

# *Soy and Cancer*

## **Sense and Sensibility** **The truth about soy and cancer**

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Acknowledgement

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# Jan. 14 Sydney - Shock! Horror!

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## Herald Sun

Australia's biggest-selling daily newspaper

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### Soy cancer alert

Clair Weaver

January 14, 2007 12:00am

**CANCER patients are being warned to avoid foods rich in soy because they can accelerate the growth of tumours.**

Cancer Council NSW will for the first time issue guidelines today warning about the dangers of high soy diets and soy supplements for cancer patients and those in remission. At particular risk are people suffering from hormone-dependent cancers including breast and prostate cancers, the two most common forms in Australia.

Cancer survivors are also being urged to avoid high doses of soy as they may be more vulnerable to a relapse.

Research has found that high consumption of soy products can also prevent the effectiveness of conventional medicines used to treat the disease.

# Jan. 14 Sydney - Shock! Horror!

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## Cancer patients warned to avoid soy products

January 14, 2007 - 12:44PM

Cancer patients are being urged to avoid soy food products due to fears they can cause tumours to grow faster.

The Cancer Council NSW will today issue guidelines warning of the dangers of consuming high amounts of soy products, a newspaper reports.

People with breast and prostate cancer - Australia's most common cancers - are most at risk as both forms of the disease are hormone dependent.

Research has found consuming high amounts of soy can limit the effectiveness of medicines used to treat the disease.

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# The truth is out there!

SOY the food of illness



SOY JUNK and how People are unaware of the Dangers of Soy

## SOY AND CANCER !!!!!!!!!!!!!!!

The new FDA ruling does not allow any claims about cancer prevention on food packages, but that has not restrained the industry and its marketeers from making them in their promotional literature. "In addition to protecting the heart," says a vitamin company brochure, "soy has demonstrated powerful anticancer benefits...the

Japanese, who eat 30 times as much soy as North Americans, have a lower incidence of cancers of the breast, uterus and prostate."<sup>37</sup> **Indeed they do. But the Japanese, and Asians in general, have much higher rates of other types of cancer, particularly cancer of the oesophagus, stomach, pancreas and liver.**<sup>38</sup> **Asians throughout the world also have high rates of thyroid cancer.**<sup>39</sup> The logic that links low rates of reproductive cancers to soy consumption requires attribution of high rates of thyroid and digestive cancers to the same foods, particularly as soy causes these types of cancers in laboratory rats.

Just how much soy do Asians eat? A 1998 survey found that the **average daily amount of soy protein consumed in Japan was about eight grams for men and seven for women - less than two teaspoons.**<sup>40</sup> The famous Cornell China Study, conducted by Colin T. Campbell, **found that legume consumption in China varied from 0 to 58 grams per day, with a mean of about twelve.**<sup>41</sup> **Assuming that two-thirds of legume consumption is soy, then the maximum consumption is about 40 grams, or less than three tablespoons per day, with an average consumption of about nine grams, or less than two teaspoons.** A survey conducted in the 1930s found that soy foods accounted for only 1.5 per cent of calories in the Chinese diet, compared with 65 per cent of calories from pork.<sup>42</sup> **(Asians traditionally cooked with lard, not vegetable oil!)** Traditionally fermented soy products make a delicious, natural seasoning that may supply important nutritional factors in the Asian diet. But except in times of famine, **Asians consume soy products only in small amounts, as condiments, and not as a replacement for animal foods** - with one exception. Celibate monks living in monasteries and leading a vegetarian lifestyle find

**soy foods quite helpful because they dampen libido.**

It was a 1994 meta-analysis by Mark Messina, published in Nutrition and Cancer, that fuelled speculation on soy's anticarcinogenic properties.<sup>43</sup> Messina noted that in 26 animal studies, 65 per cent reported protective effects from soy. He conveniently **neglected to include at least one study in which soy feeding caused pancreatic cancer** - the 1985 study by Rackis.<sup>44</sup> In the human studies he listed, the results were mixed. **A few showed some protective effect, but most showed no correlation at all between soy consumption and cancer rates.** He concluded that "the data in this review cannot be used as a

<http://augmentinforce.50webs.com/ANTI%20SOY.htm>

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## *Why is this important?*

- **74% - food and nutrition has a significant effect on the maintenance and improvement of their overall health.**
- **33% - add particular foods or ingredients to their diet to improve or maintain health (27% in Australia).**
- ***59% - eat up to three foods specifically for functional health benefits.***

USA survey data 1998; National Nutrition Survey, 1995

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# Why is this important?

- Cancer is the leading cause of death in Australia – 29.4% as the sole underlying cause, 40.6% as contributing cause

STANDARDISED DEATH RATES, Selected Malignant neoplasms—Females



STANDARDISED DEATH RATES, Selected Malignant neoplasms—Males



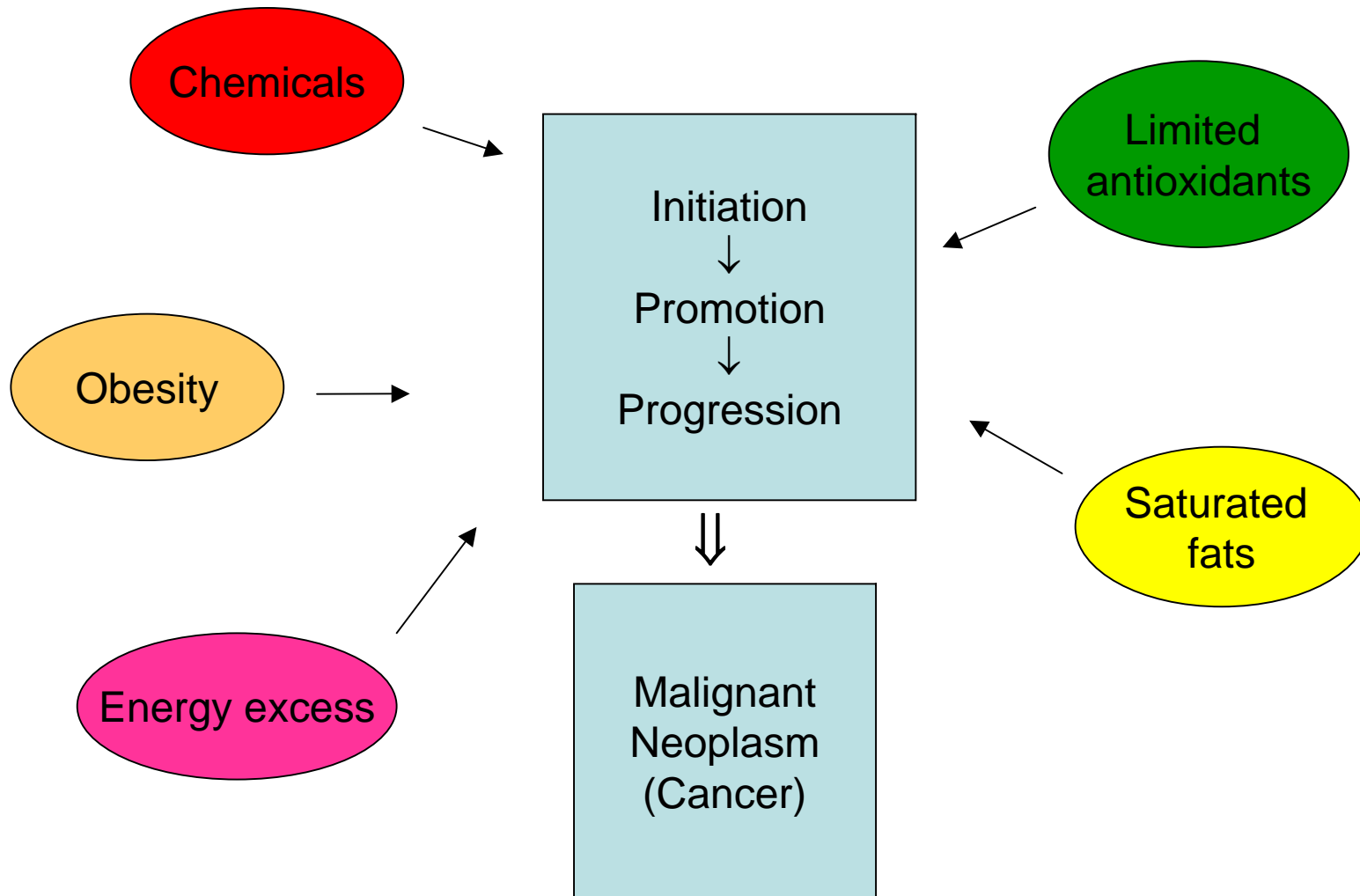
- Breast and prostate cancers are leading causes of mortality

ABS statistics 2005

(a) Per 100,000 estimated resident population.



