**Table E-2. Design Details Comparative Studies**

| **Author, year, PMID, country, trial name** | **Study Design, study start date** | **Funding source/Conflict of interest** | **Duration of Intervention/ duration of washout period** | **Eligibility Criteria** | **Study Population** | **Registration (prospective/retrospective)\*** |
| --- | --- | --- | --- | --- | --- | --- |
| Baxheinrich, 2012, 22894911, Germany  | Trial: Randomized Parallel, 2010 (approx.) | Industry funded/No conflict of interest (explicitly stated)  | 6 months | To be enrolled in the study, subjects had to meet the diagnosis criteria of the metabolic syndrome according to the definition of the International Diabetes Federation (Table 1). Exclusion criteria were CVD, severe illnesses such as renal failure or liver disease, food allergy or intolerance, pregnancy or lactation, smoking, alcohol abuse and insulin therapy or severe diabetic complications in case of diagnosed type 2 diabetes mellitus. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Diabetes and/or metabolic syndrome\*  |  |
| DRKS00006232 (Baxheinrich, 2012, 22894911) | Trial: Randomized Parallel, 2008 | Industry funded/ Conflict of interest stated | 6 months | Inclusion Criteria: 18-70 years old, male and female. Participants who had the following traits of metabolic syndrome were included: central obesity (waist circumference ≥94 cm for men and ≥80 cm for women) plus two of the following criteria (i) fasting serum concentrations of triacylglycerols ≥1.7 mmol/L, (ii) reduced serum HDL cholesterol (<1.03 mmol/L in men; <1.29 mmol/L in women), (iii) elevated blood pressure (systolic ≥130 mmHg; diastolic ≥85 mmHg), (iv) fasting plasma glucose ≥6.5 mmol/LExclusion Criteria:smoking; insulin-dependent diabetes mellitus; liver, gastrointestinal, or inﬂammatory diseases; a history of cardiovascular events; use of anti-obesity medications or antiinﬂammatory drugs; cancer; pregnancy or breast-feeding; alcohol abuse | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): elevated blood pressure (systolic ≥130 mmHg; diastolic ≥85 mmHg), triacylglycerols ≥1.7 mmol/L; reduced serum HDL cholesterol (<1.03 mmol/L in men; <1.29 mmol/L in women),  | Retrospective |
| Bosch, 2012, 22686415, Canada, ORIGIN | Trial: Randomized Factorial Design, 2003 | Industry funded | 2 years | At least 50 years old; a diagnosis of diabetes with receipt of no more than one oral glucose-lowering drug, impaired glucose tolerance (plasma glucose level at 2 hours, =7.8 mM [140 mg per deciliter] and <11.1 mM [200 mg per deciliter] after a 75-g oral glucose load), or impaired fasting glucose (range, =6.1 mM [110 mg per deciliter] to <7.0 mM [126 mg per deciliter]); a history of myocardial infarction, stroke, or revascularization; angina with documented ischemia; a ratio of urinary albumin to creatinine of more than 30 mg per gram; left ventricular hypertrophy; 50% or more stenosis of a coronary, carotid, or lower-limb artery on angiography; or an ankle brachial index of less than 0.9. Participants were excluded if they were unwilling to discontinue use of a nonstudy preparation of n 3 fatty acids, had a locally measured glycated hemoglobin level of 9% or more, had undergone coronary-artery bypass grafting within the previous 4 years with no intervening cardiovascular event, had severe heart failure, or had a cancer that might affect survival. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Diabetes and/or metabolic syndrome\*; Hypertension; Cardiac disease; Cerebrovascular disease; Peripheral vascular disease; Arrhythmia  |  |
| NCT00069784 (Bosch, 2012, 22686415) | Trial: Randomized Factorial Design, 2003 | Industry funded/Conflict of interest stated (principal Investigators are NOT employed by the organization sponsoring the study. | 6.2 years | Ages Eligible for Study: 50 Years and older. Genders Eligible for Study: Both. Inclusion criteria:Individuals with IFG and/or IGT, or early diabetes, as defined below.Glucose tolerance status was determined by a 75 g oral glucose tolerance test (OGTT) that was performed fasting (ie, no consumption of food or beverage other than water for at least 8 hours) at the time of screening for all candidates who were not known to have diabetes. The qualifying OGTT could be obtained up to 4 weeks prior to screening provided that anti-diabetic therapy (if any) remained unchanged between the qualifying OGTT and the screening visit. Two plasma glucose values were drawn during the OGTT - a fasting value (FPG) and a value drawn two hours after the 75 g oral glucose load was administered (postprandial plasma glucose [PPG]).Impaired glucose tolerance (IGT), defined as a PPG value ≥140 and <200 mg/dL (ie, ≥7.8 and <11.1 mmol/L), with a FPG <126 mg/dL (7.0 mmol/L). OR - Impaired fasting glucose (IFG), defined as an FPG ≥110 and <126 mg/dL (≥6.1 and <7 mmol/L), without diabetes mellitus (PPG must be <200 mg/dL [11.1 mmol/L]). OR Early type 2 diabetes, defined as a FPG ≥126 mg/dL (7.0 mmol/L) or a PPG of ≥200 mg/dL (11.1 mmol/L), or a previous diagnosis of diabetes, and either:on no pharmacological treatment (while ambulatory) for at least 10 weeks prior to screening, with screening glycated hemoglobin <150% of the upper limit of normal (ULN) for the laboratory (eg, <9% if the ULN is 6%)or taking one oral antidiabetic drug (OAD) from among sulfonylureas (SU), biguanides, thiazolidinediones (TZDs), alpha-glucosidase inhibitors (AGIs), and meglitinides (MGTs) at a stable dose while ambulatory for at least 10 weeks at the time of screening (or for the 10 weeks prior to hospitalization if identified while hospitalized for a CV event), with screening glycated hemoglobin <133% of the ULN for the laboratory (eg, <8% if the ULN is 6%) if taking this medication at half-maximum dose or greater, and glycated hemoglobin <142% of the ULN for the laboratory (eg, <8.5% if the ULN is 6%) if taking this medication at less than half-maximum dose. Individuals taking combination products containing two or more OADs were not eligible.Men or women aged 50 years and olderAt least one of the following CV risk factors:previous myocardial infarction (MI) (≥ 5 days prior to randomization)previous stroke (≥ 5 days prior to randomization)previous coronary, carotid or peripheral arterial revascularizationangina with documented ischemic changes (at least 2 mm ST segment depression on electrocardiogram during a Graded Exercise Test [GXT]; or with a cardiac imaging study positive for ischemia); or unstable angina with documented ischemic changes (either ST segment depression of at least 1 mm or an increase in troponin above the normal range but below the range diagnostic for acute myocardial infarction)microalbuminuria or clinical albuminuria (an albumin: creatinine ratio ≥ 30 μg/mg in at least one or timed collection of urine with albumin excretion ≥20 μg/min or ≥30 mg/24 hours or total protein excretion ≥500 mg/24 hours)left ventricular hypertrophy by electrocardiogram or echocardiogramsignificant stenosis on angiography of coronary, carotid, or lower extremity arteries (ie, 50% or more stenosis)ankle-brachial index < 0.9.Provision of signed and dated informed consent prior to any study procedures.Ability and willingness to complete study diaries and questionnaires.Demonstrated ability to use the self-glucose-monitoring device, and to self-inject insulin prior to