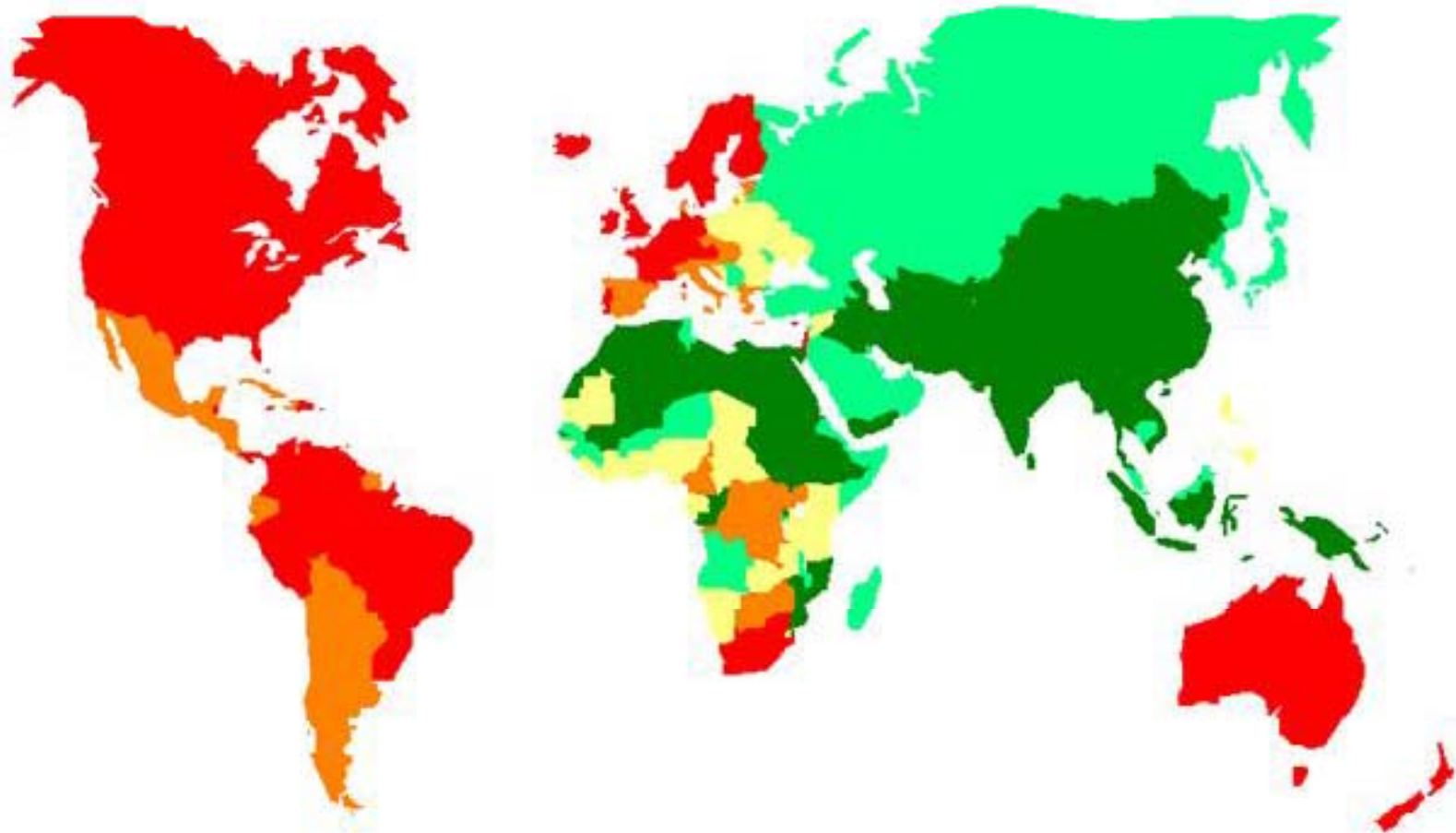


Prostate Cancer – Is the Asian diet protective?

Woon-Puay KOH
Associate Professor
Department of Epidemiology and Public Health
National University of Singapore

