

Food factors for atherosclerosis prevention: Asian perspective derived from analyses of worldwide dietary biomarkers

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Y Yamori, on behalf of the WHO-CARDIAC Study Group. Food factors for atherosclerosis prevention: Asian perspective derived from analyses of worldwide dietary biomarkers. *Exp Clin Cardiol* 2006;11(2):94-98.

Worldwide epidemiological surveys covering 61 populations in 25 countries have shown that fish and soybean diets contribute to healthy longevity through the prevention of cardiovascular diseases in the Japanese population, particularly in Okinawans who consume a lot of fish and soy products. This is supported by the finding that 24 h urinary excretions of taurine and isoflavones, which are rich in fish and soybeans, are inversely related to mortality rates of coronary artery disease (CAD). Immigrant studies of Okinawans in Hawaii (USA) and Brazil

showed that dietary factors were more important determinants of cardiovascular diseases than genetic factors. Intervention studies in these immigrants and Scottish people, whose CAD mortality rates are among the highest in the world, confirmed that diets fortified with fish oil (docosahexaenoic acid) and soy protein (isoflavone) alleviated the risks of CAD and osteoporosis. Asian eating patterns, consisting of daily seafood and/or soy consumption, confer protection against CAD despite a Westernized life style; moreover, dietary biomarkers indicate that approximately 100 g of soybean curd (tofu) or fish may contribute to lower CAD mortality, as low as that found among the Japanese.

Key Words: *Coronary artery disease; DHA; Soy isoflavones; Soy protein; Stroke; Taurine*

Japanese women are now enjoying the longest average life expectancy (85.2 years) in the world. A World Health Organization (WHO) report also indicates that the disability-adjusted life-years (an average of 74.5 years) of the Japanese population are the longest in the world. Because average life expectancies are inversely related to the age-adjusted mortality rates of coronary artery disease (CAD) and all cancers in the world, the lowest mortality rates of these diseases in Japan contribute to the longest life expectancy among developed countries (Figure 1).

The WHO-Coordinated Cardiovascular Diseases and Alimentary Comparison (CARDIAC) Study (1-6) has been carried out in 61 communities in 25 countries around the world since the proposal of the study in 1983 (Figure 2). The WHO-CARDIAC Study aims to confirm the relationship between diets containing high seafood and soybean content and the widely known healthy longevity of Japanese; this is being confirmed based on the analysis of biological markers of these dietary intakes, such as taurine and isoflavones, in 24 h urinary (hu) excretions (7,8)

WHO-CARDIAC STUDY

The WHO-CARDIAC Study successfully showed, for the first time, that mortality rates of CAD are positively related to serum cholesterol (Cho) concentrations (Figure 3), and inversely related to 24 hu taurine excretions and to the ratio of n-3 fatty acids in plasma phospholipids (Figure 4) (indexes of seafood consumption) (4,5,9,10), and particularly to 24 hu isoflavone excretions (an index of soy product intake) (Figure 5) (11). On the other hand, stroke mortality is positively related to 24 hu Na excretions (Figure 6) and the Na/K ratio, and is inversely related to serum Cho concentrations (Figure 7) (5,6,10). Risk factors of stroke in Okinawans were shown to be

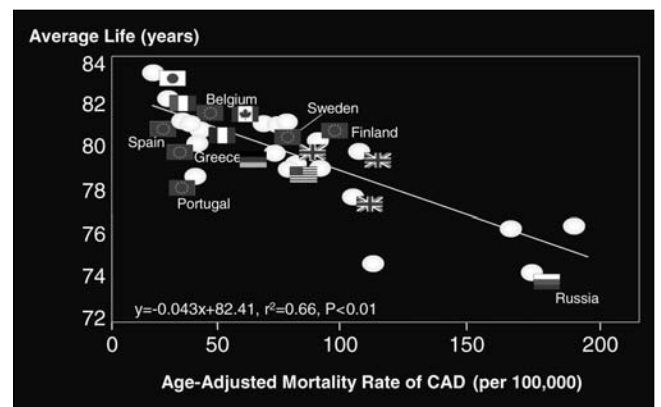


Figure 1 Relationship between age-adjusted coronary artery disease (CAD) mortality rate and average female life expectancy

the lowest among the Japanese due to their lowest 24 hu Na excretion (corresponding to NaCl intake [8 g a day in Japan]), and their lower cardiovascular disease (CVD) mortality rates were ascribed to their medium serum Cho concentrations (an average of 180 mg/dL to 200 mg/dL) (5), which contributed to their stroke and CAD mortalities being the lowest; in addition, their marked soybean consumption and fish intake also contributed to these low mortality rates, as shown by the biological dietary markers in 24 hu samples and blood.

