IL TRATTAMENTO NUTRIZIONALE DELLE DISLIPIDEMIE

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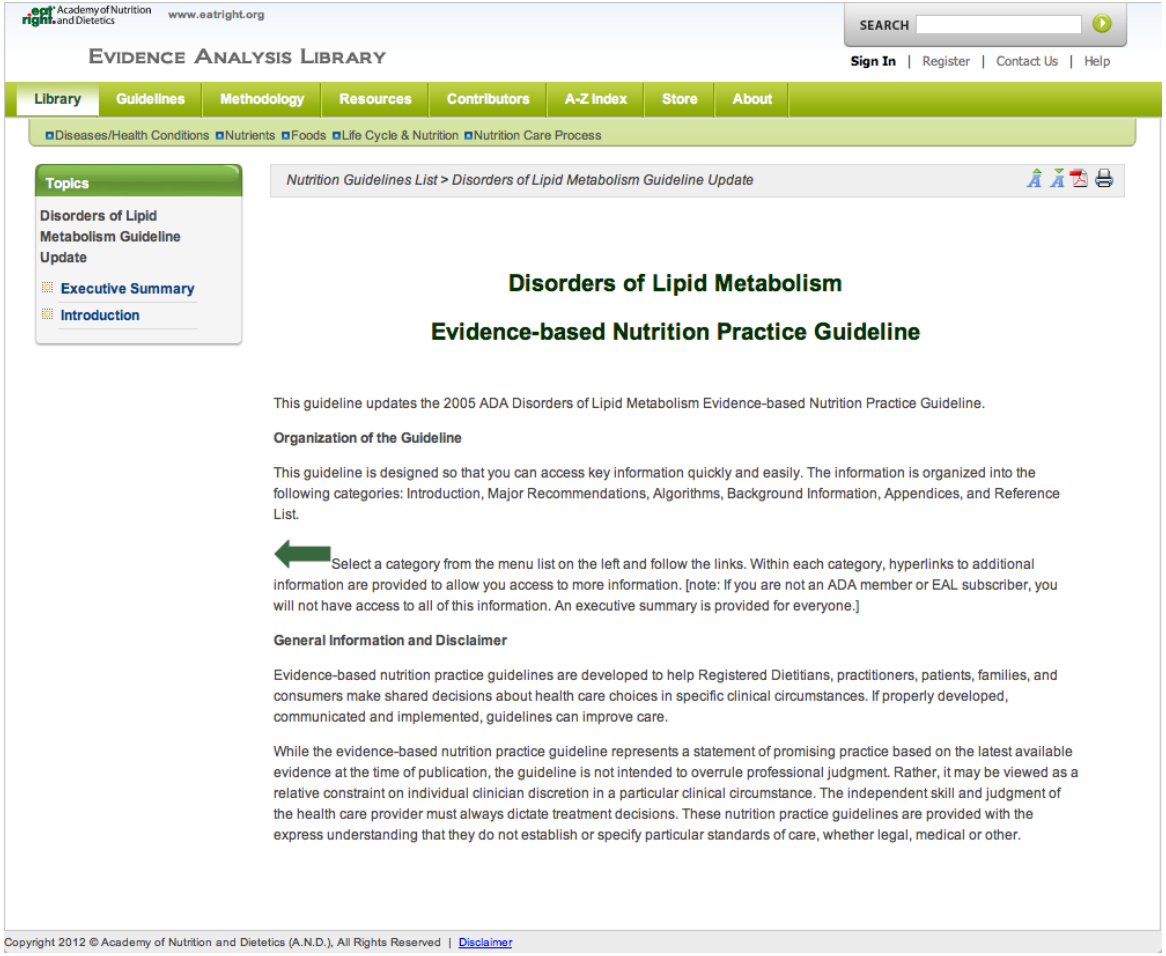
Obiettivo

- Discutere la base di evidenza disponibile per il trattamento nutrizionale delle displipidemie e la sua implementazione in forma di linee guida per la pratica professionale (Academy of Nutrition and Dietetics, AND ex American Dietetic Association, ADA)

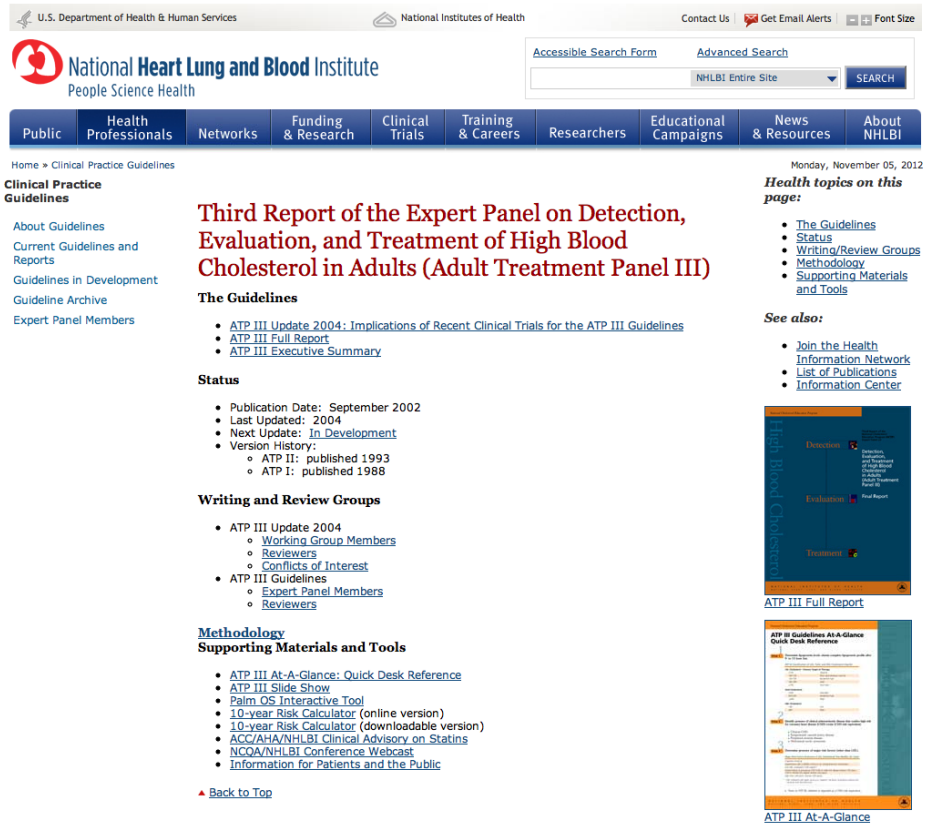
ADA guidelines (updated Mar 2011)



MNT and Referral to a RD (1)

MNT provided by a registered dietitian RD is recommended for patients with an abnormal lipid profile as defined by *current National Heart, Lung and Blood Institute (NHLBI) Clinical Practice Guidelines* and low-density lipoprotein cholesterol (LDL-C) goals.

