

ILSI SEA REGION

Dr Woon-Puay Koh is Associate Professor at the Department of Epidemiology and Public Health in the National University of Singapore. She is also honorary consultant to the Singapore Cancer Registry in the Ministry of Health. For her research, Dr Koh is site principal investigator to the Singapore Chinese Health Study, a 63,000 strong cohort supported by US-NIH in Singapore. Together with her research team in US and Singapore, she has used the cohort to understand etiology of chronic diseases common in Singapore. She has over 80 publications in international, peer-reviewed journals, most of which are in the area of cancer research.



A Microcosm of Industrializing Asia (The Singapore Chinese Health Study)

Dr Woon-Puay Koh
Associate Professor
Department of Epidemiology & Public Health
National University of Singapore
Scientific Advisor, ILSI SEAR

ILSI SEA REGION

“Industrialized Nations”

- Countries with developed economies
- High gross domestic product (GDP) per capita/high income countries
- High human development index (HDI)
 - Life expectancy
 - Literacy/education
 - Standard of living
 - Child welfare
- Change in lifestyle and diet
- Change in disease patterns
- Wave of industrialization sweeping across Asia

ILSI SINGAPORE

Singapore



INDIANS 8.9%



CHINESE 74.7%



MALAYS 13.6%



ILSI SEA REGION

TOP 10 CAUSES OF DEATH IN SINGAPORE 2009

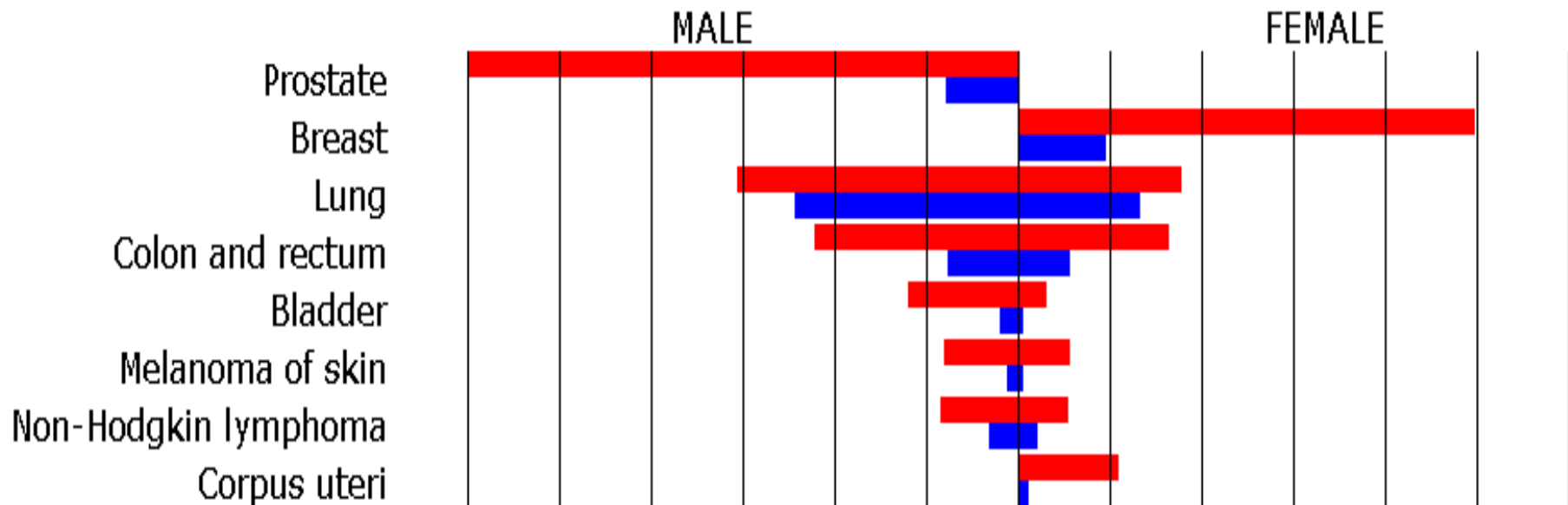
Rank	Cause of death	% of total deaths	% in 2007
1	Cancer	29.3	27.7
2	Ischemic heart disease	19.2	19.8
3	Pneumonia	15.3	13.9
4	Cerebrovascular disease (including stroke)	8.0	8.7

ILSI SEA REGION

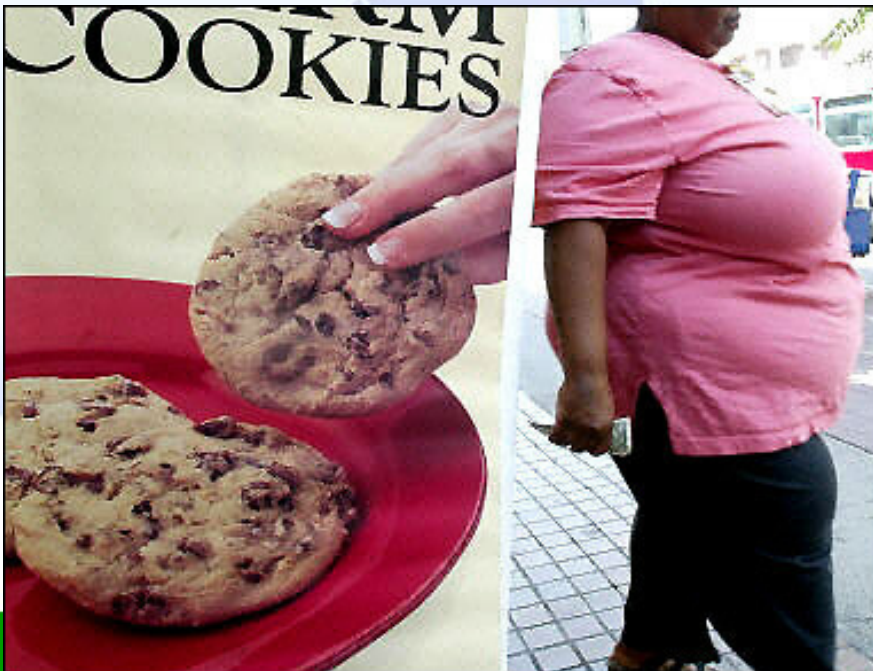
Top cancers in developed regions

■ Incidence
■ Mortality

Northern America
Age-Standardized rate per 100,000 (all ages)



ILSI SEA REGION

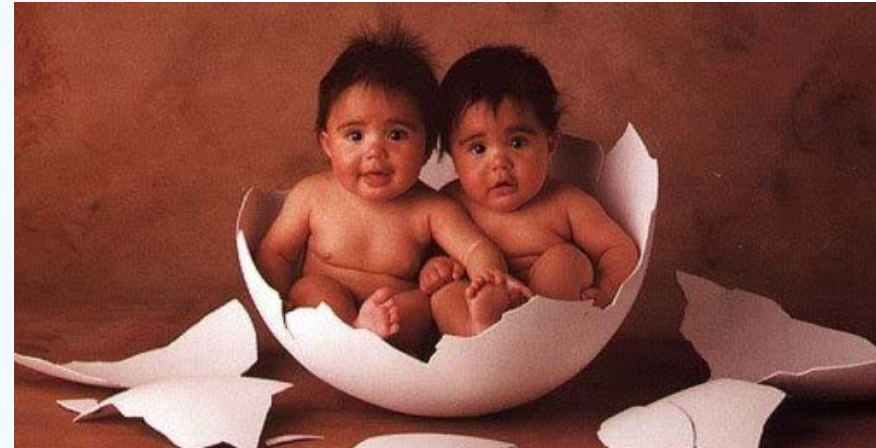


“Lifestyle” cancers

- Cigarette Smoking
- Obesity
- Western diet

ANNUAL MEETING 2011

ILSI SEA REGION



Female cancers

- Delayed first birth
- Nulliparity
- Decline in breastfeeding
- Hormone replacement