randomization.A negative pregnancy test for all women of childbearing potential (ie, ovulating, pre- menopausal, and not surgically sterile) and the agreement of these women to use a reliable method of birth control to prevent pregnancy during the duration of the study .Willingness to discontinue prior omega-3 PUFA supplements for the duration of the study.Exclusion criteriaType 1 diabetes.Requiring ambulatory insulin treatment or uncontrolled or symptomatic hyperglycemia that is likely to require the addition of ambulatory insulin therapy or a new antidiabetic agent either before or within 2 weeks after randomization.Known anti-glutamic acid decarboxylase antibody (anti-GAD Ab) positivity in the past.Screening glycated hemoglobin ≥150% of the ULN for the laboratory (eg, ≥9% if the ULN is 6%).Unwillingness to inject insulin or perform self-monitoring of blood glucose.Nonadherence to the run-in requirement to inject placebo insulin and do capillary glucose monitoring for at least 4 days prior to randomization.Coronary artery bypass grafting (CABG) either planned at the time of screening, or CABG within the 4 years prior to screening - however, participants with angina, MI, or stroke since a previous CABG will be eligible for randomization, even if the last CABG was within 4 years.Serum creatinine >2.0 mg/dL (176 μmol/L) at screening.Active liver disease, or alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >2.5 times ULN at screening.Chronic or recurrent treatment with systemic corticosteroids, or niacin treatment for hyperlipidemia.Heart failure of New York Heart Association (NYHA) Functional Class III or IV.Expected survival of <3 years for non-CV causes such as cancer.Any other factor likely to limit protocol compliance or reporting of adverse events (AEs).Unwilling or unable to discontinue TZDs.Simultaneous participation in any other clinical trial of an active pharmacologic agent.Unwillingness to permit sites to contact their primary physicians to communicate information about the study and the participant's data and treatment assignment.History of hypersensitivity to the investigational products.Previous randomization in this study.A prior heart transplant, or awaiting a heart transplant.Known infection with human immunodeficiency virus (HIV). | Primary Prevention, Increased CVD Risk: Diabetes and/or metabolic syndrome, Hypertension; Cardiac disease; Cerebrovascular disease; Peripheral vascular disease; Arrhythmia | Retrospective |
| Brinton, 2013, 23835245, US, ANCHOR | Trial: Randomized Parallel | Industry funded | 12 weeks | >18 years of age at high risk for CVD (patients with clinical coronary heart disease [CHD] or CHD risk equivalents [10-year risk 20%]) as defined by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines. On stable statin therapy (atorvastatin, rosuvastatin, or simvastatin with or without ezetimibe) for 4 weeks at doses expected to produce "optimal" LDLC levels for high-risk patients ( 40 and <100 mg/dL). Patients who had A1c >9.5% or were being treated with antidiabetes medication that had not been stable for 4 weeks at screening were excluded from the ANCHOR study. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease) |  |
| NCT01047501 (Brinton, 2013, 23835245) | Trial: Randomized Parallel, 2009 | Industry funded/No Data regarding conflict of interest | 12 weeks | Inclusion Criteria: Men and women, ages >18; Fasting triglyceride ≥200 mg/dL and <500 mg/dL; LDL-C (low density lipoprotein - cholesterol) ≥40 mg/dL and <100mg/dL; High risk for Coronary heart disease; On stable dose of statin (atorvastatin, rosuvastatin or simvastatin); Provide written informed consent and authorization for protected health information disclosure. Exclusion Criteria: Women who are pregnant or lactating, or planning to become pregnant; Use of non-statin lipid-altering drugs which cannot be stopped including fibrates, niacin, fish oil and other products containing omega-3 fatty acids or other dietary supplements with potential lipid-altering effects; History of bariatric surgery or currently on weight loss drugs; Uncontrolled hypertension (BP > 160/100); HIV infection or on treatment with HIV-protease inhibitors, cyclophosphamide,or isotretinoin; Consumption of more than 2 alcoholic beverages per day; History of cancers (except if been disease free for >5 years OR history was basal or squamous cell skin cancer); Participation in another clinical trial involving an investigational agent in the last 30 days; Other parameters will be assessed at the study center to ensure eligibility for this study. | Primary Prevention, Increased CVD Risk:  | Retrospective |
| Brouwer, 2006, 16772624, Germany, Netherlands, Sweden, UK, Poland, Czech Republic, Belgium, Austria, SOFA trial | Trial: Randomized Parallel, 2001 | No industry relationship reported (funding or affiliations reported)/No Data regarding conflict of interest  | 12 months | Men and women >=18 years old, experienced at least 1 true, confirmed, spontaneous VT or VF in the preceding year, and either had and ICD or were about to receive one. Exclusion: receipt of an ICD for prophylactic reasons; ICD as a "bridge" to heart transplantation; refractory supraventricular arrhythmia with rapid ventricular rates despite antiarrhythmic therapy; a projected life span of <1 year; use of supplemental omega-3 PUFA during the past 3 months or consumption >8g of omega-3 PUFAs from fish or seafood per month (267 mg/d) as judged by a seafood FFQ; pregnant women; women of childbearing age who did not use adequate contraception, and patients with a known history of recent drug or alcohol abuse.. excluded patients with high baseline omega-3 intake from supplements and/or foods | Secondary Prevention (history of CVD event): Arrhythmia (at least 1 true, confirmed, spontaneous VT or VF in the preceding year, and either had and ICD or were about to receive one.) |  |
| NCT00110838 (Brouwer, 2006, 16772624) | Trial: Randomized Parallel, 2001 | No industry relationship reported/No Data regarding conflict of interest | 12 months | Inclusion Criteria: ICD is capable of recording ECG strips for at least 10 of its (attempted) therapeutic interventions; 18 years or older; written informed consent. Exclusion Criteria: Primary prophylactic indication; ICD implantation as a ‘bridge’ to heart transplantation; Refractory supraventricular arrhythmias with rapid ventricular rates despite antiarrhythmic therapy; a projected lifespan of less than 1 year; participation in another trial (during or within 30 days before SOFA); use of any supplemental n-3 fatty acid during the last 3 months; intake of more than 8g of n-3 fatty acids from fish per month as judged by a fish frequency questionnaire; pregnant women and women of childbearing potential who do not use adequate contraception; patients known to have a history of recent drug or alcohol abuse | Primary Prevention, Increased CVD Risk: Arrhythmia | Prospective |
| Damsgaard, 2008, 18492834, Denmark | Trial: Randomized Factorial Design, 2005 | Industry only donated materials (eg, supplements)/No conflict of interest (explicitly stated)  | 8 weeks | Healthy males, aged 18-40 y, with no chronic diseases, no regular medication, and no strong allergies who were smoking <5 cigarettes/week, exercising strenuously <7 h/wk, eating homemade meals >5 d/wk, and consumed butter/margarine/or oil daily. | Primary Prevention, Healthy |  |