# *The dietary origins of cancer*



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# Why is this important?

- Diet is the single largest contributing factor
  - multifactorial in effect

| Factor                       | Best Estimate | Range of Acceptable Estimates |
|------------------------------|---------------|-------------------------------|
| Tobacco                      | 30            | 25-40                         |
| Alcohol                      | 3             | 2-4                           |
| Diet                         | 35            | 10-70                         |
| Food Additives               | 1             | (-5**)-2                      |
| Reproductive/Sexual Behavior | 7             | 1-13                          |
| Occupation                   | 4             | 2-8                           |
| Pollution                    | 2             | 1-5                           |
| Industrial Products          | 1             | 1-2                           |
| Medicines/Medical Products   | 1             | 0.5-3                         |
| Geophysical Factors          | 3             | 2-4                           |
| Infection                    | 10            | 1-?                           |

Doll and Peto (1981)



# Why single out soy for attention?

- Soybeans contain chemicals known as **phytoestrogens**
- Natural plant substances
  - Three main classes
    - Isoflavones
    - Coumestans
    - lignans
- Phytoestrogens plant relatives of the hormone oestrogen
  - They weakly mimic or modulate the hormone's effects on some body tissues
- They have anti-carcinogenic properties
- But also due the oestrogenic properties they can also promote cancer

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# Soy and cancer

How do we establish an evidence-based relationship between diet and cancer?

## Epidemiology

- inverse relationship with nutrient intake
- incidence of site specific tumors varied with diet
- patterns between countries

## Clinical Studies

- mainly retrospective
- used supplements
- equivocal findings

## Randomized Clinical Trials

- large prospective underway
- biomarkers as endpoints

## Animal Studies

- compelling but not generalizable

## Cell Lines

- elucidation of mechanisms
- evaluate genetic interactions

## Molecular Biology

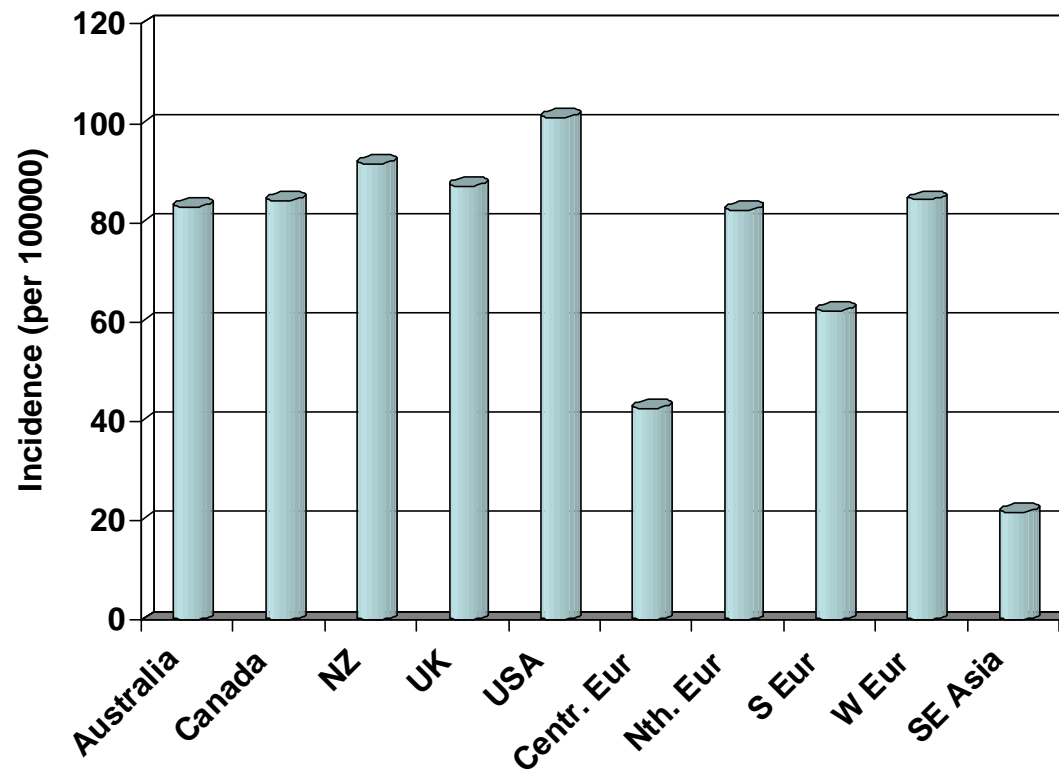
- confirmation of mechanisms
- demonstration of gene binding

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# *What is the evidence - epidemiologic*

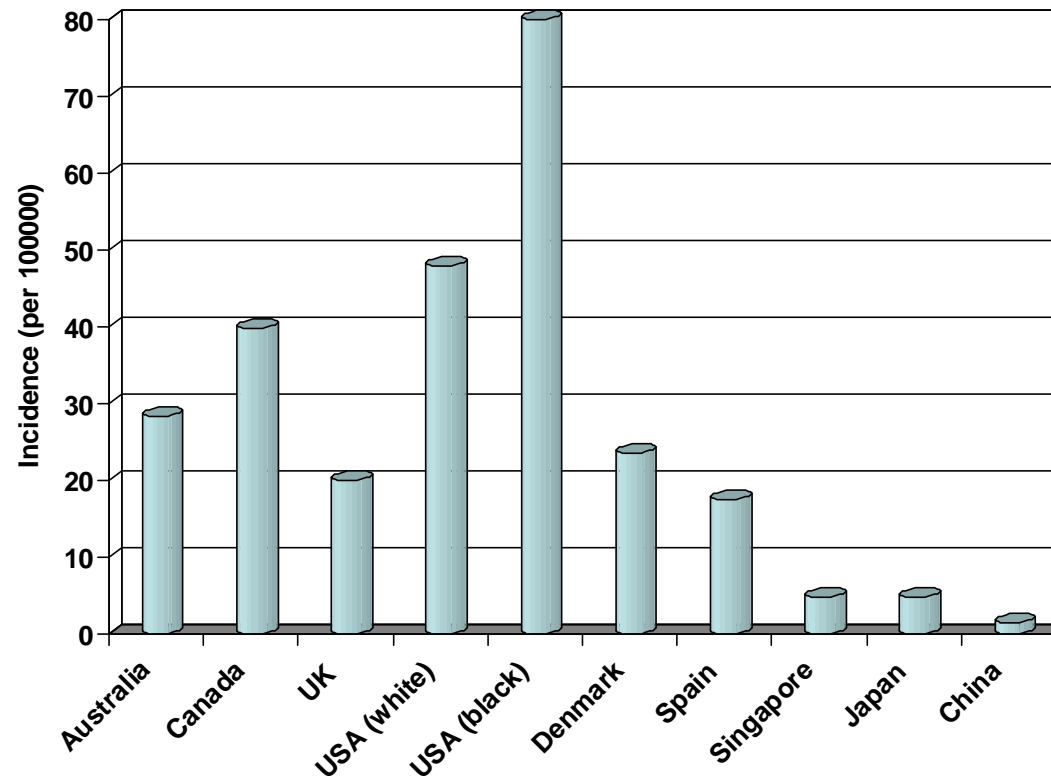
- Populations with high soy food intake tend to have lower rates of breast, prostate, and colon cancer