IMMIGRANT STUDY ON THE JAPANESE (OKINAWANS) IN HAWAII AND BRAZIL

Three Okinawan populations were comparatively studied for their CVD risk factors in Hilo (Hawaii, USA), Campo Grande (Brazil) and Nago (Okinawa), where approximately 100 men

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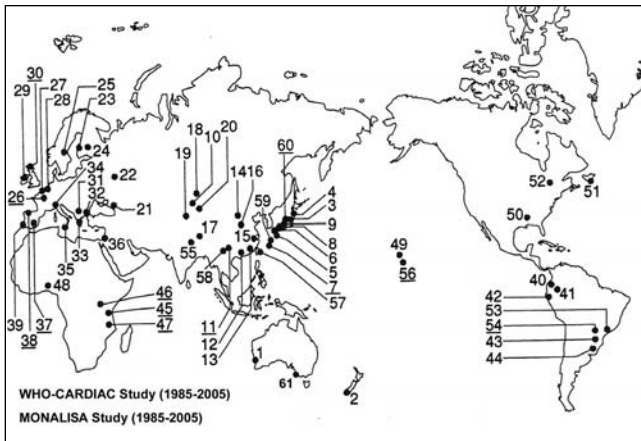


Figure 2) Worldwide distribution of populations studied by the World Health Organization- Coordinated Cardiovascular Diseases and Alimentary Comparison (WHO-CARDIAC) Study (1985 to 2005).
 1. Australia (Perth); 2. New Zealand (Dunedin); 3. Japan (Toyama); 4. Japan (Hirosaki); 5. Japan (Beppu); 6. Japan (Kurume); 7. Japan (Naha); 8. Japan (Hiroshima); 9. Japan (Ohta); 10. People's Republic of China (Urumqi); 11. People's Republic of China (Guiyang); 12. People's Republic of China (Guangzhou); 13. People's Republic of China (Meixian); 14. People's Republic of China (Beijing); 15. People's Republic of China (Shanghai); 16. People's Republic of China (Shijiazhuang); 17. People's Republic of China (Lhasa); 18. People's Republic of China (Altai); 19. People's Republic of China (Khotan); 20. People's Republic of China (Turpan); 21. Georgia (Java); 22. Russian Federation (Moscow); 23. Finland (North Carelia); 24. Finland (North Carelia); 25. Kingdom of Sweden (Göteborg); 26. France Republic (Orleans); 27. Kingdom of Belgium (Leuven); 28. Kingdom of Belgium (Ghent); 29. United Kingdom of Great Britain (Belfast); 30. United Kingdom (Lewis); 31. Republic of Bulgaria (Sofia); 32. Republic of Bulgaria (Sofia); 33. Hellenic Republic (Athens); 34. Republic of Italy (Milan); 35. Republic of Italy (Palermo); 36. State of Israel (Tel Aviv); 37. Kingdom of Spain (Navas); 38. Kingdom of Spain (Madrid); 39. Portuguese Republic (Lisbon); 40. Republic of Ecuador (Quito); 41. Republic of Ecuador (Vilcabamba); 42. Republic of Ecuador (Manta); 43. Federative Republic of Brazil (Uruguaina); 44. Federative Republic of Brazil (Bage); 45. United Republic of Tanzania (Handeni); 46. United Republic of Tanzania (Monduli); 47. United Republic of Tanzania (Dar es Salaam); 48. Federal Republic of Nigeria (Ibadan); 49. United States of America (Honolulu); 50. United States of America (Jockson); 51. Canada (Newfoundland); 52. Canada (Montreal); 53. Federative Republic of Brazil (San Paulo); 54. Federative Republic of Brazil (Campo Grande); 55. Kingdom of Nepal (Namchebazar); 56. United States of America (Hilo); 57. Republic of China (Taipei); 58. People's Republic of China (Guiyang); 59. Japan (Nago); 60. Japan (Kyoto); 61. Australia (Melbourne)

