© Med Sci Monit, 2007; 13(7): CR307-312
PMID: 17599024

Received: 2006.11.22
Accepted: 2007.02.28
Published: 2007.07.01

Long-term fish intake is associated with better lipid profile, arterial blood pressure, and blood glucose levels in elderly people from Mediterranean islands (MEDIS epidemiological study)

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Demosthenes B. Panagiotakos[1ABCDE], Akis Zeimbekis[1BE], Vassiliki Boutziouka[1BE], Mary Economou[1BE], Georgia Kourlaba[1DF], Pavlos Toutouzas[2FG], Evangelos Polychronopoulos[1AF]

[1] Department of Nutrition-Dietetics, Harokopio University, Athens, Greece
[2] Hellenic Heart Foundation, Athens, Greece

Source of support: The study was funded by research grants by the Hellenic Heart Foundation

Summary

Background: A study to evaluate the link between long-term fish intake and health status in a sample of elderly adults was undertaken.

Material/Methods: Three hundred men and women from Cyprus, 142 from Mitilini, and 100 from Samothraki islands (aged 65 to 100 years) were enrolled in this study during 2005-2006. Dietary habits (including fish consumption) were assessed through a food frequency questionnaire. Among various factors, fasting blood glucose, arterial blood pressures, and blood lipids were measured.

Results: Sixty-one percent of the participants reported that they had consumed fish approximately once a week (mean intake: 1.9±1.2 servings/week) for a mean period of 30 years. After adjusting for various confounders, fish intake was inversely associated with systolic blood pressure (p=0.026), fasting glucose (p<0.001), total serum cholesterol (p=0.012), and triglyceride levels (p=0.024). Multinomial logistic regression revealed that a decrease of 100 g per week in fish intake was associated with a 19% (95%*CI*: 1–41) higher likelihood of having one additional cardiovascular risk factor (i.e. hypertension, hypercholesterolemia, diabetes, obesity).

Conclusions: The results indicate that long-term fish intake is associated with reduced levels of the most common cardiovascular disease risk markers in a cohort of elderly people.

key words: **cardiovascular disease • risk factors • fish • elderly**

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/487376

Word count: 2556
Tables: 3
Figures: –
References: 30

Author's address: Demosthenes B. Panagiotakos, Harokopio University, 70 El. Venizelou St, 17671, Athens, Greece, e-mail: dbpanag@hua.gr

Background

Long-term research and observation have shown that diet has a significant impact on the development and progression of cardiovascular diseases [1]. An important component of a healthy dietary pattern is fish. During the last two decades, several epidemiological studies and clinical trials have indicated the beneficial effects of fish intake in the primary and secondary prevention of several diseases, including cardiovascular disease [3–9]. In addition, the hypotriglyceridemic effects of n-3 fatty acids from fish oils are well established [10]. Furthermore, n-3 fatty acids have been associated with a small, dose-dependent hypotensive effect [11, 12] and they may protect against heart disease mortality by stabilizing ion transport through heart cell membranes, which is essential for heart rhythm [13]. Moreover, animal experiments and clinical intervention studies indicate that n-3 fatty acids have anti-inflammatory properties and, therefore, might be useful in the management of inflammatory and autoimmune diseases [14,15]. However, the majority of these results are based on middle-aged populations were the disease burden is not so high. The effect of fish intake, as well as other dietary habits, on health status in the elderly has rarely been investigated and presented in the literature. In this age-group of people it is known that the burden of disease is much higher, with hypertension, hypercholesterolemia, and diabetes affecting at least one third of them, and their nutritional status and needs are associated with several biological and, frequently, socioeconomic changes. Therefore, in the context of the Mediterranean Islands Epidemiological Study (MedIS), which is a health and nutrition survey among elderly people living in the Mediterranean islands, we sought to evaluate whether fish intake is independently associated with the levels of the most common cardiovascular risk markers, i.e. arterial blood pressures, fasting blood glucose, and blood lipids.

Material and Methods

Participants

A random, population-based, multistage sampling method was used to select men and women 65 years of age or older from several Cypriot cities (Arsos, Lemessos, Pachna, Pafos, Empa, Kallapia and Yeroskipu) as well as from the islands of Mitilini and Samothraki in Greece. Individuals residing in assisted-living centers as well as those with a clinical history of cardiovascular disease were not included in this research. Of the initially selected population, 234 men and 308 women agreed to participate (Cyprus: n=300, Mitilini: n=142, and Samothraki: n=100; 79% participation rate). The final number of enrolled participants (N=542) was high enough for a standardized difference evaluation between the investigated parameters greater than 0.5, achieving a statistical power of <0.80 at the probability level of p<0.05.