*ATP III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The Guidelines
ATP III Update 2004: Implications of Recent Clinical Trials for the ATP III Guidelines
ATP III Full Report
ATP III Executive Summary
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ATP III At-A-Glance: Quick Desk Reference
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*Still waiting for ATP IV…

ATP III Guidelines At-A-Glance Quick Desk Reference

Step 1

Determine lipoprotein levels–obtain complete lipoprotein profile after 9- to 12-hour fast.

ATP III Classification of LDL, Total, and HDL Cholesterol (mg/dL)

LDL Cholesterol – Primary Target of Therapy	
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
≥190	Very high
Total Cholesterol	
<200	Desirable
200-239	Borderline high
≥240	High
HDL Cholesterol	
<40	Low
≥60	High

Step 2

Identify presence of clinical atherosclerotic disease that confers high risk for coronary heart disease (CHD) events (CHD risk equivalent):

- Clinical CHD
- Symptomatic carotid artery disease
- Peripheral arterial disease
- Abdominal aortic aneurysm.

Step 3

Determine presence of major risk factors (other than LDL):

Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals

Cigarette smoking
Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)
Low HDL cholesterol (<40 mg/dL)*
Family history of premature CHD (CHD in male first degree relative <55 years; CHD in female first degree relative <65 years)
Age (men ≥45 years; women ≥55 years)

** HDL cholesterol ≥60 mg/dL counts as a "negative" risk factor; its presence removes one risk factor from the total count.*

- Note: in ATP III, diabetes is regarded as a CHD risk equivalent.

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Step 4

If 2+ risk factors (other than LDL) are present without CHD or CHD risk equivalent, assess 10-year (short-term) CHD risk (see Framingham tables).
Three levels of 10-year risk:

- >20% — CHD risk equivalent
- 10-20%
- <10%

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Step 5

Determine risk category:

- Establish LDL goal of therapy
- Determine need for therapeutic lifestyle changes (TLC)
- Determine level for drug consideration

LDL Cholesterol Goals and Cutpoints for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories.

Risk Category	LDL Goal	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)	LDL Level at Which to Consider Drug Therapy
CHD or CHD Risk Equivalents (10-year risk >20%)	<100 mg/dL	≥100 mg/dL	≥130 mg/dL (100-129 mg/dL: drug optional)*
2+ Risk Factors (10-year risk ≤20%)	<130 mg/dL	≥130 mg/dL	10-year risk 10-20%: ≥130 mg/dL 10-year risk <10%: ≥160 mg/dL
0-1 Risk Factor†	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)

* *Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol <100 mg/dL cannot be achieved by therapeutic lifestyle changes. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g., nicotinic acid or fibrate. Clinical judgment also may call for deferring drug therapy in this subcategory.*
† *Almost all people with 0-1 risk factor have a 10-year risk <10%, thus 10-year risk assessment in people with 0-1 risk factor is not necessary.*

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Step 6

Initiate therapeutic lifestyle changes (TLC) if LDL is above goal.

TLC Features

- TLC Diet:
  - Saturated fat <7% of calories, cholesterol <200 mg/day
  - Consider increased viscous (soluble) fiber (10-25 g/day) and plant stanols/sterols (2g/day) as therapeutic options to enhance LDL lowering
- Weight management
- Increased physical activity.

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Step 7

Consider adding drug therapy if LDL exceeds levels shown in Step 5 table:

- Consider drug simultaneously with TLC for CHD and CHD equivalents
- Consider adding drug to TLC after 3 months for other risk categories.

Drugs Affecting Lipoprotein Metabolism

Drug Class	Agents and Daily Doses	Lipid/Lipoprotein Effects		Side Effects	Contraindications
HMG CoA reductase inhibitors (statins)	Lovastatin (20-80 mg) Pravastatin (20-40 mg) Simvastatin (20-80 mg) Fluvastatin (20-80 mg) Atorvastatin (10-80 mg) Cerivastatin (0.4-0.8 mg)	LDL HDL TG	↓18-55% ↑5-15% ↓7-30%	Myopathy Increased liver enzymes	Absolute: • Active or chronic liver disease Relative: • Concomitant use of certain drugs*
Bile acid sequestrants	Cholestyramine (4-16 g) Colestipol (5-20 g) Colesevelam (2.6-3.8 g)	LDL HDL TG	↓15-30% ↑3-5% No change or increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute: • dysbeta-lipoproteinemia • TG >400 mg/dL Relative: • TG >200 mg/dL
Nicotinic acid	Immediate release (crystalline) nicotinic acid (1.5-3 gm), extended release nicotinic acid (Niaspan®) (1-2 g), sustained release nicotinic acid (1-2 g)	LDL HDL TG	↓5-25% ↑15-35% ↓20-50%	Flushing Hyperglycemia Hyperuricemia (or gout) Upper GI distress Hepatotoxicity	Absolute: • Chronic liver disease • Severe gout Relative: • Diabetes • Hyperuricemia • Peptic ulcer disease
Fibric acids	Gemfibrozil (600 mg BID) Fenofibrate (200 mg) Clofibrate (1000 mg BID)	LDL *(may be increased in patients with high TG)* HDL TG	↓5-20% ↑10-20% ↓20-50%	Dyspepsia Gallstones Myopathy	Absolute: • Severe renal disease • Severe hepatic disease

* *Cyclosporine, macrolide antibiotics, various anti-fungal agents, and cytochrome P-450 inhibitors (fibrates and niacin should be used with appropriate caution).*

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Step 8

Identify metabolic syndrome and treat, if present, after 3 months of TLC.

Clinical Identification of the Metabolic Syndrome – Any 3 of the Following:

Risk Factor	Defining Level
Abdominal obesity*	Waist circumference†
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥110 mg/dL

* *Overweight and obesity are associated with insulin resistance and the metabolic syndrome. However, the presence of abdominal obesity is more highly correlated with the metabolic risk factors than is an elevated body mass index (BMI). Therefore, the simple measure of waist circumference is recommended to identify the body weight component of the metabolic syndrome.*

† *Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased, e.g., 94-102 cm (37-39 in). Such patients may have a strong genetic contribution to insulin resistance. They should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.*

Treatment of the metabolic syndrome

- Treat underlying causes (overweight/obesity and physical inactivity):
  - Intensify weight management
  - Increase physical activity.

- Treat lipid and non-lipid risk factors if they persist despite these lifestyle therapies:
  - Treat hypertension
  - Use aspirin for CHD patients to reduce prothrombotic state
  - Treat elevated triglycerides and/or low HDL (as shown in Step 9).

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Step 9

Treat elevated triglycerides.

ATP III Classification of Serum Triglycerides (mg/dL)

<150	Normal
150-199	Borderline high
200-499	High
≥500	Very high

Treatment of elevated triglycerides (≥150 mg/dL)

- Primary aim of therapy is to reach LDL goal
- Intensify weight management
- Increase physical activity
- If triglycerides are ≥200 mg/dL after LDL goal is reached, set secondary goal for non-HDL cholesterol (total – HDL) 30 mg/dL higher than LDL goal.

