What dietary changes and supplements effectively lower LDL cholesterol?

**Evidence-Based Answer**

A low-fat diet reduces low-density lipoprotein cholesterol (LDL-C), especially when the diet is rich in unsaturated fats (SOR: A, meta-analysis). Supplementing with 2 g phytosterols or phytostanols daily, 67 g of nuts daily, and probiotics daily reduces LDL-C (SOR: B, lower quality meta-analyses).

A 2012 Cochrane review of 48 RCTs involving nearly 81,000 adult participants evaluated the effect of low-fat and modified diets on a variety of measures. Reduced-fat diets (<30% total daily calories from fat) resulted in a significant reduction in LDL-C (14 trials, N=6,971; mean difference [MD] –3.9 mg/dL; 95% CI, –5.4 to –1.9) compared with control or usual diet. Reduced and modified-fat diets (<30% total daily calories from fat with higher levels of mono- and polyunsaturated fats) also resulted in reduced LDL-C (4 trials, N=627; MD –8.1 mg/dL; 95% CI, –14 to –3.1) compared with control or usual diet.

A 2009 meta-analysis of 19 RCTs involving 1,273 participants examined the efficacy of plant sterols and stanols on lipids. Patients consumed plant sterols, plant stanols, or plant stanol esters delivered in spreads, bread, yogurt, etc, with a mean dose of 2.1 g/d. The duration of the trials ranged from 3 weeks to 1 year. Compared with usual diet in patients with or without hypercholesterolemia, plant sterols and stanols significantly reduced LDL-C (MD –14 mg/dL; 95% CI, –18 to –8.5).

A 2010 pooled analysis of 25 trials (16 crossover and 2 parallel-design controlled trials and 7 consecutive uncontrolled trials) with 583 patients assessed the effect of nut consumption on blood lipids in patients not taking lipid-lowering medication. When taken for at least 3 weeks, 67 g of daily nut consumption reduced LDL-C 7.4% (MD –10 mg/dL; 95% CI, –13 to –7.4) compared with usual diet.

A 2011 meta-analysis of 13 RCTs with 485 patients measured the effect of a daily dose of probiotic capsules or yogurt on serum lipids. None of the participants were taking cholesterol-reducing drugs. Mean baseline LDL-C ranged from 100 to 172 mg/dL. Probiotics reduced LDL (MD –4.9 mg/dL; 95% CI, –7.9 to –1.9) compared with the control group. Only 1 RCT showed a significant difference between intervention and control groups and 10 RCTs showed only a trend toward benefit with intervention.

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Should the male partner of someone with HPV changes on cervical biopsy have androscopy?

**Evidence-Based Answer**

Based on limited evidence, male partners of women with human papillomavirus (HPV) infection should probably not be referred for androscopy (SOR: C, disease-oriented outcomes in cohort studies).

A prospective cohort trial examined the HPV prevalence among 30 couples in which the women had any grade of cervical intraepithelial neoplasia (CIN) and 60 couples without CIN. Women with CIN lesions had more HPV infections than women without CIN lesions (76% vs 15%; P<.01), but no difference was noted in the male partners between the 2 groups (23% vs 11%; P=.26). There were no differences in positive findings on male androscopy between the 2 groups (17% vs 15%; P=.92). Both partners were HPV positive in 23 (of 90) couples; of these, only 13% (3 of 23) of couples were positive for the same HPV type.

To study the prognostic significance of penile acetowhite staining, a large cohort of 3,210 male partners of women with either HPV infection and/or præneoplastic lesions of the lower genital tract were examined by gross examination and then androscopy with acetowhite staining. Of those men, 39% had gross HPV lesions and 3.6% had lesions identified by acetowhite staining. Only 43% of the acetowhite stained lesions were positive for HPV by cytology or biopsy and only 37% were HPV positive by DNA testing. Only 30 samples were positive by both biopsy/cytology and DNA typing.

A case-control trial of 60 married couples, half with a diagnosis of cervical cancer and half with no cervical cancer—designed to compare urine HPV testing versus genital scraping/biopsies—also reported the prevalence and concordance of HPV infection in these couples. Positive results for high-risk HPV (types 16 and 18) were found in 70% of women with cervical cancer and 30% of their partners, and in 17% of healthy women and 10% of their partners ($P \leq 0.001$ comparing female cases vs female controls).

No statistically significant difference was noted when comparing male cases with male controls. Additionally, this study found type-specific concordance (HPV 16) in 9 of 21 dually HPV-positive couples in the group with female cervical cancer and 1 of 5 dually HPV-positive couples in the control group (43% vs 20%; $P$ not significant).

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How accurate is D-dimer for predicting recurrence of VTE in a patient with a history or current treatment of VTE?

Evidence-Based Answer
A persistently elevated D-dimer is associated with an approximate doubling of the odds of recurrent venous thromboembolism (VTE) (SOR: B, meta-analysis of and individual cohort studies). It is unclear how this information is best used clinically.

A meta-analysis of 4 cohort trials (N=1,539) evaluated the use of D-dimer as a prognostic test for recurrence of idiopathic VTE 1 month after discontinuation of oral anticoagulant therapy. The risk of VTE recurrence was greater in patients with persistently elevated D-dimer: 16% compared with 7.2% of patients with normal D-dimer (OR 2.4; 95% CI, 1.7–3.4). Variability between the 4 studies in D-dimer cutoff points and length of follow-up may have been potential weaknesses of this review.

A prospective cohort trial evaluated the value of D-dimer, measured at hospital discharge, for predicting recurrent VTE in patients with provoked (coagulopathies, cancer, immobilization, trauma, pregnancy, and surgery) and unprovoked acute pulmonary embolism (PE). The primary outcome measure was recurrent, symptomatic VTE. All patients (N=204) had a 3-month minimum treatment with vitamin K antagonists. D-dimer was tested at discharge; follow-up occurred at 3, 6, and 12 months and then every 12 months thereafter. Additionally, patients were assessed for PE by clinical history and physical examination, 12-lead electrocardiography, arterial blood gas analysis, chest x-ray examination, and lower-limb venous ultrasonography and confirmed by chest CT.

More patients with persistently elevated D-dimer experienced VTE recurrence: 21% compared with 6% for patients with decreasing D-dimer values ($P=0.001$). This gave the D-dimer test a sensitivity of 64% and specificity of 71% (positive likelihood ratio of 2.2, negative likelihood ratio of 0.51) for all subjects and 67% and 71%, respectively, for those with unprovoked PE.

An observational, prospective multicenter study (N=355) examined the value of serial D-dimer testing, beginning after at least 6 months of anticoagulation therapy, for predicting recurrence in subjects with idiopathic VTE. At the end of anticoagulation treatment, patients with elevated D-dimer values (n=19) continued treatment and were reevaluated at 6 months. Patients with normal D-dimer values (n=336) stopped treatment and were retested 1 month later. At 1 month, some patients (n=85) had abnormal D-dimer values and restarted anticoagulation and were retested bimonthly for a year. For patients whose D-dimer value became abnormal (and remained abnormal) at 3 months, the risk of VTE recurrence was higher than in patients with persistently normal D-dimer values (22% vs 4.6%; $P=0.003$).

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