| NCT00266292 (Damsgaard, 2008, 18492834) | Trial: Randomized Factorial Design, 2005 | No industry relationship reported/No Data regarding conflict of interest | 2 months | Ages Eligible for Study: 18 Years to 40 Years ;Genders Eligible for Study: Male; Accepts Healthy Volunteers: Yes; Healthy (no chronic diseases and no regular medications); BMI >18.5 and <27.5 kg/m2; Daily use of fats and home cooking >5 d/wk; Heavy exercise <7 h/wk; Not daily smokers (<5 cigarets/wk) | Primary Prevention, Healthy | Retrospective |
| Galan, 2010, 21115589, France, SU.FOL.OM3 | Trial: Randomized Parallel, 2003 | Industry funded | Median 4.7 years (mean 4.2, SD 1.0) | History of CVD (acute coronary event, including ACS, or cerebral ischemic event, excluding TIA, within 12 mo), 45-80 y. Exclude disease or treatment that might interfere with metabolism of homocysteine or n-3 FA (eg, methotrexate), SCr >200 mcmol/L, CrCl <40 ml/min.  | Secondary Prevention (history of CVD event): Cardiac disease (Coronary event w/in 12 mo, including MI, ACS or suspected ACS); Cerebrovascular disease (CVA (not TIA)) |  |
| ISRCTN41926726 (Galan, 2010, 21115589) | Trial: Randomized Factorial Design 2003 | Industry funded/ Conflict of interest stated | nd | Participant inclusion criteria1. Participants should have experienced a coronary or cerebral event during 1 to 12 months before baseline. A coronary or cerebral event is defined as:a. Myocardial infarction (validated and documented by a combination of clinical, enzymatic, or electrocardiogram [ECG] parameters)b. Acute coronary syndrome without necrosis (validated and documented by a combination of clinical, enzymatic or ECG parameters)c. A cerebral vascular ischemic accident (defined by criteria validated in epidemiological studies)2. The participants should be 45-80 years at baselineExclusion criteria1. Age <45 years or >80 years2. Cardiovascular pathology not well defined3. Patients that are incapable of understanding the study protocol4. Patients with a pathology that might interfere with homocysteine or omega-3 fatty acid metabolism, in particular those that use methotrexate for the treatment of a cancer or rheumatoid arthritis and chronic renal failure (plasma level of creatinine >200 µmol/l or creatinine clearance <40 ml/min)5. Patients with a non-cardiovascular pathology with a suspected survival time less than the 5 years period of the study (solid cancer, evolved dementia, leukemia etc.) | Secondary Prevention (history of CVD event): MI, ACS, stroke within a year | Retrospective |
| Holman, 2009, 19002433, UK, AFORRD | Trial: Randomized Factorial Design, 2004 | Industry funded | 4 months | Patients with type 2 diabetes for at least 3 months, aged 18 years, with no known CVD events, and not thought by their general practitioner to be at high enough CVD risk to require immediate lipid-lowering therapy.  | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Diabetes and/or metabolic syndrome\*  |  |
| NCT00141232 and ISRCTN76737502 (Holman, 2009, 19002433) | Trial: Randomized Factorial Design, 2004 | Industry funded/No Data regarding conflict of interest | 1 year | Aged 18 years or above; have had Type 2 Diabetes for at least 3 months; not known to have had a cardiovascular event; have provided written informed consent; in UK general practice. | Primary Prevention, Increased CVD Risk: Diabetes and/or metabolic syndrome | Retrospective |
| Jones, 2014, 24829493, Canada, COMIT | Trial: Randomized Cross-over, 2010 | Industry funded/Conflict of interest stated (All authors report having received grants and funding from food companies) | 4 weeks/4 weeks | Inclusion: any of the following: triglyceride level (TG) 1.7 mmol/L, high density lipoprotein cholesterol level (HDL) <1 mmol/L (males) or <1.3 mmol/L (females), blood pressure 130 mmHg (systolic) and/or 85 mmHg (diastolic) and glucose level 5.5 mmol/L, waist circumference 94 cm for men and 80 cm for women. Exclusion: thyroid disease (unless controlled by medication), diabetes mellitus, kidney disease, liver disease, current smokers, or those consuming more than two alcoholic drinks per week, or medications known to affect lipid metabolism or endothelial function (including aspirin or other non-steroidal anti-inflammatory drugs), cholestyramine, colestipol, niacin, clofibrate, gemfibrozil, probucol, or 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase inhibitors.. At the beginning of the study, the Adult Treatment Panel III (ATP III) metabolic syndrome criteria for waist circumference (>102 cm for men and >88 cm for women) were followed [28]. As the trial progressed, the International Diabetes Federation (IDF) metabolic syndrome criteria for waist circumference (94 cm for men and 80 cm for women) were adopted to identify individuals in the initial stages of abdominal obesity who might benefit from dietary intervention. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Hypertension (blood pressure 130 mmHg (systolic) and/or 85 mmHg (diastolic)); Dyslipidemia (TG 1.7 mmol/L, HDL <1 mmol/L (males) or <1.3 mmol/L (females)); Obesity/Overweight (waist circumference 94 cm for men and 80 cm for women); Other (glucose level 5.5 mmol/L) |  |
| NCT01351012 (Jones, 2014, 24829493) | Trial: Randomized Cross-over, 2010 | No industry relationship reported/No Data regarding conflict of interest | 4 weeks/4 weeks | Inclusion Criteria: Waist circumference ≥94 cm (males) or ≥80 cm (females); age 18-65 years; plus at least one of the following: Triglycerides ≥1.7 mmol/L; High density lipoprotein (HDL) cholesterol <1 mmol/L (males) or <1.3 mmol/L (females); Low density lipoprotein (LDL) cholesterol ≥3.5 mmol/L; Blood pressure ≥130 mmHg (systolic) and/or ≥85 mmHg (diastolic); Glucose ≥5.5 mmol/L. Exclusion Criteria: Thyroid disease; Diabetes mellitus; Kidney disease; Liver disease; Smoking; Heavy drinking; Use of medication known to affect lipid metabolism during the last 3 months(cholestyramine, colestipol, niacin, clofibrate, gemfibrozil, probucol, HMG CoA reductase inhibitors). | Primary Prevention, Increased CVD Risk: Hypertension; Dyslipidemia; Obesity/Overweight | Retrospective |
| Kastelein, 2014, 24528690, US, Denmark, Netherlands, India, Hungary, Ukraine, Russia, EVOLVE | Trial: Randomized Parallel, 2011 | Industry funded/Conflict of interest stated (The authors acknowledge that they have either received research grant funding from, or are employees of, or have ownership in Omthera Pharmaceuticals, Inc, the manufacturer of the product studied. The relationship of authors Dr Kastelein, Mr Machielse, Mr Kling, and Dr Davidson to Omthera are considered significant according to the definitions used by the Food and Drug Administration. The following authors further disclose that they have other modest relationships with industry that might pose a potential conflict of interest(s): Dr Kastelein (Amarin), Dr Maki (Abbott, Amarin, DSM, GSK, Pharmavite, Trygg Pharma), Dr Susekov (Abbott, Actavis, Amarin, Amgen, AstraZeneca, Gedeon-Richter, Genzyme, KRKA, Merck, Novartis, Pfizer, Promed, Sandoz, Sanofi-Aventis, Teva, Zentiva), Dr Ezhov (KRKA, Pfizer), and Dr Nordestgaard (AstraZeneca, Kara-Bio, Merck, Pfizer, Regeneron, Sanofi-Aventis).) | 12 weeks | Participants included men and women (nonpregnant, nonlactating) >=18 years of age with average serum TG concentrations >=500 mg/dL but <2000 mg/dL at screening (1 and 2 weeks before random assignment) who were either untreated for dyslipidemia or were using a stable (for at least 6 weeks before the first qualifying lipid measurement) dosage of a statin, CAI, or their combination. Subjects were also required to have a body mass index (calculated as weight divided by height squared; kg/m2) >=20 and be willing to maintain their customary activity level, follow the TLC diet with weight maintenance, and restrict their consumption of fish to no more than twice per week throughout the study. Persons with known lipoprotein lipase impairment or deficiency, apolipoprotein (Apo) CII deficiency, or familial dysbetalipoproteinemia were excluded from the study, as were persons with a history of pancreatitis, symptomatic gallstone disease (unless treated with cholecystectomy), uncontrolled diabetes (glycosylated hemoglobin $9%), or cancer in the past 2 years (basal cell carcinoma was not exclusionary). Persons with a recent history (past 6 months) of a cardiovascular event (ie, myocardial infarction, acute coronary syndrome, new onset angina, stroke, transient ischemic attack, or unstable congestive heart failure that required a change in treatment); revascularization procedure; aortic aneurysm; nephrotic syndrome; or pulmonary, hepatic, biliary, gastrointestinal, or immunologic disease were also excluded. Persons with uncontrolled hypothyroidism, thyroid-stimulating hormone >5 mIU/L, or poorly controlled hypertension (resting blood pressure >=160 mm Hg systolic or >=100 mm Hg diastolic) at 2 consecutive visits before random assignment were not enrolled, nor were persons with any of the following laboratory results: serum alanine aminotransferase or aspartate aminotransferase <3 times the upper limit of normal, fasting serum glucose <200 mg/dL, calculated glomerular filtration rate <30 mL/min, platelet counts <60 X 10^9/L, or hemoglobin <10.0 g/dL. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Dyslipidemia (average serum TG concentrations 500-2000 mg/dL); Obesity/Overweight (body mass index >=20) |  |
| NCT01242527 (Kastelein, 2014, 24528690)  | Trial: Randomized Parallel, 2011 | Industry funded/ Conflict of interest stated | 12 weeks | Inclusion Criteria:Men or women, >=18 years of age.Very high serum TG values in the range >=500 mg/dL and <2000 mg/dL (>=5.65 mmol/L and <22.60 mmol/L)Exclusion Criteria:Allergy or intolerance to omega-3 fatty acids, omega-3-acid ethyl esters, or fish.Known lipoprotein lipase impairment or deficiency or apolipoprotein C-II deficiency or familial dysbetalipoproteinemia.Unable to discontinue use of omega-3 drugs/supplements.Unable to discontinue use of bile acid sequestrants, fibrates or niacin (other than niacin-containing vitamins <200 mg), or any supplement used to alter lipid metabolism.Women who are pregnant, lactating, or planning to become pregnant. Women of childbearing potential who are not using acceptable contraceptive methods.Use of tamoxifen, estrogens or progestins that has not been stable for >4 weeks prior to Visit 1.Use of oral or injected corticosteroids or anabolic steroids.History of pancreatitis.History of symptomatic gallstone disease, unless treated with cholecystectomy.Uncontrolled diabetes.Uncontrolled hypothyroidism or thyroid stimulating hormone (TSH).History of cancer (other than basal cell carcinoma) in the past 2 years.Cardiovascular event (i.e., myocardial infarction, acute coronary syndrome, new onset angina, stroke, transient ischemic attack, unstable congestive heart failure requiring a change in treatment) or revascularization procedure within six months prior to Visit 1.Use of anticoagulants (e.g. warfarin [Coumadin®], coumarin, heparin, enoxaparin, clopidogrel).Presence of an aortic aneurysm or resection of an aortic aneurysm within six months prior to Visit 1.Recent history (within six months prior to Visit 1) or current significant nephrotic syndrome, pulmonary, hepatic, biliary, gastrointestinal or immunologic disease.Poorly controlled hypertension.Any of the following laboratory criteria: serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST), glucose, glomerular filtration rate (GFR), platelet count,or hemoglobin outside of study range.Recent history (past 12 months) of drug abuse or alcohol abuse.Exposure to any investigational product, within 4 weeks prior to Visit 1.Presence of any other condition the Investigator believes would interfere with the subject's ability to provide informed consent, comply with study instructions, or which might confound the interpretation of the study results or put the subject at undue risk | Primary Prevention, Increased CVD Risk: Dyslipidemia: serum TG values in the range >=500 mg/dL and <2000 mg/dL (>=5.65 mmol/L and <22.60 mmol/L) | Retrospective |
| Kromhout, 2010, 20929341, Netherlands, DART | Trial: Randomized Factorial Design, 2002 | Industry only donated materials (eg, supplements)/No conflict of interest (explicitly stated)  | 40 months | Men and women 60 to 80 years of age, who had had a clinical diagnosed MI up to 10 years before randomization. Exclusion criteria: daily consumption of <10 10 g of margarine, use of n-3 fatty-acid supplements, unintended weight loss of >5 kg in the previous year, and a diagnosis of cancer with an estimated life expectancy of <1 year. | Secondary Prevention (history of CVD event): Cardiac disease (myocardial infarction) |  |
| NCT00127452 (Kromhout, 2010,20929341) Alpha Omega | Trial: Randomized Parallel, 2002 | No industry relationship reported/No Data regarding conflict of interest | 40 months | Inclusion criteria: Men and women; Aged 60 through 80 y; Verified clinically diagnosed myocardial infarction up to 10 y before randomization; Written informed consent. Exclusion criteria: Living in a nursing home or other institution; Participation in another scientific study; Habitual margarine intake < 10 g per day; Habitual fish intake > 150 g per day; Habitual alcohol intake > 6 drinks per day; Use of fish oil capsules or other supplements containing omega-3 fatty acids; Presence of cancer with < 1 y of life expectancy; Cognitive impairment, as indicated by the Mini Mental State Examination (score <= 21); Unintended weight loss > 5 kg in the past year; Lack of facilities for cooled margarine storage at home; Inability or unwillingness to comply with study procedures | Secondary Prevention (history of CVD event): Cardiac disease (verified clinically diagnosed myocardial infarction up to 10 y before randomization) | Retrospective |
| Kuhnt 2014, 24553695, Germany | Trial: Randomized Parallel, 2011 | No conflict of interest (explicitly stated) | 8 weeks | Normolipidemic and normal-weight (BMI 18-25) individuals were recruited for 2 age groups: group I, 20-35 y; and group II 49-69 y. Older overweight individuals were recruited for echium oil (EO) intervention only (49-69 y; BMI >25 with markers of metabolic syndrome or BMI >= 30). Patients with markers of metabolic syndrome were mainly enlisted from the diabetes research center. This subgroup - EO III (older overweight individuals who were recruited for echium oil intervention only; 49-69 y; BMI >25 with markers of metabolic syndrome) was not included in this systematic review. | Primary Prevention, Healthy |  |