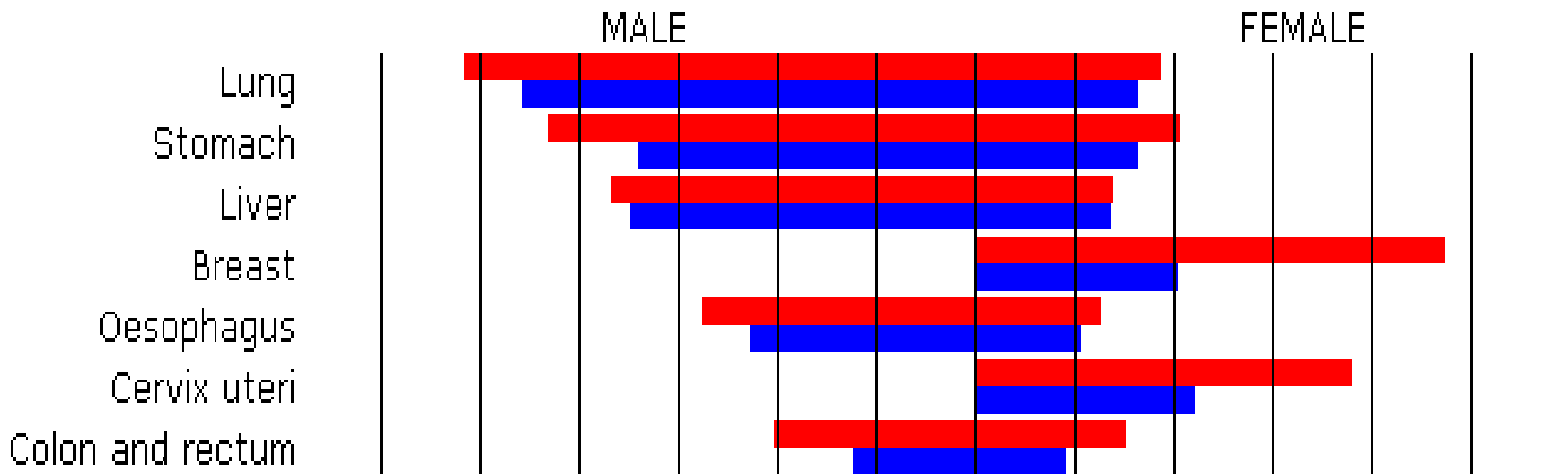


ILSI SEA REGION

Top cancers in less developed regions

■ Incidence
■ Mortality

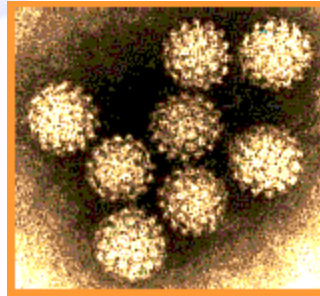
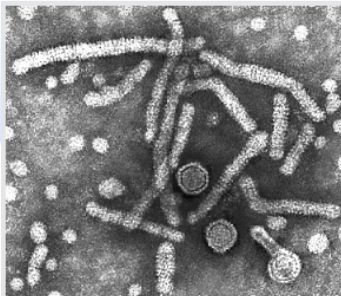
Less developed regions
Age-Standardized rate per 100,000 (all ages)



ILSI SEA REGION

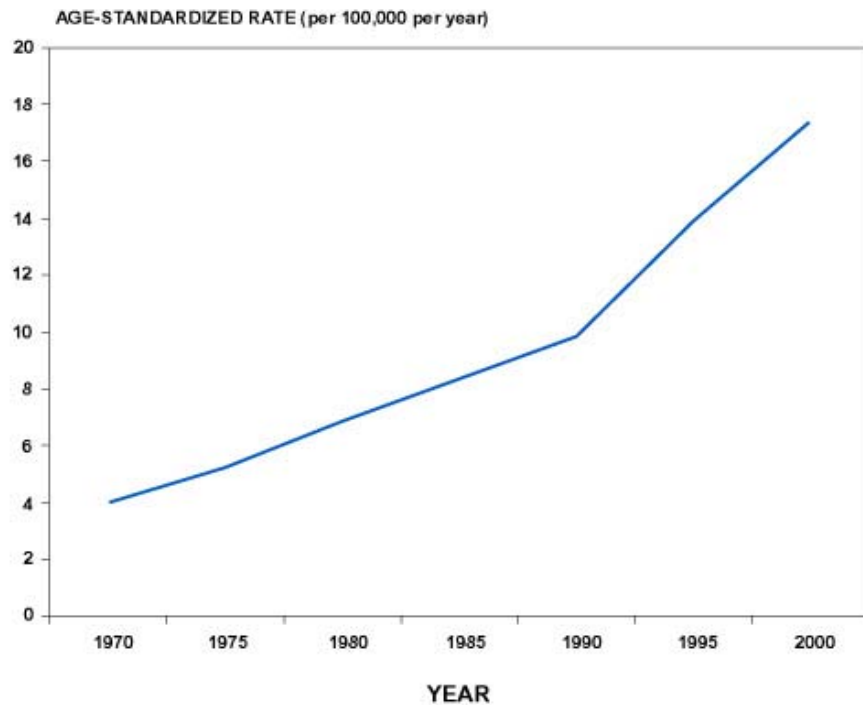
Cancers related to chronic infections and malnutrition

- Liver cancer with Hepatitis B virus
- Cervical cancer with Human papillomaviruses
- Gastric and esophageal cancers with salt-preserved foods, food contaminants or nutritional deficiencies

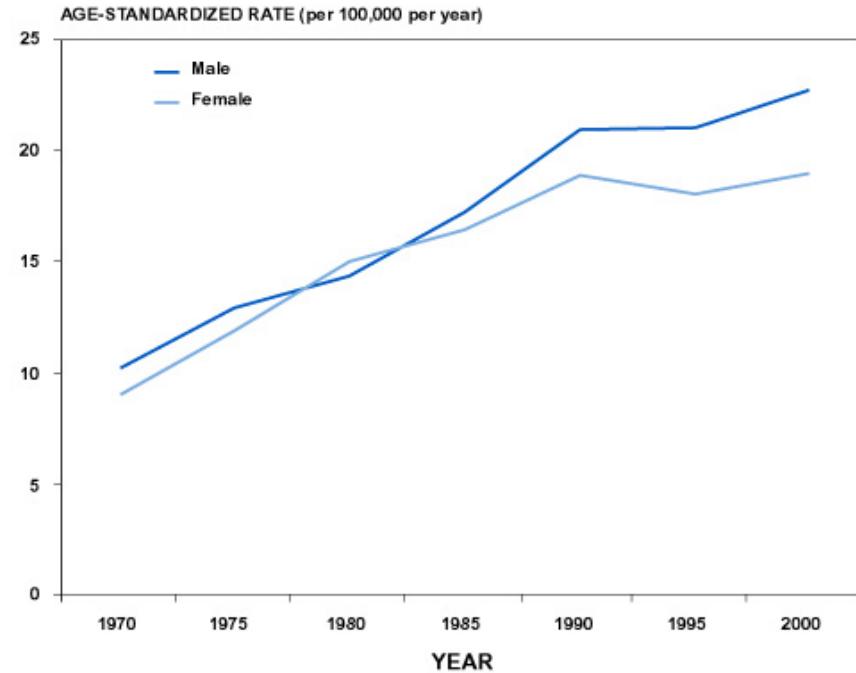


ILSI SEA REGION

Cancers of rising incidence in Singapore



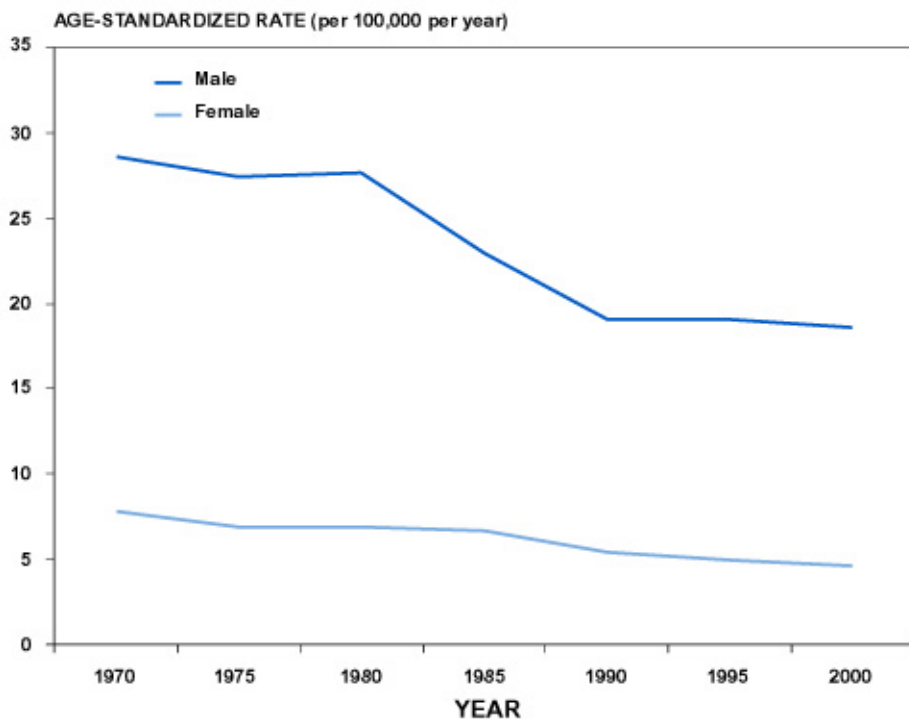
PROSTATE: AGE-STANDARDIZED INCIDENCE, 1968-2002



