Much of the traditional focus on the modification of circulating lipids/lipoprotein factors for the primary prevention and secondary management of cardiovascular disease (CVD) has emphasized a reduction in total cholesterol levels and LDL-cholesterol levels because of the established relationship between these latter two risk parameters and serious CVD end-points. More recently, evidence has come forth that fasting plasma (serum) triglycerides are important and independent risk factors for coronary heart disease (CHD). For example, a progressive increase in the incidence of major coronary events over an eight year period in men was associated with progressively increased levels of fasting triglyceride levels over eight years of follow-up (see Figure 1).

![Figure 1: Relation between fasting triglyceride levels and major coronary events in men](image)

Very recently, a prospective study based on a population with prevalent metabolic syndrome (as seen with increasing occurrence in our societies today) supported plasma triglyceride as an independent predictor of cardiovascular disease (see Figure 2).

![Figure 2:](image)

The protective effect of higher circulating levels of HDL-cholesterol has long been recognized. More recently, the ratio of fasting triglyceride: HDL-cholesterol levels has been recognized as potentially a stronger predictor of myocardial infarction than even the total cholesterol: HDL-cholesterol or LDL-cholesterol: HDL-cholesterol ratios. A pattern of high circulating triglyceride levels together with low HDL-cholesterol concentrations has been involved in a more aggressive transition from atheroma to atherothrombosis. Very recently, the ratio of triglyceride: HDL-cholesterol has been found to be closely correlated with the small, dense LDL particles (which are regarded as highly atherogenic). Higher ratios of triglyceride: HDL-cholesterol are inversely related to the LDL size and positively with the particle concentration. Thus, lowering circulating triglyceride levels as well as the triglyceride: HDL-cholesterol ratio is becoming of increased importance in reducing the risk of CVD and hard end-points (non-fatal and fatal myocardial infarctions). Since lowering of fasting triglyceride levels often leads to a moderate reduction (rise) in the calculated LDL-cholesterol concentrations (because of the use of the Friedwald equation for indirectly assessing LDL-cholesterol levels via calculations) and the recognition that cholesterol associated with lower density lipoprotein particles in addition to LDL-cholesterol represent a risk factor for CHD, the non-HDL-cholesterol levels are of considerable interest in risk assessment. The non-HDL-cholesterol levels appear to be at least as useful as LDL-cholesterol measurements for risk assessment and, for some populations and sectors, may be of greater predictability.

The ability of supplementation with fish oil and derived concentrates containing DHA/EPA omega-3 fatty acids have long been recognized. Appropriate review articles on this topic are available (including the reviews by Harris and Balk et al. as provided below). Figure 3 below gives the average expected percentage reduction in fasting triglyceride levels as determined from the review of various published trials by Harris. The expected reductions for each gram of DHA/EPA (combined) as consumed daily over a period of at least a few weeks (in amounts ranging from 1gm up to 4 gm DHA/EPA daily) are given in relation to the fasting baseline serum (plasma) triglyceride levels in the target populations. It is apparent, that the reductions in fasting triglyceride levels range from 20 and up to approximately 35% for dosages of 3-4 gm of DHA/EPA (combined) per day.
Figure 3: Average expected % change in fasting triglyceride (TG) levels based on baseline triglyceride status in various cross-over and parallel studies.

Figure 4 indicates that little or no change (plus or minus 1% overall) in the non-HDL-cholesterol levels is realized per gram of DHA/EPA (omega-3) intake daily based on the various cross-over and parallel studies reviewed by Harris.

Figure 5 indicates that a moderate elevation in HDL-cholesterol levels per gram of DHA/EPA (combined) consumed daily can be expected ranging from approximately 1-3% overall depending upon the baseline triglyceride levels. Studies on the ability of DHA/EPA supplementation to lower the ratio of circulating triglyceride: HDL-cholesterol as well as the fasting triglyceride levels have begun to emerge in the recent literature. For example, Stark et al. (see reference below) reported a 28% lowering of the overall ratio of serum triglyceride:HDL-cholesterol ratio with supplementation of post-menopausal women at the level of 4 gm/day of DHA/EPA (combined) over a 28 day period. Based on the review by Harris wherein the effect of DHA/EPA (fish oil and derived concentrates) on fasting triglyceride and HDL-cholesterol levels had been provided from various clinical trials, the expected percentage reductions in the fasting triglyceride:HDL-cholesterol ratios based on segmented baseline triglyceride levels have been calculated and provided in Figure 6. The progressive increase in the reduction of triglyceride:HDL-cholesterol ratios (increasing per gram of consumed DHA/EPA) provided overall reductions ranging from approximately 25 -40% overall with daily dosages of 3-4 gm /day over a period of a few weeks in duration.

Figure 5: Average expected % change in high density lipoprotein (HDL)-cholesterol levels based on baseline triglyceride status in various cross-over and parallel studies.

Figure 6: Average expected % change in the fasting TG:HDL-cholesterol ratio based on baseline triglyceride status in various cross-over and parallel studies.


