

function underpins all NHS purchaser and provider activity" and that this requires "an assessment of the health needs of any given population to inform decision-making on aims and priorities so as to achieve appropriate and effective services leading to improved health and value for money."⁶ The most recent guidance from the former NHS Management Executive exhorts health authorities to purchase procedures specifically in relation to their effectiveness in conditions for which clearcut clinical guidelines are merited.⁷ Of course, patients on waiting lists have had their needs assessed by individual clinicians. Yet most health authorities—and to an even greater extent general practice fundholders—do not consider the needs of people on waiting lists as requiring further assessment. They are happy to accept the waiting list as reflecting an aggregate of unquestioned clinical decisions, which may be influenced by factors such as the visibility of waiting lists and the perverse incentives built into the NHS market rather than by evidence of effectiveness. The driving force behind this acceptance is the patient's charter.

The assumption that waiting lists reflect need (that is, ability to benefit) may be tested by considering the indications for various procedures. Increasingly, systematic reviews and techniques for identifying consensus have been used to set criteria of appropriateness for clinical procedures. There seems, however, to have been little interest in using this work to tackle waiting lists. The appropriateness of some procedures may be questioned regardless of the clinical indications (for example, dilatation and curettage in women under 40⁸), but for most procedures for which there is a waiting list, the situation is far more complex. The intended procedure, the precise indication for that procedure (the condition and its severity), and any comorbidity must be assessed. These factors could be used to generate an appropriateness rating.⁹

For example, in coronary artery bypass grafting the procedure has been judged inappropriate in patients with single vessel disease, moderate or severe myocardial ischaemia, and mild left ventricular dysfunction.¹⁰ Yet such patients continue to be operated on. Furthermore, a recent study of a waiting list for tonsillectomy showed that nearly one third of patients had waited more than one year.¹¹ The natural course of recurrent throat infection, the main indication for tonsillectomy, may be one of improvement¹²; a prospective study to determine the morbidity caused by a delay in tonsil surgery found that a fifth of patients grew out of their

condition and were spared surgery.¹³ This raises the possibility that, in certain circumstances, need may fall with longer waits.

Maximum waiting periods for procedures of accepted effectiveness have some appeal, although surgery may be inappropriate when judged against local guidelines or when resources are constrained.¹⁴ Existing criteria for appropriateness may require refinement,¹⁵ but they offer a reasonable tool, possibly with local modification, for examining waiting lists. The next stage is for commissioners to agree with general practitioners and providers the criteria for appropriateness for entry to and clearance from a waiting list. Such an approach should be widely debated in local community settings. Furthermore, the criteria for appropriateness should be linked with a commitment to audit. This would allow the standards given in the patient's charter to be achieved on the basis of need rather than political whim. For all those concerned with appropriateness, the time spent on waiting lists allows an opportunity to assess the costs and benefits of intended treatment.

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- 1 Department of Health. *Statistical Bulletin 1995-1. Elective admissions and patients waiting: England*. London: Government Statistical Service, 1995.
- 2 Labour Party. *Health 2000: the health and wealth of the nation in the 21st century*. London: Labour Party, 1994.
- 3 Wilcock GK. The prevalence of osteoarthritis of the hip requiring total hip replacement in the elderly. *Int J Epidemiol* 1979;8:247-50.
- 4 NHS Executive. *Clinical priority on waiting lists*. Leeds: NHSE, 1994. (EL(94)19.)
- 5 NHS Management Executive. *Waiting time initiative 1993-1994*. Leeds: NHSME, 1993. (EL(93)23.)
- 6 NHS Management Executive. *Public health: responsibilities of the NHS and the roles of others*. Leeds: NHSME, 1993. (HSG(93)56.)
- 7 NHS Management Executive. *Improving clinical effectiveness*. Leeds: NHSME, 1993. (EL(93)115.)
- 8 Coulter A, Klassen A, MacKenzie IZ, McPherson K. Diagnostic dilatation and curettage: is it used appropriately? *BMJ* 1993;306:236-9.
- 9 Brook RH. Appropriateness: the next frontier. *BMJ* 1994;308:218-9.
- 10 American College of Cardiology and American Heart Association Task Force. Guidelines and indications for coronary artery bypass graft surgery. *JACC* 1991;17:543-89.
- 11 Hemingway H. *Needs assessment of a resident based tonsillectomy waiting list*. London: City and Hackney Health Authority, 1992.
- 12 Paradise JL, Bluestone CD, Bachman RZ, Colborn DK, Bernard BS, Taylor FH, et al. Efficacy of tonsillectomy for recurrent throat infection in severely affected children: results of parallel randomised and non-randomised trials. *N Engl J Med* 1984;310:674-83.
- 13 Freeland AP, Curley JW. The consequences of delay in tonsil surgery. *Otolaryngol Clin North Am* 1987;20:405-8.
- 14 Gray D, Hampton JR, Bernstein SJ, Kosecoff J, Brook RH. Audit of coronary angiography and bypass surgery. *Lancet* 1990;335:1317-20.
- 15 Hicks N. Some observations on attempts to measure appropriateness of care. *BMJ* 1994;309:730-3.