and 100 women aged 47 to 57 years were randomly selected for the health examination of the WHO-CARDIAC Study (11-13). The prevalences of hypertension, hypercholesterolemia, obesity and diabetes mellitus were lowest in Okinawans in Okinawa. CVD risk factors were particularly increased in Okinawan immigrants in Brazil (Figure 8), indicating that the extreme Westernization of dietary habits, particularly the loss of habitual fish and soybean consumption (as shown by their biomarkers), appears to be involved in the shortening of life expectancy due to high CVD mortality.

INTERVENTION STUDIES

Study of Japanese immigrants in Brazil

A selected group of high-risk Japanese immigrants in Brazil (10 men and 10 women aged between 47 and 57 years) were

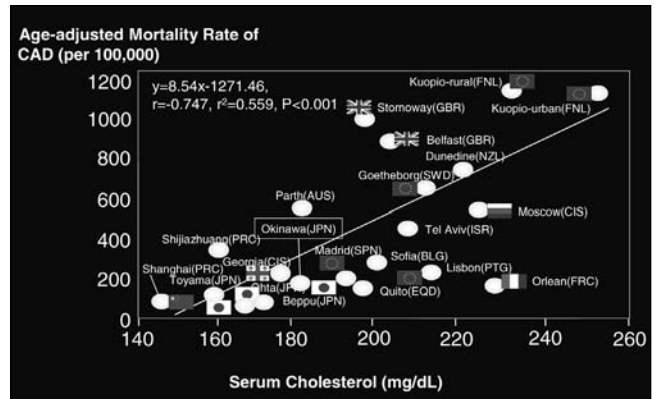


Figure 3) Relationship between age-adjusted coronary artery disease (CAD) mortality rate and total serum cholesterol in men

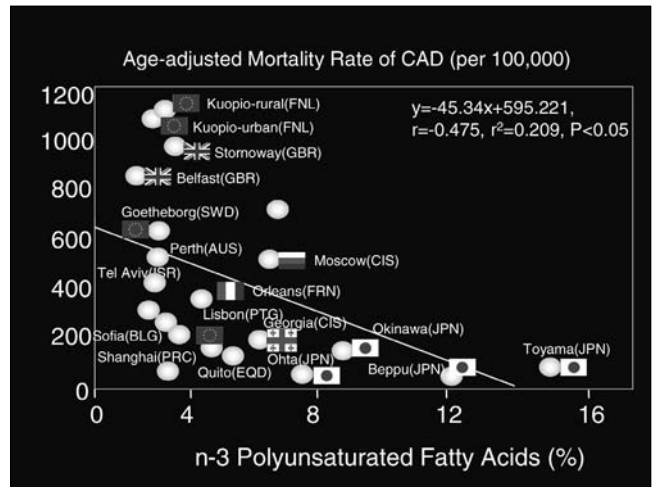


Figure 4) Relationship between age-adjusted coronary artery disease (CAD) mortality rate and the n-3 polyunsaturated fatty acid ratio in plasma phospholipids in men

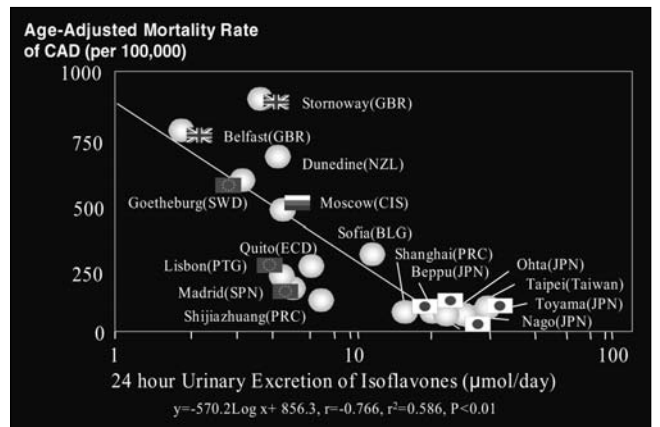


Figure 5) Relationship between age-adjusted coronary artery disease (CAD) mortality rate and 24 h urinary isoflavones excretion in men

given 3 g of docosahexaenoic acid daily, and showed a significant reduction in blood pressure (BP) (Figure 9); in addition, the same number of people were given 5 g of seaweed powder daily, and showed a significant reduction in serum Cho (11). Twenty women aged 47 to 57 years were given 50 mg of soy

