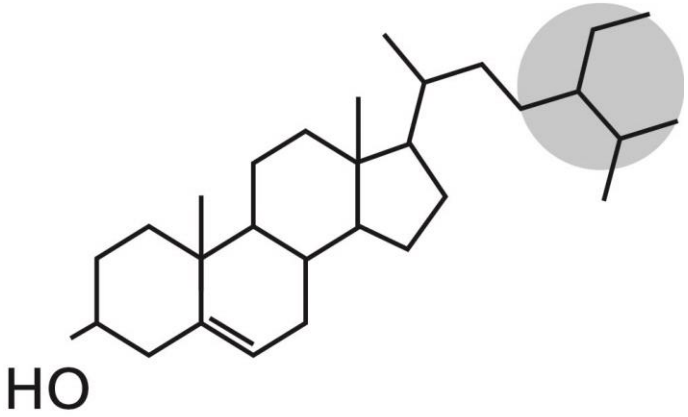


- **Found primarily in soybeans**
- **Phytoestrogens but *different* from estrogen**
- **Sometimes effects opposite to estrogen**

Cholesterol
(animal foods)



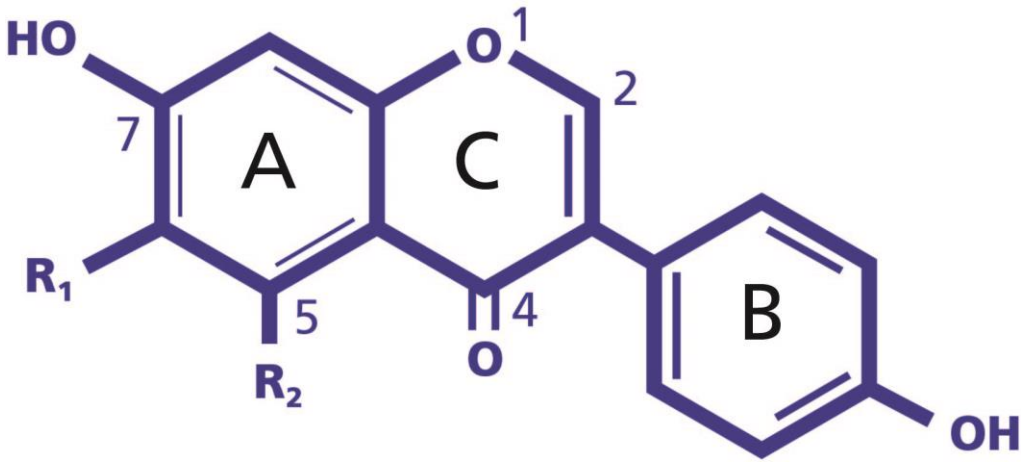
↑ **Blood cholesterol**



↓ **Blood cholesterol**

Phytosterols
(plant foods)