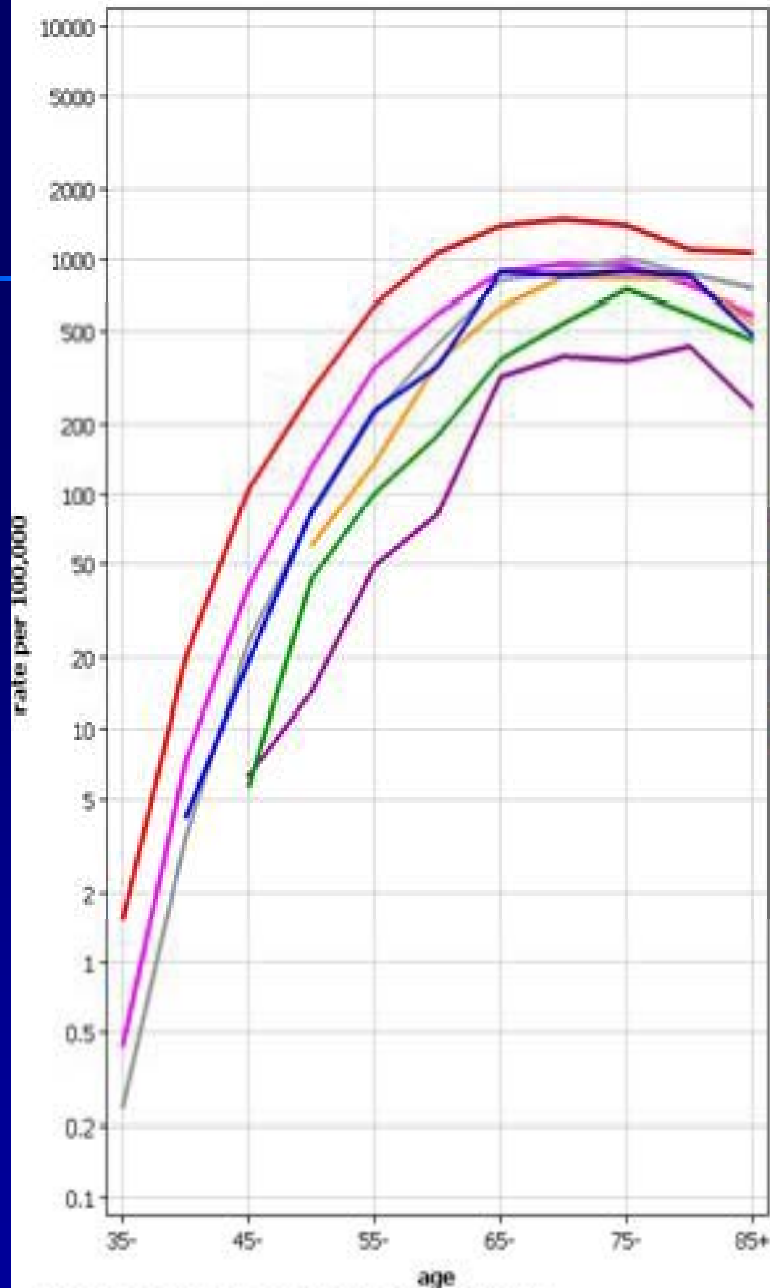
PROSTATE CANCER MAP: AGE-STANDARDIZED INCIDENCE RATE



■ < 7.4 ■ < 13.8 ■ < 24.5 ■ < 40.7 ■ < 124.8

GLOBOCAN 2002, IARC

Prostate



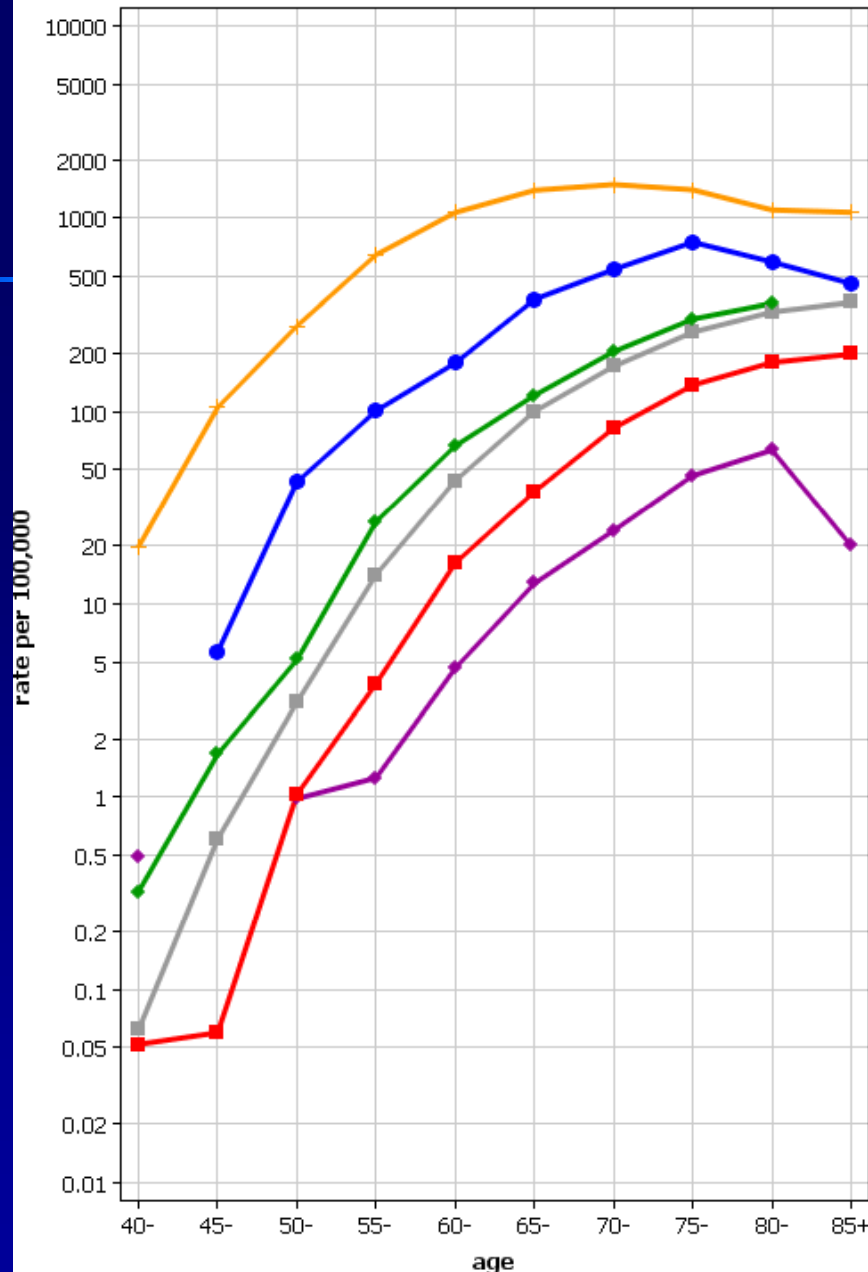
International Agency for Research on Cancer (IARC) - 19.1.2010

COMPARISON OF PROSTATE CANCER INCIDENCE IN DIFFERENT ETHNICITIES IN ONE REGION

- USA, Los Angeles: Black
- USA, Los Angeles: Chinese
- USA, Los Angeles: Filipino
- USA, Los Angeles: Japanese
- USA, Los Angeles: Hispanic White
- USA, Los Angeles: Korean
- USA, Los Angeles: Non-Hispanic White