Fish oils and cardiovascular disease

Beneficial effects on lipids and the haemostatic system

Oily fish contains large quantities of the long chain n-3 (ω -3) polyunsaturated fatty acids (eicosapentaenoic acid (C20:5) and docosahexaenoic acid (C22:6)). Low rates of coronary heart disease in various populations with high intakes of fish suggested health preserving effects of these fatty acids. For example, mortality from coronary heart disease was found to be low among Greenland Inuits who ate large amounts of fish and whale meat (400-500 g/day, 14 g n-3 fatty acids/day)¹ and in Japanese fish eaters.² In the Netherlands 30 g of fish daily was associated with 50% fewer deaths from coronary heart disease.³ In the multiple risk factor intervention trial cardiovascular mortality was inversely proportional to the intake of n-3 fatty acids over the 10.5 years of follow up.⁴ Not

all investigators, however, have confirmed these findings.^{5,6}

Suggested mechanisms for this cardioprotective effect focused first on serum lipids.⁷ In healthy subjects increased consumption of long chain n-3 fatty acids is associated with falls in serum concentrations of triglycerides and very low density lipoprotein^{8,9}; cholesterol concentration is unchanged except at high doses (24 g/day), when concentrations of both low density lipoprotein cholesterol and apoprotein B fall. Postprandial lipoprotein concentrations also fall.¹⁰ Concentrations of high density lipoprotein cholesterol (principally high density lipoprotein-2 cholesterol) increase with moderate supplementation with fish oil. In the various dyslipidaemias serum triglyceride concentrations tend to fall.

Although no consistent changes have been observed in lipoprotein (a) concentrations,¹¹ low density lipoprotein cholesterol concentrations may increase in diabetic subjects receiving fish oil.^{12,13} These effects on lipids did not seem adequately to explain the cardioprotective effect of fish oil; the effect on the haemostatic system has also been examined.

N-3 polyunsaturated fatty acids are rapidly incorporated into platelets, where they compete with arachidonic acid for the 2-acyl position of membrane phospholipid and as substrate for the cyclo-oxygenase enzyme complex that modulates the production of prothrombotic eicosanoids.¹⁴ Inuits have a lower platelet count, less platelet aggregation, and a longer bleeding time than Danish controls¹⁵; urinary concentrations of prostacyclin metabolites are higher and of thromboxane metabolites lower than those in controls.¹⁶ Similar effects have been found after an increased dietary intake of fish or fish oil supplements.¹⁷ The reported effects of dietary fish oil on coagulation and fibrinolysis vary.¹⁸ No consistent effects on the prothrombin time, clotting factors, or anticoagulant proteins have been reported. The fibrinogen concentration fell in some^{19,20} but not all studies.²¹ Red cell deformability and blood viscosity are increased even at a low dose,^{22,23} but fish oil may inhibit fibrinolysis in normal subjects and patients with cardiac ischaemia.^{18,24,25}

Experimentally, n-3 polyunsaturated fatty acids reduce adhesion and migration of monocytes, which is important in atherogenesis. Concentrations of interleukin-1, tumour necrosis factor, platelet activating factor, and platelet derived growth factor fall, as does the production of free radicals and endothelial production of fibroblast growth factor. Dietary n-3 polyunsaturated fatty acids enhance production of endothelial derived relaxing factor, which is reduced in atherosclerotic vessels.^{5,6} Improved endothelial function is suggested by the observation that vasodilatation in response to acetylcholine intra-arterially was restored in coronary arteries of patients who had received heart transplants and took fish oil supplements for three weeks, whereas vasoconstriction still occurred in control subjects.²⁶ Supplementation with fish oil inhibits atherogenesis in animals.^{5,6}