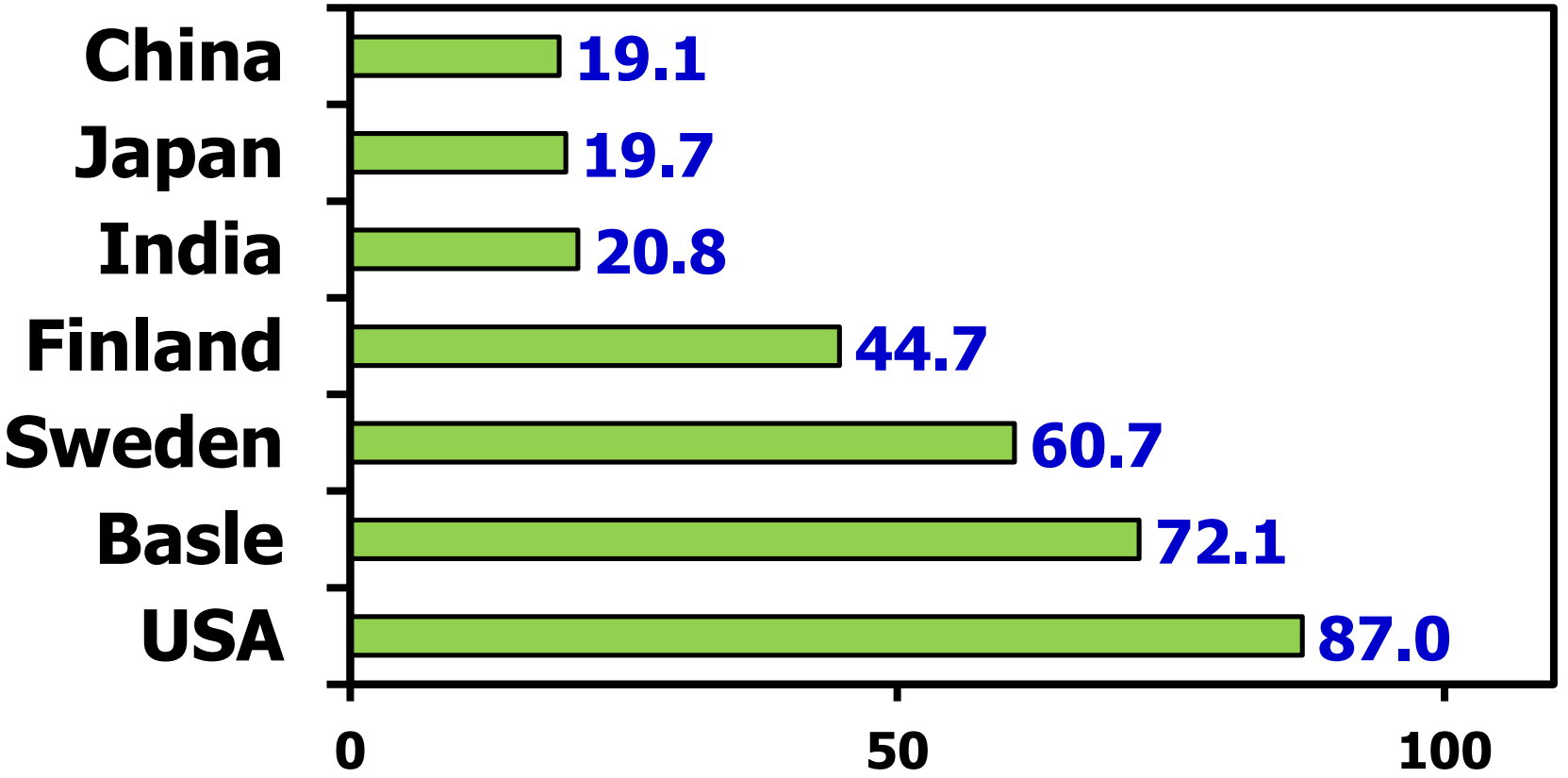
Isoflavones



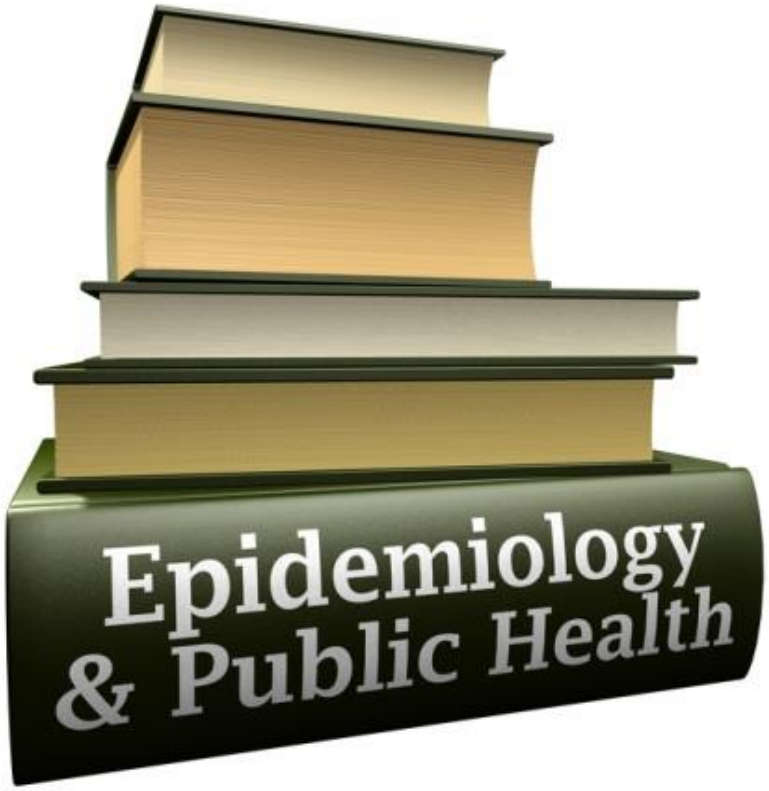
- Found primarily in soybeans
- Phytoestrogens but *different* from estrogen
- Sometimes effects opposite to estrogen
- Sometimes no effects in estrogen-sensitive tissues
- Estrogen-independent effects

Soyfoods and breast cancer prevention

Age-Adjusted Breast Cancer Incidence Rates (per 100,000) for Selected Countries



BCa: Shanghai, Osaka, Madras, Geneva, San Francisco (W).



Are women who consume soy less likely to develop breast cancer?

Isoflavone consumption and risk of breast cancer: a dose-response meta-analysis of observational studies

Qi Xie MM, Ming-Liang Chen MM, Yu Qin MD, Qian-Yong Zhang MD, Hong-Xia Xu MD, Yong Zhou MD, Man-Tian Mi MD, Jun-Dong Zhu MD

Research Center for Nutrition and Food Safety, Chongqing Key Laboratory of Nutrition and Food Safety, College of Military Preventive Medicine, Third Military Medical University, Chongqing, China

Epidemiologic studies that examine whether isoflavone consumption protects against breast cancer have yielded inconsistent results. The controversy focuses on the effects of the menopausal status and exposure dose of isoflavone. We aim to conduct a meta-analysis on the association between isoflavone intake and breast cancer risk by comprehensively assessing isoflavone exposure in the targeted populations. We searched PUBMED and EMBASE databases for case-control and cohort studies that assess the association between isoflavone intake and breast cancer risk. We extracted relative risks

Asia Pac J Clin Nutr, 22: 118, 2013

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Higher soy intake is associated with a one-third reduction in breast cancer risk

exposure dose of isoflavone. We aim to conduct a meta-analysis on the association between isoflavone intake and breast cancer risk by comprehensively assessing isoflavone exposure in the targeted populations. We searched PUBMED and EMBASE databases for case-control and cohort studies that assess the association between isoflavone intake and breast cancer risk. We extracted relative risks

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Hypothesis

Early Soy (Isoflavone) Intake Decreases Breast Cancer Risk

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Support

- **Rodent data**
- **Epidemiologic data**
- **Proposed mechanisms**

Hypothesis

Early Soy (Isoflavone) Intake Decreases Breast Cancer Risk

Support

- Rodent data
- **Epidemiologic data**
- Proposed mechanisms

Early Soy Intake and BCa Risk: Summary of Retrospective Studies

High vs low soy intake during adolescence

Author/Y	Location	(N)	Risk % ↓	Statistically Significant?
Shu, 2001	China	3,015		
Wu, 2009	USA	345		
Korde, 2009	USA	250		
Baglia, 2016	China	36,297		

*Premenopausal only Ref.: Shu: CEBP;10:483, 2001; Wu: AJCN 89: 1145, 2009; Korde: CEBP 18: 1050, 2009; Int J Cancer 139: 742, 2016 *(95% CI: 0.31, 1.00)

Early Soy Intake and BCa Risk: Summary of Retrospective Studies

High vs low soy intake during adolescence

Author/Y	Location	(N)	Risk % ↓	Statistically Significant?
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Wu, 2009	USA	345	28	Yes
Korde, 2009	USA	250	60	Yes
Baglia, 2016	China	36,297	44*	Almost

*Premenopausal only Ref.: Shu: CEBP;10:483, 2001; Wu: AJCN 89: 1145, 2009; Korde: CEBP 18: 1050, 2009; Int J Cancer 139: 742, 2016 *(95% CI: 0.31, 1.00)

100 g

240 ml

245 g

100 g

100 g

Young girls should be sure to eat ≥1 serving of soy per day

Can soyfoods be safely consumed by breast cancer patients?

Why the controversy?

SOY & BREAST CANCER

Estrogen and Breast Cancer

Menopausal hormone therapy for the primary prevention of chronic conditions: U.S. Preventive Services Task Force recommendation statement

Moyer, V. A. U.S. Preventive Services Task Force

Description: Update of the 2005 U.S. Preventive Services Task Force (USPSTF) recommendation statement on hormone therapy for the prevention of chronic conditions in postmenopausal women. Methods: The USPSTF commissioned a review of the literature to update evidence about the benefits and harms of hormone therapy differ by population subgroups defined by age; the presence of comorbid medical conditions; and the type, dose, and method of hormonal delivery. Population: This recommendation applies to postmenopausal women who are considering hormone therapy for the primary prevention of chronic medical conditions. It does not apply to women who are considering hormone therapy for the management of menopausal

Ann Intern Med, 158: 47, 2013

Menopausal hormone therapy for the primary prevention of chronic conditions: U.S. Preventive Services Task Force recommendation statement