Measurements

Consumption of 15 food groups was measured as averages per week during the past year through a semi-quantitative food-frequency questionnaire (FFQ). The frequency of food consumption was then calculated by month. Consumption of various alcoholic beverages (wine, beer, retsina, etc) was measured in terms of wineglasses adjusted for ethanol intake (for example, one 100-ml glass of wine was considered to be 12% ethanol). Diets were scored with reference to the Mediterranean dietary pattern (which is characterized by moderate consumption of fat and a high monounsaturated-to-saturated fat ratio) consisting of:

1. daily consumption of unrefined cereals and their products (whole grain bread, pasta, brown rice, etc), vegetables (2–3 servings/day), fruits (6 servings/day), olive oil (as the main added lipid), and dairy products (1–2 servings/day);
2. weekly consumption of fish (4–5 servings/week), poultry (3–4 servings/week), olives, pulses, and nuts (3 servings/week), potatoes, eggs, sweets (e.g. grapes, walnut cake, honey and sesame fritters, kantaifi, baklava, milk pie, other homemade spoon sweets) (3–4 servings/week), and
3. monthly consumption of red meat and meat products (4-5 servings/month).

Based on the FFQ, all participants were also asked about their usual average frequency of fish consumption, which was coded as follows: 0 for none or very rare (<4 units per month), 1 for rare (<4 units, or ca. 150 g/week), 2 for moderate (4–12 units, or 150–300 g/week), and 3 for frequent (>12 units or >300 g/week). Moreover, the participants were asked about the duration (in years) of eating fish.

Physical activity was evaluated using a shortened version of the self-reported International Physical Activity Questionnaire (IPAQ) for the elderly [16]. Frequency (times per week), duration (minutes per time), and intensity of physical activity during sports, occupation, and/or free-time activities were assessed. Participants who did not report any physical activity were defined as sedentary. In accordance with the standard IPAQ scoring procedures, physically active participants were classified into one of the following groups: upper tertile: "vigorous" physical activity (i.e. <2500 MET/min/week), middle tertile: "moderate" physical activity (i.e. 500–2500 MET/min/week), or lower tertile: "low" physical activity (i.e. <500 MET/min/week).

The survey also included basic demographic items such as age, gender, financial status (average annual income during the past three years), and educational level (years of school). Weight and height were measured to attain body mass index (BMI) scores (kg/m^2). Obesity was defined as a BMI >29.9 kg/m^2. The participants' blood pressure levels were retrieved from their medical records. People who had blood pressure levels ≥140/90 mmHg or used antihypertensive medications were classified as hypertensive. Fasting blood lipids were recorded. Hypercholesterolemia was defined as total serum cholesterol levels >200 mg/dl or the use of lipid-lowering agents. Participants' medical records were also consulted to determine high- and low-density lipoprotein (HDL, LDL) cholesterols and triglyceride levels. Diabetes mellitus (type 2) was determined by fasting plasma glucose tests and was analyzed in accordance with the American Diabetes Association diagnostic criteria (i.e. fasting blood glucose levels greater than 125 mg/dl indicated the presence of diabetes). Current smokers were defined as those who smoked at least one cigarette per day or had stopped cigarette smoking during the past 12 months. Former smokers were defined as those who previously smoked, but had not done so for a year or more. The remaining participants were defined as rare- or non-smokers.

CR

Table 1. Participant's socio-demographic and lifestyle characteristics.

	Fish consumption				Overall	p
	No.	<150 g/wk	150–300 g/wk	>300 g/wk		
% of participants	10%	29%	42%	19%	–	–
Male sex (%)	42	39	46	45	43	0.65
Age (years)	77±12	78±8	75±7	74±6	76±7	0.01
Years of school	3.9±2	5.1±3*	5.6±3*	6.4±3**	5.5±3	<0.001
Current smokers (%)	10	4	8	14*	8	<0.001
Physically inactive (%)	75	68	67	41**	63	0.001

Data are expressed as mean ± standard deviation or percentages.
* $p<0.05$ and ** $p<0.01$ (Tukey corrected) for the differences between fish consumption groups vs. no consumption. Probability values derived from the ANOVA or the chi-squared tests.