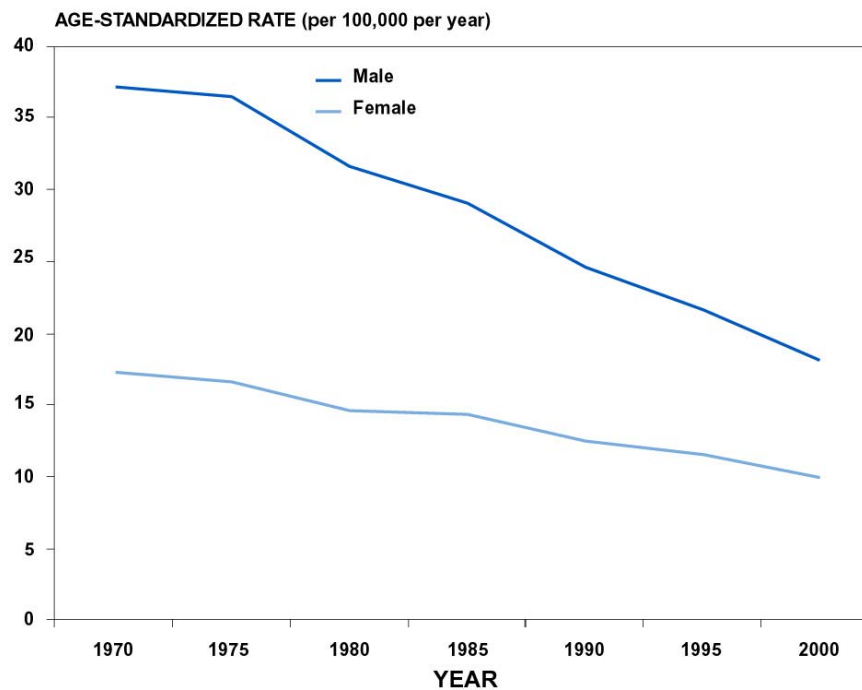
COLON: AGE-STANDARDIZED INCIDENCE BY SEX, 1968-2002

ILSI SEA REGION

Cancers of falling incidence in Singapore



LIVER: AGE-STANDARDIZED INCIDENCE BY SEX, 1968-2002



STOMACH: AGE-STANDARDIZED INCIDENCE BY SEX, 1968-2002

MAJOR RISK FACTORS

Diabetes in Asia

Epidemiology, Risk Factors, and Pathophysiology

Juliana C. N. Chan, MBChB, MD

“Metabolically obese”

Over-nutrition
Sedentary lifestyle

Frank B. Hu, MD, PhD

ONCE CONSIDERED A DISEASE OF THE WEST, type 2 diabetes is now a global health priority.¹ The International Diabetes Federation has predicted that the number of individuals with diabetes will increase from 240 million in 2007 to 380 million in 2025, with 80% of the disease burden in low- and middle-income countries.² More than 60% of the world's population with diabetes will come from Asia, because it remains the world's most populous region. The number of individuals with diabetes and impaired glucose tolerance (IGT) in each Asian country will increase substantially in coming de-

Context With increasing globalization and East-West exchanges, the increasing epidemic of type 2 diabetes in Asia has far-reaching public health and socioeconomic implications.

Objective To review recent data in epidemiologic trends, risk factors, and complications of type 2 diabetes in Asia.

Evidence Acquisition Search of MEDLINE using the term *diabetes* and other relevant keywords to identify meta-analyses, systematic reviews, large surveys, and cohort studies. Separate searches were performed for specific Asian countries. The review was limited to English-language articles published between January 1980 and March 2009; publications on type 1 diabetes were excluded.

Evidence Synthesis The prevalence of diabetes in Asian populations has increased rapidly in recent decades. In 2007, more than 110 million individuals in Asia were living with diabetes, with a disproportionate burden among the young and middle aged. Similarly, rates of overweight and obesity are increasing sharply, driven by economic development, nutrition transition, and increasingly sedentary lifestyles. The “metabolically obese” phenotype (ie, normal body weight with increased abdominal adiposity) is common in Asian populations. The increased risk of gestational diabetes, combined with exposure to poor nutrition in utero and overnutrition in later life in some populations, may contribute to the increasing diabetes epidemic through “diabetes begetting diabetes” in Asia. While young age of onset and long disease duration place Asian patients with diabetes at high risk for cardiorenal complications, cancer is emerging as an important cause of morbidity and mortality.

Conclusions Type 2 diabetes is an increasing epidemic in Asia, characterized by rapid rates of increase over short periods and onset at a relatively young age and low body mass index. Prevention and control of diabetes should be a top public health priority in Asian populations.

JAMA. 2009;301(20):2129-2140

www.jama.com

ILSI SEA REGION

Common diseases in industrialized nations

- Ischaemic heart disease and stroke
- “Lifestyle” cancers, eg colorectal, lung, breast, prostate
- Diabetes mellitus

Common/shared causes

- Cigarette smoking
- Obesity
- Dietary patterns

ILSI SEA REGION

The Singapore Chinese Health Study

- **A population-based prospective cohort of middle-aged and elderly Chinese in Singapore for long-term study of genetic, dietary and other environmental determinants to cancer and other chronic diseases**
- **Funded by NIH grants**



Dr Woon-Puay Koh (NUS)
Dr Hin-Peng Lee (NUS)

Dr Mimi Yu (UM)
Dr Jian-Min Yuan (UM)

UNIVERSITY
OF MINNESOTA *TWIN CITIES*



ILSI ANNUAL MEETING 2011

ILSI SEA REGION

Singapore Chinese Health Study

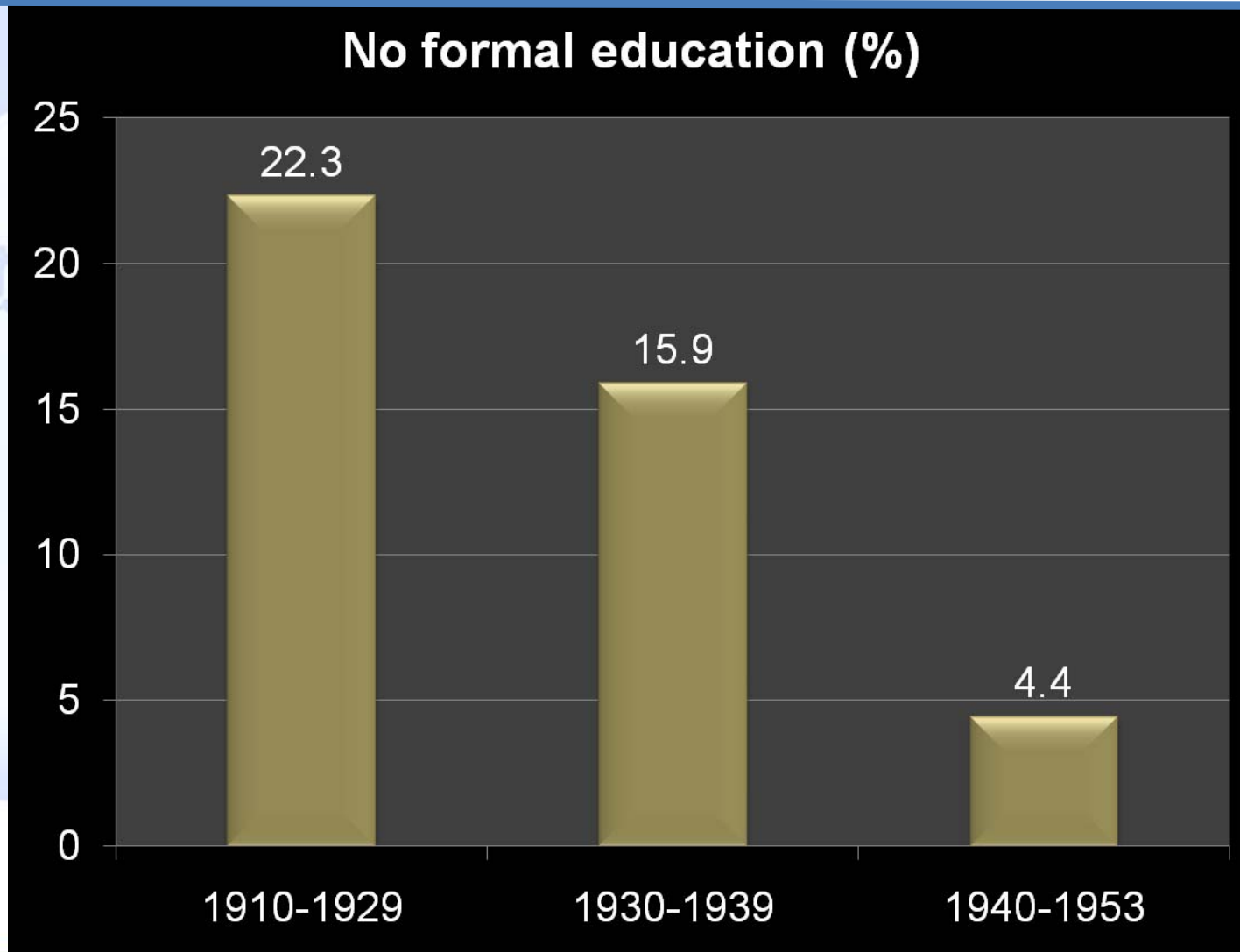
- Eligibility criteria: Housing estate residents, ages 45-74 years,
- Recruitment period: April 1993 to December 1998
- Cohort size: Total of 63,257, with 35,298 women and 27,959 men
- Baseline data: In-person interview, focus on current diet-validated 165-item food frequency questionnaire, smoking, physical activity and lifestyle detailed menstrual and reproductive history from women
- Biospecimen Subcohort: Since April 1994, blood/buccal cells and spot urine from all incident breast/colorectal cancers and 3% cohort. Expand to entire cohort in January 2000. Currently, a total of 32,575 subjects contributed biospecimens, representing 51% of the cohort.
- Follow-up: Cancer Registry, death certificates, address/phone updates via linkage
- Follow-up interviews: I: 1999-2004, II: 2006-2010; Telephone and in-person interviews to update smoking, drinking, tea, coffee, exercise, medical history and for women, menstrual history