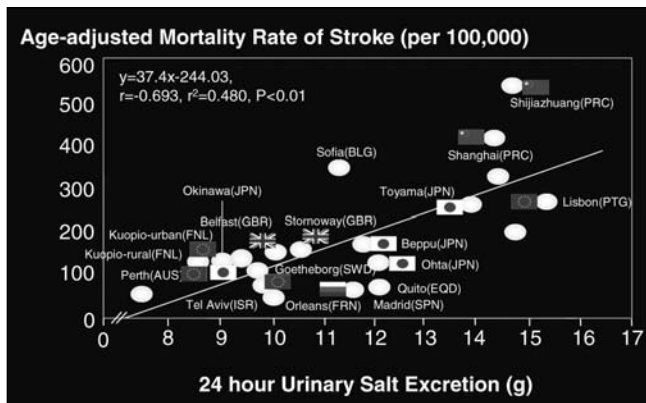


Figure 6) Relationship between age-adjusted stroke mortality rate and 24 h urinary salt excretion in men

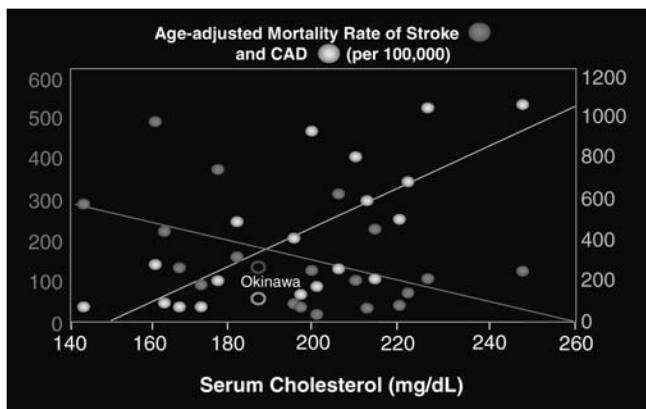


Figure 7) Relationship between age-adjusted coronary artery disease (CAD) and stroke mortality rates and total serum cholesterol in men

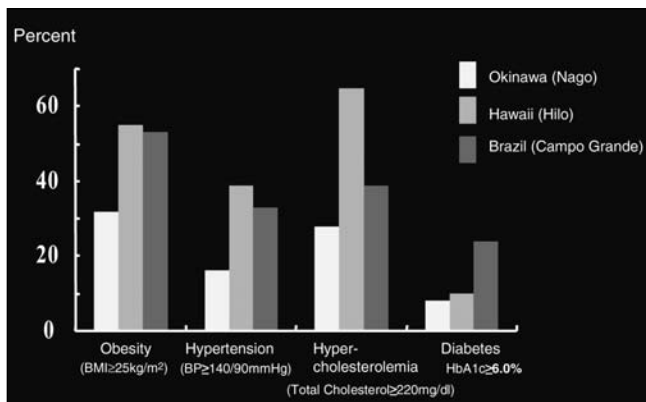


Figure 8) Prevalence of risks of life style-related diseases in Japanese immigrants from Okinawa living in Brazil and Hawaii, and in Japanese living in Okinawa (men). BP Blood pressure; HbA1c Hemoglobin A1c

isoflavones daily, and showed significant reductions in BP and Cho (Figure 10) (11), as well as reductions in 24 hu pyridinoline and deoxypyridinoline, which are markers of Ca resorption from the bone.

Because risk factors in these Japanese immigrants were beneficially affected within three to 10 weeks by typical nutrients from fish, seaweed and soybeans common in Japanese (particularly Okinawan) diets, CAD is expected to be prevented by these nutritional factors.