Statistical analyses

Continuous variables are presented as mean values ±standard deviation. The categorical variables are presented as absolute and relative (%) frequencies. After controlling for equality of variances, associations between continuous variables and group of participants were evaluated with analyses of variance (ANOVA). Tukey's honestly significant difference post hoc test was used to test for differences among comparisons between groups of fish intake. Associations between continuous variables were tested with Spearman's correlation coefficient. Multiple regression models were then applied for all the investigated biological markers on fish consumption after adjusting for various potential confounders. Fish intake interaction with potential confounding factors was also assessed. Assumptions of linearity for the continuous independent variables and constant variance of the standardized residuals were assessed by plotting the residuals against the fitted values. We also calculated R^2 in order to find how well each fitted model predicts the dependent variables. Multinomial logistic regression analysis evaluated the association between fish intake and the number of cardiovascular risk factors prevailed in our sample. p-values <0.05 from two-sided hypotheses were considered as statistically significant. All statistical calculations were performed using SPSS version 14.0 software (SPSS Inc., Chicago, IL, USA).

Results

The majority of the participants (90%) reported that they consumed fish at least once per week. Moreover, the types of fish consumed include mainly small, lean fishes, such as sardine, tope, gilthead, goatfish, anchovy, fry, and the like. The participants reported that they had had the same habits regarding fish intake for at least the past 30 years. Table 1 presents the characteristics of the participants by fish consumption group. As one can see, no differences were observed between the gender and fish-intake groups, while people with higher fish intake were more educated, less physically inactive, more obese, and more frequently smokers compared with the no-fish-intake group.

Table 2 presents the biological characteristics of the participants by fish-intake group. An inverse relationship was found between fish intake and systolic blood pressure (p=0.03), total cholesterol level (p=0.001), triglyceride level (p=0.01), and fasting blood glucose level (p=0.002). No significant associations were observed between fish intake and diastolic blood pressure, HDL, and LDL cholesterol levels. Moreover, an inverse relationship was observed between fish intake and the prevalence of hypertension. Particularly, people in the higher group of fish intake were 13% less likely to have hypertension (p=0.02). Similarly, an inverse relationship was observed between fish intake and the prevalence of type 2 diabetes, since people in the higher group of fish intake were 14% less likely to have diabetes (p=0.01). Furthermore, fish intake positively correlated with the consumption of greens and vegetables (r=0.29, p<0.001), legumes (r=0.08, p=0.05), and olive oil (r=0.25, p<0.001), while fish consumption was inversely correlated with cereal (r=–0.16, p=0.001) and fruit (r=-0.10, p=0.025) intake.

However, residual confounding may exist. Thus, after adjusting for age, sex, educational status, physical activity level, BMI, and dietary and smoking habits, we observed that weekly fish intake was associated with lower systolic blood pressure levels, lower triglyceride and fasting glucose concentrations, as well as lower (but not significant at the 5% level) total serum cholesterol and higher HDL cholesterol concentrations (Table 3). Comparing the net effect of fish intake on the investigated biological markers, we observed that the more prominent results were observed in glucose levels, followed by triglyceride and cholesterol levels (i.e. the higher the B coefficient, the more prominent the effect). Moreover, the effect of fish intake on the aforementioned biological factors showed higher explanatory ability, as expressed by the changes in the R^2 values.

Then we added the number of the common cardiovascular risk factors (i.e. hypertension, hypercholesterolemia, diabetes, and obesity) and observed that increased fish intake was associated with a lower burden of cardiovascular risk factors (Table 2). In addition, a decrease of 100 g per week in fish intake was associated with a 19% higher likelihood of having one additional risk factor (95%CI: 1–41).

Table 2. Participant's biological characteristics.