Changing dietary pattern

- To capture changing dietary trends in view of Singapore's rapid industrialization
- A cross sectional study of Chinese men (45-74 years old), belonging to 3 different birth cohorts in SCHS
- 1910-29 (mean age 68.7 years, SD 2.9 years)
 - 1930-39 (mean age 59.5 years, SD 3.3 years)
 - 1940-53 (mean age 49.6 years, SD 3.3 years)
- Excluded individuals with diabetes, ischemic heart disease, stroke and hypertension

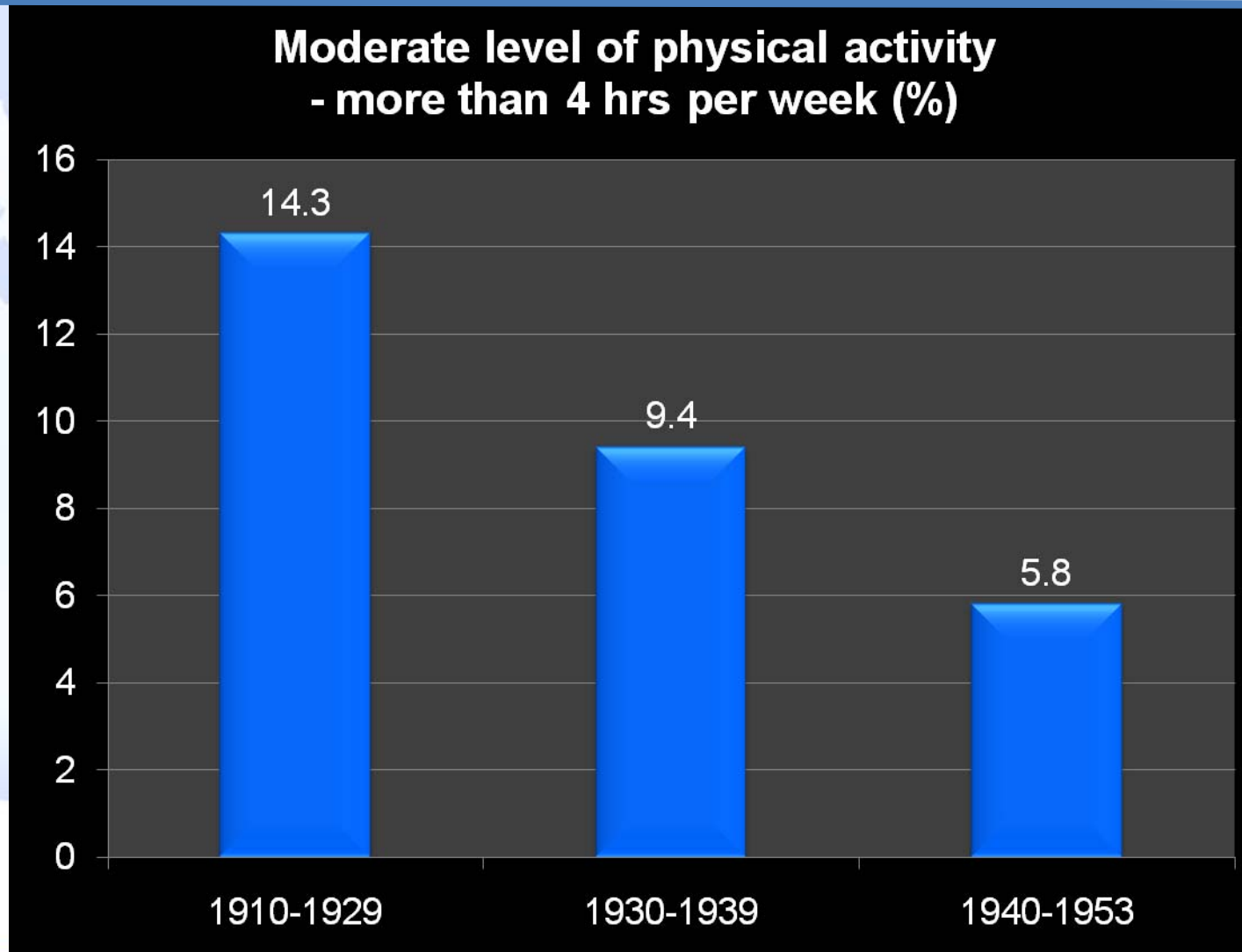
ILSI SEA REGION

- Educational level



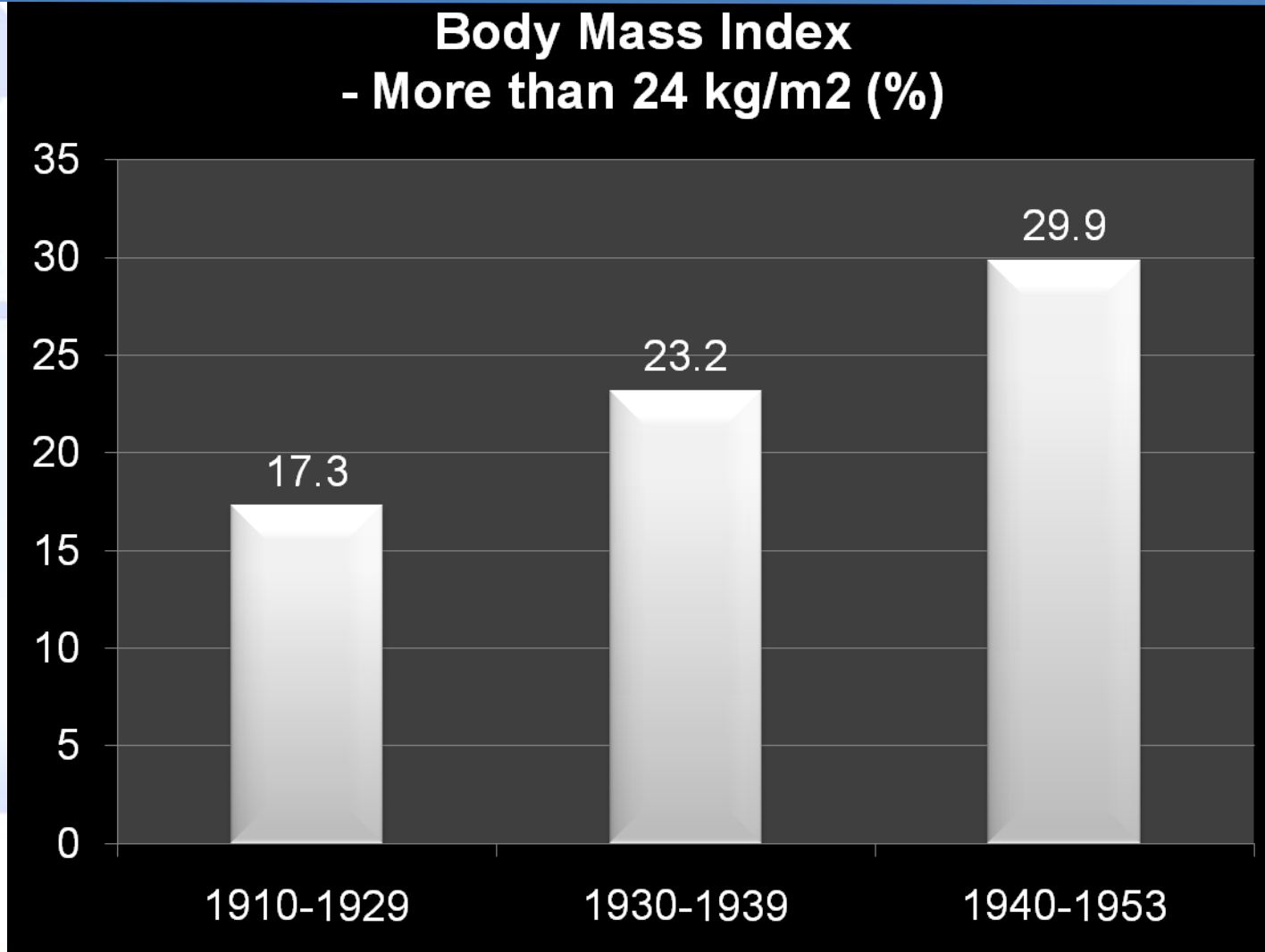
ILSI SEA REGION

- Physical Activity



ILSI SEA REGION

- Obesity



Negative trends

Decreased Physical Activity

Increased total Caloric Intake

Increased Sodium Intake

