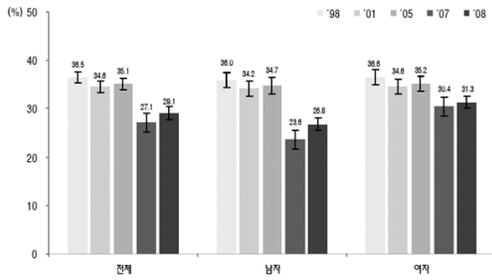


일차의료에서의 스트레스 관리지침

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국민건강 영양조사의 스트레스 인지율



※스트레스 인지율 : 평소 일상생활 중에 스트레스를 많이 느끼는 분을, 만일세이삼 ※2009년 추계연구로 연장표준화

Psychosocial distress for cardiovascular disease

- Emotional factors
 - Depression
 - Anxiety
 - Anger, hostility
- Chronic stressors
 - Low social support
 - Low socioeconomic status
 - Work stress
 - Marital stress

Risk of acute myocardial infarction

Risk Factor	Gender	Cont. %	Case %	OR (95%CI)	PAR (95%CI)
Curr Smok	female	9.3	20.1	2.86 (2.36-3.46)	15.8 (12.9, 19.3)
	male	33.0	53.1	3.05 (2.78-3.33)	44.0 (40.9, 47.2)
Diabetes	female	7.9	25.5	4.26 (3.51-5.18)	19.1 (16.4, 21.7)
	male	7.4	18.2	2.67 (2.36-3.02)	10.1 (8.8, 11.4)
Hypertension	female	28.3	53.0	2.95 (2.57-3.39)	35.8 (32.1, 39.6)
	male	19.7	34.8	2.32 (2.12-2.53)	19.5 (17.7, 21.5)
Abd Obesity	female	33.3	45.8	2.26 (1.90-2.68)	35.9 (28.9, 43.6)
	male	33.3	46.5	2.24 (2.03-2.47)	32.1 (28.0, 36.5)
PS Index	female	-	-	3.49 (2.41-5.04)	40.0 (28.6, 52.8)
	male	-	-	2.58 (2.11-3.14)	25.3 (19.2, 34.0)
Fruits/Veg	female	50.3	39.4	0.58 (0.48-0.71)	17.8 (12.9, 24.1)
	male	39.6	34.7	0.74 (0.66-0.83)	10.3 (6.9, 15.2)
Exercise	female	16.5	9.3	0.48 (0.39-0.59)	37.3 (26.1, 50.0)
	male	20.3	15.8	0.77 (0.69-0.85)	22.9 (16.9, 30.2)
Alcohol	female	11.2	6.3	0.41 (0.32-0.53)	48.9 (34.3, 60.0)
	male	29.1	29.8	0.88 (0.81-0.96)	10.5 (6.1, 17.5)
ApoB/ApoA-1 Ratio	female	14.1	27.0	4.42 (3.43-5.70)	52.1 (44.0, 60.2)
	male	21.9	35.5	3.76 (3.23-4.38)	53.8 (45.3, 59.2)

Risk of acute myocardial infarction for men and women for each of nine coronary artery disease (CAD) risk factors evaluated in the international INTERHEART case-control study. Results are adjusted for age, gender, and geographic location. The prevalence of each CAD risk factor is presented for controls and cases in the third and fourth columns.



Lancet 2004;364:937-52

Table 4. Cause of Death and Relative Risk During the 9-Year Posttrial Period Associated With Work Stress*

Cause of Death (No. of Deaths)	No. of Different Work Stressors During Trial. RR (95% CI)				P Value for Linear Trend
	0 (n = 3688)	1 (n = 4381)	2 (n = 2478)	≥3 (n = 1730)	
All causes (1505)	1.00	1.12 (0.98-1.27)†	1.19 (1.03-1.38)‡	1.26 (1.07-1.48)§	.004
All cardiovascular (771)	1.00	1.07 (0.89-1.29)	1.19 (0.97-1.46)†	1.34 (1.07-1.67)‡	.006
CHD (539)	1.00	1.10 (0.88-1.35)	1.41 (1.11-1.78)‡	1.35 (1.03-1.76)‡	.007
Acute MI (270)	1.00	1.28 (0.92-1.73)	1.50 (1.07-2.12)‡	1.27 (0.85-1.89)	.16
Other CHD (289)	1.00	0.96 (0.70-1.30)	1.32 (0.96-1.83)†	1.42 (0.99-2.02)†	.02
All noncardiovascular (722)	1.00	1.16 (0.97-1.40)†	1.20 (0.97-1.48)†	1.16 (0.91-1.47)	.22
Neoplastic disease (485)	1.00	1.05 (0.85-1.31)	1.11 (0.96-1.42)	0.83 (0.61-1.14)	.31
Respiratory disease (43)	1.00	2.25 (0.93-5.44)†	3.12 (1.23-7.87)‡	2.15 (0.72-6.48)	.13
Digestive system disease (53)	1.00	1.38 (0.64-2.98)	1.55 (0.65-3.68)	3.71 (1.69-8.13)§	.001
Accidents (57)	1.00	0.86 (0.44-1.70)	0.82 (0.36-1.85)	1.84 (0.89-3.77)†	.13

*In all Cox proportional hazard models, the following characteristics were included as covariates: age, study group (special intervention vs usual care), educational attainment, occurrence of nonfatal cardiovascular event during the trial, smoking, diastolic blood pressure, alcohol consumption, and serum cholesterol level (the latter 4 variables were trial averages). Relative risks (RRs) correspond to comparison between no stress and increasing numbers of different work stressors (ie, 0, 1, 2, or ≥3). Numbers vary slightly from those in Table 2 because of missing covariate values in each analysis. CI indicates confidence interval; CHD, coronary heart disease; and MI, myocardial infarction.