	Fish consumption				Overall	p
	No.	<150 g/wk	150–300 g/wk	>300 g/wk		
% of participants	10%	29%	42%	19%	–	–
Systolic blood pressure (mmHg)	141±17	138±16	139±16	133±11*	137±16	0.03
Diastolic blood pressure (mmHg)	80±9	79±9	80±9	80±8	80±9	0.89
Total cholesterol (mg/dl)	241±56	220±43**	228±47*	226±48*	228±43	0.001
HDL cholesterol (mg/dl)	54±16	54±11	55±11	59±10	57±11	0.13
LDL cholesterol (mg/dl)	158±38	136±35	140±41	140±37	141±38	0.15
Triglycerides (mg/dl)	158±84	140±51*	139±45*	126±31**	136±60	0.01
Blood glucose (mg/dl)	154±84	111±37**	116±35**	110±29**	114±37	0.002
Obese (%)	33	41*	39*	55**	42	0.02
No. of CVD risk factors (0–4)***	2.1	2.1	1.7	1.6	1.8	0.001

No gender differences were observed.
* $p<0.05$ and ** $p<0.01$ (Tukey corrected) for the differences between fish consumption groups vs. no consumption. Probability values derived from the ANOVA or the chi-squared tests.
*** Factors added in this variable were: hypertension, diabetes, hypercholesterolemia, and obesity.

Table 3. Results from multiple linear regression analyses that evaluated the association between levels of biological markers and fish consumption (in g/wk) after adjusting for various covariates*.

	Standardized Beta coefficient	Adjusted R^2 with fish-intake variable in the model	Adjusted R^2 without fish-intake variable in the model	*p*
Model 1: Systolic blood pressure (mmHg)	–0.09	2.9%	1.5%	0.05
Model 2: Diastolic blood pressure (mmHg)	+0.03	0.7%	0.6%	0.58
Model 3: Total cholesterol (mg/dl)	–0.02	4.6%	4.1%	0.06
Model 4: HDL cholesterol (mg/dl)	+0.09	7.7%	5.9%	0.07
Model 5: LDL cholesterol (mg/dl)	–0.06	5.7%	5.1%	0.25
Model 6: Triglycerides (mg/dl)	–0.10	5.5%	3.1%	0.01
Model 7: Blood glucose (mg/dl)	–0.16	6.9%	4.1%	0.008

** *p* values derived from multiple linear regression models.
* The regression models evaluated the association of fish consumption (in g/week) on biological markers (dependent) after adjusting for age in years, sex, smoking (y/n), physical activity status (sedentary, light, moderate, and vigorous), body mass index in kg/m^2, the use of medication (y/n), and the average weekly frequency of the food groups included in the FFQ.

Discussion

In this study we investigated the association between fish intake and the most common serum markers of cardiovascular disease risk in a sample of elderly men and women living on Mediterranean islands. This is one of few studies focusing on elderly individuals, in whom disease burden may be high and dietary habits may have less influence. We revealed that long-term increased fish consumption is related to a significant reduction in systolic blood pressure, total serum cholesterol, triglyceride, and fasting blood glucose levels, while no effect of fish intake was observed on diastolic blood pressure, HDL, and LDL cholesterol levels. Moreover, people in the higher fish intake groups were more physically active, but also more likely to be smokers and obese (Tables 1, 2). These associations may be explained by the fact that individuals that are close to a healthy dietary pattern are also close to a healthy lifestyle that includes physical activity [17]; however, this healthy lifestyle also includes abstinence from smoking, which does not seem to hold in the present study. This could be explained by the increased smoking frequency that people in Greece have shown during the last decades, irrespective of other lifestyle habits [18,19]. Finally, the fact that increased fish intake was associated with a higher prevalence of obesity may be explained by other dietary habits of the participants presented above (i.e. increased olive oil use and reduced fruit intake);

however, since no data about energy or nutrient intake were available in this study, it is hard to draw any conclusions.

The effects of fish, fish oil, and n-3 fatty acids consumption on biomarkers of cardiovascular disease risk has been extensively examined in middle-aged adults [3–12,20] and the majority of studies have demonstrated their beneficial effect on reducing triglyceride and blood pressure levels. In particular, a recently published review, after performing a meta-analysis on 21 trials evaluating fish oil consumption and lipid profile, revealed that fish oil intake resulted in a 27 mg/dl reduction in triglycerides, while no significant association was detected between fish oil intake and total serum cholesterol levels [21]. Moreover, a meta-regression analysis revealed that high intake of fish oil is associated with lower blood pressure, especially in hypertensive subjects [22]. The benefits of fish and n-3 fatty acids consumption on triglyceride levels could be attributed to a decrease in the hepatic production of triglyceride in the liver and on an increment in fractional clearance rates [23,24]. Moreover, it has been reported that n-3 fatty acids increase the conversion rate of VLDL to LDL, similarly to fibrate drugs [25]. The hypotensive effect of fish may be explained by the ability of fish oil and n-3 fat acid to inhibit hemostasis and platelet aggregation [26]. Furthermore, it is possible for fish to stimulate the synthesis of prostacyclin (a vasolidator) and inhibit thromboxane (a vasoconstrictor).