Genes play a role

Prostate



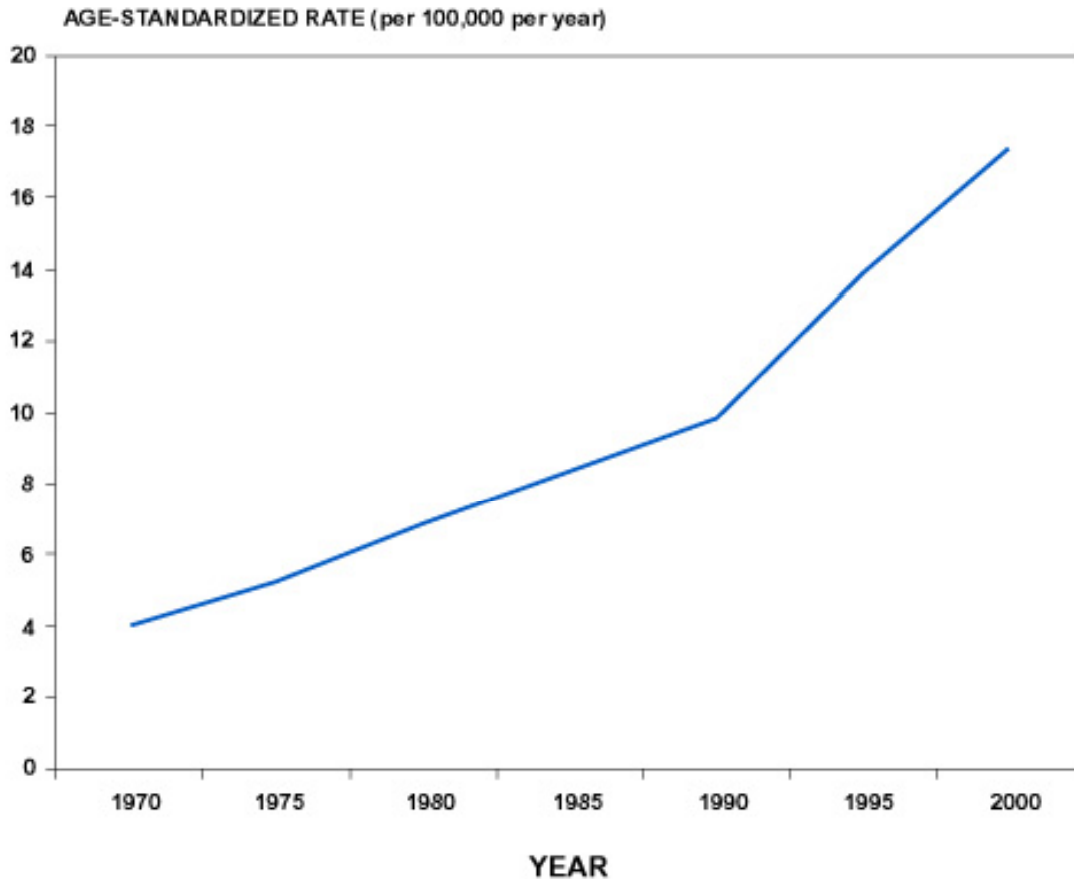
International Agency for Research on Cancer (IARC) - 26.3.2010

COMPARISON OF PROSTATE CANCER INCIDENCE IN ONE ETHNICITY IN DIFFERENT REGIONS

- China, Shanghai
- Singapore: Chinese
- USA, Los Angeles: Chinese
- USA, Los Angeles: Black
- China, Hong Kong
- China, Harbin

Environmental (lifestyle & diet) factors are important

Prostate cancer incidence in Singapore



**PROSTATE: AGE-STANDARDIZED INCIDENCE,
1968-2002**

Large increases seen between 1985-2000 among low-risk countries:

Singapore (104%)
China (84%)
Japan (55%)

Can screening explain the rapid increase in incidence?

- Increased availability of PSA screening has led to detection of many prostate cancers that are small and may or may not have developed further into high stage
- Up to 30% incidence of cancers in autopsies of men aged 50 years or older, most of these tumors being defined as latent.
- Rates were already increasing before the availability of PSA testing, and have continued to rise in Asian countries, such as Singapore, where screening is still not widely available.

Why are prostate cancer rates less common in Asia?

“A diet characteristic of Asian countries such as Japan and China, essentially a low fat intake with consequent low body weight, with an intake of relatively high phytoestrogens in isoflavonoids, lignans and possibly certain flavonoids, may provide the means of restraining the growth and progression of prostate cancer.”

WHO, IARC, World Cancer Report 2003

Body size and composition and prostate cancer risk

- Meta-analysis of 31 cohort and 25 case-control studies
- The overall RR for BMI was 1.05 per 5 kg/m² increment, 95% CI 1.01–1.08; stronger for advanced stage
- Height was also positively associated with risk (RR 1.05 per 10 cm increment, 95% CI 1.02–1.09)

MacInnis RJ et al, Cancer Causes Control. 2006 (8):989-1003.

- Rapid increase of BMI across Asian countries

Dietary factors and prostate cancer

Convincing Evidence

World Cancer Research Fund/AICR, 2007

(↑) (none)

(↓) (none)

Probable Evidence

(↑) diets high in calcium

(↓) foods containing lycopene (foods), selenium (supplements)

Limited Evidence, suggestive

(↑) preserved meat, milk/dairy products

(↓) legumes (including soy foods), vitamin E (foods), alpha-tocopherol (supplements)

Lycopene-rich foods

- Tomato and tomato products
- Grapefruit, watermelon, guava and apricot
- Potent carotenoid antioxidant
- Antiproliferative
- Anti-inflammatory