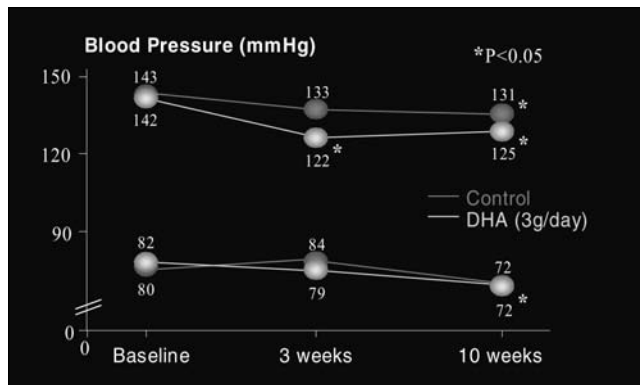


Figure 9) Blood pressure changes after fish oil (docosahexaenoic acid [DHA], 3 g/day) supplementation

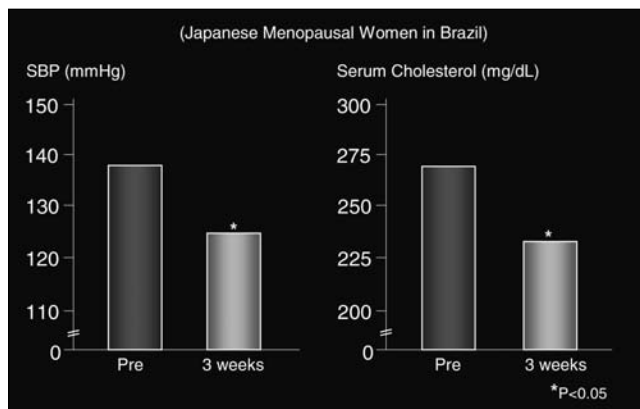


Figure 10) Changes in systolic blood pressure (SBP) and serum total cholesterol in women after soy isoflavone (50 mg/day) supplementation

Studies of Japanese immigrants in Hawaii

Two hundred thirty-eight Japanese immigrants aged between 45 and 59 years underwent a health examination according to the WHO-CARDIAC Study protocol. After which, 80 individuals (43 men and 37 women) with mild hypertension and hypercholesterolemia were invited to participate in an eight-week nutritional intervention, taking soy protein (over 25 g daily) fortified diets (14). After the eight-week intervention, their BP and serum total Cho were significantly reduced from the initial levels, but no reduction was observed in the control group (14).

Studies in Scottish people with a high CVD mortality rate

The WHO-CARDIAC/MONALISA study (MONALISA is an acronym of Moneo Alimentationis Sanae, meaning ‘Reminding of Healthy Diets’) of Scottish people (Isles of Lewis and Skye) in 1999 (15) confirmed a further increase in CAD risk factors compared with the results from the previous study in 1987. Sixty menopausal women with relatively high CVD risk factors were randomly assigned into two groups (30 in each) to take (daily for five weeks) either a jelly containing 50 mg of isoflavones or placebo jelly. Urinary isoflavone excretion was significantly increased and a significant BP reduction was observed in the isoflavone group but not in the placebo group.

OKINAWAN DIETS AND CANCERS

Stomach cancer mortality in Okinawans, the lowest in Japan, is related to the lowest Na intake, and the lower mortalities of

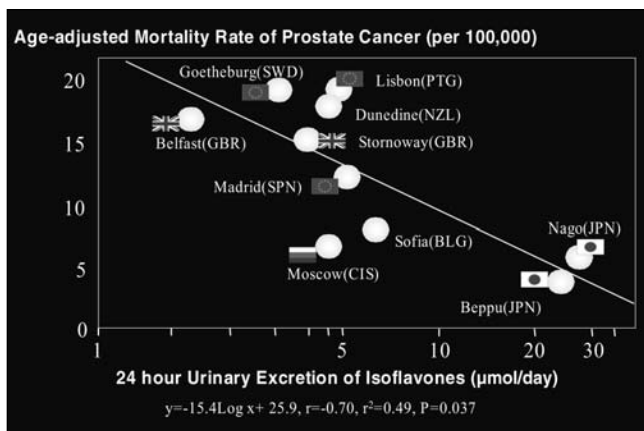


Figure 11) Relationship between age-adjusted mortality rates of prostate cancer and 24 h urinary isoflavone excretion in men