| NCT01856179 (Kuhnt,2014, 24553695) | Trial: Randomized Parallel, 2011 | No industry relationship reported | 56 days | Inclusion Criteria: healthy subjects, 20-70 years. Exclusion Criteria: cholesterol lowering drugs; chronic diseases; pregnancy, lactation; intake of nutritional supplements. | Primary Prevention, Healthy | Retrospective |
| Leaf, 2005, 16267249, US, FAAT | Trial: Randomized Parallel, 1999 | Industry only donated materials (eg, supplements)/No Data regarding conflict of interest  | 1 year | Subjects were included who had an ICD implanted because of a history of cardiac arrest, sustained ventricular tachycardia (VT), or syncope with inducible, sustained VT or ventricular fibrillation (VF) during electrophysiologic studies. The qualifying ICD implantation was required to have occurred within 12 months before entry into the study or if the patient had experienced at least 1 spontaneous ICD event for VT/VF in the preceding 12 months.. - | Secondary Prevention (history of CVD event): Arrhythmia (ICD implanted) |  |
| NCT00004559 (Leaf, 2005, 16267249)  | Trial: Randomized Parallel, 1999 | No industry relationship reported/No Data regarding conflict of interest | nd | Ages Eligible for Study: 18 Years to 75 Years; Genders Eligible for Study: Both; Accepts Healthy Volunteers: No | Secondary Prevention (history of CVD event): Cardiac disease, Arrhythmia | Prospective |
| Macchia, 2013, 23265344, Italy, Argentina, FORWARD | Trial: Randomized Parallel, 2008 | Industry funded/No conflict of interest (explicitly stated)  | 12 months | Patients with previous persistent AF (>=2 symptomatic episodes of documented AF in the 6 months before randomization, with last episode occurring within 3 to 90 days before randomization (paroxysmal AF); or successful electrical or pharmacological cardioversion for persistent AF performed within 3 to 28 days before randomization. | Secondary Prevention (history of CVD event): Arrhythmia  |  |
| NCT00597220 (Macchia, 2013, 23265344) | Trial: Randomized Parallel, 2008 | Industry funded/ No Data regarding conflict of interest | 12 months | Inclusion Criteria: Persistent atrial fibrillation; Age 21+Exclusion Criteria: Contraindications or known hypersensitivity to n-3 PUFA; Current treatment with n-3 PUFA for any reason; Heart failure NYHA class IV; Coronary artery bypass surgery or valve replacement within the past 3 months; Planned cardiac procedures; Known sick-sinus syndrome; Diagnosis of Wolff-Parkinson-White; Clinical significant valvular etiologies; Presence of arrhythmia associated with an acute reversible condition; Advanced chronic lung disease; Contraindications for anticoagulation therapy; Pregnancy or lactation; Any non cardiac illness associated with a life expectancy of < 2 years; Treatment with any investigational agent within 3 month before randomization; Any condition that in the opinion of the investigator would jeopardize the evaluation of efficacy or safety or be associated with poor adherence to the protocol | Secondary Prevention (history of CVD event): Arrhythmia | Prospective |
| Maki, 2010, 20451686, US, COMBOS | Trial: Randomized Parallel, 2005 | Industry funded | 8 weeks | Eligible patients were men or women between the ages of 18 and 79 years who had been receiving a stable dose of a statin for the control of LDL-C levels for =>8 weeks before screening and were judged to be in good health on the basis of a medical history, physical examination, electrocardiogram, and laboratory tests, including serum chemistry, hematology, and urinalysis. Major inclusion criteria included a mean fasting TG level >=200 and <500 mg/dL, and a mean LDL-C level below or within 10% of the patient's NCEP ATPIII goal. Major exclusion criteria included poorly controlled diabetes mellitus (glycosylated hemoglobin [HbAlc] >8.0% at screening); history of a cardiovascular event, a revascularization procedure, or an aortic aneurysm or resection within 6 months of screening; history of pancreatitis; sensitivity to statins or omega-3 fatty acids; poorly controlled hypertension (resting blood pressure =>160 mm Hg systolic and/or =>100 mm Hg diastolic at 2 consecutive visits); serum creatinine level =>2.0 mg/dL; serum transaminase (aspartate aminotransferase lAST] or alanine aminotransferase [ALT]) >1.5 times the upper limit of normal (ULN) (45 U/L for ALT, 31 U/L for AST); or creatine kinase (CK) level >2 times the ULN. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Dyslipidemia (mean fasting TG level \_>200 and <500 mg/dL, and a mean LDL-C level below or within 10% of the patient's NCEP ATP III goal.) |  |
| NCT00246701 (Maki, 2010,20451686) | Trial: Randomized Parallel, 2005 | Industry funded/ No Data regarding conflict of interest | 8 weeks | Inclusion Criteria: Men and women ages 18-79 years, inclusive; Current therapy with a statin drug; Triglyceride levels between 200 and 499 mg/dL; Normally active and in good health on the basis of medical history, brief physical examination, electrocardiogram, and routine laboratory tests; Provide written informed consent and authorization for protected health information disclosureExclusion Criteria: Sensitivity to statin drugs or omega-3 fatty acids; Lipoprotein lipase impairment or apo C-2 deficiency or type III hyperlipidemia; Unexplained muscle pain or weakness; History of pancreatitis; Recent history of certain heart, kidney, liver, lung, or gastrointestinal diseases, or cancer (except non-melanoma skin cancer); Poorly controlled diabetes, or receiving insulin therapy; Pregnant or lactating females; Women of childbearing potential who are not using a medically approved method of contraception; Use of certain types of hormones, anticonvulsant drugs, immunologic drugs, antibiotic, antifungal and antiviral drugs, and cardiac drugs; Use of warfarin (Coumadin) | Primary Prevention, Increased CVD Risk: Dyslipidemia | Prospective |
| Maki, 2013, 23998969, US, ESPRIT TRIAL | Trial: Randomized Parallel, 2011 | Industry funded | 6 weeks | Participants included men and non pregnant, nonlactating women 18 years of age with fasting triglyceride (TG) levels 200 mg/dL and <500 mg/dL(after 4 weeks of the statin/diet lead-in) and at high risk for a future cardiovascular event. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Dyslipidemia ((TG) levels 200 mg/dL and <500 mg/dL) |  |