Tomatoes, lycopene and prostate cancer

Tomatoes and prostate cancer

Lycopene and prostate cancer

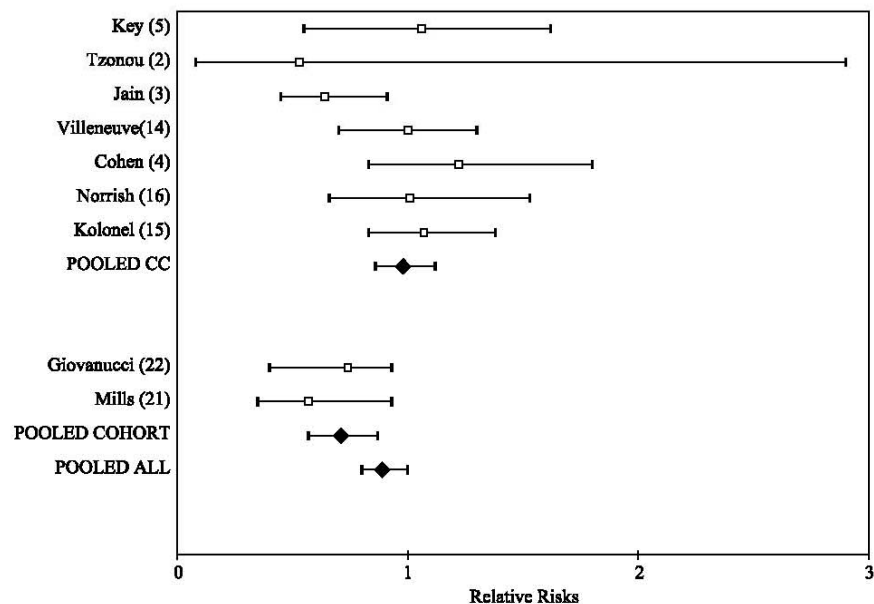


Fig. 1. RRs and 95% CIs for studies of high intake of raw tomatoes and prostate cancer.

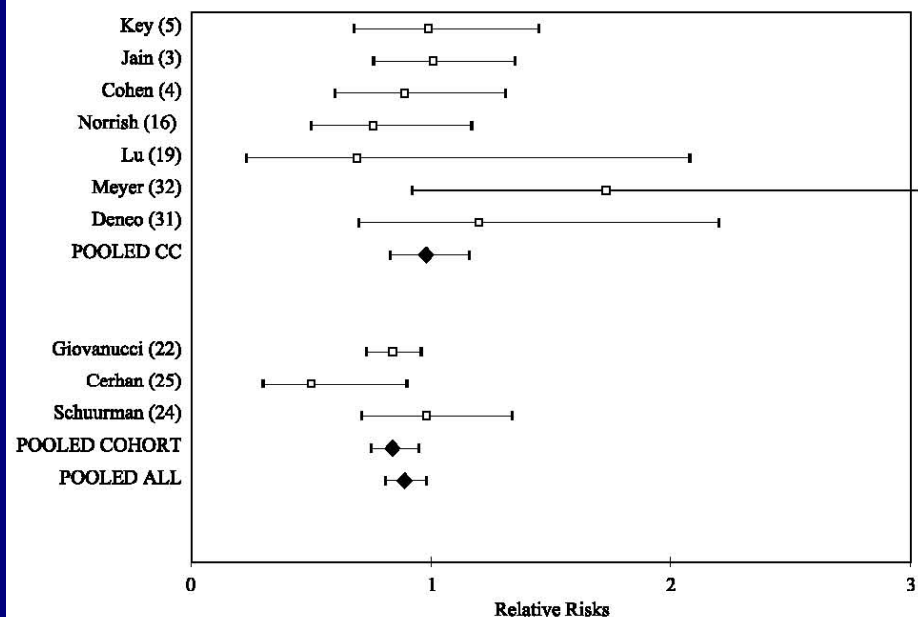


Fig. 2. RRs and 95% CIs for studies of high intake of lycopene and prostate cancer.

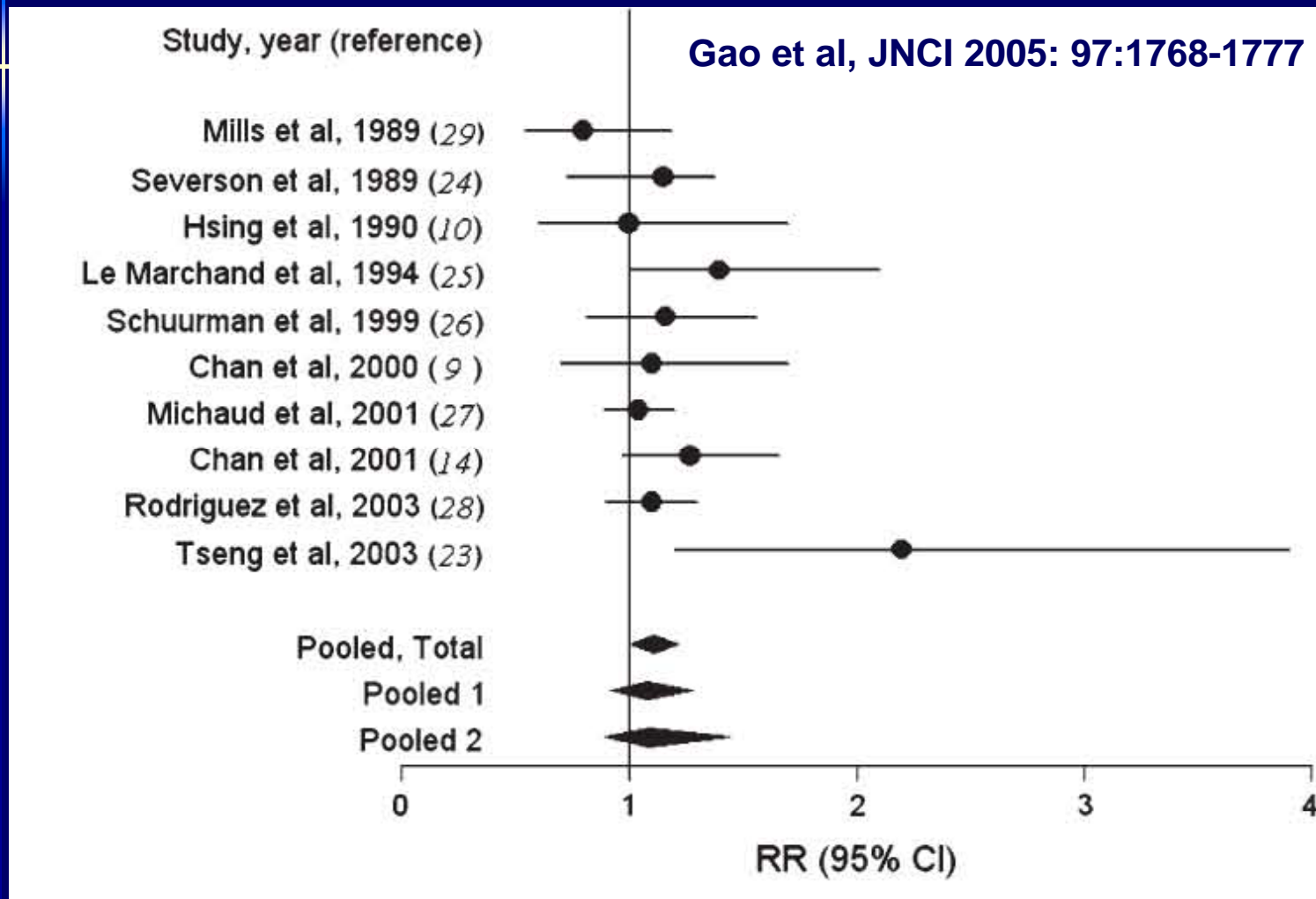
Summary RR: 0.81 (0.71-0.92)