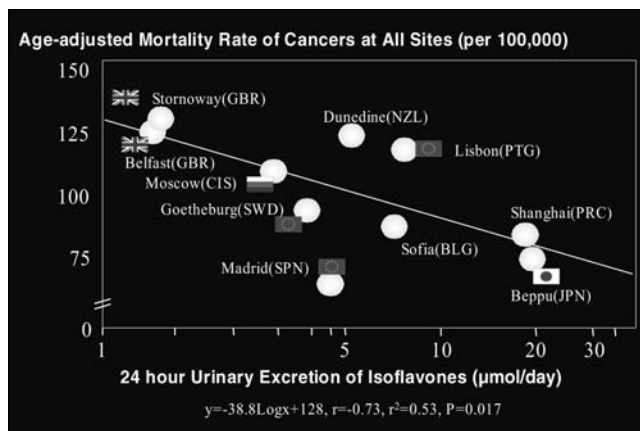


Figure 13) Relationship between age-adjusted mortality rate of cancers at all sites and 24 h urinary isoflavone excretion in women

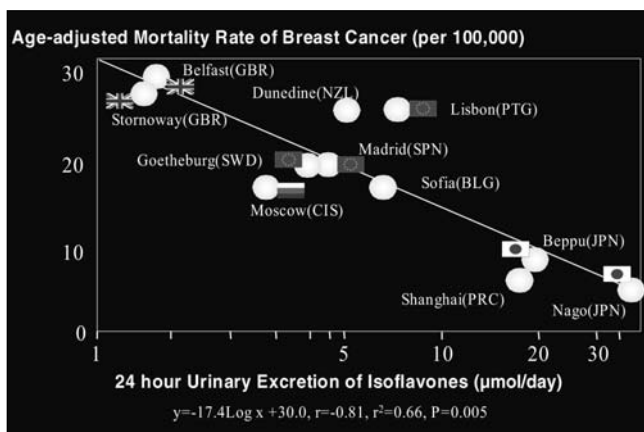


Figure 12) Relationship between age-adjusted mortality rates of breast cancer and 24 h urinary isoflavone excretion in women

prostate, breast and all cancers were inversely related to 24 hu isoflavone excretion in the WHO-CARDIAC Study populations (Figures 11, 12 and 13, respectively) (11). The preventive mechanism of isoflavones, which traditional Okinawan soybean dishes are rich in, is ascribed to reduced estrogenic and estrogen receptor-blocking activity, and to the inhibition of angiogenesis. Therefore, Okinawans' healthy longevity can be ascribed to their lower CAD and cancer mortalities due to the merits of the Okinawan daily diet, which is characterized by low salt and is rich in soybeans, fish and seaweeds, and probably green vegetables containing antioxidants, which are all popular in other Asian countries.

CONCLUSIONS

The WHO-CARDIAC Study indicates, by a worldwide comparison of biological markers of fish consumption (24 hu taurine excretion and the n-3 fatty acid ratio in plasma phospholipids) and soybean consumption (24 hu isoflavone excretion), that increased fish and soybean consumption reduces CAD mortality and, thus, may contribute to healthy longevity. Moreover, soy consumption, popular in Japan and other Asian countries, may decrease not only CAD mortality but also prostate, breast and all cancer mortalities, and thus, may also contribute to healthy longevity worldwide, as typically shown in Okinawa, where soy

product consumption is the highest in Japan. Because CAD and cancer mortalities are higher in populations consuming less fish and soybeans, the promotion of seafood and soybean utilization as human nutrients by the technological improvement of seafood and soybean production and processing, as well as by harmonizing oriental and occidental or traditional and modern dietary customs, will hopefully contribute to 'health for all' and solve serious problems of protein supply to the expanding population on the earth.

ACKNOWLEDGEMENTS: The WHO-CARDIAC Study was supported by Grants-in-Aids from the Japanese Government and donations to the WHO through the Japan Heart Foundation (Tokyo, Japan), from Otsuka Pharmaceutical Co (Tokyo) and many other companies, and also individual donations from approximately 300,000 Japanese in total since 1983 to the International (former WHO) Collaborating Center for Research on Primary Prevention of Diseases (Kyoto, Japan).

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