In a study of 2033 male survivors of myocardial infarction fatty fish (300 g/week, or 0.35g n-3 polyunsaturated fatty acids daily) reduced overall mortality by 29% and mortality from coronary heart disease by a third. A reduced intake of saturated fat with a proportional increased intake of polyunsaturated fat and a high fibre diet were ineffective.²⁷ Benefits occurred early in the trial, suggesting non-atherosclerotic mechanism(s). Fibrinogen concentration and plasma viscosity were unchanged.²⁸ An antiarrhythmic effect, which is observed in animals, is possible.²⁹

Meta-analyses of trials of supplementation with fish oil to prevent restenosis after coronary angioplasty have suggested a small benefit of fish oil (odds ratio 0.71, 95% confidence interval 0.54 to 0.94).^{30,31} Paradoxically, a study of restenosis that used a high dose of n-3 fatty acids produced a negative result.³² High doses may be detrimental through enhanced peroxidation of lipids; perhaps antioxidants such as vitamin E should also be given.³¹

A meta-analysis of placebo controlled trials in 1356 subjects has shown modest falls of blood pressure with n-3 polyunsaturated fatty acids³³; systolic blood pressure fell by 3.4 mmHg and diastolic pressure fell by 2.0 mmHg. A further meta-analysis gave comparable results.³⁴ Most of the individual trials used amounts of fish oil that patients may find hard to sustain (six to 10 capsules or two 100 g helpings of fish). Only two trials lasted longer than three months.³⁴

Fish oil therefore affects lipid and lipoprotein metabolism and interactions between platelets and the vessel wall. Therapeutic possibilities exist after myocardial infarction, in

restenosis after angioplasty, and in hypertension. Despite fish oil's effect on the platelet count and aggregation the trials do not provide convincing evidence of increased bleeding; although deaths from cerebrovascular disease are more common among Inuits, they are less common in Japanese people who eat fish than in other Japanese people.⁵ More studies are needed in diseases related to atherosclerosis.