Summary RR: 0.78 (0.61-1.00)

High intakes of calcium and dairy products may

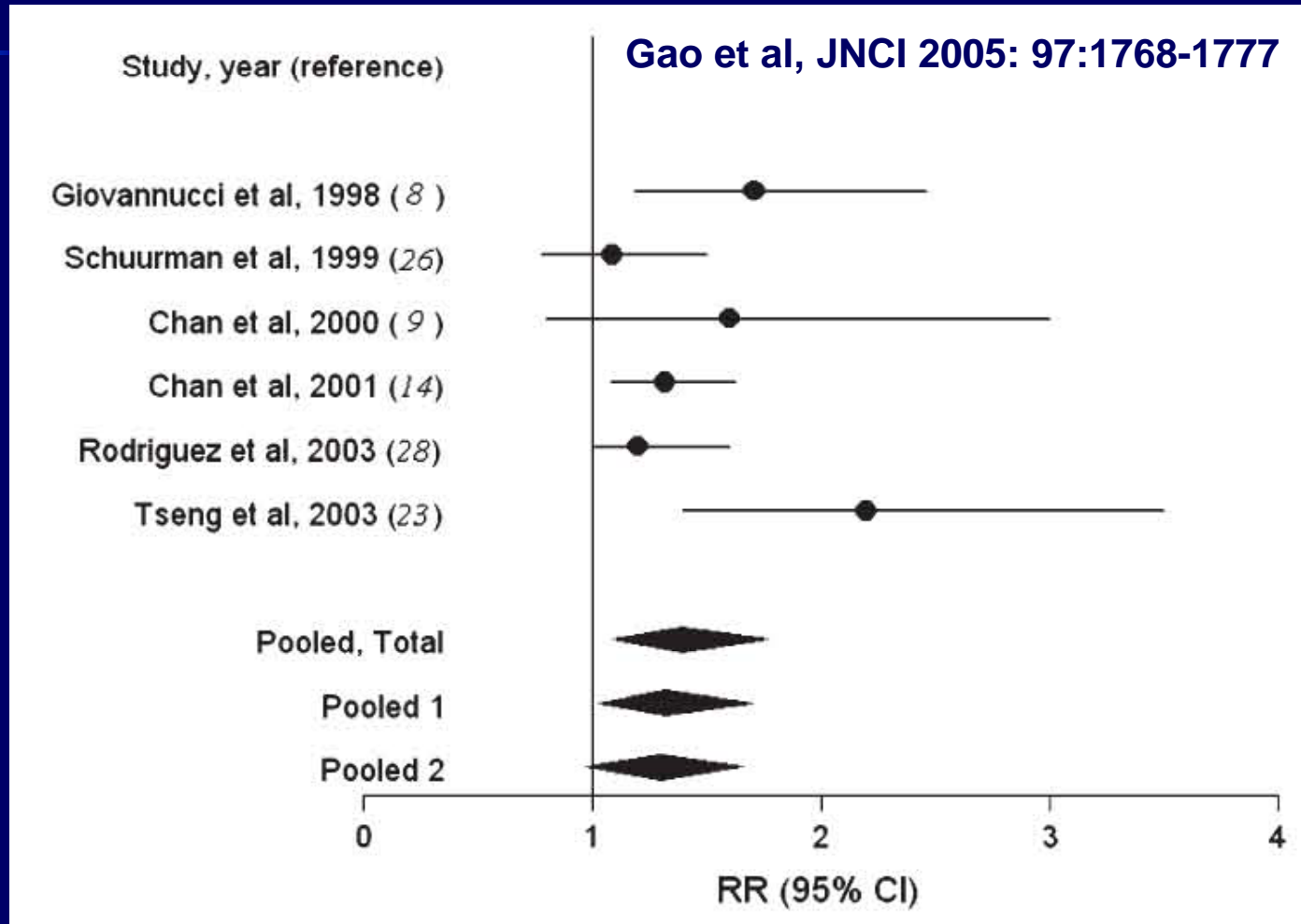
- increase the risk of prostate cancer by suppressing the production of 1,25-dihydroxyvitamin D₃ , the active form of vitamin D₃, which binds to vitamin D receptors and inhibits proliferation of normal and malignant prostate cells
- increase plasma levels of IGF-I. Results of a recent meta-analysis showed that high plasma concentrations of IGF-I were associated with a 49% increased risk of prostate cancer
- be a source of phosphorus and saturated fatty acid, e.g. phytanic acid

Meta-analysis: dairy products & prostate cancer



Pooled RR: 1.11 (95% CI = 1.00 to 1.22, $P = .047$)

Meta-analysis: calcium & prostate cancer



Pooled RR: 1.39 (95% CI = 1.09 to 1.77, $P=.018$).