Moyer, V. A. U.S. Preventive Services Task Force

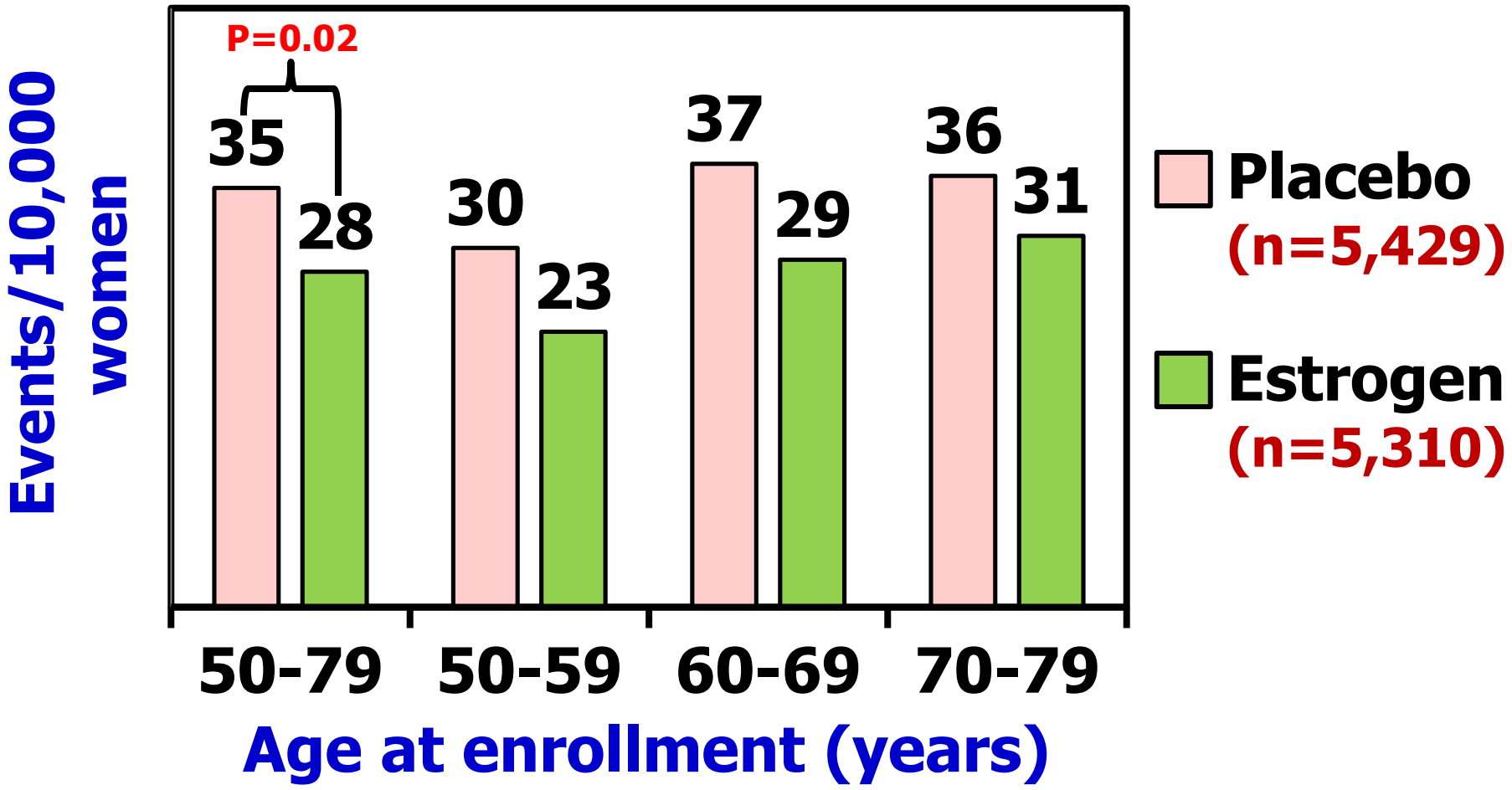
Description: Update of the 2005 U.S. Preventive Services Task

"… the use of estrogen alone results in a small reduction in the risk for developing or dying of invasive breast cancer."

the presence of comorbid medical conditions; and the type, dose, and method of hormonal delivery. Population: This recommendation applies to postmenopausal women who are considering hormone therapy for the primary prevention of chronic medical conditions. It does not apply to women who are considering hormone therapy for the management of menopausal

Ann Intern Med, 158: 47, 2013

Estrogen* Use and Annual Breast Cancer Incidence in the WHI Trial



Conjugated equine estrogens (0.625 mg/d); mean use, 7.2 y; 13 y follow up. Events=invasive BCa. JAMA 310: 1353, 2013

No clinical trials have evaluated the effects of soyfoods or isoflavones on breast cancer recurrence or mortality

BUT

Trials Involving Soy & Soy Components

Mammographic density (N=11*)

Breast cell proliferation (N=6*)

Nipple aspirate fluid (N=3*)

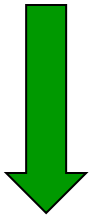
Hormone levels (N=50*)

***Number of studies**

No effects on markers of cancer risk

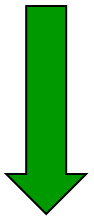
Oncology 2013;430:430-37

Combined Hormone Therapy
(estrogen + progestin)



12 weeks

Increases breast cell proliferation 4 to 10-fold



Increases breast cancer risk

Fertility Sterility 95: 1188, 2011; Breast Cancer Res Tx 78: 159, 2003

American Institute for Cancer Research

American Cancer Society

Soyfoods are safe for breast cancer patients

CA Cancer J Clin, 62 242, 2012; http://wwwaicrorg/cancer-research-update/november_21_2012/cru-soy-safehtml (accessed Feburary 5, 2013). 2012.

European Food Safety Authority

Scientific opinion on the risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2015

The EFSA ANS Panel was asked to deliver a scientific opinion on the possible association between the intake of isoflavones from food supplements and harmful effects on mammary gland, uterus and thyroid in peri- and post-menopausal women. Isoflavones are naturally occurring substances which can be found in, among other sources, soy, red clover and kudzu root. The main isoflavones are genistein, daidzein, glycitein, formononetin, biochanin A and puerarin. Their chemical structure

EFSA J. 13,4246 (342 pp).

European Food Safety Authority

Scientific opinion on the risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones

EFSA ANS Panel (EFSA Panel on Food Additives

Isoflavones don't adversely affect breast tissue in postmenopausal women

od supplements and harmful effects on mammary gland, uterus and thyroid in peri- and post-menopausal women. Isoflavones are naturally occurring substances which can be found in, among other sources, soy, red clover and kudzu root. The main isoflavones are genistein, daidzein, glycitein, formononetin, biochanin A and puerarin. Their chemical structure

EFSA J. 13,4246 (342 pp).