Comparison of LDL Cholesterol and Non-HDL Cholesterol Goals for Three Risk Categories

Risk Category	LDL Goal (mg/dL)	Non-HDL Goal (mg/dL)
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	<100	<130
Multiple (2+) Risk Factors and 10-year risk ≤20%	<130	<160
0-1 Risk Factor	<160	<190

If triglycerides 200-499 mg/dL after LDL goal is reached, consider adding drug if needed to reach non-HDL goal:

- intensify therapy with LDL-lowering drug, or
- add nicotinic acid or fibrate to further lower VLDL.

If triglycerides ≥500 mg/dL, first lower triglycerides to prevent pancreatitis:

- very low-fat diet (≤15% of calories from fat)
- weight management and physical activity
- fibrate or nicotinic acid
- when triglycerides <500 mg/dL, turn to LDL-lowering therapy.

Treatment of low HDL cholesterol (<40 mg/dL)

- First reach LDL goal, then:
- Intensify weight management and increase physical activity
- If triglycerides 200-499 mg/dL, achieve non-HDL goal
- If triglycerides <200 mg/dL (isolated low HDL) in CHD or CHD equivalent consider nicotinic acid or fibrate.

Men

Estimate of 10-Year Risk for Men

(Framingham Point Scores)

Age	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Total Cholesterol	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Point Total	10-Year Risk %
<0	< 1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥17	≥ 30

10-Year risk _____%

Women

Estimate of 10-Year Risk for Women

(Framingham Point Scores)

Age	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Total Cholesterol	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
≥280	13	10	7	4	2

	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

Point Total	10-Year Risk %
< 9	< 1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥25	≥ 30

10-Year risk _____%

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health
National Heart, Lung, and Blood Institute

NIH Publication No. 01-3305
May 2001

*TLC ATP III

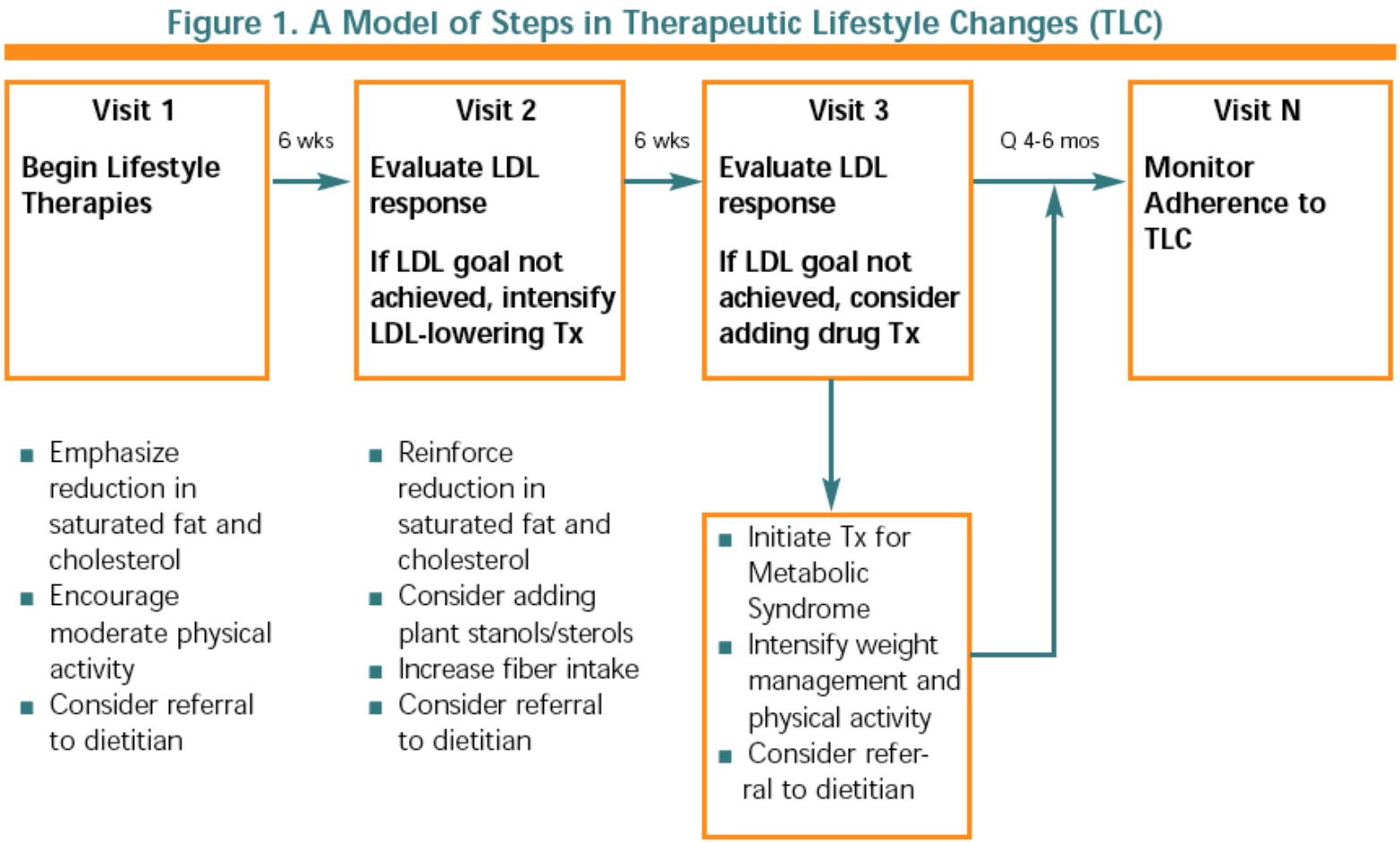


Figure 1. A Model of Steps in Therapeutic Lifestyle Changes (TLC)
Visit 1
Begin Lifestyle Therapies
6 wks
Visit 2
Evaluate LDL response
If LDL goal not achieved, intensify LDL-lowering Tx
6 wks
Visit 3
Evaluate LDL response
If LDL goal not achieved, consider adding drug Tx
Q 4-6 mos
Visit N
Monitor Adherence to TLC
Emphasize reduction in saturated fat and cholesterol
Encourage moderate physical activity
Consider referral to dietitian
Reinforce reduction in saturated fat and cholesterol
Consider adding plant stanols/sterols
Increase fiber intake
Consider referral to dietitian
Initiate Tx for Metabolic Syndrome
Intensify weight management and physical activity
Consider referral to dietitian

*Dieta ATP III

SFA	< 7% E
PUFA	sino a 10% E
MUFA	sino a 20% E
FAT	25-35% E
CHO	50-60% E
Fibra	20-30 g/die
CH	< 200 mg/die
PRO	15%
Energia	In base al peso

MNT and Referral to a RD (2)

Patients who attend multiple RD visits for MNT lasting an average of 45 minutes (30-60 minutes per session) over 6 to 12 weeks can reduce daily dietary fat (5% to 8%), saturated fat (2% to 4%) and energy intake (232-710 kcal per day).

This can result in a reduction in serum total cholesterol (TC) (↓7% to 21%), LDL-C (↓7% to 22%) and triglycerides (↓11% to 31%).

Strong, Imperative

MNT Number and Duration of Visits (1)

RD should provide more than 2 visits for MNT (3 to 6 visits) to further improve a patient's lipid profile.