Epidemiologic Evidence

- Previous studies have been conducted primarily among populations with very high dairy intakes, and with high use of calcium containing supplements.
- Only one prospective study among Japanese, where a positive, statistically significant association was reported.
- Among Singapore Chinese, we would be able to examine the lower end of intake
 - Median daily calcium intake among Asian populations is within the range of 388 mg and 500mg, or about 2-fold lower than among Western populations
- In addition, the food sources of calcium differ among Chinese, compared to Western diets.

What are potential foods protective against prostate cancer in the Asian diet?

Soy and legumes

- A major plant source of dietary protein for Asians for centuries



Tea

- Green tea drunk mainly in China, Southeast Asia and Japan



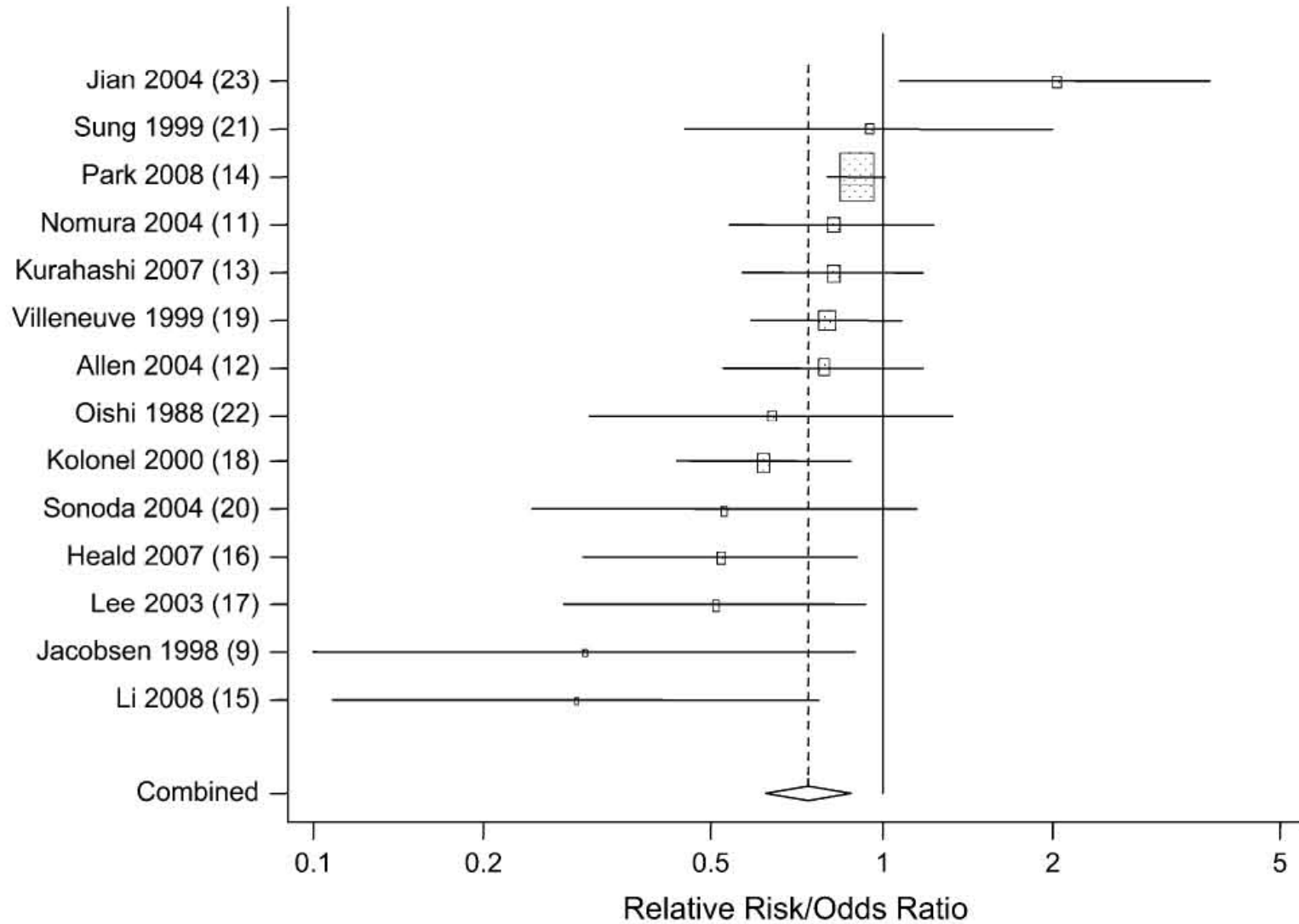
Legumes and Soy

- Phytoestrogens plausibly influence oestrogen metabolism
- Androgenic effects, potentially inhibiting testosterone-induced growth of the prostate
- Dietary soy protein and soy phytochemical extracts inhibit experimentally induced prostate tumorigenesis
- Genistein, a major soy isoflavone, inhibits prostate tumor development in animals and proliferation of prostate cancer cells in culture
- The proposed anticancer mechanisms of isoflavones may be associated with an inhibition in 5- α reductase activity and an increase in vitamin D concentrations in prostate tissue