Increased Fat Intake

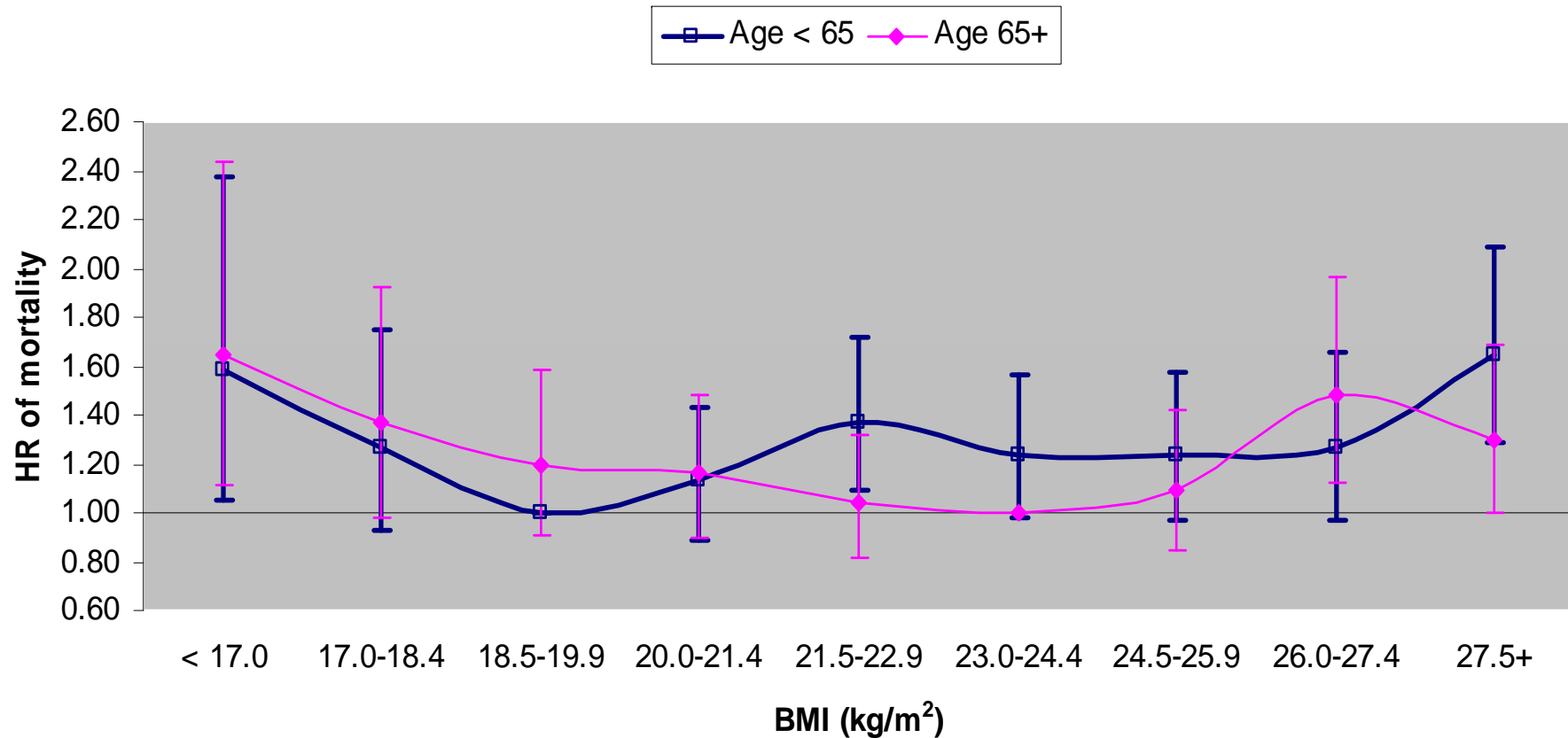
Increased Cholesterol Intake



ILSI SEA REGION

BMI and total mortality (SCHS)

Age stratified hazard ratios of all cause mortality



30,538 subjects, non-smokers without reported prevalent disease and excluding deaths occurring within first 5 years of baseline, adjusted for age, sex, year of enrolment, dialect, education, dietary pattern scores and physical activities.

Odegaard et al, *PLoS One*. 2010 Nov 15;5(11):e14000.

ILSI ANNUAL MEETING 2011



Asian Diabetes / Obesity Paradox

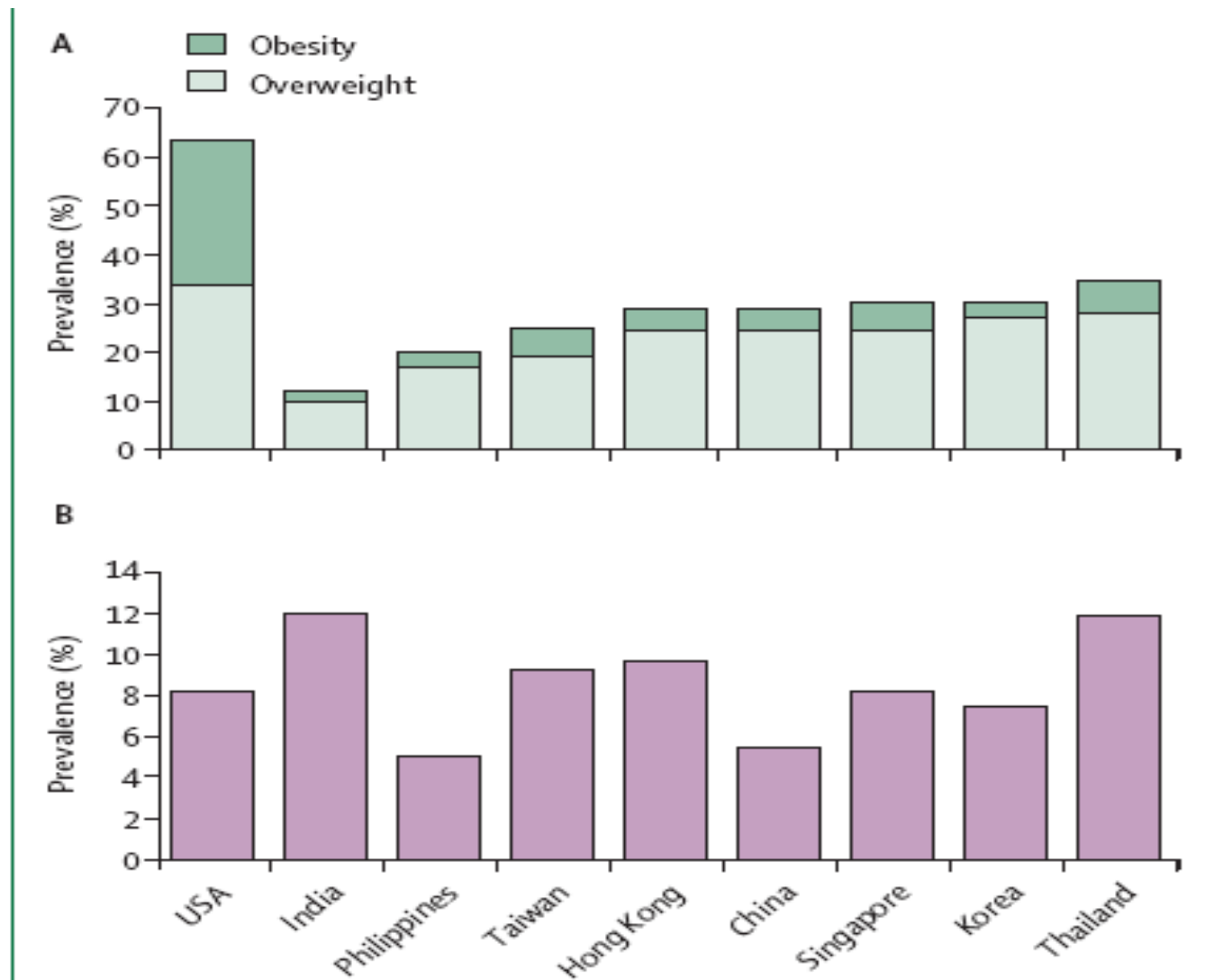


Figure 4: International comparison of prevalence of adult obesity and diabetes

(A) Proportion of overweight and obese adults. (B) Prevalence of diabetes.