The magnitude of low-density lipoprotein cholesterol (LDL-C) reduction increases with additional visits or time spent with the RD.

MNT Number and Duration of Visits (2)

Studies report that further reduction in TC (↓19% with 4 RD visits vs. ↓12% with 2 RD visits) and LDL-C (↓21% with 4 RD visits/180 minutes vs. ↓12% with 2 RD visits/120 minutes were observed.

Further research is needed to define the optimal duration and frequency of follow-up visits with the RD.

Fair, imperative

Lipid-Lowering Medication (1)

If a patient is on lipid-lowering medications, the RD should provide 3 or more visits for MNT averaging 45 minutes per session over a 6 to 8 week period to improve the patient's lipid profile.

Lipid-Lowering Medication (2)

Two retrospective studies showed 50% of patients were obviated from lipid drug eligibility after three MNT visits with the RD.

In a randomized controlled trial (RCT), at the end of 12 months, no subject in the MNT group needed lipid-lowering drugs, while six of 44 in the Usual Care group needed medication at an average cost of $446 (in 1995 dollars) for months 7 to 12 of the trial.

Fair, conditional

Assessment of Food and Nutrient Intake (1)

The registered dietitian (RD) should assess the food/nutrition intake and related history of adults with disorders of lipid metabolism (DLM) including, but not limited to the following:

1. Energy intake, serving sizes, meal-snack pattern, fat, types of fat and cholesterol, carbohydrate, fiber, micronutrient intake
2. Bioactive substances (alcohol intake, plant stanols and sterols, soy protein, psyllium, fish oil)
3. Food and nutrient administration (patient's experience with food)
4. Previous and current diet history, diet orders, exclusions and experience, cultural and religious preferences

Assessment of Food and Nutrient Intake (2)

5. Eating environment, eating out

6. Medication and herbal supplement use: Prescription and over-the-counter medications, herbal and complementary product use (coenzyme Q-10, red yeast rice)

7. Knowledge, beliefs or attitudes: Motivation, readiness to change, self-efficacy

8. Behavior: Diet adherence, disordered eating, meal timing and duration

9. Factors affecting access to food: Psychosocial/economic issues (e.g., social support) impacting nutrition therapy

10. Physical activity and function: Exercise patterns, functionality for activities of daily living, sleep patterns.

Assessment of Food and Nutrient Intake (3)

Assessment of the above factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions. Inability to achieve optimal nutrient intake may contribute to poor outcomes.

Assessment of Food and Nutrient Intake (4)

Dietary intake can be assessed using a variety of approaches, including multiple 24-hour recalls or three non-consecutive days of food records (i.e., two weekdays and one weekend day). In addition, the more sophisticated multiple-pass technology may be used.

Dietary results can be analyzed using nutrient analysis software programs that have complete nutrient data. Manufacturers' nutrition facts labels may also be included.

Consensus, *Imperative*

Assessment of Anthropometric Data

In addition to body mass index (BMI), the RD should use waist circumference (WC) or waist-to-hip ratio (WHR) to assess obesity and cardiovascular disease (CVD) risk.

BMI alone is not a good predictor of CVD risk in persons over 65 years old.

Increases in WC, WHR, and BMI are associated with coronary heart disease (CHD) events and CVD mortality.

Strong, Imperative

Assessment of Biochemical Data (1)

The RD should assess the biochemical data, medical tests and procedures of adults with disorders of lipid metabolism (DLM) including, but not limited to lipid profile [total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), non-HDL-C, low-density lipoprotein cholesterol (LDL-C), triglycerides (TG)], *blood pressure*, and fasting glucose.

Assessment of Biochemical Data (2)

Additional values such as Lp(a), hemoglobin A1c (HbA1c), 25-OH vitamin D, thyroid function tests and C-reactive protein (CRP) *may* also be assessed.

Assessment of these factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions. Inability to achieve optimal nutrient intake may contribute to poor outcomes.

Consensus, Imperative

Assessment of Medical and Health History and Physical Findings (1)

RD should assess the medical and health history of adults with disorders of lipid metabolism (DLM) for the presence of other disease states and conditions, such as endocrine/metabolism disorders, metabolic syndrome, HIV/AIDS, hypertension, obesity and food allergies and intolerances.

Assessment of Medical and Health History and Physical Findings (2)

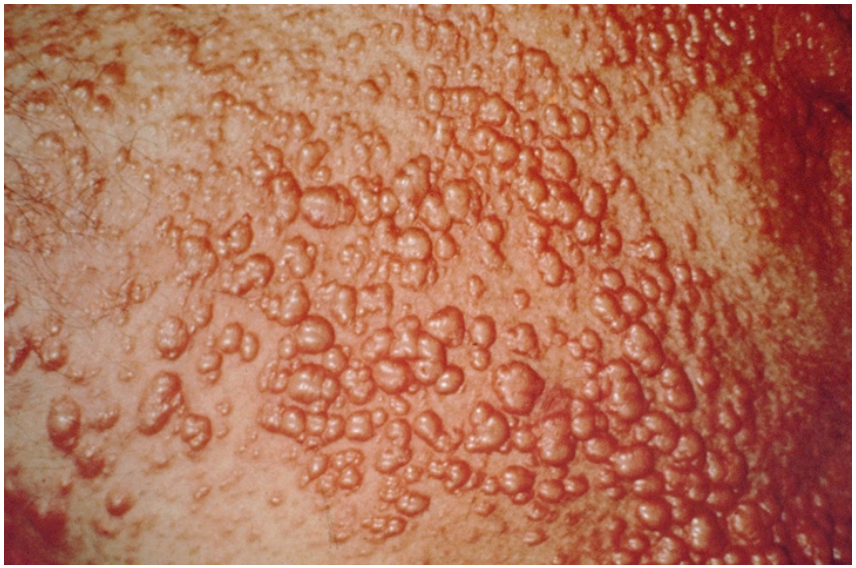
Adults with DLM, have a higher prevalence of comorbidities, which are *risk factors* for the progression of cardiovascular disease (CVD).

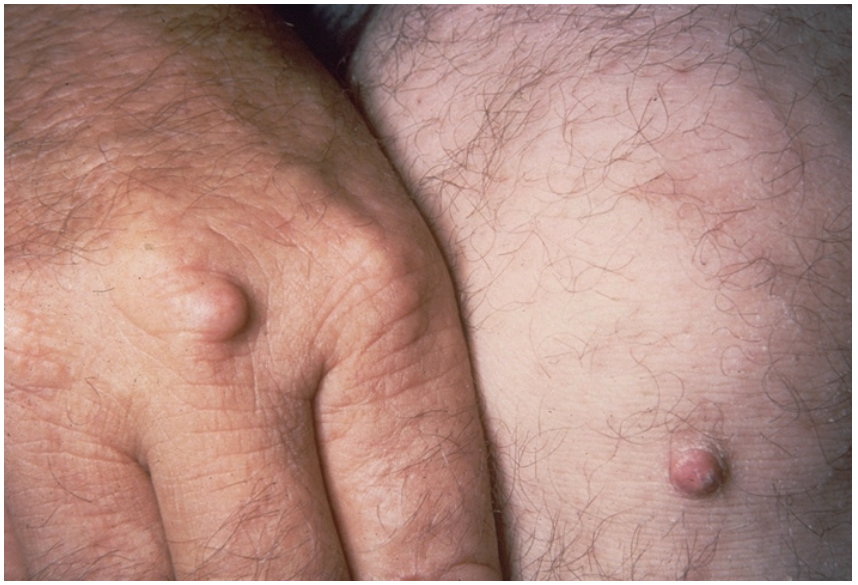
The RD should note observations of fat distribution (i.e., abdominal obesity or lipodystrophy) and fluid retention (i.e., edema or ascites), as well as any evidence of xanthomas, xanthelasma, corneal arcus, and palmar discolorations.