Soy consumption and prostate cancer risk in men

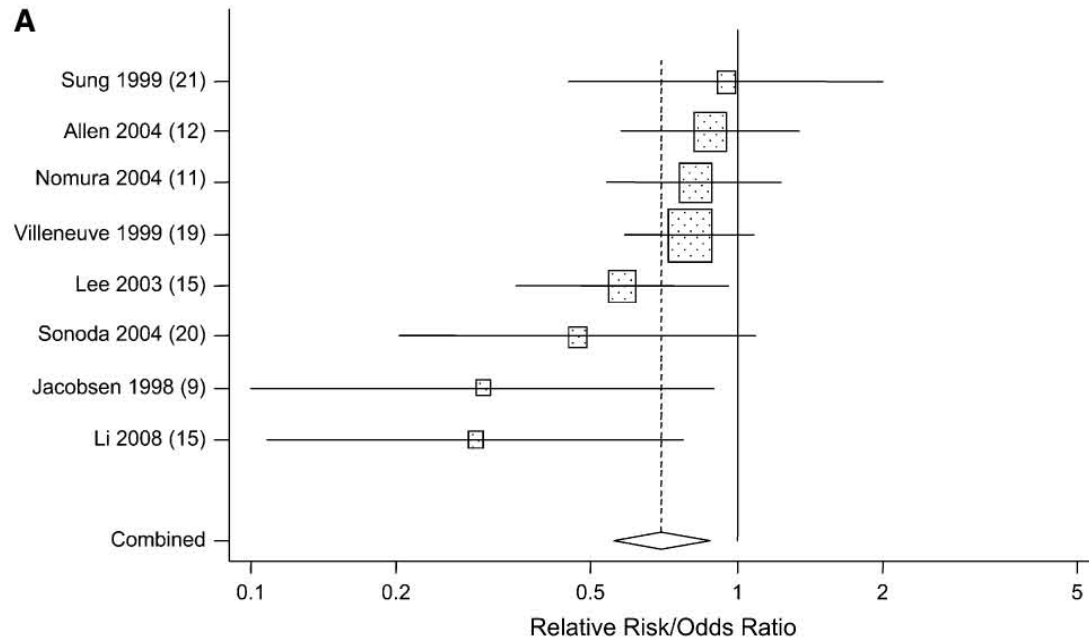
- 15 epidemiologic publications on soy consumption in association with prostate cancer risk.
- Six are cohort studies and 9 are case-control studies
- China and Japan, multiethnic groups in USA, Canada and Scotland

Lin et al Am J Clin Nutr 2009;89:1155–63.



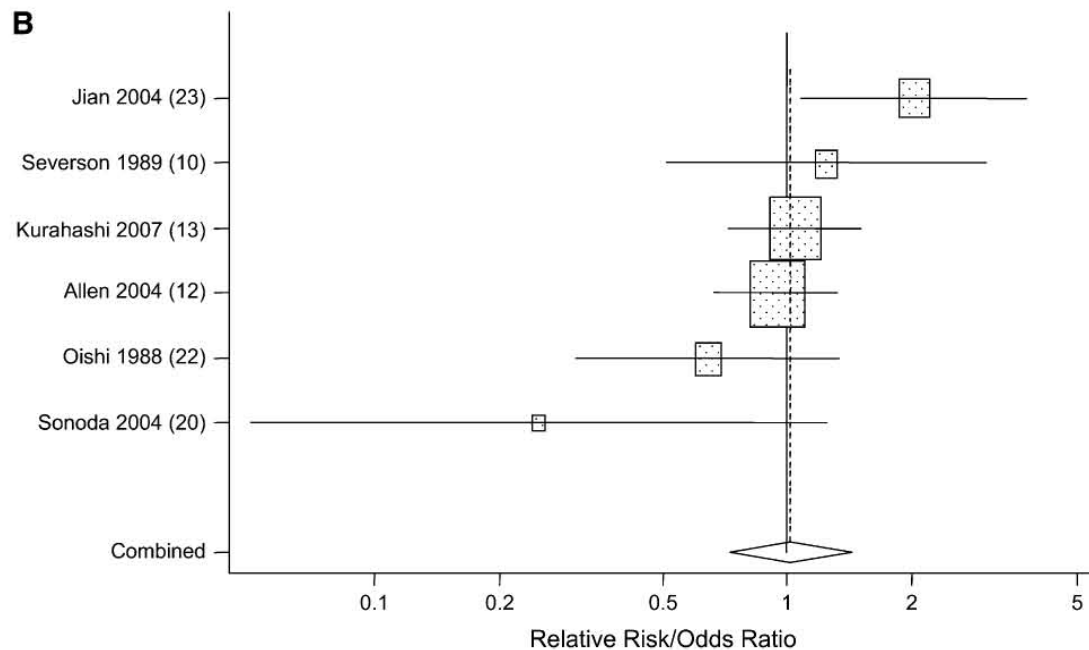
RR of 0.74 (95% CI: 0.63, 0.89; P = 0.01).

YAN AND SPITZNAGEL



Non-fermented soy food
: tofu and soy milk

RR: 0.70 (95% CI: 0.56, 0.88)