AIHW/NBCC (2006) #34 "Breast cancer in Australia: an overview"



# Prostate cancer by country

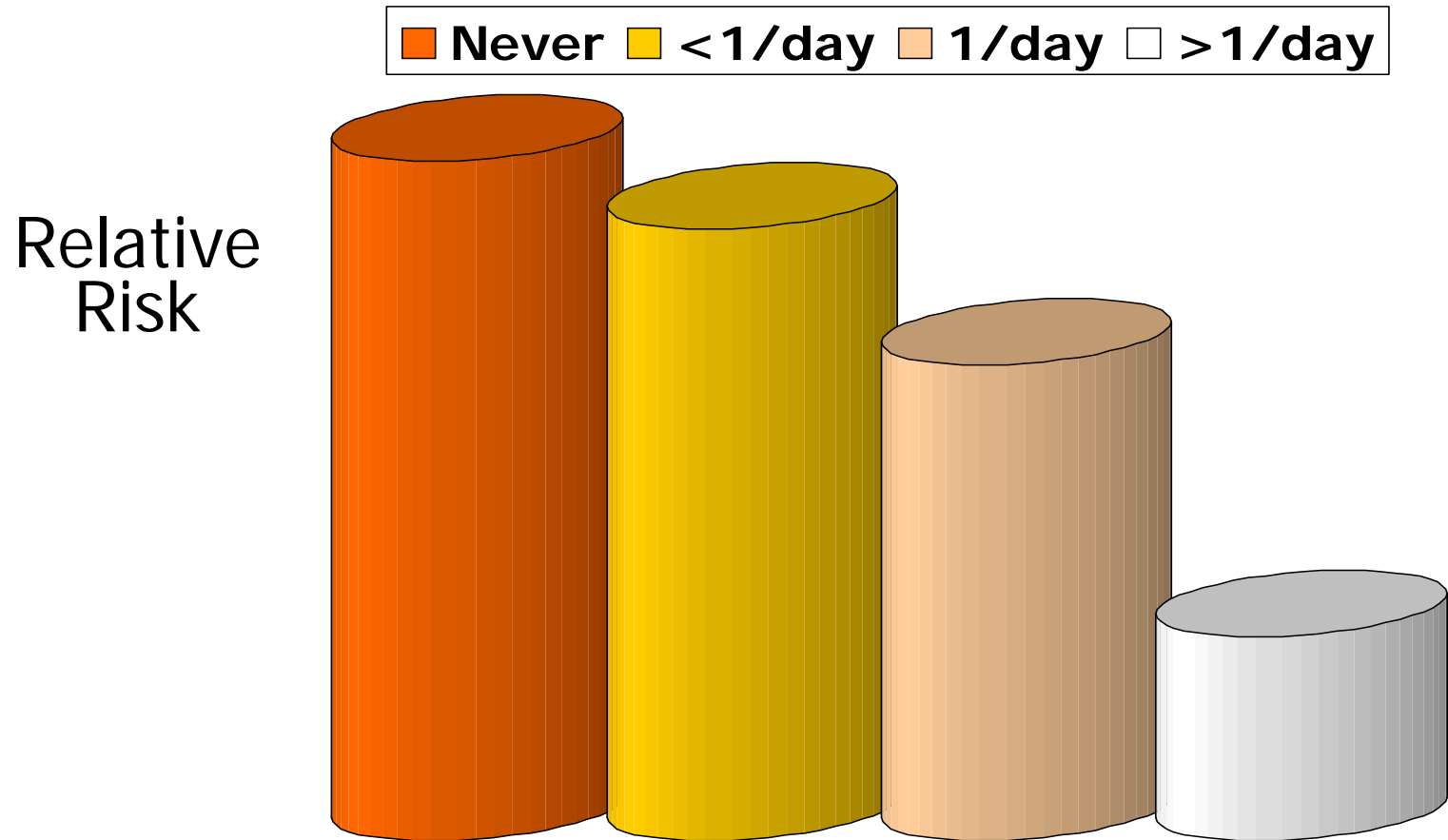


Hsing et al. (2000) Int. J. Canc. 85: 60

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# Soy milk intake and prostate cancer



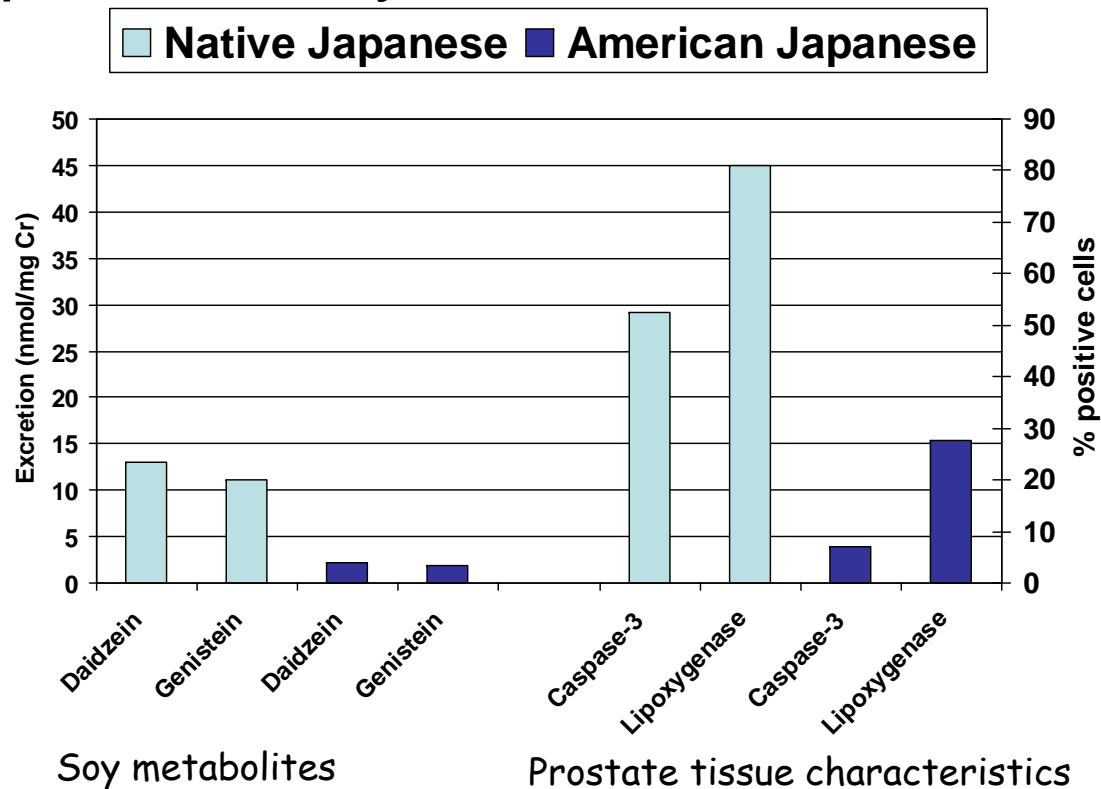
Adventists Health Study - 1 1976-1988

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# Epidemiologic evidence - 2