ILSI SEA REGION

Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship

© 2002 The International Association for the Study of Obesity. *obesity* reviews 3, 141–146

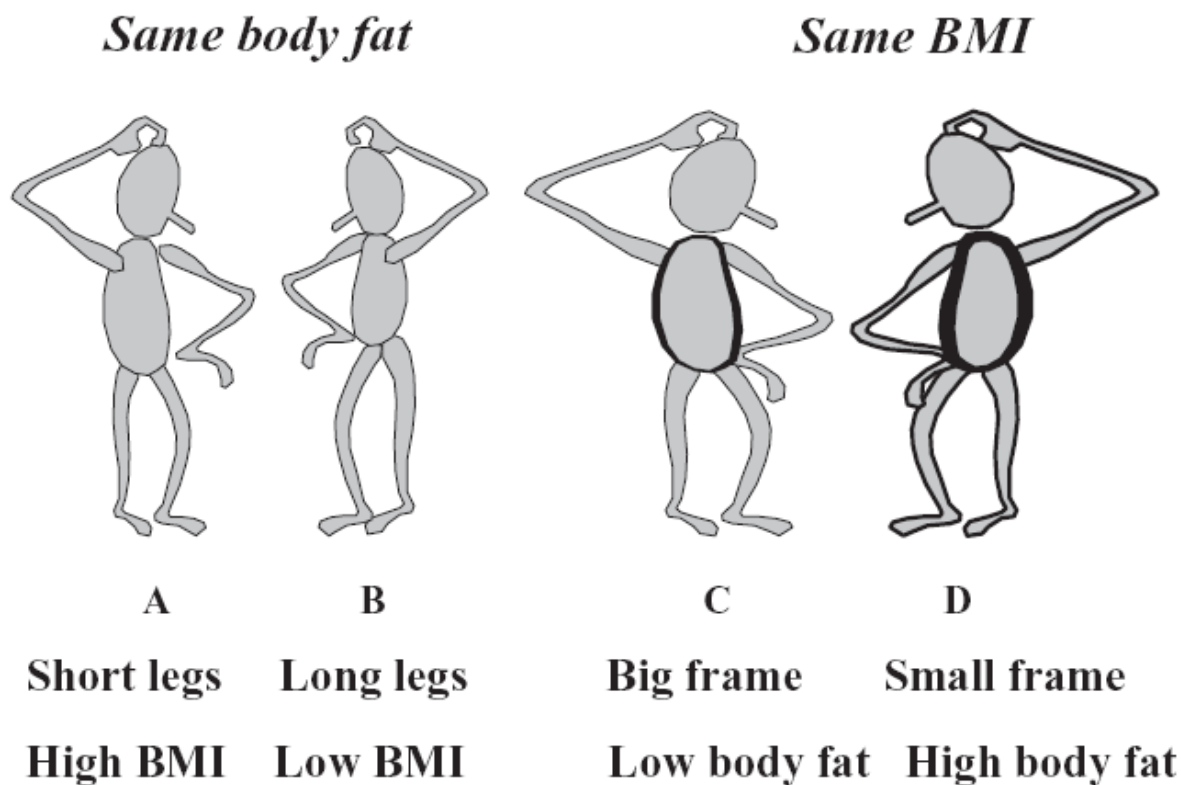
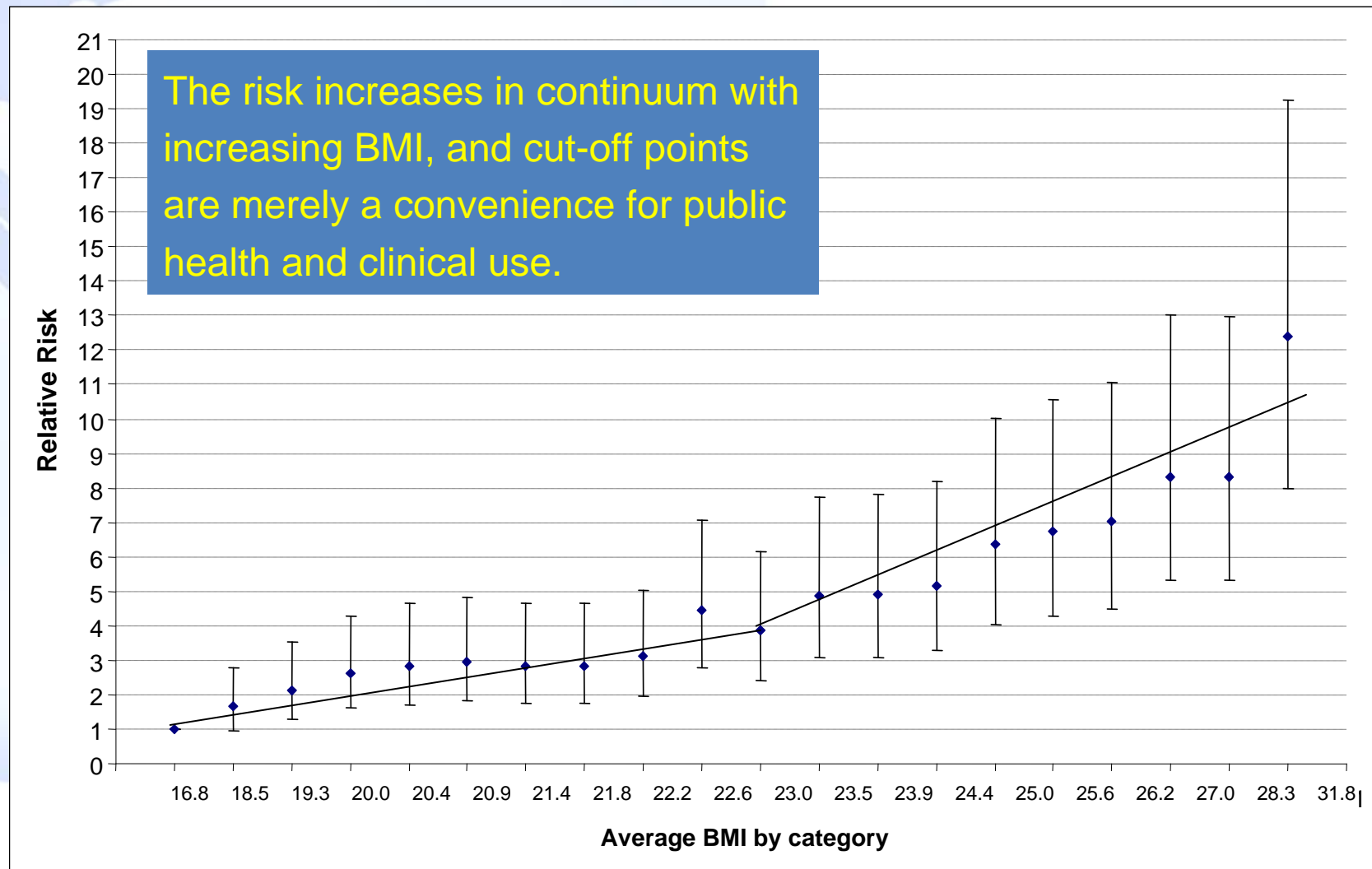


Figure 3 The effect of relative leg length and frame size on the body mass index (BMI)/body fat per cent (BF%) relationship. Subject A has the same BF% as subject B, but because he has shorter legs his BMI will be higher (more mass per cm length in the trunk). Subject C has the same BMI as subject D, but because his frame is bigger (stockier) he will have more skeletal mass, more muscle mass and more connective tissue. Therefore, for the same BMI he will have less BF%.