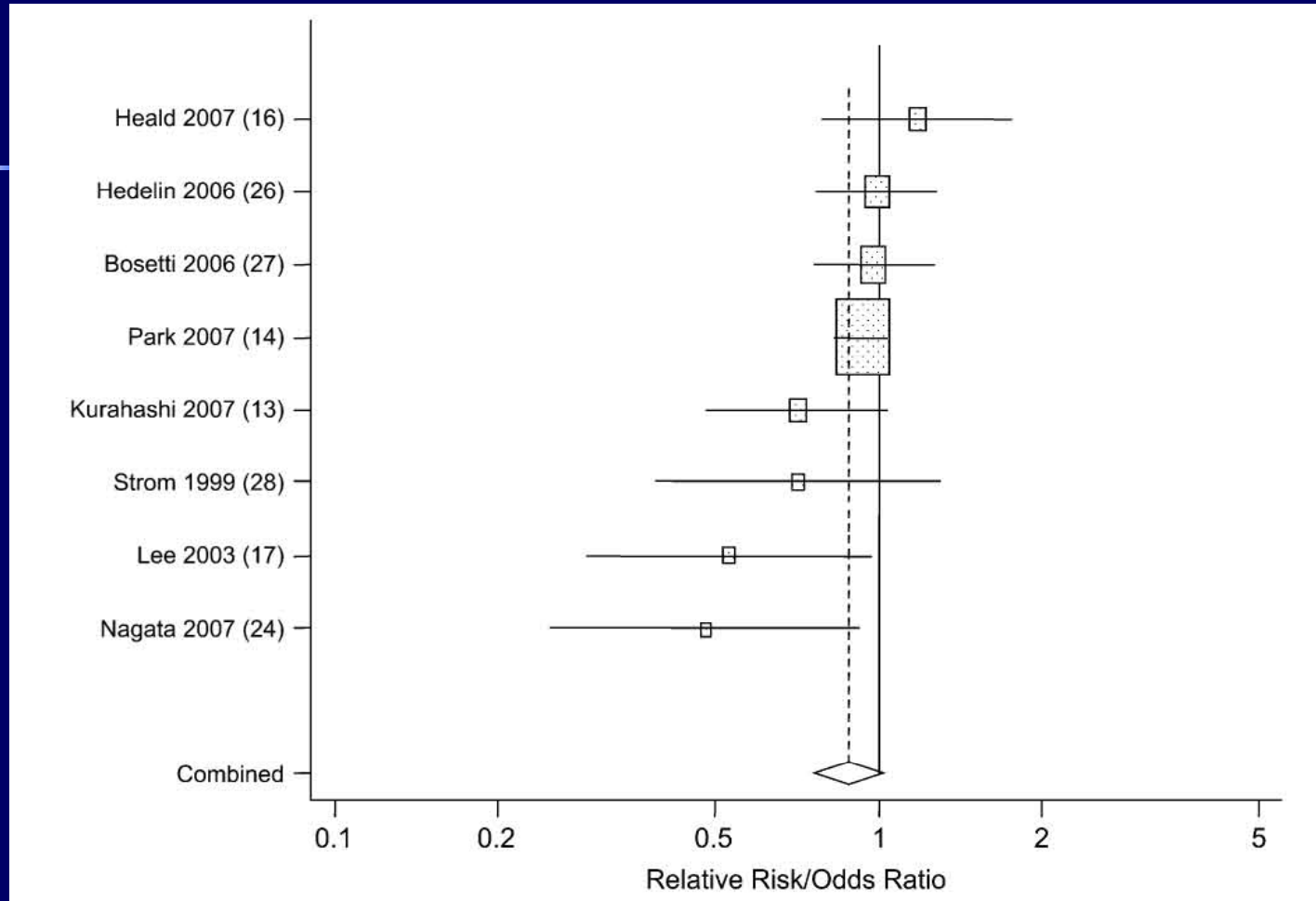


Fermented soy foods,
: including miso and natto.

RR: 1.02 (95% CI: 0.73, 1.42)



Isoflavones and prostate cancer risk



RR: 0.88 (95% CI: 0.76, 1.02; P= 0.09).

Lin et al Am J Clin Nutr 2009;89:1155–63.

Isoflavones and prostate cancer risk

- 8 studies (2 cohort and 6 case-control studies)
- A significant risk reduction from studies in the Asian populations, but not from those in the Western populations.
- Asian populations yielded a combined RR of 0.52 (95% CI: 0.34, 0.81) and that in Western populations yielded a combined RR of 0.99 (95% CI: 0.85, 1.16)
- Interestingly, the estimated isoflavone intakes from the Asian populations are all reported in mg/d, whereas those from Western populations are all reported in ug/d
- Type and quantity of soy foods are important in conferring protection against prostate cancer risk.

Strong experimental evidence for green tea catechins and prostate cancer

- Green tea polyphenols such as EGCG have broad chemopreventive properties
 - from inhibition of carcinogenesis formation to suppression of prostate cancer progression (e.g. inhibition of cellular proliferation and induction of apoptosis), angiogenesis and metastasis
- From the TRAMP mouse model, EGCG
 - inhibits 5-alpha reductase and the androgen receptor
 - down-regulates IGF-1
 - inhibits matrix metalloproteinases (MMP-2) implicated in prostate cancer progression

Prospective Epidemiologic Results *are Mixed*

Inverse association

US Japanese

- RR=0.6, P=0.02 for daily black tea. N=149 cases

Japan

- RR= 0.52 (0.28, 0.96) for 5+ cups/day green tea.
N=404 cases

No association Two studies (England and Japan)

- Limitations of previous studies: Narrow range of intake and not able to evaluate tea types.

Tea Catechins and Genes

- Green tea catechins are rapidly metabolised by human COMT and other enzymes
- Genes of these enzymes are polymorphic and determine interindividual variation in bioavailability of tea catechins
- More studies are needed to see if tea is protective for prostate cancer after taking into account the bioavailability of tea polyphenols

Why examine dietary patterns?

Traditional analyses evaluate individual nutrients or foods in relation to disease are useful to address etiologic hypotheses

However, individual foods/nutrients:

- Do not always reflect actual eating habits or behavior
- Highly correlated with each other and with certain dietary, lifestyle and socio-demographic factors
- Are not always as interpretable as dietary patterns for communicating dietary recommendations

“Western Pattern” is not associated with prostate cancer

Harvard HPFS (Wu, 2006), N=678 cases

Western pattern RR = 1.03 (95% CI: 0.92-1.17)

- For advanced disease RR=1.13; (95% CI: 0.77-1.67)
- Among older men RR= 1.35; (95% CI: 0.97-1.90)

NHANES (Tseng, 2004), N=136 cases

- No association with red meat-starch pattern

Melbourne Collaborative Cohort Study (Muller, 2009), 1,018 cases

- No association with Mediterranean, vegetable, meat & potatoes, and fruit & salad

AICR Cancer Prevention Recommendations (2007)

- *Stop smoking*
- *Eat more vegetables and fruits*
- *Limit energy-dense foods*
- *Limit alcohol*
- *Limit red meat*
- *Limit processed food*
- *Be active*
- *Be as lean as possible within normal body weight*