Assessment of the above factors is needed to effectively determine nutrition diagnoses and plan the nutrition interventions. Inability to achieve optimal nutrient intake may contribute to poor outcomes.

Consensus, Imperative

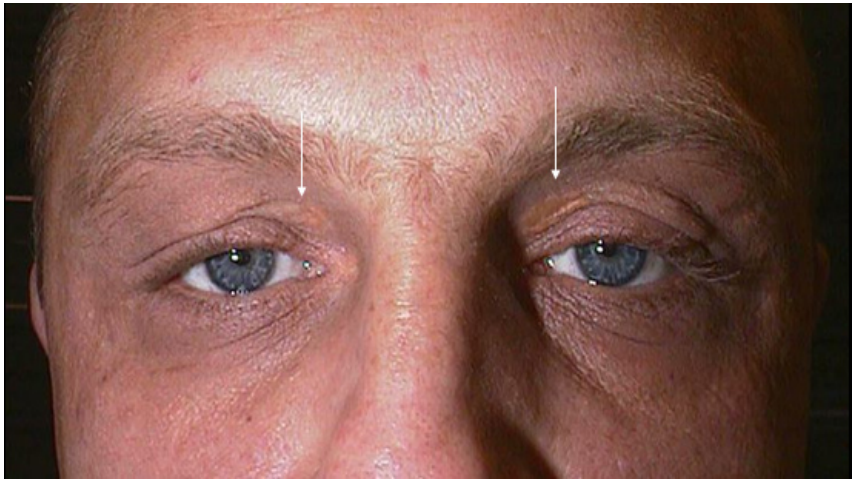
*Xantoma

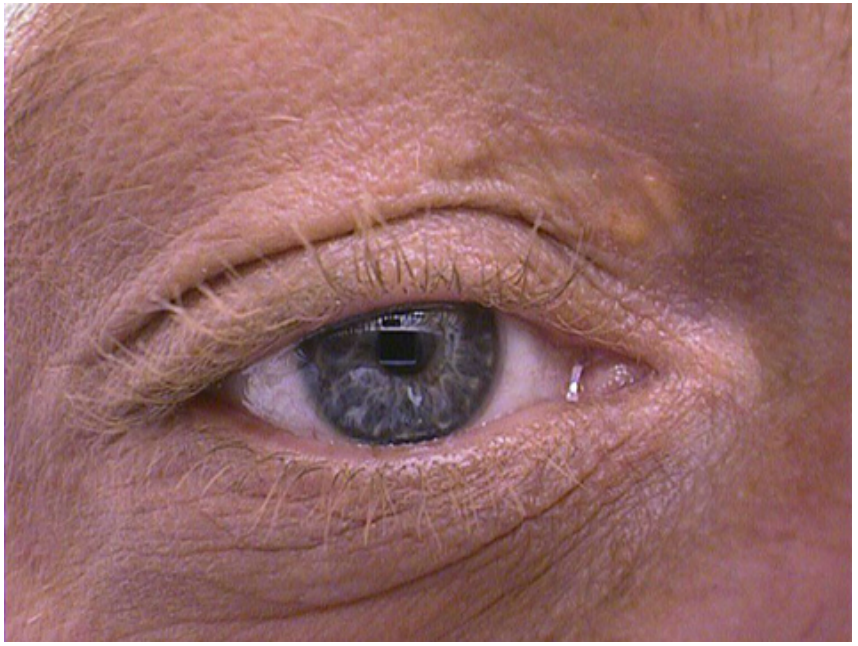




http://emedicine.medscape.com/article/1103971-clinical

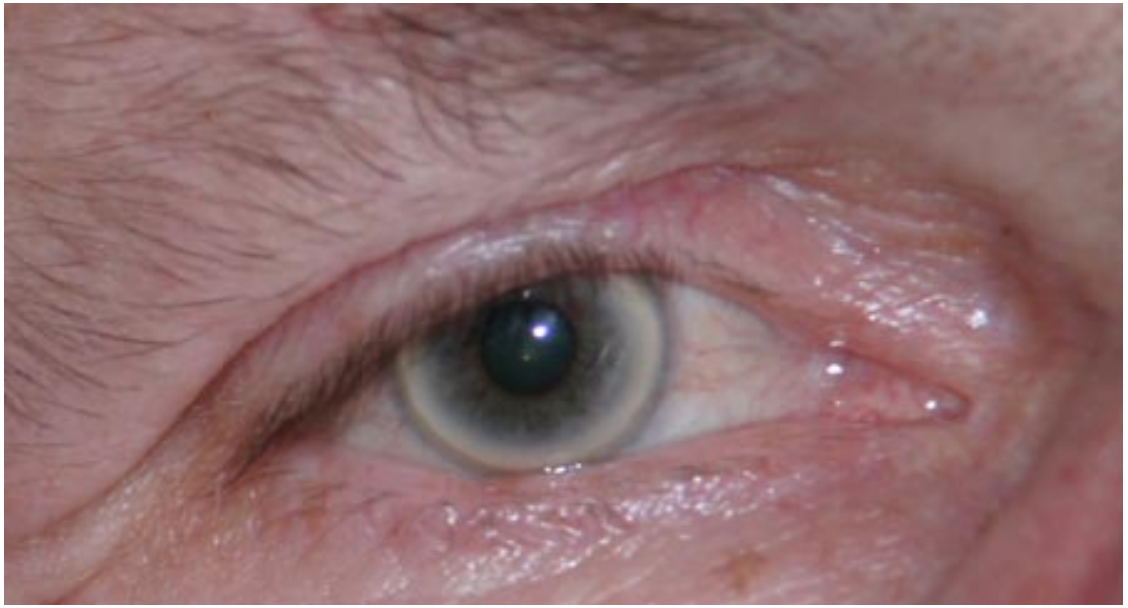
*Xantelasma





http://emedicine.medscape.com/article/1213423-overview

*Arcus cornealis



Energy and Macronutrient Needs (1)

- The RD should determine energy and macronutrient needs (e.g., quantity and quality of fat, carbohydrate and protein) of adults with disorders of lipid metabolism (DLM).

- Use of indirect calorimetry is preferred for measuring energy needs. When indirect calorimetry is not available, predictive equations can be used. After estimation of current energy needs, a recommended energy intake can be developed with consideration of whether the goal is weight maintenance or weight loss.