- Migrant populations (presumably adapting western diet) tend to develop cancer rates of adopted country



Marks et al. (2004) Urology 64: 765



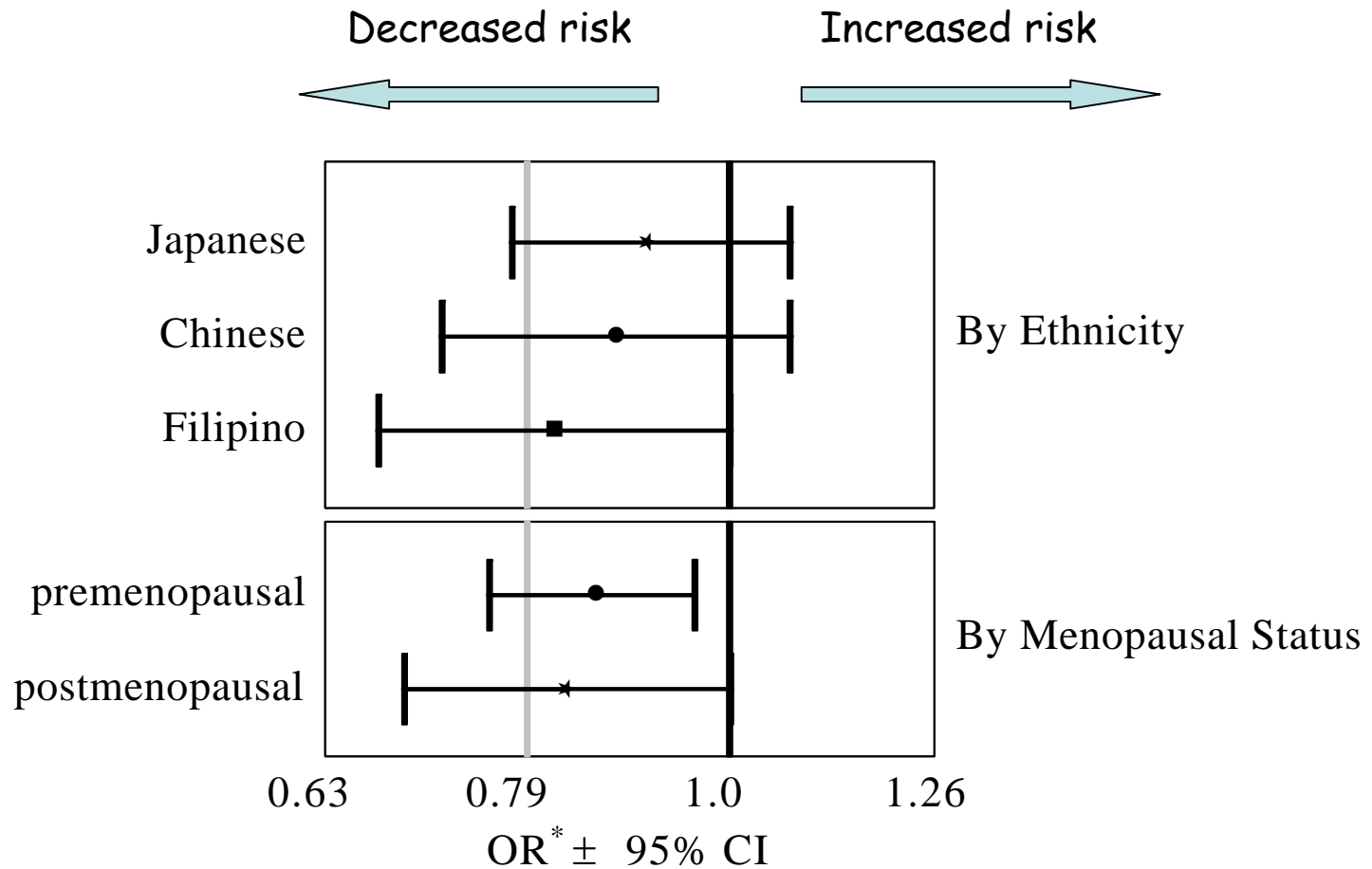
# *Soy and Breast Cancer in Asian Americans*

- Population-based case-control study (n=597 cases, 966 controls)
- Chinese-, Japanese-, Filipino-American women in Los Angeles, San Francisco, Oahu
- Age 20-55 years at diagnosis, 1983-1987
- First primary breast cancer
- FFQ: usual frequency of intake during adult life, 50 items common, 10 items specific to ethnic group
- Exposure: tofu (for Jap-Am tofu/miso/natto)



Wu et al, *Cancer Epidemiol, Biomarkers, Prev*, 1996

# Soy and Breast Cancer in Asian Americans



\* multi-adj OR per 1 category difference in tofu intake

Wu et al, Cancer Epidemiol, Biomarkers, Prev, 1996

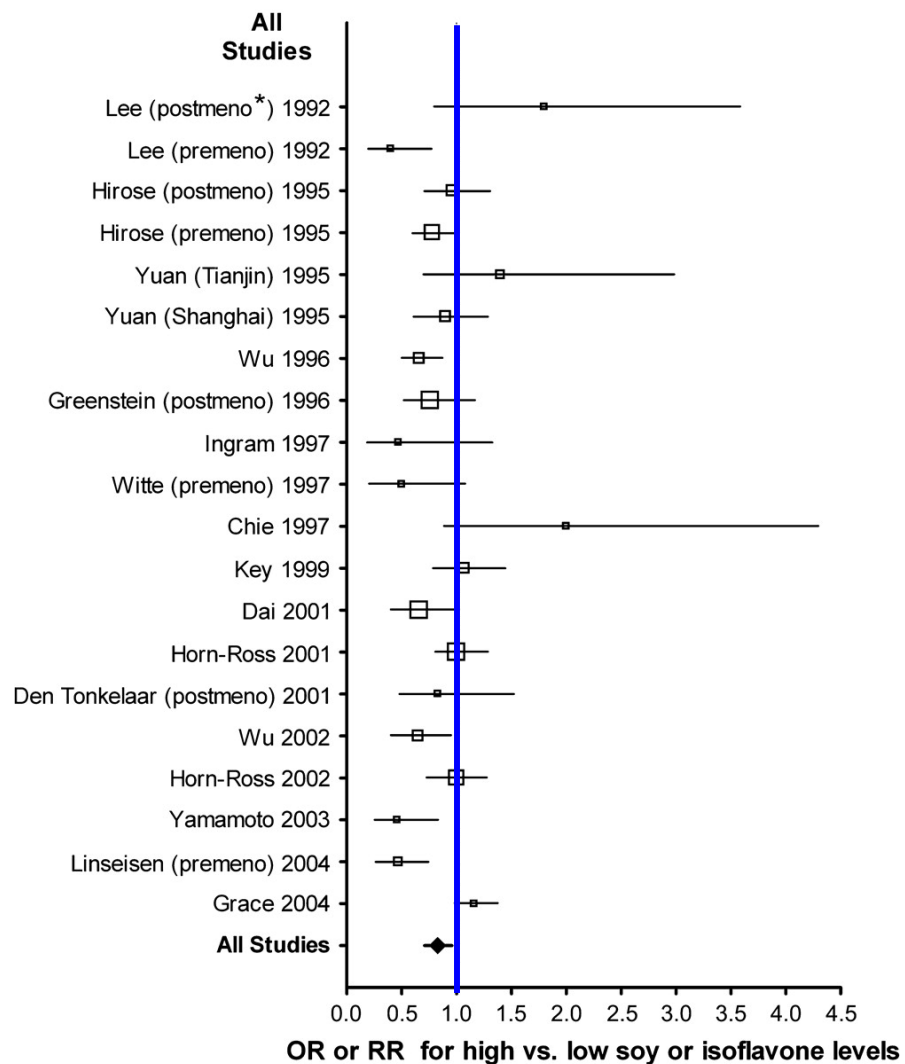


# Epidemiologic studies: meta-analysis

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Association Between Soy and Breast Cancer Risk