| NCT01408303 (Maki, 2013, 23998969) | Trial: Randomized Parallel, 2011 | Industry funded | 6 weeks | Inclusion Criteria:Men or women, ≥18 years of age.Fasting triglyceride (TG) level ≥200 mg/dL and <500 mg/dL. The subject is a high risk for a future cardiovascular event. The subject is treated with a statin and at or near LDL-C goal.Exclusion Criteria:Allergy or intolerance to omega-3 fatty acids and omega-3-acid ethyl esters.Use of fibrates, bile acid sequestrants, or niacin or its analogues (greater than 200 mg/d) during screening. Use of simvastatin 80 mg or Vytorin10/80 mg during screening. Use of any eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA) products. Use of any supplement for the purpose of lowering plasma cholesterol during screening. Use of weight loss drugs or programs during screening. Use of erythromycin, telithromycin, clarithromycin, cyclosporine, itraconazole, ketoconazole, protease inhibitors, or nefazodone during screening. Use of anticoagulants during screening. Use of oral or injected corticosteroids during screening.Use of tamoxifen, estrogens, progestins, or testosterone, that has not been stable for >4 weeks at Visit 1, or is unstable during screening. Use of >750 mL/d grapefruit juice during screening.Known lipoprotein lipase impairment or deficiency, or apolipoprotein C-II deficiency or familial dysbetalipoproteinemia. History of pancreatitis. Type I diabetes mellitus, use of insulin, or HbA1c >10% at Visit 1. Poorly controlled hypertensionUncontrolled hypothyroidism, or thyroid stimulating hormone (TSH) >1.5xULN at Visit 2. Recent history or current significant nephrotic syndrome, pulmonary, hepatic, biliary, gastrointestinal or immunologic disease. History of cancer (except non-melanoma skin cancer, or carcinoma in situ of cervix) within the previous two years. Females who are pregnant, planning to be pregnant during the study period, lactating, or women of childbearing potential who are not using an acceptable method of contraception. Creatine kinase >5.0 times upper limit of normal (ULN); aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >2.5 times ULN at Visit 2. Current or recent history (past 12 months) of drug or alcohol abuse. Exposure to any investigational agent within 4 weeks prior to Visit 1. Any other condition the investigator believes would interfere with the subject's ability to provide informed consent, comply with study instructions, or which might confound the interpretation of the study results or put the subject at undue risk. | Primary Prevention, Increased CVD Risk: Dyslipidemia (Fasting triglyceride (TG) level ≥200 mg/dL and <500 mg/dL.) | Prospective |
| Nodari, 2011, 21844082, Italy | Trial: Randomized Parallel, 2006 | No industry relationship reported (funding or affiliations reported) | 1 year | Eligibility was determined at a screening visit that included medical history, physical examination, 12-lead ECG, chest x-ray, and 2-dimensional Doppler echocardiography, plus complete blood count, routine chemistry, thyroid function tests, and pregnancy test in fertile women. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Arrhythmia  |  |
| NCT01198275 (Nodari, 2011, 21844082) ATRIA | Trial: Randomized Parallel, 2006 | No industry relationship reported/ No Data regarding conflict of interest | 12 months | Inclusion Criteria:persistent Atrial Fibrillation (AF) lasting > one month history of at least one AF relapse after previous electrical or Pharmacological cardioversionExclusion Criteria:left atrium size > 6 cm severe valvulopathy myocardial infarction during the previous 6 months unstable angina NYHA heart failure class IV or hemodynamic instability cardiac surgery during the previous 3 months significant pulmonary thyroid and hepatic disease contraindications to treatment with amiodarone or RASS inhibitors chronic renal dysfunction QT > 480 msec in the absence of bundle-branch block bradycardia < 50 b/min diagnosis of paroxysmal AF hyperkalemia pregnancy any disease or other medical treatment that, in the opinion of the investigators, could interfere with the study. | Secondary Prevention (history of CVD event): Arrhythmia | Retrospective |
| Raitt, 2005, 15956633, US | Trial: Randomized Parallel, 2001 | No industry relationship reported (funding or affiliations reported) | 718 days (median) | Patients were eligible for entry if they were receiving an implantable cardioverter defibrillator (ICD) for an electrocardiogram-documented episode of sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) that was not the result of acute myocardial infarction or a reversible cause or who had a preexisting ICD and had received ICD therapy for an episode of electrogramdocumented VT/VF within the previous 3 months. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Arrhythmia  |  |
| NCT00004558 (Raitt, 2005, 15956633) | Trial: Randomized Parallel, 2000 | No data/no data | nd | Survivors of VT and VF with an implantable defibrillator. 18 Years to 75 Years | Secondary Prevention (history of CVD event): Arrhythmia | Retrospective |
| Ras, 2014, 25122648, Sweden | Trial: Randomized Parallel, 2011 | Industry funded/conflict of interest: Ras, Demonty, Zebregs, and Trautwein were employed by Unilever Research and Development at the time of study conduct. Unilever markets food products enriched with plant sterols. | 4 weeks | Apparently healthy; aged 25–75 y; fasting TC concentration between 5 and 8 mmol/L; BMI between 18 and 30 kg/m2; systolic blood pressure >=160 mm Hg, diastolic blood pressure >=90 mm Hg and heart rate between 50 and 100 beats/min; no use of medication that could influence the study outcomes; no use of nicotine-containing products; 10-y cardiovascular disease risk >=10 according to the Systematic Coronary Risk Evaluation (SCORE); willing to comply with the study protocol; and having signed the informed and biobank consents | Primary Prevention, Healthy |  |
| NCT01313988 (Ras, 2015, 25122648) | Trial: Randomized Parallel, 2011 | Authors report industry affiliation | 4 weeks | Inclusion Criteria: Apparently healthy men and women; Age ≥ 25 and ≤ 75 years old; Body mass index (BMI) ≥ 18 and ≤ 30 kg/m2; Total cholesterol levels at screening ≥ 5.0 and ≤ 8.0 mmol/L; 10-year CVD risk equal or lower than 10% according to "SCORE"; Blood pressure, heart rate, hematological parameters, clinical chemical parameters within normal reference ranges; Informed consent and biobank consent signed; Willing to comply to study protocol during study; Agreeing to be informed about medically relevant personal test-results by a physician; Not smoking; Accessible veins on the forearm; Habitually consuming spreads. Exclusion Criteria: Pregnant or having the wish to become pregnant, or lactating; Use of prescribed medication which may interfere with study measurements; Use of antibiotics in the 3 months before screening or during the study; Use of any medically- or self-prescribed diet with the purpose to reduce weight; Intolerance for gluten or lactose; Reported food allergy; Having bleeding disorders; Recent blood donation; Excessive alcohol consumption; Strenuous exercise; Reported weight change ≥ 10 % of body weight or use of prescribed weight reduction drugs; Recent participation in another nutritional or medical trial; Participation in night shift work. | Primary Prevention, Healthy | Retrospective |
| Rauch, 2010, 21060071, Germany, OMEGA | Trial: Randomized Parallel, 2003 | Industry funded | 1 year | Minimum age of 18 who were admitted to hospital for acute STEMI or non-STEMI and gave written informed consent to participate in the study. | Secondary Prevention (history of CVD event): Cardiac disease (Myocardial infarction) |  |
| NCT00251134 (Rauch, 2010, 21060071) | Trial: Randomized Parallel, 2003 | Industry funded/No Data regarding conflict of interest | 12 months | Inclusion Criteria: Myocardial infarction 3-14 days before randomisation (STEMI and NSTEMI), Ability to take Ω-3-FAE or olive oil without risk, Informed consentExclusion Criteria: Premenopausal women who are not surgically sterile, who are pregnant or nursing, who are of child-bearing potential and are not practising acceptable means of birth control (pregnancy testing required before randomisation), Known hypersensitivity to study medication, Dislike of fish oil, Haemorrhagic diathesis, Unwillingness to discontinue other medications containing fish oil, Legal incapacity, History of drug or alcohol abuse within 6 months, Any investigational therapy within one month of signing informed consent form | Secondary Prevention (history of CVD event): Cardiac disease (Myocardial infarction) | Retrospective |