Energy and Macronutrient Needs (2)

The recommended macronutrient intake is:

Total fat of 25-35% (achieving goals of saturated fat (SFA) and trans fat <7% of kcals and dietary cholesterol <200 mg per day is typically feasible only with total fat ≤30% kcals per day)

Total protein of 15-20% (encourage vegetable protein to help achieve SFA goals and cholesterol goals)

Total carbohydrates (CHO) of 45-60% of kcals (with emphasis on high fiber/ complex CHO sources and avoidance of refined CHO foods).

Energy and Macronutrient Needs (3)

Comparison of the *assessed food and nutrient intake* with estimated needs will help the RD to develop strategies to meet the recommendations of the cardioprotective diet.

Estimating current (or baseline) energy and macronutrient intake, is essential to establishing the relevant nutrition diagnoses and tailoring the MNT.

Consensus, Imperative

Plant-derived Omega-3 Fatty Acids and CVD (1)

If consistent with patient preference and not contraindicated by risks or harms, the RD can recommend *foods* rich in plant-derived omega-3 fatty acids (ALA; alpha-linolenic acid) to reduce the risk of cardiovascular disease (CVD) or CVD events.

In persons with coronary heart disease (CHD), higher intakes of plant-derived omega-3 fatty acids, are associated with a decreased rate of cardiac death and non-fatal myocardial infarction (MI) and may be protective against recurrence of MI. One study reported use of 4.8% of calories from ALA.

Plant-derived Omega-3 Fatty Acids and CVD (2)

In persons without CHD, higher intakes of food sources of ALA are associated with a lower risk of fatal ischemic heart disease (IHD) and prolonged repolarization (mean intake 0.74 g per day of ALA).

In case-control studies, ALA lowered the risk of IHD in men and women (amount of ALA from mustard oil not specified) and sudden cardiac death in women (median intake 1.16g per day ALA). Alpha-linolenic acid, however, was not related to other non-sudden fatal CVD events or to non-fatal MI.

Plant-derived Omega-3 Fatty Acids and CVD (3)

These studies contrasted lower intake of approximately 0.6 g per day with higher intakes of approximately 1.4 g per day. This recommendation can be followed within the context of diets that meet the Adequate Intake (AI) for ALA of 1.6 g per day for men and 1.1 g per day for women (within the Acceptable Macronutrient Distribution Range of 0.6% to 1.2% of energy) (DRI).

Fair, Conditional

Marine-Derived *Food Sources* of Omega-3 Fatty Acids and CVD (1)

- If consistent with patient preference and not contraindicated by risks or harms, the Registered Dietitian (RD) should encourage food sources of marine-derived omega-3 fatty acids, preferably from fish to reduce risk of cardiovascular disease (CVD).

- For patients without CHD: recommend 2 fish servings per week (4 oz servings each)

- For patients with CHD: Recommend 2 or more fish servings per week (4oz servings each).

Marine-Derived *Food Sources* of Omega-3 Fatty Acids and CVD (2)

Studies report, that in persons with CHD higher plasma levels of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are associated with a reduction in arrhythmias and fatal heart disease and reduced progression of coronary atherosclerosis.

In persons without CHD, consumption of fish and marine-derived omega-3 fatty acids may or may not be associated with reduced incidence of arrhythmia, including atrial fibrillation.

Fair, Conditional

Marine-Derived *Food Sources* of Omega-3 Fatty Acids and CVD (3)

If persons choose to consume eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) supplements or EPA alone to reduce the risk of CVD) mortality and events (sudden death and re-infarction), the RD should advise:

Omega-3 *Supplements* and Risk for CVD (2)

Patients without CHD: Intervention studies of omega-3 supplementation have not been done in patients without CHD

Patients with CHD, but no angina or implantable cardioverter defibrillators (ICD): supplementation with 850mg per day EPA and/or DHA reduced sudden death by 45%

Patients with CHD with angina or ICDs: EPA and DHA supplements may be contraindicated.

Omega-3 *Supplements* and Risk for CVD (3)

The US Food and Drug Administration advises that consumption of more than three grams of omega-3 fatty acids per day may cause gastrointestinal symptoms.

Fair, Conditional

*Quale evidenza?

Association Between Omega-3 Fatty Acid Supplementation and Risk of Major Cardiovascular Disease Events

A Systematic Review and Meta-analysis

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Context Considerable controversy exists regarding the association of omega-3 polyunsaturated fatty acids (PUFAs) and major cardiovascular end points.

Objective To assess the role of omega-3 supplementation on major cardiovascular outcomes.

Conclusion Overall, omega-3 PUFA supplementation was not associated with a lower risk of all-cause mortality, cardiac death, sudden death, myocardial infarction, or stroke based on relative and absolute measures of association.

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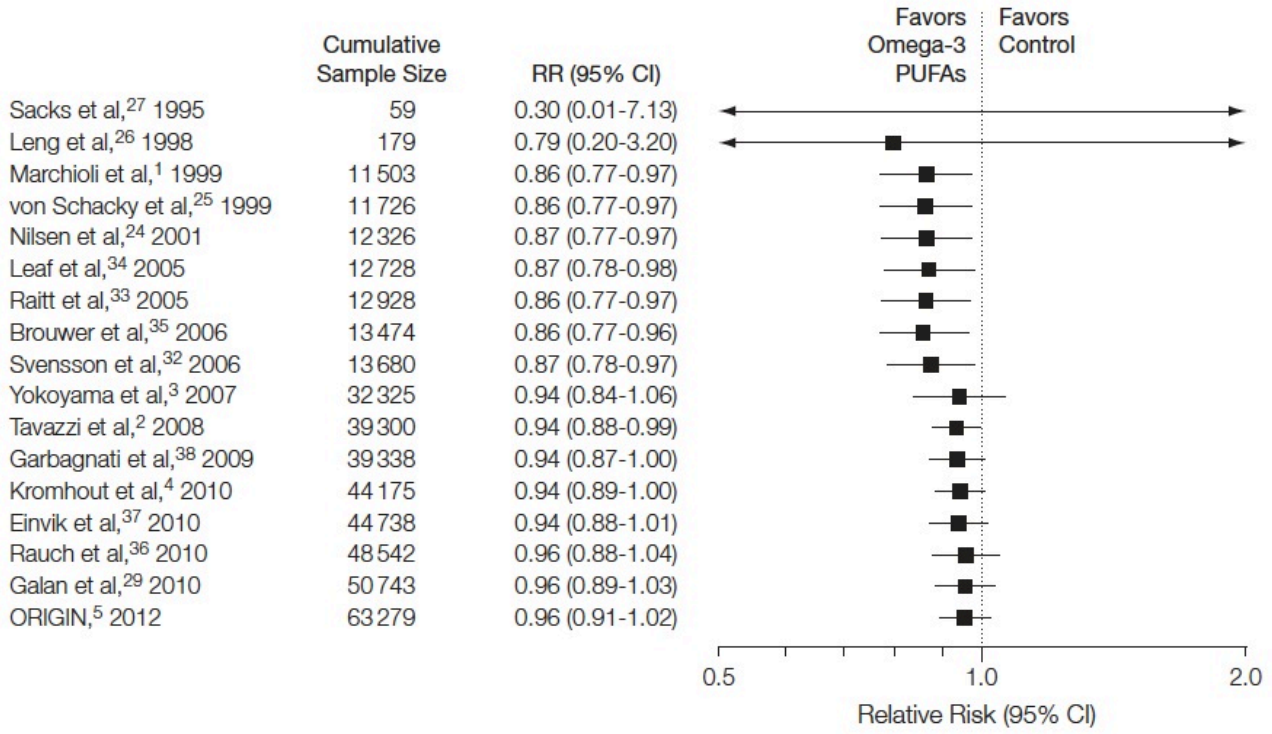
Figure 5. Cumulative Meta-analysis of the Omega-3 Supplements for All-Cause Mortality



Error bars indicate the 95% CI of the cumulative meta-analysis estimates as randomized patients accumulate through time. PUFAs indicates polyunsaturated fatty acids; RR, relative risk.