\* Premeno = premenopausal women, postmeno = postmenopausal women

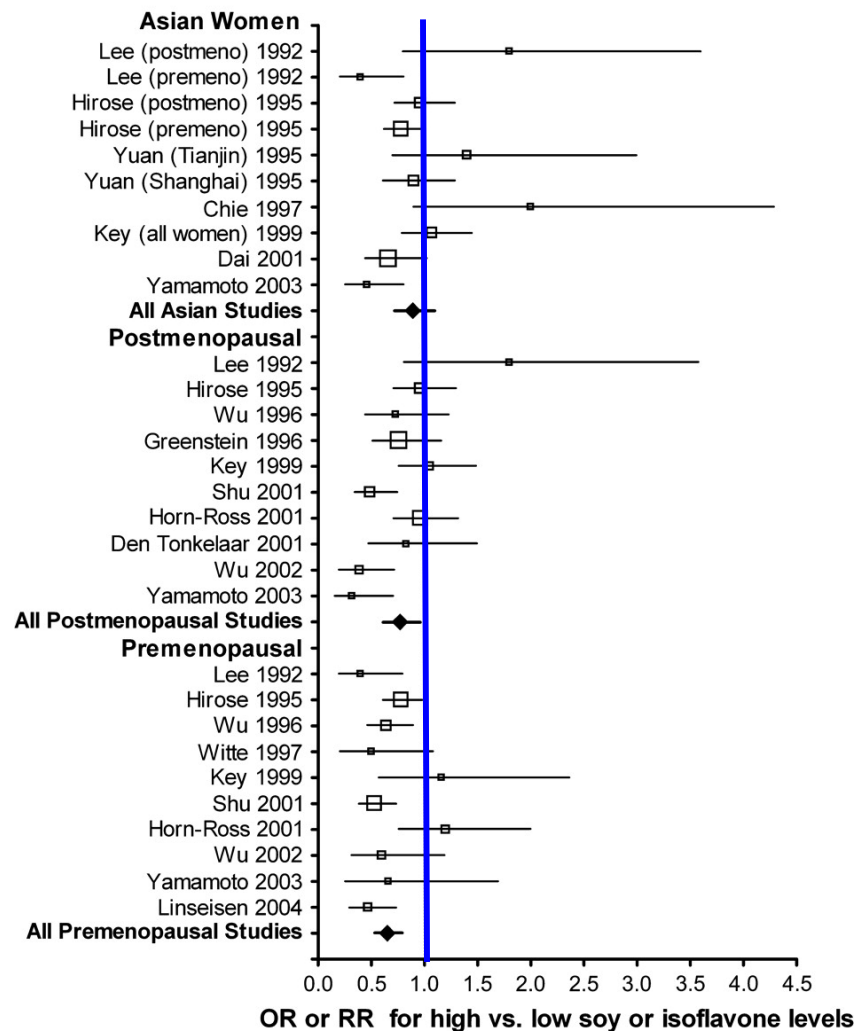
Trock, et al. J. Natl. Cancer Inst. 2006 98: 459

# Epidemiologic studies: meta-analysis

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**Association Between Soy and Breast Cancer Risk, by Population Subgroups**



\* Premeno = premenopausal women, postmeno = postmenopausal women

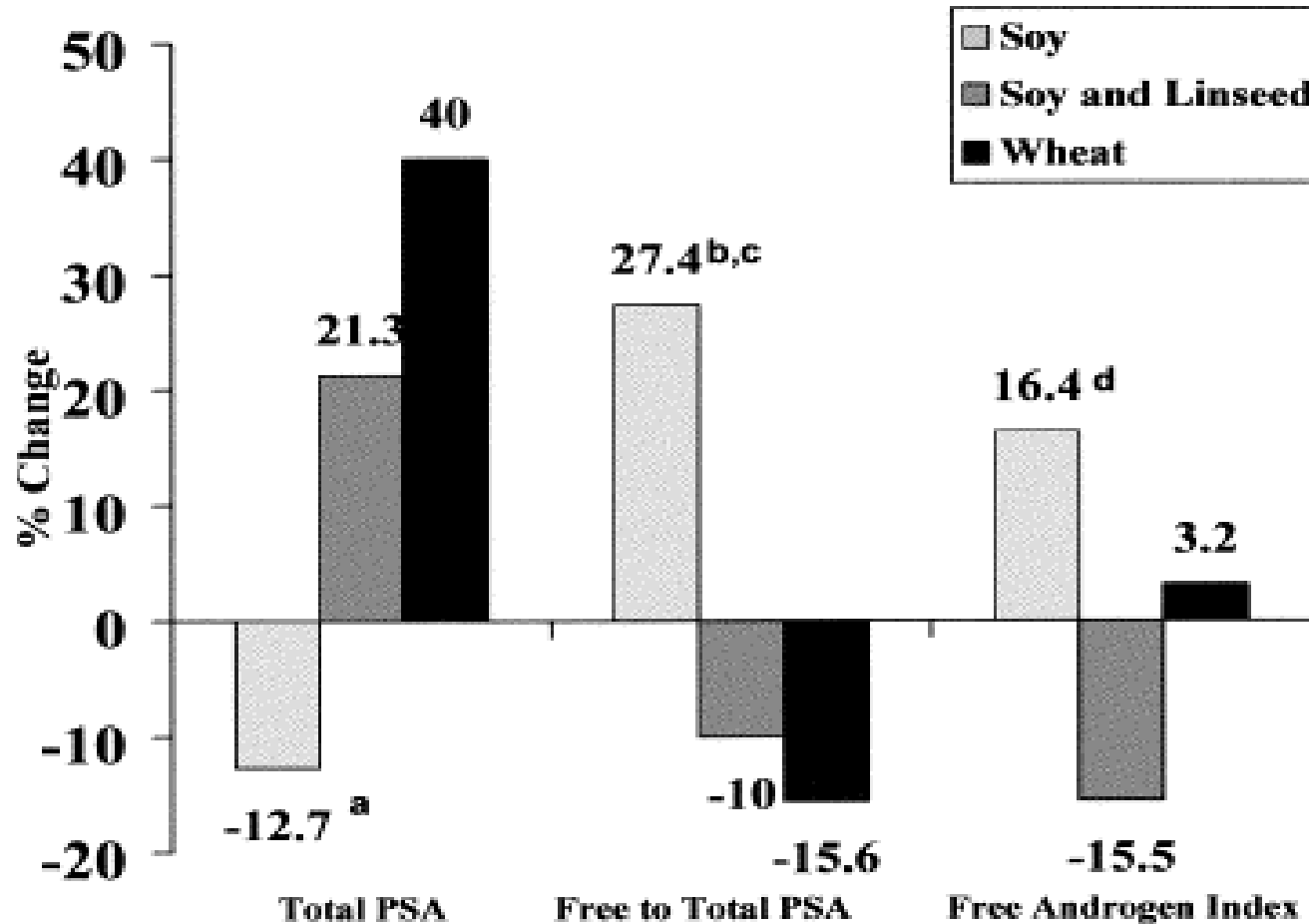
Trock, et al. J. Natl. Cancer Inst. 2006 98: 459

# Case-control studies

| Study    | Country   | Phytoestrogen                          | Cancer   | Odds Ratio<br>(95% CI)              |
|----------|-----------|--|----------|-------------------------------------|
| Pietinen | Finland   | Lignans<br>enterolactone               | Breast   | 0.38 (0.18-0.77)                    |
| Ingram   | Australia | Urinary equol<br>Urinary enterolactone | Breast   | 0.27 (0.10-0.69)<br>1.1 (0.15-0.86) |
| Zheng    | China     | Total isoflavanoids                    | Breast   | 0.14 (0.02-0.88)                    |
| Sonoda   | Japan     | Total dietary soy                      | Prostate | 0.53 (0.24-1.24)                    |



# Clinical studies – prostate cancer



"This work provides some evidence..that male populations who consume high phytoestrogen diets have a reduced risk of prostate cancer development and progression"

Dalais et al. (2004) Urology 64: 510

# *Epidemiologic studies & clinical trials*

## *– Take home message*

Soy foods are not harmful...