ILSI SEA REGION

Diabetes Relative Risk by BMI category



37,109 participants, adjusted for education, smoking status, alcohol use, hypertension, dietary factors and physical activity

ILSI SEA REGION

Dietary patterns in Chinese diet

- **Meat-dim sum diet**
 - Chicken, pork, fish
 - Noodle and rice dishes
 - Preserved foods
- **Vegetable-fruit-soy diet**
 - Vegetables
 - Fruits
 - Soyfood



Scores in dietary patterns correlated with disease risk

ILSI SEA REGION

Relative Risk (95% CI) of postmenopausal breast cancer according to dietary patterns in SCHS (1993 – 2005)

Pattern	Q1 (low)	Q2	Q3	Q4 (high)	P for trend
Vegetable-fruit-soy					
RR (95% CI)	1	1.08 (0.84-1.39)	0.86 (0.65-1.14)	0.70 (0.51-0.95)	0.01
Meat-dim sum					
RR (95% CI)	1	1.17 (0.90-1.51)	1.32 (1.01-1.72)	0.85 (0.62-1.17)	0.73

Adjusted for age, dialect group, interview year, education, parity, body mass index, family history of breast cancer and total daily energy intake

Butler et al, AJCN 2010; 91: 1013-9.

ILSI ANNUAL MEETING 2011



ILSI SEA REGION

Relative Risk for Type 2 Diabetes Mellitus, according to Quintile of Dietary Pattern Scores: SCHS

Pattern	Q1 (low)	Q2	Q3	Q4	Q5 (high)	P for trend
Vegetable-fruit-soy rich pattern						
RR (95% CI)	1	0.79 (0.68-0.93)	0.83 (0.71-0.97)	0.75 (0.63-0.88)	0.80 (0.68-0.95)	0.02
Meat-dim sum rich pattern						
RR (95% CI)	1	1.18 (1.02-1.37)	1.14 (0.97-1.33)	1.21 (1.02-1.43)	1.46 (1.21-1.75)	0.0002

Adjusted for age, sex, dialect, year of interview, energy intake, hypertension, education, physical activity and BMI

Odegaard et al, Diabetes Care, in press, 2011



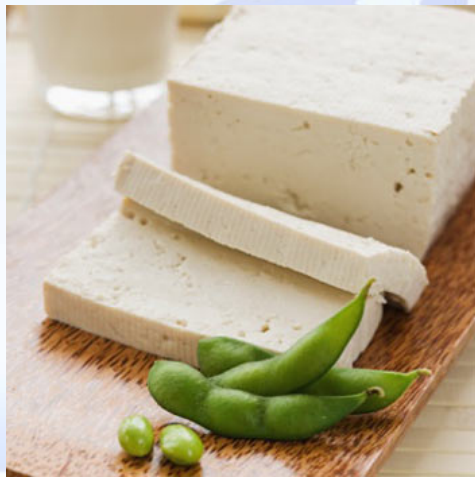
ILSI SEA REGION

Other published findings from SCHS

1. Phytoestrogen in soy-based products may help reduce the risk of breast cancer and osteoporotic hip fractures in elderly women. *Wu et al, Brit J Cancer 2008;99:196*
2. Beta-cryptoxanthin in orange-yellow fruits and vegetables such as papaya, tangerines and pumpkins may reduce the risk of lung cancer in smokers. *Yuan et al, CEBP 2003;12:890*
3. Isothiocyanates in cruciferous vegetables may reduce the risk of colon cancers. *Seow et al, Carcinogenesis 2002;23:2055*
4. Omega-3 FA in fish frequently may reduce the risk of breast cancer. *Gago-Dominguez et al, Brit J Cancer 2003;89:1686*
5. Coffee may help reduce the risk of Parkinson's disease and diabetes mellitus. *Tan et al, Am J Epid 2008;167:553; Odegaard et al, Am J Clin Nutr 2008;88:979*
6. Catechins in green tea may help reduce the risk of breast cancer in some women. *Inoue et al Carcinogenesis 2008;29:1967; Yuan et al Carcinogenesis 2005*

ILSI SEA REGION

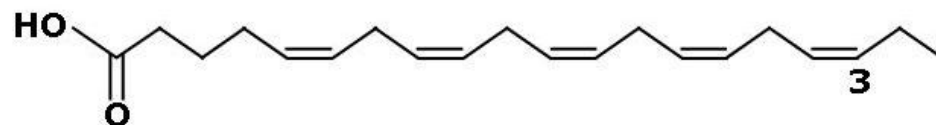
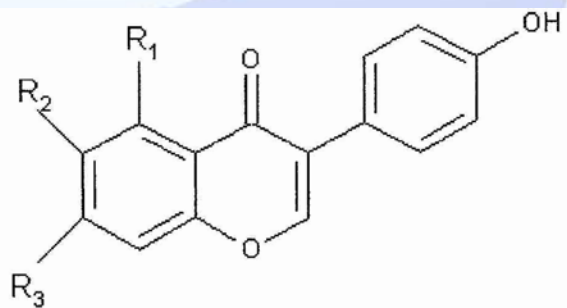
Soy and fish –
can they prevent breast cancer?



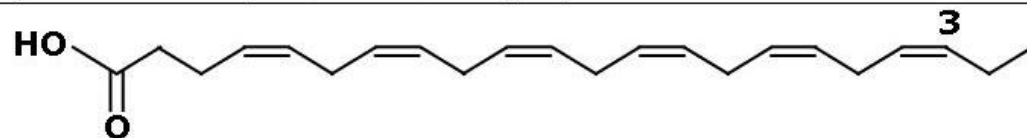
ILSI SEA REGION

Isoflavones and omega-3 fatty acids

can they prevent breast cancer?



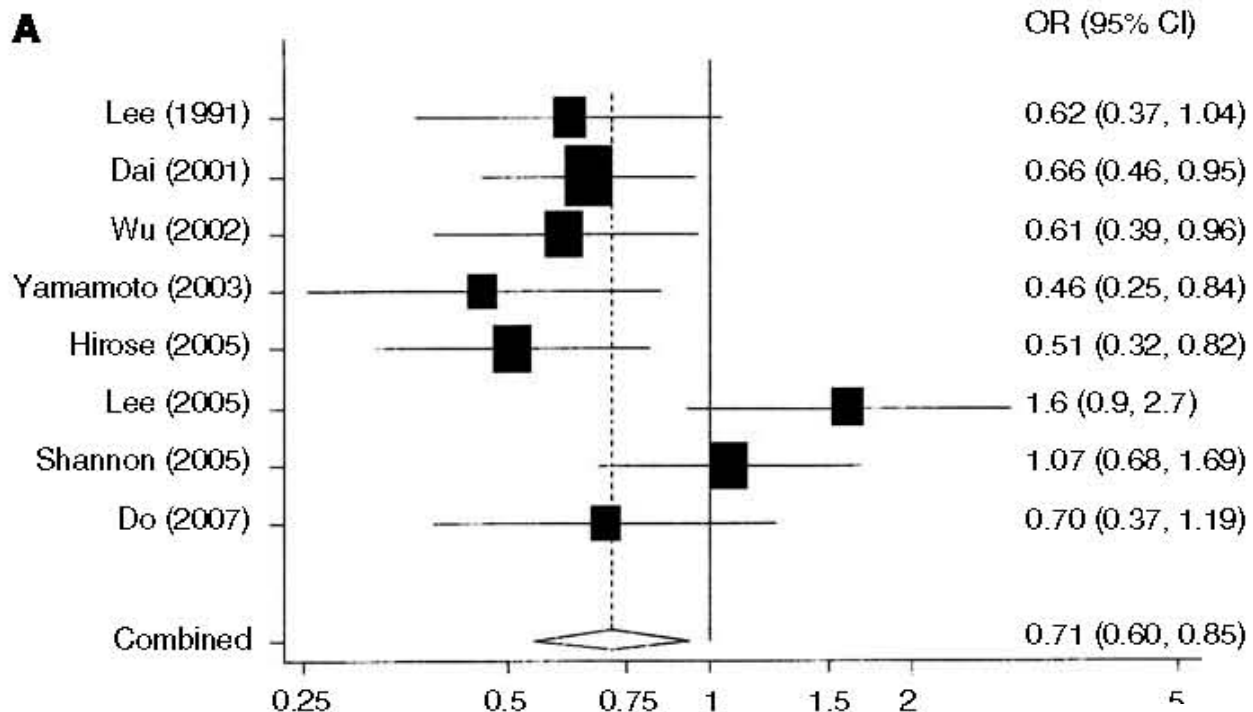
Eicosapentaenoic acid (EPA, C20:5, omega-3)



Docosahexaenoic acid (DHA, C22:6, omega-3)

ILSI SEA REGION

Studies in Japan, China and among Asian Americans



High intake
Highest (~20 mg
isoflavones per day) vs
lowest (~5 mg per day)

Wu et al, Br J Cancer 98:9, 2008

ILSI SEA REGION

Measurement of soy intake

- 7 common soy products, unfermented
- Soy intake expressed in grams of soy protein, soy isoflavones and equivalent amounts of tofu per day
- Soy intake estimated from summation of genistein, daidzein and glycitein previously measured in market samples of common soy foods in Singapore



ILSI SEA REGION

Soy and breast cancer risk

Soy intake	N	Person-year	HR (95% CI)
All subjects			
<10.6 mg*	339	167312	1.00
>=10.6 mg*	290	170930	0.82 (0.70-0.97)

Premenopausal	N	Person-year	HR (95% CI)
<10.6 mg*	84	43668	1.00
>=10.6 mg*	106	52937	1.04 (0.77-1.40)
Postmenopausal			
<10.6 mg*	255	123608	1.00
>=10.6 mg*	184	117960	0.74 (0.61-0.90)

* isoflavone/1000 kcal/day

P for interaction=0.08



ILSI SEA REGION

How about fish
(omega-3 fatty acids)?