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- Dyerberg J. Linolenate-derived polyunsaturated fatty acids and prevention of atherosclerosis. *Nutr Rev* 1986;44:125-8.
- Kagawa Y, Nishizawa M, Suzuki M, Miyatake T, Hamamoto T, Goto K, et al. Eicosapolyenoic acids of serum lipids of Japanese islanders with low incidence of cardiovascular diseases. *J Nutr Sci Vitaminol (Tokyo)* 1982;28:441-53.
- Kromhout D, Bosschieter EB, de Lezenne Coulander C. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. *N Engl J Med* 1985;312:1205-9.
- Dolecek TA. Epidemiological evidence of relationships between dietary polyunsaturated fatty acids and mortality in the multiple risk factor intervention trial. *Proc Soc Exp Biol Med* 1992;200:177-82.
- Goodnight SH, Cairns JA, Fisher M, Fitzgerald GA. Assessment of the therapeutic use of n-3 fatty acids in vascular disease and thrombosis. *Chest* 1992;102:374-84S.
- Israel DH, Gorlin R. Fish oils in the prevention of atherosclerosis. *J Am Coll Cardiol* 1992;19:174-85.
- Bang HO, Dyerberg J, Nielsen AB. Plasma lipid and lipoprotein pattern in Greenlandic west-coast Eskimos. *Lancet* 1971;ii:1143-6.
- Harris WS. Fish oils and plasma lipid and lipoprotein metabolism in humans: a critical review. *J Lipid Res* 1989;30:785-807.
- Sanders TAB, Hinds A, Pereira CC. Influence of n-3 fatty acids on blood lipids in normal subjects. *J Intern Med* 1989;225(suppl 1):99-104.
- Weintraub MS, Zechner R, Brown A, Eisenberg S, Breslow JL. Dietary polyunsaturated fats of the W-6 and W-3 series reduce postprandial lipoprotein levels. Chronic and acute effects of fat saturation on postprandial lipoprotein metabolism. *J Clin Invest* 1988;82:1884-93.
- Schmidt EB. n-3 polyunsaturated fatty acids and ischaemic heart disease. *Current Opinions in Lipidology* 1993;4:27-33.
- Haines AP, Sanders TAB, Imeson JD, Mahler RF, Martin J, Mistry M, et al. Effects of a fish oil supplement on platelet function, haemostatic variables and albuminuria in insulin-dependent diabetics. *Thromb Res* 1986;43:643-55.
- Schectman G, Kaul S, Kissebah AH. Heterogeneity of low density lipoprotein responses to fish-oil supplementation in hypertriglyceridemic subjects. *Atherosclerosis* 1989;9:345-54.
- Leaf A, Weber PC. Cardiovascular effects on n-3 fatty acids. *N Engl J Med* 1988;322:697-8.
- Dyerberg J, Bang HO. Haemostatic function and platelet polyunsaturated fatty acids in Eskimos. *Lancet* 1979;ii:433-5.
- Fischer S, Weber PC, Dyerberg J. The prostacyclin/thromboxane balance is favourably shifted in Greenland Eskimos. *Prostaglandins* 1986;32:235-41.
- Kristensen SD, Schmidt EB, Dyerberg J. Dietary supplementation with n-3 polyunsaturated fatty acids and human platelet function: a review with particular emphasis on implications for cardiovascular disease. *J Intern Med* 1989;225(suppl 1):141-50.
- Goodnight SH. Fish oil: effects on atherogenesis and thrombosis. *Current Opinions in Lipidology* 1990;1:334-40.
- Hostmark AT, Bjerkedal T, Kierulf P, Flaten H, Ulshagen K. Fish oil and plasma fibrinogen. *BMJ* 1988;297:180-1.
- Radack K, Deck C, Huster G. Dietary supplementation with low-dose fish oils lowers fibrinogen levels: a randomized, double-blind controlled study. *Ann Intern Med* 1989;111:757-8.
- Brown AJ, Roberts DCK. Fish and fish oil intake: effect on haematological variables related to cardiovascular disease. *Thromb Res* 1991;64:169-78.
- Cartwright IJ, Pockley AG, Galloway JH, Greaves M, Preston FE. The effects of dietary omega-3 polyunsaturated fatty acids on erythrocyte membrane phospholipids, erythrocyte deformability and blood viscosity in healthy volunteers. *Atherosclerosis* 1985;55:267-81.
- Ernst E. Effects of n-3 fatty acids on blood rheology. *J Intern Med* 1989;225(suppl 1):129-32.
- Schmidt EB, Varming K, Ernst E, Madsen P, Dyerberg J. Dose-response studies on the effect of n-3 polyunsaturated fatty acids on lipids and haemostasis. *Thromb Haemost* 1990;63:1-5.
- Schmidt EB, Kristensen SD, Dyerberg J. The effect of fish oil on lipids, coagulation and fibrinolysis in patients with angina pectoris. *Artery* 1988;15:316-29.
- Fleischhauer FJ, Yan W-D, Fischell TA. Fish oil improves endothelium-dependent coronary vasodilatation in heart transplant recipients. *J Am Coll Cardiol* 1993;21:982-9.
- Burr ML, Fehily AM, Gilbert JF, Rogers S, Holliday RM, Sweetnam PM, et al. Effects of changes in fat, fish and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* 1989;ii:757-61.
- Burr ML, Holliday RM, Fehily AM, Whitehead PJ. Haematological prognostic indices after myocardial infarction: evidence from the diet and reinfarction trial (DART). *Eur Heart J* 1992;13:166-70.
- Charnock JS. Antiarrhythmic effects of fish oils. *World Rev Nutr Diet* 1991;66:278-91.
- Gapinski JP, VanRuiswyk JV, Heudebert GR, Schectman GS. Preventing restenosis with fish oils following coronary angioplasty. A meta-analysis. *Arch Intern Med* 1993;153:1595-601.
- O'Connor GT, Malenka DJ, Olmstead EM, Johnson PS, Hennekens CH. A meta-analysis of randomized trials of fish oil in prevention of restenosis following coronary angioplasty. *Am J Prev Med* 1992;8:186-92.
- Reis GJ, Boucher TM, Sipperly ME, Silverman DI, McCabe CH, Baim DS, et al. Randomised trial of fish oil for prevention of restenosis after coronary angioplasty. *Lancet* 1989;ii:177-81.
- Morris MC, Sacks F, Rosner B. Does fish oil lower blood pressure? A meta-analysis of controlled trials. *Circulation* 1993;88:523-33.
- Appel LJ, Miller ER, Seidler AJ, Whelton PK. Does supplementation of diet with "fish oil" reduce blood pressure? A meta-analysis of controlled clinical trials. *Arch Intern Med* 1993;153:1429-38.