Links between better survival after breast cancer and:

World Cancer Research Fund International

- **Healthy body weight**
- **Being physically active**
- **Eating foods containing fiber**
- **Eating foods containing soy**
- **A lower intake of total fat, & in particular, saturated fat**

RESEARCH ARTICLE

Post-diagnosis soy food intake and breast cancer survival: A meta-analysis of cohort studies

Feng Chi*, Rong Wu, Yue-Can Zeng, Rui Xing, Yang Liu, Zhao-Guo Xu

Abstract

Background and Objectives: Data on associations between soy food intake after cancer diagnosis with breast cancer survival are conflicting, so we conducted this meta-analysis for more accurate evaluation. Methods: Comprehensive searches were conducted to find cohort studies of the relationship between soy food intake after cancer diagnosis and breast cancer survival. Data were analyzed with comprehensive meta-analysis software. Results: Five cohort studies (11,206 patients) were included. Pooling all comparisons, soy food intake after diagnosis was associated with reduced mortality (HR 0.85, 95%CI 0.77 0.93) and recurrence

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Abstract

Consuming soy after a diagnosis of breast cancer is associated with reduced recurrence and increased survival

after cancer diagnosis and breast cancer survival. Data were analyzed with comprehensive meta-analysis software. Results: Five cohort studies (11,206 patients) were included. Pooling all comparisons, soy food intake after diagnosis was associated with reduced mortality (HR 0.85, 95%CI 0.77 0.93) and recurrence

RESEARCH ARTICLE

Post-diagnosis soy food intake and breast cancer survival: A meta-analysis of cohort studies

Details

- 5 studies (3 Chinese, 2 American)
- 11,224 women with breast cancer
- Followed for 3.9 to 7.3 years
- 948 breast cancer deaths
- 1449 recurrences

High versus low soy intake

Results:

↓ 16% mortality

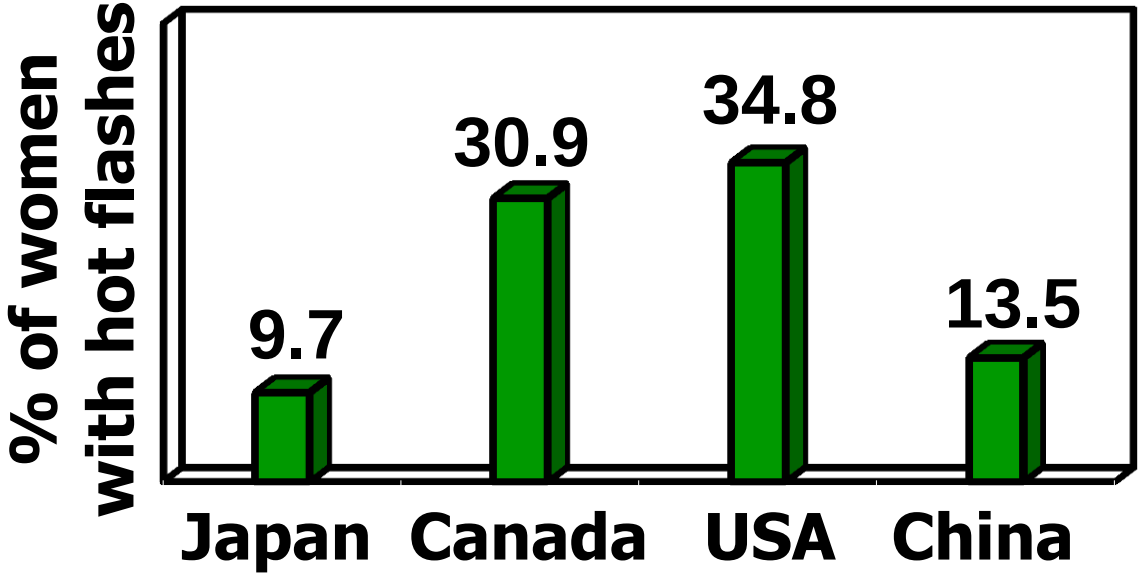
↓ 24% recurrence

Soy and hot flashes

The Hot Flash Hypothesis

Isoflavones can mitigate the drop in estrogen levels

Herman Adlercreutz, MD, PhD
University of Helsinki, Finland



1992

Lancet 339 (8803), 1233

Exp Gerontol 29: 307, 1994; Maturitas 2006

Extracted or synthesized soybean isoflavones reduce menopausal hot flash frequency and severity: systematic review and meta-analysis of randomized controlled trials

Kyoko Taku, PhD, MD,[1] Melissa K. Melby, PhD,[2] Fredi Kronenberg, PhD,[3] Mindy S. Kurzer, PhD,[4] and Mark Messina, PhD[5]

Abstract

Objective: This analysis was conducted to determine the efficacy of extracted or synthesized soybean isoflavones in the alleviation of hot flashes in perimenopausal and postmenopausal women. METHODS: PubMed and The Cochrane Controlled Clinical Trials Register Database were searched for relevant articles reporting double-blinded randomized controlled trials through December 14, 2010. References within identified articles, as well as peer-reviewed articles that had come to the attention of the authors through other means, were also examined for suitability. This systematic review and meta-analysis, which evaluated the effects of isoflavones on the frequency, severity, or composite score

Menopause 19: 776, 2012

Extracted or synthesized soybean isoflavones reduce menopausal hot flash frequency and severity: systematic review and meta-analysis of randomized controlled trials

Kyoko Taku, PhD, MD,[1] Melissa K. Melby, PhD,[2] Fredi Kronenberg, PhD,[3] Mindy S. Kurzer, PhD,[4] and Mark Messina, PhD[5]

Abstract

Whole soybean-derived isoflavone supplements significantly reduce hot flash frequency and severity in comparison to placebo