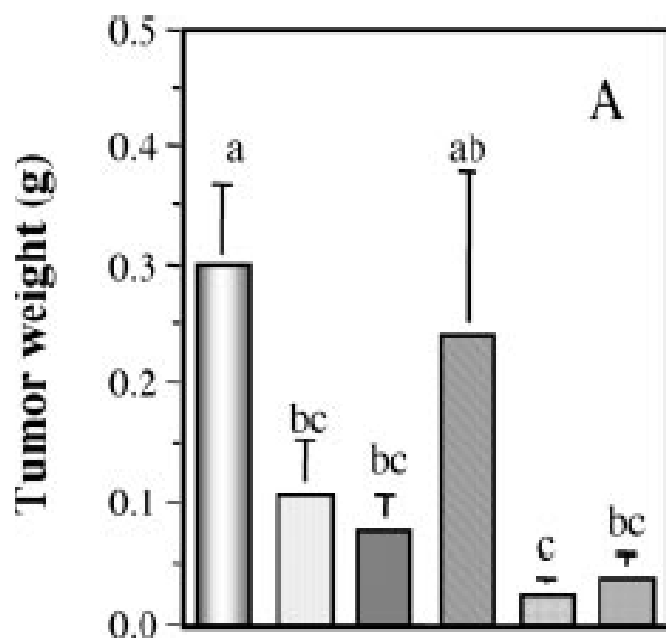
... and in fact maybe protective against cancer

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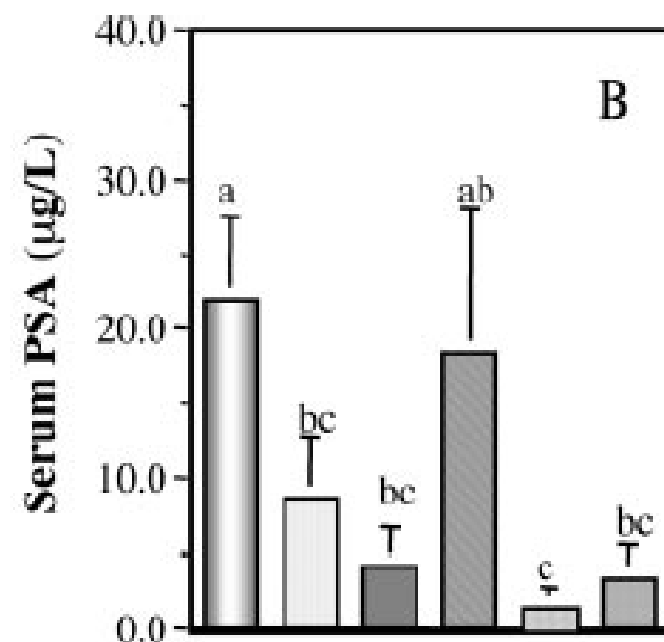


# Animal studies

Soy phytochemicals and tea bioactive components synergistically inhibit human prostate tumors in mice



|                  |   |   |   |   |   |   |
|------------------|---|---|---|---|---|---|
| <b>SPC</b>       | - | + | - | - | + | + |
| <b>Black tea</b> | - | - | + | - | + | - |
| <b>Green tea</b> | - | - | - | + | - | + |

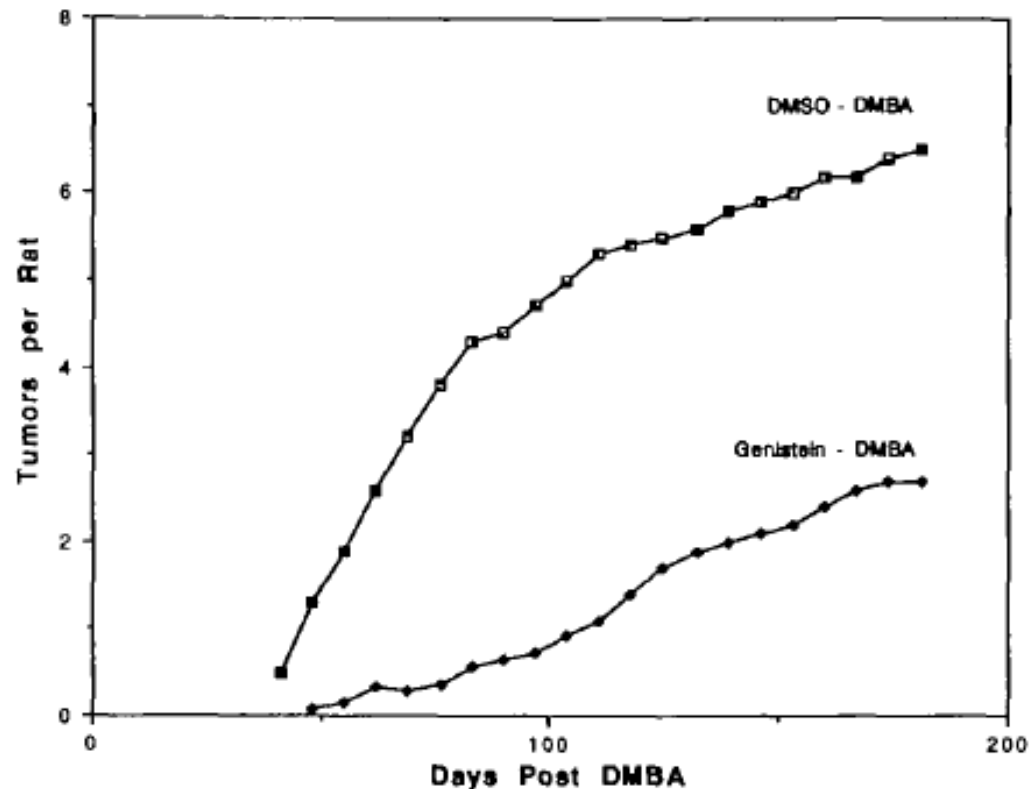


|                  |   |   |   |   |   |   |
|------------------|---|---|---|---|---|---|
| <b>SPC</b>       | - | + | - | - | + | + |
| <b>Black tea</b> | - | - | + | - | + | - |
| <b>Green tea</b> | - | - | - | + | - | + |