Antioxidants and the Cardioprotective Diet

The Registered Dietitian (RD) should specifically plan antioxidant-rich *foods* such as fruits, vegetables, whole grains and nuts containing Vitamin E, vitamin C and β-carotene (and other carotenoids), into a cardioprotective dietary pattern. These *foods* have been shown to be associated with reduced coronary heart disease (CHD) risk.

Consensus, Imperative

Nuts and Coronary Heart Disease (1)

If consistent with patient preference and not contraindicated by risks or harms, the RD may isocalorically incorporate daily consumption of *unsalted* peanuts and lower saturated fat tree nuts, specifically walnuts [noci], almonds [mandorle], pecans [noci americani], and pistachios [pistacchi] into a cardioprotective dietary pattern.

Nuts and Coronary Heart Disease (2)

Consuming five ounces (average 900 kcals) of nuts per week is associated with a reduced risk of coronary heart disease (CHD) [*OBSERVATIONAL STUDIES].

Because of their beneficial fatty acid profile, as well as other nutritional components, nuts may be isocalorically incorporated into a cardioprotective dietary pattern to achieve lipid lowering.

Nuts and Coronary Heart Disease (3)

Studies demonstrate that 1.75 to 4 oz (½ to 1 cup or 315 to 720 kcals) nuts per day lowers total cholesterol (TC) by 4% to 21% and low-density lipoprotein cholesterol (LDL-C) by 6% to 29%.

The practicality of this recommendation is limited, because of the significant caloric contribution this amount of nuts provides.

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Fat Components of the Cardioprotective Diet (1)

The RD should tailor the cardioprotective dietary pattern to the individual's needs to provide a total fat intake of 25% to 35% of calories (ATP III) with < 7% of calories from saturated fat and trans-fatty acids (TFA).

Because TFAs raise total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and may decrease high-density lipoprotein cholesterol (HDL-C), TFA consumption should be as low as possible.

Alcohol Intake

If a patient currently drinks alcohol, and if not contraindicated by risks and harms, then the RD could incorporate a maximum of 1 drink per day for women and up to 2 drinks per day for men into a cardioprotective dietary pattern that meets the patient's caloric needs.

This level of alcohol consumption has been associated with a reduced risk of CVD. One type of alcohol does not appear to be better than another. Current evidence does not justify recommending that non-drinkers begin drinking alcohol.

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Physical Activity and CHD

If not contraindicated by risks and harms, the RD should recommend resistance exercise for a minimum of 2 days a week and moderate intensity physical activity for at least 30 minutes most, if not all, days of the week. Many individuals will have to start slowly and increase gradually to achieve goals.

Moderately intense physical activity reduces the risk of cardiovascular disease (CVD) events, decreases low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG), and increases high-density lipoprotein cholesterol (HDL-C).

Strong, Conditional

Fat Components of the Cardioprotective Diet (1)

Cholesterol should be <200mg per day. The majority of total fat intake should be derived from unsaturated fat sources.

For individuals at their appropriate body weight, without elevated LDL-C or triglyceride (TG) levels, and with normal HDL-C levels, saturated fat calories could be replaced by unsaturated fat and/or complex carbohydrate (CHO). This dietary pattern can lower LDL-C up to 16% and decrease risk of coronary heart disease (CHD) and CHD events.

Strong, Imperative

Replacing Saturated Fats (1)

- The RD should develop a nutrition prescription within a cardioprotective dietary pattern that replaces saturated fat calories with calories from *either complex carbohydrate* (CHO) principally contributed by fruits, vegetables and whole grains, protein *and/or unsaturated fat*.

- Robust evidence documents that saturated fat increases low-density lipoprotein cholesterol (LDL-C). Under isocaloric conditions, large scale, randomized controlled trials (RCTs) indicate that a cardioprotective diet reduced LDL-C by 9% to 16% in both normo- and hyperlipidemic individuals.

Replacing Saturated Fats (2)

Advantages for substituting *complex CHO* for saturated fat calories include the following:

It is difficult to achieve a saturated fat reduction of <10% of calories in diets that are 30% to 35% of total calories from fat

A diet high in complex CHO includes shortfall nutrients (e.g., dietary fiber, potassium and magnesium and other micronutrients)

A diet high in complex CHO is nutrient-dense and is less likely to contribute excess calories

In addition, a diet rich in omega-3 fatty acids and/or monounsaturated fat, and reduced in refined CHO may also be effective in reducing serum triglycerides (TG) without adverse impact on high-density lipoprotein cholesterol (HDL-C).

Replacing Saturated Fats (3)

- In treating overweight or obese patients, where the goal is reduction of total energy, *reduction* rather than replacement of saturated fat calories may be warranted, depending on current intake of unsaturated fat.

- Strong, Imperative

Plant Stanols and Sterols

If consistent with patient preference and not contraindicated by risks or harms, the RD should consider incorporating plant sterol and stanol ester-enriched foods into a cardioprotective diet, to be consumed two or three times per day, for a total consumption of two to three grams per day.

These doses further lower total cholesterol (TC) by 4% to 11% and low-density lipoprotein cholesterol *(LDL-C) by 7% to 15%*. Doses beyond three grams do not provide additional benefit. To prevent weight gain, isocalorically substitute stanol- and sterol-enriched foods for other foods. Plant stanols and plant sterols are also effective in people taking statin drugs.

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Plant Stanols and Sterols and Adverse Effects

The RD should be aware that research to date has not documented adverse effects, including reduced absorption of carotenoids, retinol and tocopherols. Plant stanols and sterols may be included in a patient's nutrition prescription (e.g., two or three grams per day) to lower cholesterol.

Research from 17 randomized controlled trials (RCTs) indicates effective serum cholesterol-lowering benefits without any reported adverse effects, including no significant effect on plasma fat soluble vitamin status.

Two observational studies reported an association between plasma levels and aortic tissue concentration of stanols and sterols in a small number of individuals who consumed foods supplemented with plant sterol and stanol esters. The clinical significance of the association has not been documented.