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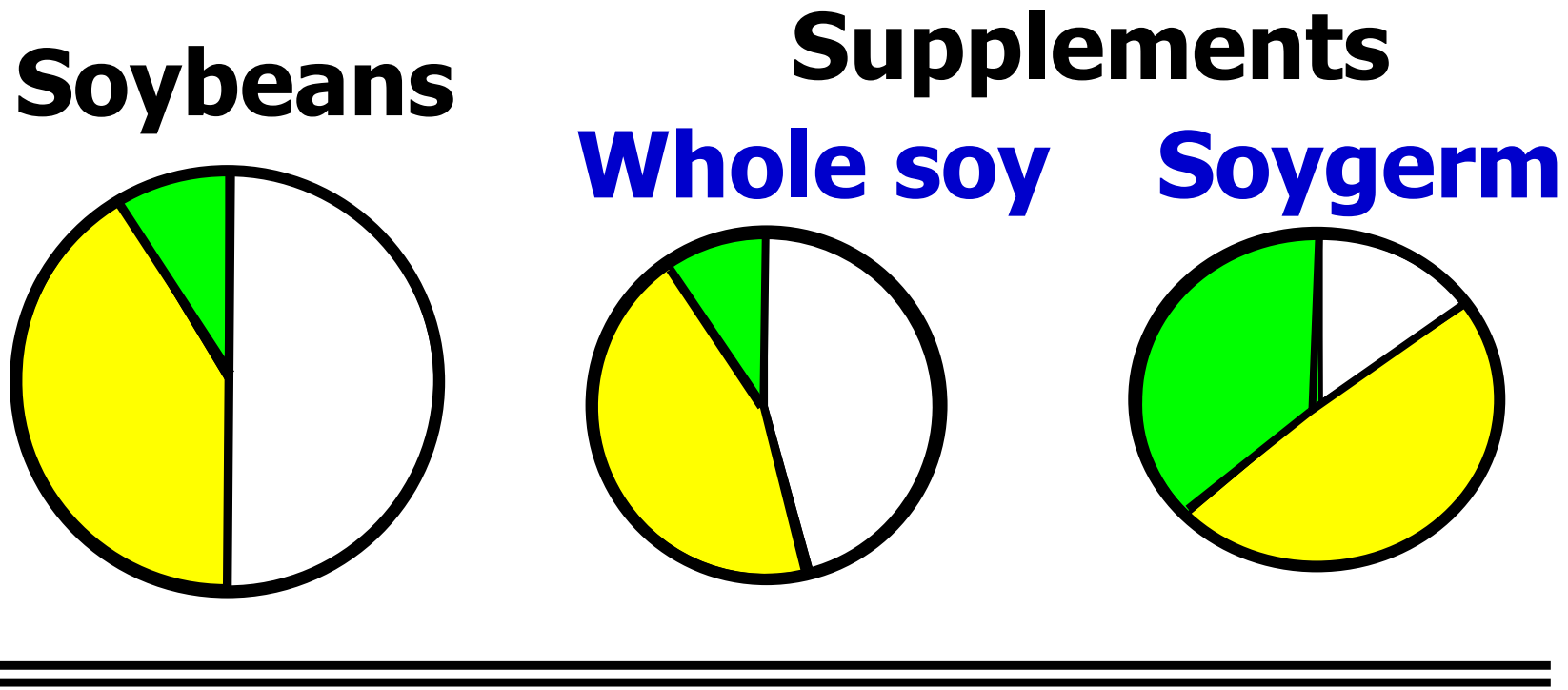
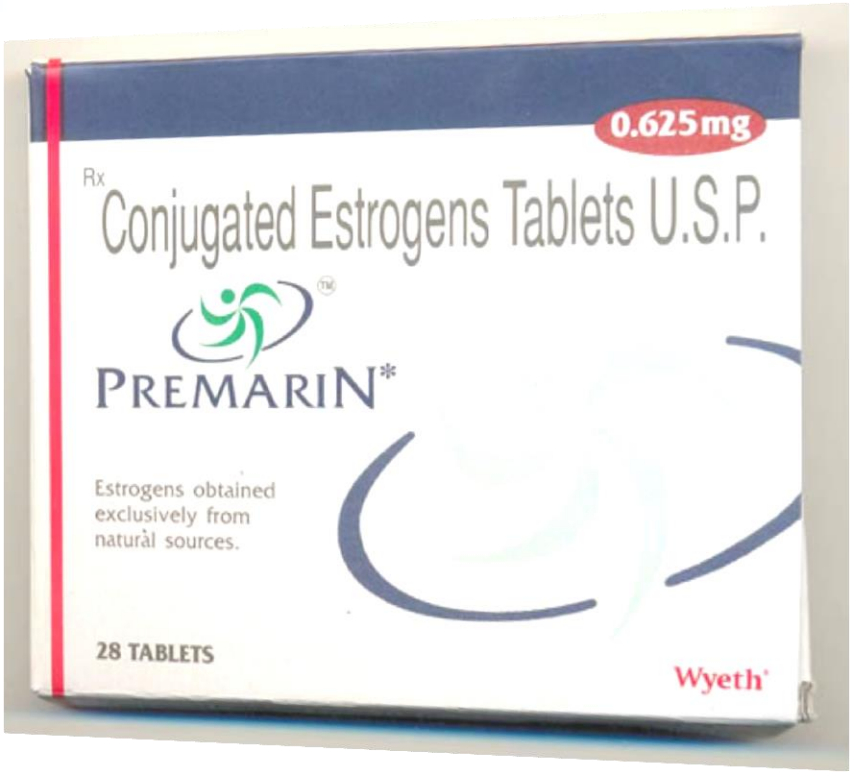
Menopause 19: 776, 2012

Isoflavone Profile of Two Commonly Used Soy Supplements



Soy and bone health



WOMEN'S HEALTH INITIATIVE

- **Inhibits bone loss**
- **Reduces fractures**

Impact of equol-producing capacity and soy-isoflavone profiles of supplements on bone calcium retention in postmenopausal women: a randomized crossover trial[1,2]

Jessica W Pawlowski,[3,8] Berdine R Martin,[3] George P McCabe,[4] Linda McCabe,[3] George S Jackson,[5] Munro Peacock,[6] Stephen Barnes,[7] and Connie M Weaver[3]*

[3]Department of Nutrition Science, College of Health and Human Sciences, [4]Department of Statistics, College of Science, and [5]Purdue Rare Isotope Measurement Laboratory, Department of Physics, Purdue University, West Lafayette, IN; [6]Indiana University School of Medicine, Indianapolis, IN; and [7]Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham, AL

BACKGROUND: Postmenopausal estrogen depletion is a major contributing factor to bone loss. Soy isoflavones have variable effects on the prevention of postmenopausal bone loss, which is possibly related to the specific isoflavone content or the variable equol-producing capacity of individuals. OBJECTIVE: We aimed to determine the effects of the content of isoflavones in a soy supplement and the equol-producing ability of the individual on

Am J Clin Nutr 102: 695, 2015

Impact of equol-producing capacity and soy-isoflavone profiles of supplements on bone calcium retention in postmenopausal women: a randomized crossover trial[1,2]

Jessica W Pawlowski,[3,8] Berdine R Martin,[3] George P McCabe,[4] Linda McCabe,[3] George Jackson,[5] Munro Peacock,[6] Stephen Barnes,[7] and Connie M Weaver[3]*

"… the use of soy isoflavones presents minimal to negligible risk to postmenopausal women … and can be used long term for some protection against postmenopausal bone loss."

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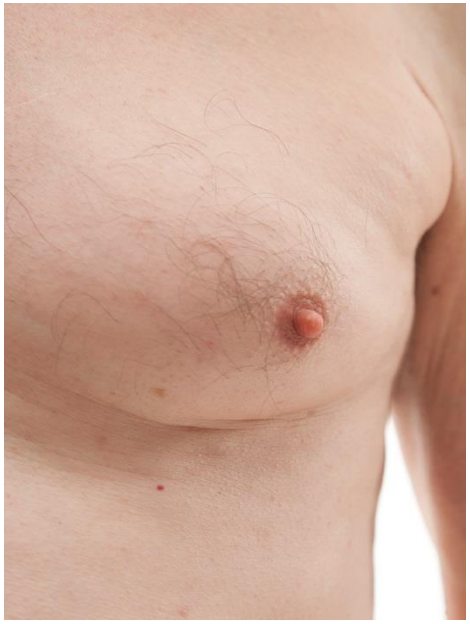
Am J Clin Nutr 102: 695, 2015

Overview of the Nutritional and Health Attributes of Soyfoods

Outline

- Macronutrient composition
- Coronary heart disease
- Isoflavones
- Breast cancer
- Hot flashes
- Bone health
- **Misunderstandings**