Zhou et al., J. Nutr. 133: 516-521, 2003

## Animal studies

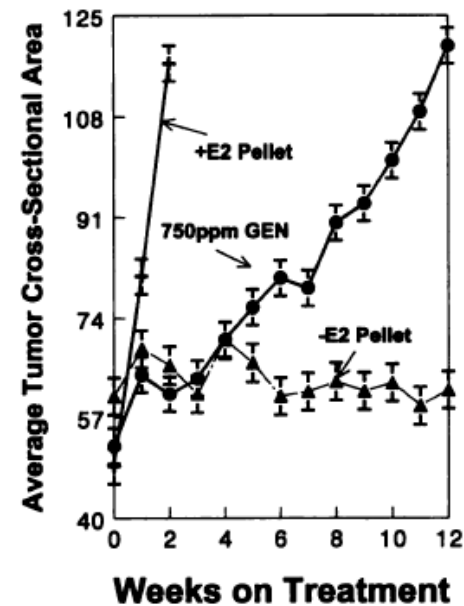
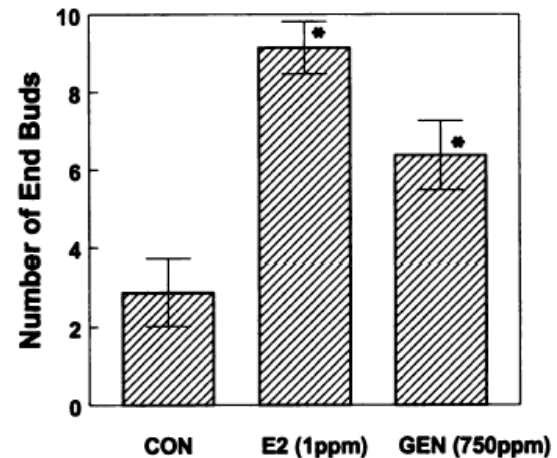
- Genistein inhibits growth of a chemically induced mammary tumour in young rats



Lamartiniere et al. (1995) Carcinogenesis 16: 2833

# Animal studies

- Genistein *promotes* mammary gland growth and mammary tumour growth in mice
- Oh dear! But..
- Mice are nude, ovariectomised and athymic – humans are not!

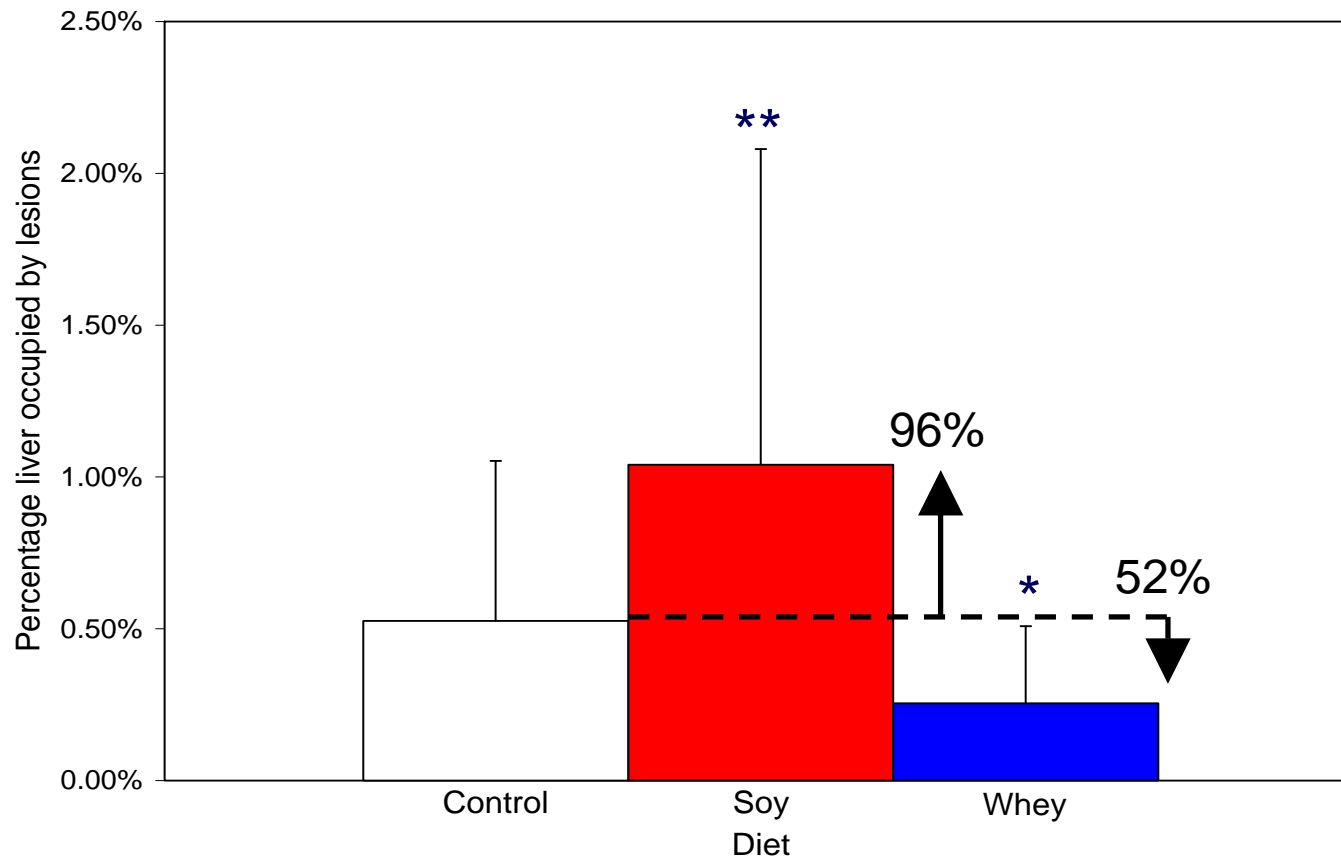


Hsieh, et al. (1998) *Cancer Res.* 58: 3833



# Animal studies

*Rats fed soy-based diets have increased preneoplastic lesions in liver*



Battersby et al. (2006) APJCN 15: S106

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# *Animal evidence*

## *– Take home message*

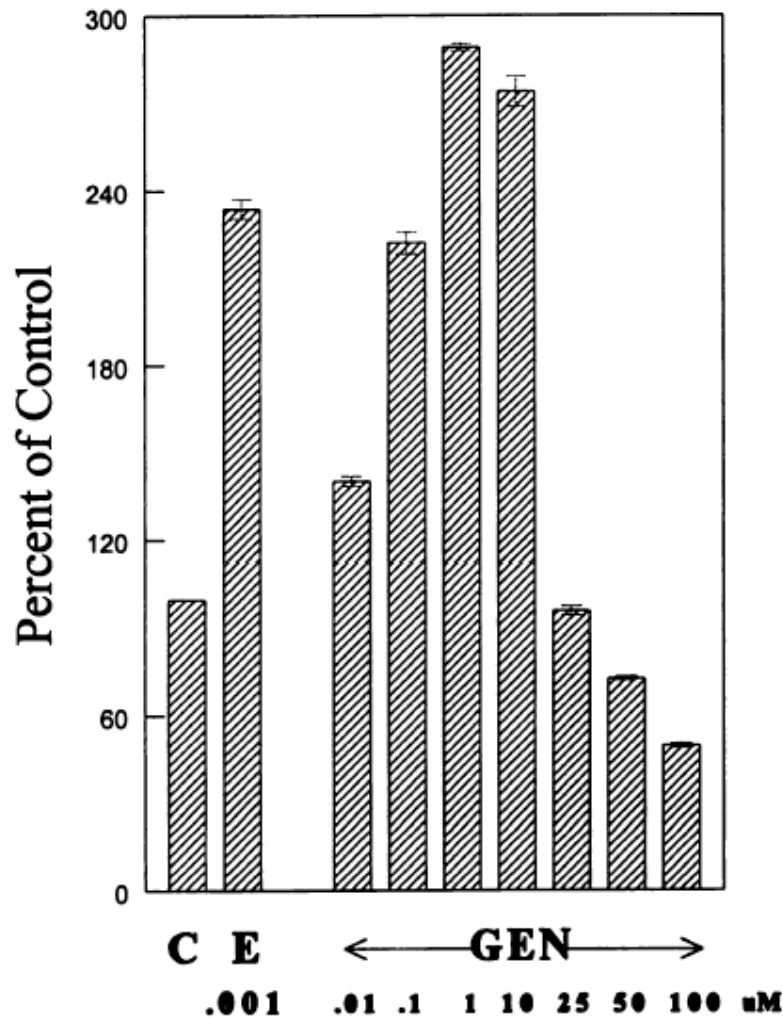
Soy phytoestrogens have been shown to reduce tumor growth but...