ILSI SEA REGION

Strong experimental evidence

- Fish contains long-chain eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are polyunsaturated n-3 fatty acids
- N-3 PUFA compete with n-6 PUFA for incorporation into cell membrane phospholipids
- N-3 PUFA incorporated into cell membrane can also influence response of protein kinase C transduction pathway, the *ras* gene or growth factor analysis
- N-3 PUFA inhibits biosynthesis of prostaglandin E2
- E2 linked to enhanced estrogen synthesis in mammary stromal tissues

ILSI SEA REGION

How about human data?

POSITIVE FINDINGS

- Ecological studies have reported a higher per capita fish consumption to be associated with lower breast cancer incidence
- Norway: women who consumed 5 or more servings of salmon per month had a 30% lower risk than those 2 or fewer servings
- Japan: 5 or more servings per week had a 20% lower risk than 1 or no serving
- Norway: fishermen's wives had 30% lower mortality from breast cancer

NEGATIVE FINDINGS

- Systematic review of 19 case-control studies on fish or n-3 PUFA: mostly non-significant or null results (Terry et al, Am J Clin Nutr 2003; 77: 532)
- 4 large cohort studies in USA have failed to show benefit (low consumption population)
- Latest study from EPIC: no association (Engeset et al, Int J Cancer. 2006;119:175)

ILSI SEA REGION

Relative Risk (95% CI) of breast cancer according to fat intake in SCHS (1993 – 2002)

Nutrient	Q1	Q2	Q3	Q4	P for trend
Total fat	1.00	0.92 (0.67-1.27)	1.13 (0.83-1.53)	0.94 (0.68-1.31)	0.95
Sat fat	1.00	0.85 (0.63-1.16)	0.86 (0.63-1.18)	0.92 (0.67-1.26)	0.59
MUFA	1.00	1.29 (0.95-1.76)	1.13 (0.82-1.56)	1.02 (0.73-1.43)	0.90
PUFA	1.00	1.24 (0.90-1.71)	0.83 (0.59-1.18)	1.27 (0.92-1.74)	0.46
N-6 FA	1.00	1.15 (0.84-1.59)	0.90 (0.64-1.26)	1.22 (0.89-1.67)	0.45

Gago-Dominguez et al, Brit J Cancer 2003: 89: 1686



ILSI SEA REGION

Relative Risk (95% CI) of breast cancer according to fat intake in SCHS (1993 – 2002)

Nutrient	Q1	Q2	Q3	Q4	P for trend
N-3 FA	1.00	0.82 (0.60-1.12)	0.84 (0.62-1.15)	0.87 (0.64-1.18)	0.40
N-3 FA marine	1.00	0.75 (0.55-1.01)	0.75 (0.55-1.02)	0.72 (0.53-0.98)	0.04
N-3 FA other foods	1.00	0.88 (0.64-1.20)	0.89 (0.64-1.22)	1.00 (0.73-1.36)	0.97

Evidence was stronger in postmenopausal women, and for advanced cancer cases

Gago-Dominguez et al, Brit J Cancer 2003: 89: 1686

ILSI ANNUAL MEETING 2011



ILSI SEA REGION

Interaction between n-3 and n-6 PUFA in breast cancer risk (SCHS)

Marine N-3 FA	N-6 FA	Advanced cancer	Marine N-3 FA	N-6 FA	Advanced cancer
Q1	Q1	1.00	Q2-Q4	Q1	1.00
	Q2	1.41 (0.67-2.97)		Q2	1.03 (0.62-1.71)
	Q3	1.59 (0.76 – 3.33)		Q3	0.69 (0.40 – 1.21)
	Q4	2.45 (1.20 – 4.97)		Q4	1.00 (0.61 – 1.64)
	P for trend	0.01		P for trend	0.73



ILSI SEA REGION

Controversies in studies



- “Yes, No, Perhaps, And only in some people.....”

ILSI SEA REGION

Problems in diet-related studies

- 1. 'Blunt' instruments to measure dietary intakes (e.g. questionnaire): better instruments are needed**
- 2. Low variability in intakes: appropriate populations**
- 3. Weak diet-disease associations: sufficient sample size**
- 4. Gene-diet or diet-diet interaction**

But population impact is great !

ILSI SEA REGION

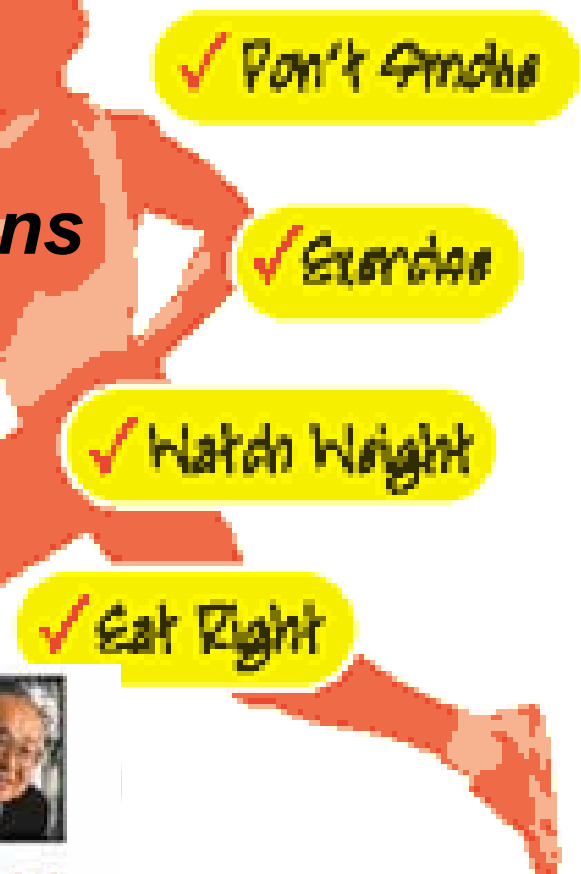
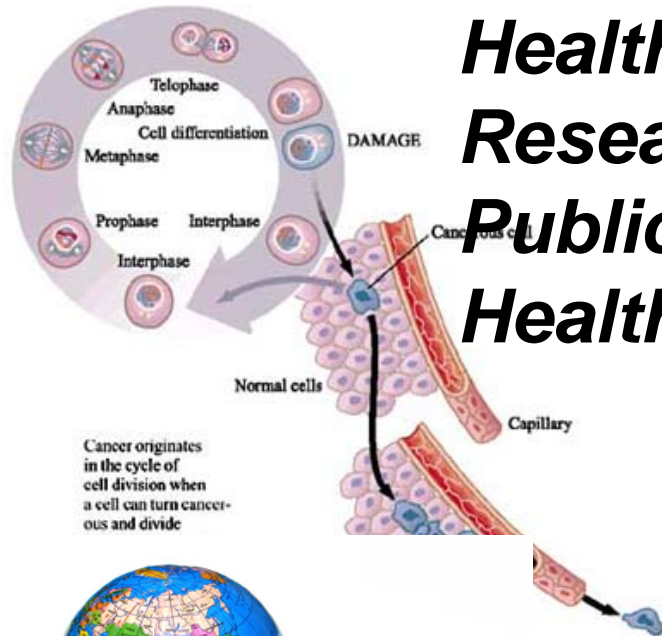
Evidence-based Nutrition

- **Randomised controlled trials (RCT) are universally regarded as the gold standard by which to determine whether a drug is appropriate in a particular clinical situation.**
- **But in the case of some chronic diseases, notably cancers, where nutritional factors may operate as promoters or protectors many years before the onset of clinical disease, RCT may not be particularly appropriate.**
- **A range of experimental studies and descriptive epidemiological approaches may be regarded as sufficient to justify nutritional recommendations or dietary guidelines.**

ILSI SEA REGION

Challenges in Disease Prevention

Healthcare Providers
Researchers
Public Health Physicians
Health Policy Makers



SCREENING DAY

ILSI ANNUAL MEETING 2011