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Coenzyme Q10 and Disorders of Lipid Metabolism

If a patient is taking coenzyme Q10 supplements, then RD may discuss the *insufficient evidence* for the association of CoQ10 and coronary heart disease (CHD) and allow the patient to make an individual decision based on his or her specific needs.

The clinical significance of normalizing CoQ10 levels in patients treated with statin medications is inconclusive.

Weak, Conditional

Metabolic Syndrome

For individuals with metabolic syndrome, the RD should recommend a calorie-controlled cardioprotective dietary pattern that avoids extremes in carbohydrate and fat intake, limits added sugar and alcohol, and includes physical activity at a moderate intensity level for at least 30 minutes on most (preferably all) days of the week.

Weight loss of 7% to 10% of body weight should be encouraged, if indicated. These lifestyle changes improve risk factors of metabolic syndrome.

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Elevated Triglycerides and Macronutrients (1)

For individuals with elevated triglycerides (TG) (≥ 150mg per dL), the RD should recommend a calorie-controlled, cardioprotective dietary pattern that avoids extremes in carbohydrate and fat intake and includes physical activity. Non-nutrient dense calorie sources including alcohol and added sugar, should be limited as much as possible.

Weight loss of 7% to 10% of body weight should be encouraged, if indicated. These lifestyle changes have been shown to lower TG levels.

Elevated Triglycerides and Macronutrients

It is unclear what the ideal macronutrient composition (e.g., protein and unsaturated fat) should be for someone with borderline high TG. At this time it seems prudent to *follow recommendations appropriate for people with the metabolic syndrome*, as moderately elevated TG are a component of this disease.

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Elevated Triglycerides and EPA/DHA Supplements

In patients with elevated triglycerides (TG), in addition to lifestyle modification with a cardioprotective diet, the RD can advise that high-dose supplemental eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (2 to 4 grams per day) may be utilized under medical supervision. High-doses of supplemental EPA and DHA have been shown to lower TG in patients with elevated TG (greater than 200mg per dL).

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Homocysteine, Folate, Vitamin B6, Vitamin B12 and CHD

The RD should include food sources of folate, vitamin B6, and vitamin B12 in the cardioprotective dietary pattern to meet the Dietary Reference Intakes (DRI).

Supplemental doses of these vitamins to lower cardiovascular disease (CVD) risk should *not* be recommended.

Although supplemental B-vitamins (folic acid, vitamin B6, and vitamin B12) may lower homocysteine in people with high serum homocysteine levels (>13umol per L), this has not translated into reduced CVD events and in fact, may be harmful.

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*Omocisteina e rischio cardiovascolare?

REVIEW

CME CREDIT

EDUCATIONAL OBJECTIVE: Readers will advise their patients that the hypothesis that elevated homocysteine should be treated to reduce the risk of cardiovascular disease has neither been proved nor disproved

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The homocysteine hypothesis: Still relevant to the prevention and treatment of cardiovascular disease?

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ABSTRACT

Although evidence suggests that the homocysteine hypothesis is still relevant as a predictor of cardiovascular risk, we cannot conclude that measuring the homocysteine level is useful in guiding treatment. Furthermore, studies of primary and secondary prevention show no evidence that taking folic acid or other B vitamins lowers the risk of cardiovascular events.

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TABLE 1

Causes of elevated homocysteine

Mild (15–30 µmol/L)
Mild-moderate renal disease
Drug use—antiepileptic drugs, methotrexate, theophylline, niacin, immunosuppressive drugs, fibrates, levodopa, metformin (Glucophage)
Hypothyroidism
Hyperproliferative disorders, certain cancers
Psoriasis
Methylene tetrahydrofolate reductase (MTHFR) 677C>T variant
Mild-moderate folate or vitamin B_{12} deficiency
Increasing age
High protein intake
Low intake of vegetables or fruits
Sickle-cell anemia

Moderate (30–100 µmol/L)
End-stage renal disease
Moderate vitamin B_{12} deficiency
Severe folate deficiency
MTHFR 677C>T variant combined with low folic acid levels

Severe (≥ 100 µmol/L)
Severe vitamin B_{12} deficiency
Cystathionine beta-synthase deficiency

BASED ON INFORMATION IN REFERENCES 9, 11, AND 12

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KEY POINTS

Factors that can cause the plasma homocysteine concentration to be high include deficiencies of vitamin B_6, vitamin B_{12}, and folic acid; renal insufficiency; and genetic variants in enzymes responsible for homocysteine metabolism.

Higher plasma homocysteine levels are associated with a higher risk of cardiovascular, cerebrovascular, and peripheral arterial disease.

Supplementation of B vitamins and folic acid can lower plasma homocysteine levels.

Randomized controlled trials of supplementation to prevent cardiovascular events and other adverse outcomes have had mostly negative results. However, most patients in these trials had normal baseline plasma homocysteine levels.

Needed are randomized trials to see if supplementation improves outcomes in patients with high homocysteine levels.

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PLoS MEDICINE

Homocysteine and Coronary Heart Disease: Meta-analysis of *MTHFR* Case-Control Studies, Avoiding Publication Bias

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- Background: Moderately elevated blood levels of homocysteine are weakly correlated with coronary heart disease (CHD) risk, but causality remains uncertain. *When folate levels are low*, the TT genotype of the common C677T polymorphism (rs1801133) of the methylene tetrahydrofolate reductase gene (MTHFR) appreciably increases homocysteine levels, so ‘‘Mendelian randomization’’ studies using this variant as an instrumental variable could help test causality.

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- Conclusions: The CI for the overall result from large unpublished datasets shows *lifelong moderate homocysteine elevation has little or no effect on CHD*. The discrepant overall result from previously published studies reflects publication bias or methodological problems.

Carbohydrates and Protein in the Cardioprotective Diet

The Registered Dietitian RD should consider replacing saturated fat and trans-fatty acids with unsaturated fatty acids, complex carbohydrates and/or protein in the cardioprotective dietary pattern.

Saturated and trans fatty acids should be as low as possible. Studies are needed to determine the ideal percentages of these macronutrients as replacements for saturated fat.

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Fiber in the Cardioprotective Diet (1)

The RD should incorporate fiber-rich foods that contribute at least 25 g to 30g of fiber per day, with special emphasis on soluble fiber sources (7g to 13 g) into the cardioprotective dietary pattern.

These foods rich in soluble fiber include: fruits, vegetables and whole grains, especially high-fiber cereals, oatmeal, and legumes, especially beans.

Fiber in the Cardioprotective Diet (2)

Risk factors associated with coronary heart disease (CHD) and cardiovascular disease (CVD) are decreased as dietary fiber intake increases.

Diets high in total and soluble fiber, as part of a cardioprotective diet, can further reduce total cholesterol (TC) by 2% to 3% and low-density lipoprotein cholesterol (LDL-C) up to 7%.

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Monitoring

Monitor and Evaluate Food and Nutrient Intake (Consensus, Imperative)

Monitor and Evaluate Anthropometric Data (Consensus, Imperative)

Monitor and Evaluate Biochemical Data (Consensus, Imperative)

Monitor and Evaluate Energy and Macronutrient Needs (Consensus, Imperative)

=> Come discusso per la valutazione <=

Grazie