... under some experimental (not real life?) circumstances the opposite is observed.

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# Cell studies

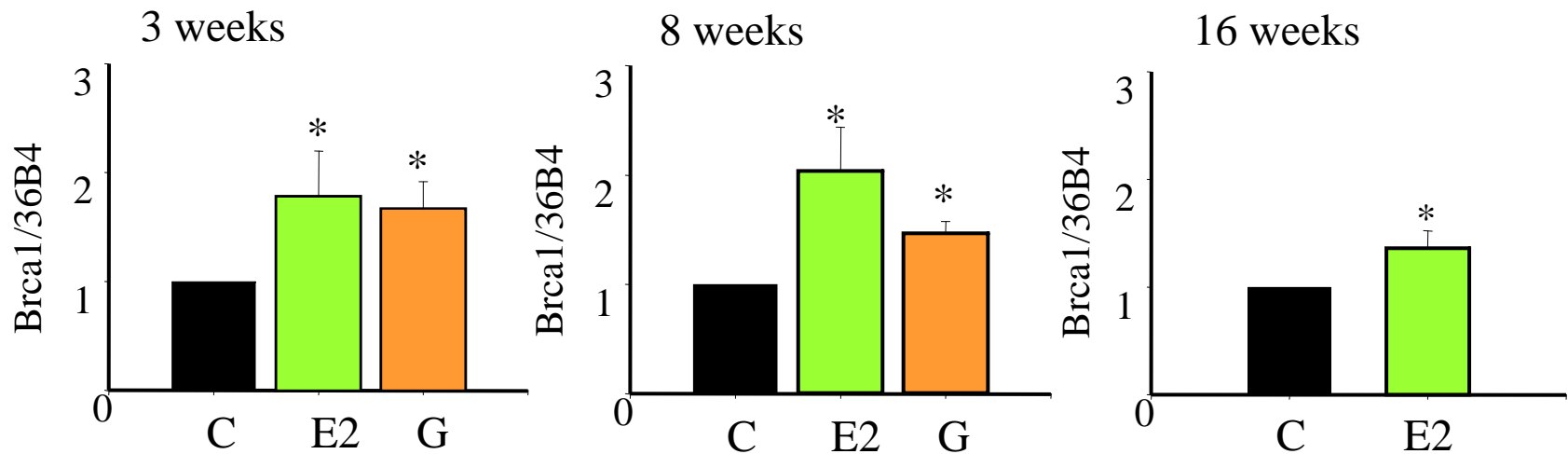
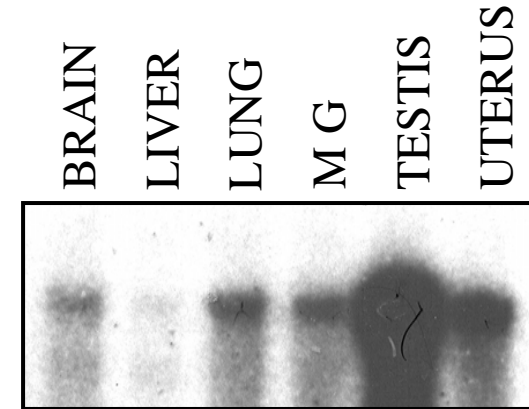


- Genistein (and oestrogen) promotes growth of mammary tumour cells in vitro.
- Soy metabolites acting as phytoestrogens

Hsieh, et al. (1998) *Cancer Res.* 58: 3833

# Cell studies

Prepubertal exposure to E2 or genistein Up-regulates Mammary BRCA1 mRNA Expression.



Cabanes et al. (2004) Carcinogenesis. 25: 741

# Cell studies

## – *Take home message*

Soy phytoestrogen genistein, like oestrogen, can promote tumor growth in the test tube but...

... it is very difficult to extrapolate results in a test tube to the whole human being. For example, we have an antioxidant system that may be promoted by soy as its metabolites are known antioxidants.

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# Conclusions

## Soy and breast cancer:

- Cannot draw definitive conclusions on
  - Soy & breast cancer risk and
  - Soy & survival of breast cancer patients
- To establish that soy foods do not adversely affect the survival of breast cancer patients may not be possible
  - Long-term clinical trials with tumor recurrence or survival as endpoints – expensive & possibly unethical



*Messina et al. (2006) J Natl Can Inst 98: 1275*

## Conclusions contd.

- Need further research to assess the potential of soy foods on breast cancer risk in high risk women
  - examine cancer risk markers (eg. cell proliferation, apoptosis)
  - assess safety and efficacy
  - use soy foods with a broad application

### Soy and prostate cancer:

- Same conclusion in recent review:
- *“After reading this review ..... what will be evident at the conclusion of this manuscript is the need for future studies of the effects of soy in prostate cancer patients.”*

*(Holzbeierlein et al. (2006) Curr opin Urol 15: 17*



# Take home message

- The jury is still out
- We know that an Asian diet containing soy foods is not detrimental to health
- Increasing consumption of soy foods in Western diets?
  - We need to do more research
  - Must not consider cancer in isolation, other well recognised and established benefits of soy (Coronary Heart Disease) may well outweigh the *possible* adverse risk consequences for cancer development.

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# The future - nutrigenomics



Molecular Nutrition  
& Genomics



Nutritional  
Systems Biology

- Identification of dietary signals
- Identification of dietary sensors
- Identification of target genes
- Reconstruction of signaling pathways



- Measurement of stress signatures
- Identification of early biomarkers

Small research groups  
Small budgets

Large research consortia  
Big money



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# The NSW Cancer Council Statement

## POSITION STATEMENT

### Soy, Phyto-oestrogens and Cancer Prevention



#### Key Messages

Phyto-oestrogens are bioactive substances found in plant foods, with naturally occurring oestrogenic activity. Soy beans and other foods containing soy, such as tofu, tempeh and soy milk, are rich sources of phyto-oestrogens.

A high consumption of soy foods may lower the risk of breast and prostate cancers, but only a little.

There is no association between soy foods and the risk of other cancers, including bowel cancer.

While they may have a protective effect, there is also some evidence that phyto-oestrogens might stimulate the growth of existing hormone dependent cancers.

The Cancer Council supports the consumption of soy foods in the diet. This is consistent with Cancer Council recommendations and national dietary guidelines to eat a diet high in plant based foods.

The Cancer Council does **not** recommend or support the use of supplements such as soy protein isolates or isoflavone capsules for healthy men and women to prevent cancer.

The Cancer Council does **not** recommend or support the use of supplements for breast cancer survivors. There is evidence to suggest that women with existing breast cancer or past breast cancer should be cautious in consuming large quantities of soy foods or phyto-oestrogen supplements.

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# Jan 28 Melbourne – Sense prevails

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## Oh, soy! Don't take scary headlines at face value

It was enough to make Sydneysiders spill their soy lattes as they read the Sunday papers - the recent tabloid headline that shrieked 'Soy cancer warning. High soy diets no good for cancer'. It was a shining example of the kind of journalism that distorts nutrition information and gets us all confused.



A A



The real story that had originated from the Cancer Council NSW, was much tamer. Soy, it turned out, didn't cause cancer. The Cancer Council NSW had never suggested we should all avoid soy foods. Instead they say they don't support the use of soy supplements for cancer survivors because there's a lack of evidence that they help. The advice for women having treatment for breast cancer with tamoxifen was that it was unclear if a diet high in the plant hormones which soyfoods contain could interfere with the treatment.