Regarding the association between fish consumption and fasting blood glucose, the findings of previous studies are inconsistent. A recent meta-analysis of 26 trials on subjects with type 1 or type 2 diabetes mellitus reported that fasting blood glucose levels rose slightly in the latter group with fish oil consumption [27], while another review including 15 studies (seven of which included only subjects with diabetes and the remaining patients with dyslipidemia or cardiovascular disease) reported an insignificant increase in fasting blood glucose with fish oil consumption [6]. In an ecological study of 41 countries, the investigators observed that high fish and seafood intake may reduce the risk of type 2 diabetes in populations with a high prevalence of obesity [28]. We have also found that fasting glucose in elderly people is reduced with increased fish consumption. This finding is novel for this age-group, and independent of various potential confounders. However, the cross-sectional design of the present study does not allow for further pathophysiological explanations, since the observed relationship may be confounded by several other unknown or unmeasured factors; therefore, further studies are needed to confirm or refute the aforementioned observation.

Before concluding that a high consumption of fish is beneficial for elderly people and recommending this, we should highlight briefly the risks involved with high fish consumption. People should be aware that fish and seafood are a major source of human exposure to methylmercury, polychlorinated biphenyls (PCBs), dioxins, and other environmental contaminants. However, for elder people, and especially for men, the benefits of fish consumption far outweigh the risks, particularly if they follow the guidelines established by the FDA and the Environmental Protection Agency [29,30].

Limitations

This study is cross-sectional and, consequently, has the potential of recall biases, particularly in the assessment of dietary habits. Although important associations were assessed, the design of this study prohibits causal interpretations.

Conclusions

In this study we revealed the beneficial effect of fish consumption on several biomarkers of cardiovascular disease risk, i.e. triglyceride, total serum cholesterol, systolic blood pressure, and fasting glucose levels, among elderly people. Our results are in agreement with those of previous studies conducted in other, middle-aged populations, with the exception of our findings relating to fasting glucose, of which previous data are lacking, especially in the elderly. Therefore we may conclude that fish consumption could be protectively associated with cardiovascular disease through the reduction of established cardiovascular risk factors among elderly people.

Acknowledgements

The authors are particularly grateful to the men and women from Cyprus, Mitilini, and Samothraki islands who participated in and collaborated in this research. The authors also wish to express their gratitude to Dr. Michael Tornaritis, Ioanna Vlachou, Kyriaki Gelastopulou, Natassa Papairakleous, Stallo Papoutsou, and Anna Polystipioti for their substantial assistance in the field investigation. The MEDIS study is funded by research grants from the Hellenic Heart Foundation.

References:

1. Keys A, Menotti A, Karvonen MJ et al: The diet and 15-year death rate in the Seven Countries Study. Am J Epidemiol, 1986; 124: 903–15
2. Breslow JL: n-3 fatty acids and cardiovascular disease. Am J Clin Nutr, 2006; 83: 1477S–82S
3. Kris-Etherton P, Harris W, Appel L for the Nutrition Committee: Fish Consumption, Fish Oil, n-3 Fatty Acids, and Cardiovascular Disease. Circulation, 2002; 106: 2747–57
4. Hu FB, Cho E, Rexrode KM et al: Fish and long-chain omega-3 fatty acid intake and risk of coronary heart disease and total mortality in diabetic women. Circulation, 2003; 107: 1852–57
5. Gillum RF, Mussolino M, Madans JH: The relation between fish consumption, death from all causes, and incidence of coronary heart disease: the NHANES I Epidemiologic Follow-up Study. J Clin Epidemiol, 2000; 53: 237–44
6. Balk EM, Lichtenstein AH, Chung M et al: Effects of omega-3 fatty acids on serum markers of cardiovascular disease risk: a systematic review. Atherosclerosis, 2006; 189: 19–30
7. Psota TL, Gebauer SK, Kris-Etherton P: Dietary omega-3 fatty acid intake and cardiovascular risk. Am J Cardiol, 2006; 98: 3i–18i
8. Jarvinen R, Knekt P, Rissanen H, Reunanen A: Intake of fish and long-chain n-3 fatty acids and the risk of coronary heart mortality in men and women. Br J Nutr, 2006; 95: 824–29
9. Panagiotakos DB, Pitsavos C, Zampelas A et al: The relationship between fish consumption and the risk of developing acute coronary syndromes among smokers: the CARDIO2000 case-control study. Nutr Metab Cardiovasc Dis, 2005; 15: 402–9
10. Harris WS: n-3 Fatty acids and serum lipoproteins: human studies. Am J Clin Nutr, 1997; 65: 1645S–54S
11. Morris MC, Sacks F, Rosner B: Does fish oil lower blood pressure? A meta-analysis of controlled trials. Circulation, 1993; 88: 523–33
12. Appel LJ, Miller ER III, Seidler AJ et al: Does supplementation of diet with 'fish oil' reduce blood pressure? A meta-analysis of controlled clinical trials. Arch Intern Med, 1993; 153: 1429–38
13. Christensen JH, Korup E, Aaroe J et al: Fish consumption, n-3 fatty acids in cell membranes, and heart rate variability in survivors of myocardial infarction with left ventricular dysfunction. Am J Cardiol, 1997; 79: 1670–73