| Rodriguez-Leyva, 2013, 24126178, Canada, FlaxPAD | Trial: Randomized Parallel, 2008 | Industry funded | 6 months | Patients must be >40 years old, had PAD (peripheral artery disease) for > 6 months with ankle brachial index <0.9.. exclusion criteria: inability to walk, bowel disease, moderate to severe renal failure, life expectancy <2 years with high baseline cardiac risk, allergies to any ingredient in the study product, patients who plan to undergo surgery during the course of the trial, and no more than 2 fish meals per week | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Peripheral vascular disease (nd) |  |
| NCT00781950 (Rodriguez-Leyva, 2013, 24126178) | Trial: Randomized Parallel, 2008 | nd | 1 year (originally 2 years) | Inclusion Criteria:Subjects with peripheral arterial disease for more than 6 months.Male or female with claudication secondary to lower extremity atherosclerotic arterial disease. (with limited IC but not incapacitated for walking on the level) confirmed with ankle/brachial pressures< or = to 0.9 in one or both legs) or who have had a previous intervention for peripheral arterial disease.Over 40 years oldAble to comply with protocol requirementsAble to provide informed consent Subjects taking anti-platelet therapy medication must be on a stable dose for 3 months prior to as well as during the study.Subjects taking lipid lowering medication must be on a stable dose for 3 months prior to as well as during the study.Exclusion Criteria:Patients with ischemic rest pain in limbs, ulceration, or gangrene.At baseline, any condition that prevents walking on a treadmill.History of major bleeding. Patients with bowel disease (including Crohn's disease, celiac disease, peptic ulcer disease, irritable bowel syndrome and diverticulosis). Patients with an estimated life expectancy less than 2 years and with high baseline cardiac risk (post ischemic or diabetic cardiomyopathy with EF<40%, Canadian Cardiovascular Society Class 3 or 4 angina or need for coronary revascularization procedures). Moderate to severe renal failure. Subjects that are on supplements other that those prescribed by their clinician for the entire duration of the study. Fish limitations (no more than 2 fish meals per week) Gluten allergy Subjects with allergies to any ingredient in the study product or placebo. Patients who plan to undergo surgery during the course of the trial. | Secondary Prevention (history of CVD event): peripheral arterial disease for more than 6 months | Prospective |
| Roncaglioni, 2013, 23656645, Italy | Trial: Randomized Parallel, 2004 | No Data on funding or affiliations/No Data regarding conflict of interest  | median 5 years | Participants with at least one of the following: multiple cardiovascular risk factors, clinical evidence of atherosclerotic vascular disease, or any other condition putting the patient at high cardiovascular risk in opinion of patient's general practitioner. multiple cardiovascular risk factors defined as at least four of the following(or for diabetic patients, one of the following): age >65 years, male sex, hypertension, hypercholesterolemia, current smoker, obesity, family history cardiovascular disease | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease) |  |
| NCT00317707 (Roncaglioni, 2013, 23656645) | Trial: Randomized Parallel, 2004 | No Data on funding or affiliations/No Data regarding conflict of interest | 5 years | Inclusion Criteria: Multiple risk factors: diabetes, age => 65 years, male sex, hypertension, hypercholesterolemia, smoking, obesity, family history of premature cardiovascular disease; Previous manifestations of atherosclerotic disease ischemic stoke, transient ischemic attack [TIA], peripheral artery disease, previous arterial revascularisation procedures, angina pectoris)Exclusion Criteria: Contraindications (known allergies to n-3 PUFA) or indications (previous myocardial infarction) for the treatment with n-3 PUFA; Serious comorbidity with an unfavourable prognosis over the short term; Expected non compliance over a long period of time; Pregnancy | Primary Prevention, Increased CVD Risk: diabetes, hypertension, dyslipidemia, obesity | Retrospective |
| Sanders, 2011, 21865334, UK, MARINA trial | Trial: Randomized Parallel, 2008 | Industry only donated materials (eg, supplements)/No conflict of interest (explicitly stated)  | 12 months | Nonsmokers (confirmed by cotinine testing) men and women aged 45 70 y. Exclusions: a medical history of CVD; overall risk of cardiovascular disease >20% over the next 10 y; cancer (excluding basal cell carcinoma) in the previous 5 y; type 1 DM; uncontrolled type 2 DM; chronic renal, liver, or inflammatory bowel disease; history of substance abuse or alcoholism; pregnancy; weight change of >3 kg in preceding 2 mo; and BMI <20 and >35. | Primary Prevention, Healthy |  |
| ISRCTN66664610 (Sanders, 2011, 21865334) | Trial: Randomized Parallel, 2008 | No industry relationship reported/No Data regarding conflict of interest | 1 year | Men and women, aged 45 - 70 years Participant exclusion criteria: 1. A reported history of angina, myocardial infarction or stroke 2. Clinical history of cancer (excluding basal cell carcinoma) in the past five years 3. Uncontrolled type 2 diabetes mellitus (fasting plasma glucose greater than 7 mmol/L) 4. Type 1 diabetes mellitus5. Chronic renal, liver or inflammatory bowel disease 6. Current cigarette smoker 7. History of substance abuse or alcoholism (previous weekly alcohol intake greater than 60 units/men or 50 units/women) 8. Current self-reported weekly alcohol intake not exceeding 21 units for women and 28 for men 9. Currently pregnant, planning pregnancy or having had a baby in the last 12 months (there are no hazards from the EPA or DHA with regard to pregnancy outcome) 10. Allergy or intolerance to any component of study capsules 11. Unwilling to follow the protocol and/or give informed consent12. Unwilling to refrain from use of dietary supplements including other sources of fish oil (e.g. cod liver oil)13. Unwilling to restrict consumption of oily fish 14. Weight change of greater than 3 kg in preceding 2 months 15. Body mass index less than 20 and greater than 35 kg/m^216. Subjects with an overall risk of cardiovascular disease over the next ten years of greater than 20% who have untreated high blood pressure or raised cholesterol (subjects who are on stable medication for blood pressure or serum cholesterol [statins] will be included) | Primary Prevention, Healthy | Retrospective |