Feminization



Hypogonadism and erectile dysfunction associated with soy product consumption

Nutrition 27: 859, 2011

Timo Siepmann M.D. [a],[*], Joseph Roofeh [a], Florian W. Kiefer M.D., Ph.D. [b], David G. Edelson M.D.[c]

19 year old vegan man

360 mg isoflavones
(12-20 servings/day)

An unusual case of gynecomastia associated with soy product consumption

Endocrine Pract 14: 415, 2008

Jorge Martinez, MD[1], Jack E. Lewi, MD, FACP, FACE[2]

60 year old man

360 mg isoflavones
(3 liters soymilk/day)

Clinical studies show no effects of soy protein or isoflavones on reproductive hormones in men: results of a meta-analysis

Jill M. Hamilton-Reeves, Ph.D.,[a] Gabriela Vazquez, Ph.D.,[b,c] Sue J. Duval, Ph.D.,[b] William R. Phipps, M.D.,[d] Mindy S. Kurzer, Ph.D.,[e] and Mark J. Messina, Ph.D.[f,g]

OBJECTIVE: To determine whether isoflavones exert estrogen-like effects in men by lowering bioavailable T through evaluation of the effects of soy protein or isoflavone intake on T, sex hormone-binding globulin (SHBG), free T, and free androgen index (FAI) in men.
DESIGN: PubMed and CAB Abstracts databases were searched through July 1, 2008, with use of controlled vocabulary specific to the databases, such as soy, isoflavones, genistein, phytoestrogens, red clover, androgen, testosterone, and SHBG. Peer-reviewed studies published in English were selected if [1] adult men consumed soy foods, isolated soy protein, or isoflavone extracts (from soy or red

Fertil Steril 94: 997, 2010

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"… No significant effects of soy protein or isoflavone intake on T, SHBG, free T, or FAI were detected regardless of statistical model."

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Fertil Steril 94: 997, 2010

Soybean isoflavone exposure does not have feminizing effects on men: a critical examination of the clinical evidence

Mark Messina, PhD
Department of Nutrition, School of Public Health, Loma Linda University, Loma Linda, California

OBJECTIVE: To critically evaluate the clinical evidence, and when not available, the animal data, most relevant to concerns that isoflavone exposure in the form of supplements or soy foods has feminizing effects on men. DESIGN: Medline literature review and cross-reference of published data. RESULT(S): In contrast to the results of some rodent studies, findings from a recently published metaanalysis and subsequently published studies show that neither isoflavone supplements nor isoflavone-rich soy affect total or free testosterone (T) levels. Similarly, there is essentially no evidence from the nine identified clinical studies that isoflavone exposure affects circulating estrogen

Fertil Steril 93: 2095, 2010

Soybean isoflavone exposure does not have feminizing effects on men: a critical examination of the clinical evidence

Mark Messina, PhD
Department of Nutrition, School of Public Health, Loma Linda University, Loma Linda, California

"… isoflavones do not exert feminizing effects on men at intake levels equal to and even considerably higher than are typical for Asian males."

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Fertil Steril 93: 2095, 2010

Soy consumption and prostate cancer risk in men: a revisit of a meta-analysis

Lin Yan and Edward L Spitznagel

Is phytoestrogen intake associated with decreased risk of prostate cancer? A systematic review of epidemiological studies based on 17,546 cases

[1]M. Zhang, [1]K. Wang, [2]L. Chen, [1]B. Yin and [1]Y. Song
[1]Departments of Urology, and [2]Ultrasound, Shengjing Hospital, China Medical University, Shenyang, China

Asian epidemiologic studies show soy intake is associated with a 20 to 50% reduction in prostate cancer risk

AJCN 89: 1155, 2009; Andrology 4: 745, 2016

Soy and thyroid function

Effects of soy protein and soybean isoflavones on thyroid function in healthy adults and hypothyroid patients: a review of the relevant literature

Mark Messina,[12] and Geoffrey Redmond[3]

Soy foods are a traditional staple of Asian diets but because of their purported health benefits they have become popular in recent years among non-Asians, especially postmenopausal women. There are many bioactive soybean components that may contribute to the hypothesized health benefits of soy but most attention has focused on the isoflavones, which have both hormonal and nonhormonal properties. However, despite the possible benefits concerns have been expressed that soy may be contraindicated for some subsets of the population. One concern is that soy may adversely affect thyroid function and interfere with the absorption of synthetic thyroid hormone. Thus, the purpose of this review is to evaluate the relevant

Thyroid 16: 249, 2006

Effects of soy protein and soybean isoflavones on thyroid function in healthy adults and hypothyroid patients: a review of the relevant literature

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No effects of soy or isoflavones on thyroid function in people with normal-functioning thyroid

Thyroid 16: 249, 2006

Genistein Aglycone Does Not Affect Thyroid Function: Results from a Three-Year, Randomized, Double-Blind, Placebo-Controlled Trial

Alessandra Bitto,* Francesca Polito,* Marco Atteritano, Domenica Altavilla, Susanna Mazzaferro, Herbert Marini, Elena Bianca Adamo, Rosario D'Anna, Roberta Granese, Francesco Corrado, Silvia Russo, Letteria Minutoli, and Francesco Squadrito

Department of Clinical and Experimental Medicine and Pharmacology, Section of Pharmacology (A.B., F.P., D.A., L.M., F.S.); Department of Internal Medicine (M.A., S.M.); Department of Biochemical, Physiological and Nutritional Sciences, Section of Physiology and Human Nutrition (H.M., E.B.A.); and Department of Obstetrical and Gynecological Sciences (R.D., R.G., F.C., S.R.), University of Messina, 98125 Messina, Italy

CONTEXT AND OBJECTIVE: Genistein aglycone positively affects postmenopausal symptoms. However, questions about its long-term safety on the thyroid gland still remain. DESIGN: The parent study was a randomized, double-blind, placebo-controlled trial involving 389 osteopenic, postmenopausal women for 24 months. A subcohort (138 patients) continued therapy for an additional year. SETTING: Patients

J Clin Endocrinol Metab 95: 3067, 2010

Genistein Aglycone Does Not Affect Thyroid Function: Results from a Three-Year, Randomized, Double-Blind, Placebo-Controlled Trial

Alessandra Bitto,* Francesca Polito,* Marco Atteritano, Domenica Altavilla, Susanna Mazzaferro, Herbert Marini, Elena Bianca Adamo, Rosario D'Anna, Roberta Granese, Francesco Corrado, Silvia Russo, Letteria Minutoli, and Francesco Squadrito

Department of Clinical and Experimental Medicine and Pharmacology, Section of Pharmacology (A.B., F.P., D.A., L.M., F.S.); Department of Internal Medicine (M.A., S.M.); Dep... Hu... (R.

No effect of isoflavones on thyroid function in postmenopausal women

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J Clin Endocrinol Metab 95: 3067, 2010

European Food Safety Authority

Scientific opinion on the risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2015

The EFSA ANS Panel was asked to deliver a scientific opinion on the possible association between the intake of isoflavones from food supplements and harmful effects on mammary gland, uterus and thyroid in peri- and post-menopausal women. Isoflavones are naturally occurring substances which can be found in, among other sources, soy, red clover and kudzu root. The main isoflavones are genistein, daidzein, glycitein, formononetin, biochanin A and puerarin. Their chemical structure

EFSA J. 13,4246 (342 pp).