14. Simopoulos AP: Omega-3 Fatty Acids in Inflammation and Autoimmune Diseases. J Am Coll Nutr, 2002; 21: 495–505
15. Zampelas A, Panagiotakos DB, Pitsavos C et al: Fish consumption among healthy adults is associated with decreased levels of inflammatory markers related to cardiovascular disease: the ATTICA study. J Am Coll Cardiol, 2005; 46: 120–24
16. Craig CL, Marshall AL, Sjostrom M et al: International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc, 2003; 35: 1381–95
17. Wannamethee SG, Shaper AG, Whincup PH: Modifiable lifestyle factors and the metabolic syndrome in older men: Effects of lifestyle changes. J Am Geriatr Soc, 2006; 54: 1909–14
18. Sichletidis LT, Chloros D, Tsiotsios I et al: High prevalence of smoking in Northern Greece. Prim Care Respir J, 2006; 15: 92–97
19. Smoking in Europe; facts and figures. Am J Health Promot, 1995; 9: 348–49
20. Geleijnse JM, Giltay EJ, Grobbee DE et al: Blood pressure response to fish oil supplementation: metaregression analysis of randomized trials. J Hypertens, 20: 1493–99
21. Harris WS, Connor WE, Illingworth DR et al: Effects of fish oil on VLDL triglyceride kinetics in humans. J Lipid Res, 1990; 31: 1549–58
22. Park Y, Harris WS: Omega-3 fatty acid supplementation accelerates chylomicron triglyceride clearance. J Lipid Res, 2003; 441: 455–63
23. Depres JP, Lemieux I, Robins SJ: Role of fibric acid derivatives in the management of risk factors for coronary heart disease. Drugs, 2004; 64: 2177–98
24. Vericel E, Calzada C, Chapuy P, Lagarde M: The influence of low intake of n-3 fatty acids on platelets in elderly people. Atherosclerosis, 1999; 147: 187–92
25. JohansenO, Seljeflot I, Hostmark AT, Amesen H: The effect of supplementation with omega-3 fatty acids on soluble markers of endothelial function in patients with coronary heart disease. Arterioscler Thromb Vasc Biol, 1999; 19: 1681–86
26. Engler MB, Engler MM: Docosahexaenoic acid-induced vasorelaxation in hypertensive rats: mechanisms of action. Biol Res Nurs, 2000; 2: 85–95
27. Friedberg CE, Janssen MJ, Heine RJ et al: Fish oil and glycemic control in diabetes: a meta-analysis. Diabetes Care, 1998; 21: 494–500
28. Nkondjock A, Receveur O: Fish-seafood consumption, obesity, and risk of type 2 diabetes: an ecological study. Diabetes Metab, 2003; 29: 635–42
29. US Environmental Protection Agency: Fish Advisories web page. Available at: *http://www.epa.gov/waterscience/fish/* Accessed October 3, 2002
30. US Food and Drug Administration, Center for Food Safety and Applied Nutrition, Office of Seafood. Mercury Levels in Seafood Species. May 2001. Available at: *http://www.cfsan.fda.gov/~frf/sea-mehg.html*. Accessed October 3, 2002