| Tavazzi, 2008, 18757090, Italy, GISSI-HF | Trial: Randomized Parallel, 2002 | Industry funded | 3.9 years | Eligible patients were men and women aged 18 years or older, with clinical evidence of heart failure of any cause that was classified according to the European Society of Cardiology (ESC) guidelines as New York Heart Association (NYHA) class II IV, provided that they had had their LVEF measured within 3 months before enrolment. When LVEF was greater than 40%, the patient had to have been admitted at least once to hospital for heart failure in the preceding year to meet the inclusion criteria. Major exclusion criteria included specific indication or contraindication to n-3 PUFA; known hypersensitivity to study treatments; presence of any non-cardiac comorbidity (eg, cancer) that was unlikely to be compatible with a sufficiently long follow-up; treatment with any investigational agent within 1 month before randomisation; acute coronary syndrome or revascularisation procedure within the preceding 1 month; planned cardiac surgery, expected to be done within 3 months after randomisation; significant liver disease; and pregnant or lactating women or women of childbearing potential who were not adequately protected against becoming pregnant..  | Secondary Prevention (history of CVD event): Cardiac disease (symptomatic heart failure of any cause and with any level of left ventricular ejection fraction (LVEF).) |  |
| NCT00336336 (Tavazzi, 2008, 18757090) | Trial: Randomized Parallel, 2002 | No industry relationship reported/No Data regarding conflict of interest | Time Frame: from enrollment to 1252 deaths in R2 arm | Clinical evidence of heart failure according to the European Society of Cardiology guidelines (New York Heart Association class II-IV) (32); Any left ventricular Ejection Fraction (EF) measured within 3 months from enrolment (if EF% >40%, at least 1 hospital admission for Congestive Heart Failure(CHF) in the previous year); 18 Years and older; Any etiology; Informed consent (obtained before any study specific procedure). Exclusion Criteria: COMMON EXCLUSION CRITERIA (R1=n-3 PUFA vs placebo and R2=rosuvastatin vs placebo): Acute Myocardial Infarction, unstable angina or revascularization procedure within 1 month; planned cardiac surgery, expected to be performed within 3 months; congenital or primary valvular etiology; known hypersensitivity to study treatments; significant liver disease; pregnant or lactating women or women of childbearing potential who are not protected from pregnancy by an accepted method of contraception; any condition that in the opinion of the investigator would jeopardize the evaluation of efficacy or safety or be associated with poor adherence to the protocol; presence of any non-cardiac disease (e.g. cancer) that is likely to significantly shorten life expectancy; treatment with any investigational agent within 1 month before randomization; patients already on treatment with n-3 PUFA or statin for whom the prescription is confirmed. EXCLUSION CRITERIA FOR R2 (statin hypothesis): current serum creatinine level >2.5 mg/dL; current ALT, AST level >1.5 times the upper normal limit; current CPK upper normal limits. | Secondary Prevention (history of CVD event): Cardiac disease | Retrospective |
| Vazquez, 2014, 24462043, Spain | Trial: Randomized Cross-over, 2011 | Industry funded/No conflict of interest (explicitly stated) | 8 weeks/0 weeks | Exclusion criteria were the following: patients taking n-3 LCFA supplements, fish allergy and positive antibodies to Anisakis spp., presence of a body mass index (BMI) 40 kg/m2, chronic kidney disease, liver failure, chronic psychopathy, neoplasia or refusal to participate in the study. | Primary Prevention, Healthy |  |
| NCT01758601 (Vazquez, 2014, 24462043) WISH-CARE | Trial: Randomized Cross-over, 2010 | Industry/No Data regarding conflict of interest | 8 weeks/0 weeks | Inclusion Criteria: We included adult patients (18 Years to 65 Years) with the metabolic syndrome as defined by the Third Report of the National Cholesterol Education Program, Adult Treatment Panel III. Exclusion Criteria: Fish allergy and positive antibodies to Anisakis spp. Morbid obesity with BMI ≥40kg/m2. Chronic renal failure. Chronic psychopathy. Neoplasia. Refusal to participate in the study. | Primary Prevention, Increased CVD Risk: Diabetes and/or metabolic syndrome | Retrospective |
| Yokoyama, 2007, 17398308, Japan, JELIS | Trial: Randomized Parallel, 1996 | Industry funded/Conflict of interest stated ('M Yokoyama received travel costs from Mochida Pharmaceutical Co Ltd, Tokyo, Japan, to participate in the scientific meeting. Other authors have no conflicts of interest.') | 5 years | Inclusion criteria: Total cholesterol concentration of 6 5 mmol/L or greater, which corresponded to a LDL cholesterol of 4 4 mmol/L or greater. Exclusion criteria: acute myocardial infarction within the past 6 months, unstable angina pectoris, a history or complication of serious heart disease (such as severe arrhythmia, heart failure, cardiomyopathy, valvular disease, or congenital disease), cardiovascular reconstruction within the past 6 months, cerebrovascular disorders within the past 6 months, complications of serious hepatic or renal disease, malignant disease, uncontrollable diabetes, hyperlipidaemia due to other disorders, hyperlipidaemia caused by drugs such as steroid hormones, haemorrhage (including haemo philia, capillary fragility, gastrointestinal ulcer, urinary tract haemorrhage, haemoptysis, and vitreous haemorrhage), haemorrhagic diathesis, hypersensitivity to the study drug formulation, patients intention to undergo surgery, and judgment by the physician in charge that a patient was inappropriate for the study. | Primary Prevention, Increased CVD Risk (ie, diabetes, metabolic syndrome\*, hypertension, dyslipidemia, or chronic kidney disease): Dyslipidemia (total cholesterol concentration of 6 5 mmol/L or greater, which corresponded to a LDL cholesterol of 4 4 mmol/L or greater) |  |
| NCT00231738 (Yokoyama, 2007, 17398308) | Trial: Randomized Parallel, 1996 | Industry funded /Authors report industry affiliation | nd | Inclusion Criteria: Age 40 Years to 75 Years; Eligible participants had a total cholesterol level of >=250mg/dL(6.5m mol/L) at baseline; Hyperlipidemic patients with serum total cholesterol of 250mg/dL or more. (Measurement of serum total cholesterol); Serum total cholesterol should be measured twice at interval of 2-4weeks. A single measurement is acceptable if the cholesterol is measured by blood collection at fasting under strict compliance with dietary advice after withdrawal of antihyperlipemic drug; (Wash Out) The wash out period of 4 weeks (8 weeks for probucol) is necessary in patients under treatment with antihyperlipemic drug. However, if treatment with the antihyperlipemic drug was started within 6 months of the initiation of the study, patient can participate in study without the washout period. Exclusion Criteria: Acute myocardial infarction occurring within last 6 months; Unstable angina pectoris; A history or complication of serious heart disease(severe arrhythmia, heart failure, cardiac myopathy, valvular disease, congenital disease, etc.); Receiving cardiovascular reconstruction within last 6 months; Cerebrovascular disorders occurring within last 6 months; Complication of serious hepatic disease or renal disease; Malignant tumor; Uncontrollable diabetes; Hyperlipidemia arising from the following disease: Nephrotic syndrome, hypothyroidism, Cushing’s syndrome, secondary hyperlipidemia due to other disease; Hyperlipidemia due to some drugs such as steroid hormone; Hemorrhage (hemophilia, capillary fragility, gastrointestinal ulcer, urinary tract hemorrhage, hemoptysis, vitreous hemorrhage, etc.); Hemorrhagic diathesis; Hypersensitivity to the study drug formulation; Patients intending to undergo surgery; Patients judged to be inappropriate by physician in charge. | Primary Prevention, Increased CVD Risk: Dyslipidemia | Retrospective |