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Scientific opinion on the risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones

EFSA ANS Panel (EFSA Panel on Food Additives

Isoflavones don't adversely affect thyroid function in postmenopausal women

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Soy and hypothyroid patients

Conditions and drugs interfering with thyroxine absorption

Llanyee Liwanpo, MD, Doctor *, Jerome M. Hershman, MD, Professor
Department of Endocrinology, VA Greater Los Angeles Healthcare System, Los Angeles, CA

- **Soy protein**

ee interfere with the absorption of levothyroxine.

Keywords:
thyroxine absorption
interfering drugs
levothyroxine
malabsorption
hypothyroidism

Malabsorptive disorders reported to affect the absorption of levothyroxine include coeliac disease, inflammatory bowel disease, lactose intolerance as well as Helicobacter pylori (H. pylori) infection and atrophic gastritis. Many commonly used drugs, such as bile acid sequestrants, ferrous sulphate, sucralfate, calcium carbonate, aluminium-containing antacids, phosphate binders, raloxifene and proton-pump inhibitors, have also been shown to interfere with the absorption of levothyroxine.

Best Pract Res Clin Endocrinol Metab 23: 781, 2009

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Department of Endocrinology, VA Greater Los Angeles Healthcare System, Los Angeles, CA

Keywords:
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hypothyroidism

- **Soy protein**
- **Calcium carbonate**
- **Fiber supplements**
- **Iron**
- **Proton pump inhibitors**
- **Bile acid sequestrants**
- **Certain herbs**
- **Etc.**

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vothyroxine.

Best Pract Res Clin Endocrinol Metab 23: 781, 2009

The Journal of Pediatrics www.jped.com

Commentary

Food and Levothyroxine Administration in Infants and Children

Philip Zeitler, MD, PhD, and Paulo Solberg, MD, for the Pharmacy and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society*

In recent years, patients receiving thyroid hormone have been told by pharmacists that the medication should be taken on an empty stomach. This advisory is found in a number of sources that pharmacists use for administration details. For example, Micromedex Drug information for levothyroxine reads: Administer tablets and capsules with water on an empty stomach, preferably one-half hour to an hour before breakfast. Administer four hours apart from antacids, iron, and calcium supplements (Prod Info

J Pediatr 157: 13, 2010

The Journal of Pediatrics www.jped.com

Commentary

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Soy not contraindicated for hypothyroid patients

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J Pediatr 157: 13, 2010

Reduces absorption of minerals – calcium, iron, zinc, and magnesium

Phytate
(phytic acid)

- **Naturally occurring compound**
- **Found in whole grains & beans**

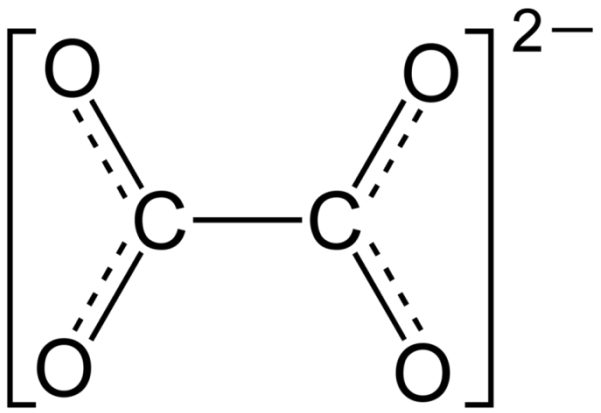
Peanuts

Spinach

Quinoa

Almonds

Rhubarb



Oxalate

Naturally-occurring plant chemical that reduces the absorption of minerals such as calcium

Soybeans are high in phytate & oxalate, but

- **Calcium absorption:**
  - **Fortified soymilk = cow's milk**
  - **Calcium set tofu = cow's milk**
- **Iron absorption:**
  - **Greatly underestimated?**
  - **Soy iron present as ferritin**

J Nutr 135: 2379, 2005; J Food Sci 68: 3144, 2002; Am J Clin Nutr 89: 1680S, 2009

Regular Consumption of a High-Phytate Diet Reduces the Inhibitory Effect of Phytate on Nonheme-Iron Absorption in Women with Suboptimal Iron Stores[1,2]

Seth M Armah,[3] Erick Boy,[4] Dan Chen,[3] Priscila Candal,[3] and Manju B Reddy[3]*

3Department of Food Science and Human Nutrition, Iowa State University, Ames, IA; and 4HarvestPlus/International Food Policy Research Institute, Washington, DC

BACKGROUND: High phytate (HP) consumption is a concern in developing countries because of the high prevalence of iron deficiency in these countries. OBJECTIVE: We investigated whether habitual consumption of an HP diet reduces the inhibitory effect of phytate on nonheme-iron absorption. METHODS: Thirty-two nonanemic females, 18-35 y of age, with normal body mass index but with suboptimal iron stores (serum ferritin, </=30 mug/L), were matched for serum ferritin concentration and randomly assigned to HP and low-phytate (LP)

J Nutr 145: 1735, 2015

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J Nutr 145: 1735, 2015

Does soy affect puberty?

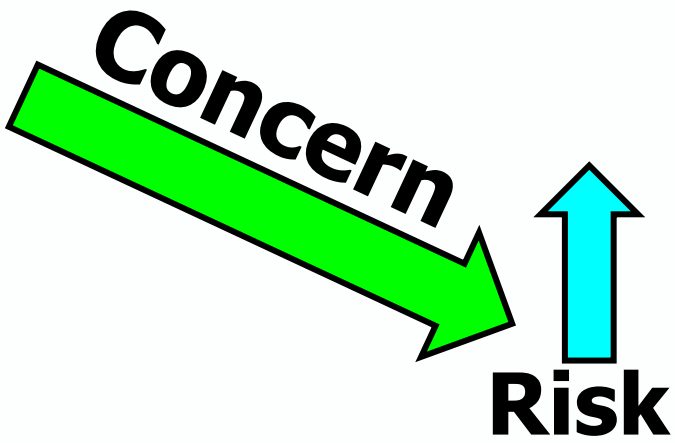
Population-based studies worldwide have observed secular trends towards earlier pubertal development

Basic & Clinical Pharmacol and Toxicol 102: 168–175, 2008

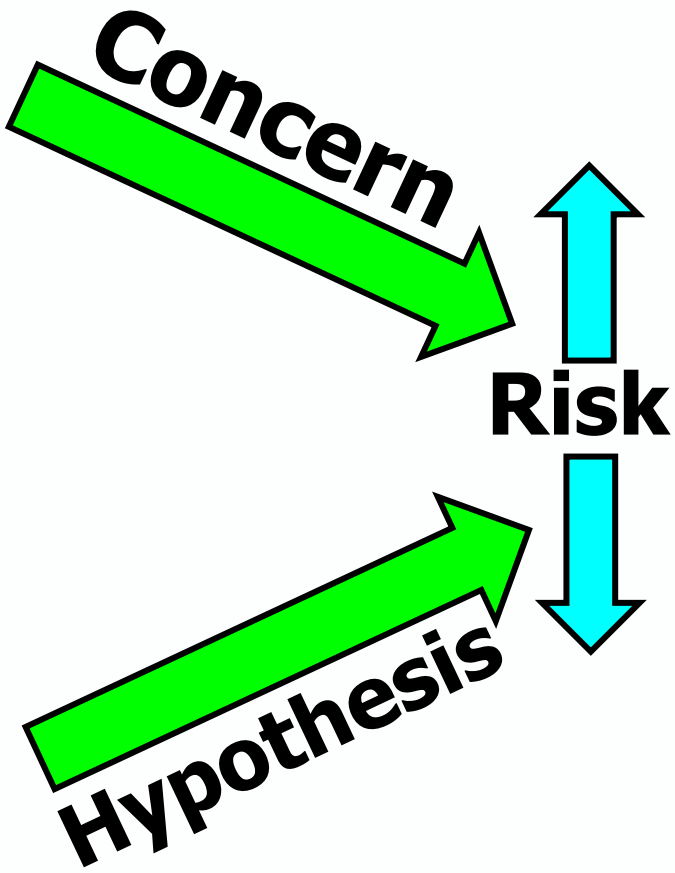
Change in Menarcheal Age (y)

Country	Time period	Beginning	Ending
Holland	1965 → 2009	13.4	12.6
Japan	1930 → 1985	13.8	12.6
Korea	1920 → 1985	16.9	13.8
UK	1910 → 1993	13.5	12.3
Spain	1925 → 1962	13.7	12.8
Canada	1933 → 1988	13.2	12.5
Brazil	(<8 y education)	13.4	11.7
	1932 → 1977		
	(>8 y education)	12.4	12.2

Early puberty



Early puberty



Childhood soy intake

Endocrine Disruptors and Abnormalities of Pubertal Development

Greet Schoeters [1,2], Elly Den Hond[1], Willem Dhooge[4], Nik van Larebeke[3] and Marike Leijs[5]

Onset and development of puberty is regulated by the neuroendocrine system. Population-based studies worldwide have observed secular trends towards earlier puberty development. These changes are apparently caused by environmental factors such as improved socio-economic status, improved health care and nutrition. However, they may also partly result from endocrine-disrupting chemicals in the environment. Epidemiological studies have investigated the relationship between pubertal development and exposure to endocrine-disrupting chemicals (polychlorinated biphenyls, polybrominated biphenyls, 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane, phthalate esters, furans and the pesticide endosulfan). Associations with both perinatal and postnatal

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Onset and development of puberty is regulated by the neuroendocrine system. Population-based studies worldwide

Earlier pubertal development may be due to exposure to hormonally active chemicals in the environment

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Is soy intake related to age at onset of menarche? A cross-sectional study among adolescents with a wide range of soy food consumption

Gina Segovia-Siapco[1]*, Peter Pribis[3], Mark Messina[4], Keiji Oda[2] and Joan Sabaté[1,2]

Abstract

Background: Early onset of menarche may negatively influence the future health of adolescent girls. Several factors affect the timing of menarche but it is not clear if soy foods consumption around pubertal years plays a role; thus, we examined its relation to age at onset of menarche (AOM) in a high soy-consuming population.

Methods: We conducted a cross-sectional study on 339 girls ages 12–18 years attending middle and high schools near two Seventh-day Adventist universities in California and Michigan using a web-based dietary questionnaire and physical development tool. Soy consumption (categorized as total soy, meat alternatives,

Is soy intake related to age at onset of menarche? A cross-sectional study among adolescents with a wide range of soy food consumption

Gina Segovia-Siapco[1]*, Peter Pribis[3], Mark Messina[4], Keiji Oda[2] and Joan Sabaté[1,2]

- 327 Seventh-day Adventists, age 12-18
- High-soy-consuming population
- Mean intake, 12.9 servings/week
- 21% consumed >4 servings/week
- Mean age of menarche, 12.5 years
- Soy intake unrelated to AOM

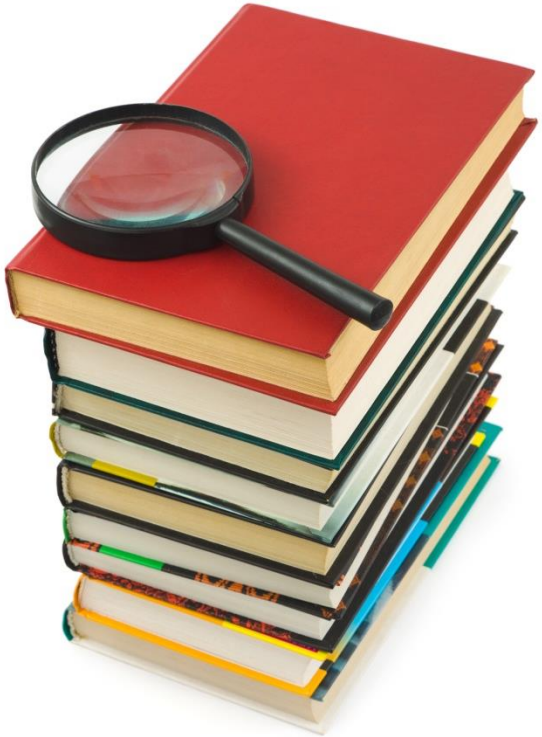
Soy Allergy Prevalence

- FDA survey of adults
  - 1 out of 2,500
  - Milk 40x > soy

- N=38,465 children
  - ~1 out of 200
  - 70% outgrow by age 10
  - Milk/peanuts 4-5x > soy

J Allergy Clin Immunol 119: 1504, 2007; Clinical Pediatr (Phila) 2012;51:856; J Allergy Clin Immunol 125: 683, 2010

- **Totality of the evidence**
- **Study type and quality**



Soyfoods promote health

Nutritional and Health Attributes of Soy

- **Excellent safety profile**
- **High quality protein**
  - **Hypocholesterolemic, hypotensive**
- **Healthy fatty acid profile**
  - **High in PUFA, both essential fats**
- **Uniquely-rich source of isoflavones**
  - **Early intake may prevent breast cancer**
  - **Reduces hot flashes**
  - **May increase BMD**
  - **May decrease prostate cancer risk**

Questions?

Contact Info:
markjohnmessina@gmail.com

Thank you for your attention

Credit Claiming

You must complete a brief evaluation of the program in order to obtain your certificate. The evaluation will be available for 1 year; you do not have to complete it today.

Credit Claiming Instructions:

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2. Click "Take Course" on the webinar description page.
3. Select "Start/Review Course" to complete and submit the evaluation.
4. Download and print your certificate.

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