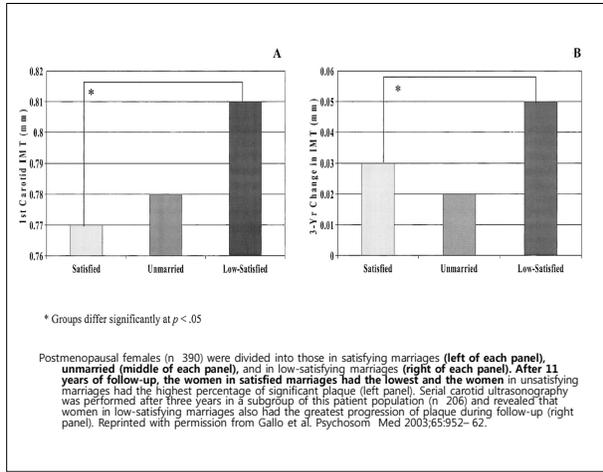
†P<.01.

‡P<.05.

§P<.01.

Matthews KA, Gump BB. Chronic work stress and marital dissolution increase risk of posttrial mortality in men from the Multiple Risk Factor Intervention Trial. Arch Intern Med. 2002;162(3):309-15.

1차 진료의가 만드는 임상진료지침(심뇌혈관질환 일차예방)



Social Relationships and Mortality Risk

- 148 studies(308,849 participants)
- OR = 1.50 (95% CI 1.42 to 1.59) survival of participants

Table 4. Weighted average effect sizes across different measures of social relationships.

Type of Measure	k	OR	95% CI
Functional	Received social support	9	1.22 [0.91, 1.63]
	Perceptions of social support	73	1.35 [1.22, 1.49]
	Loneliness (inversed)	8	1.45 [1.08, 1.94]
Structural	Living alone (inversed)	17	1.19 [0.99, 1.44]
	Marital status (married versus other)	62	1.33 [1.20, 1.46]
	Social isolation (inversed)	8	1.40 [1.06, 1.86]
	Social networks	71	1.45 [1.32, 1.59]
Combined structural and functional	Social integration	45	1.52 [1.36, 1.69]
	Complex measures of social integration	30	1.91 [1.63, 2.23]
Multifaceted measurement	67	1.47 [1.34, 1.60]	

These analyses shifted the units of analysis, with distinct effect size estimates within studies used within different categories of measurement, such that many studies contributed more than one effect size but not more than one per category of measurement.

OR, odds ratio, transformed from random effects weighted InOR.

Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. PLoS Med. 2010 Jul 27;7(7):e1000316. Review.

work stress is risk of cardiovascular disease

- 14 studies, 83,014 employees
- high versus low job strain 1.43(95% CI 1.15-1.84)
- high efforts and low rewards 1.58 (95% CI 0.84-2.97) for 11 528 employees

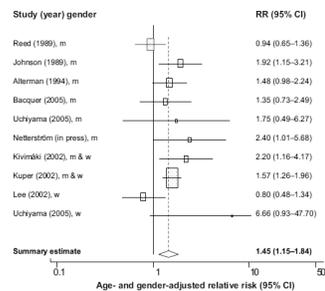
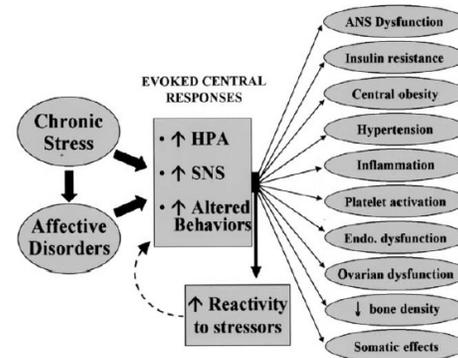


Figure 3. Relative risk (RR) of incident coronary heart disease and cardiovascular events and its summary estimate for the prospective cohort studies on the job-strain model by gender. (95% CI = 95% confidence interval, m = male study population, f = female study population)

Kivimäki M, Virtanen M, Elovainio M, Kouvonen M. Work stress and coronary heart disease--a meta-analysis. Scand J Work Environ Health. 2006 Dec;32(6):431-42.



Pathophysiological mechanisms by which chronic stress and affective disorders, such as depression, appear to promote atherosclerosis.

Rozanski A. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. J Am Coll Cardiol. 2005;45(5):637-51.

1. 일차의료 의사는 고혈압, 당뇨병 등 심뇌혈관 질환의 위험을 높이는 질환을 진료하거나 심뇌혈관 질환의 위험을 낮추기 위해 금연, 체중감량 등 생활습관 교정을 할 때 스트레스에 대한 평가와 상담을 하도록 권고한다.

ADA 2011 guideline

Psychosocial assessment and care

Assessment of psychological and social situation should be included as an on-going part of the medical management of diabetes. (E)

Psychosocial screening and follow-up should include, but is not limited to, attitudes about the illness, expectations for medical management and out-comes, affect/mood, general and diabetes-related quality of life, resources(Financial, social, and emotional), and psychiatric history. (E)

Screen for psychosocial problems such as depression and diabetes-related dis-tress, anxiety, eating disorders, and cognitive impairment when self-management is poor. (C)

ATP III guideline

Follow Obesity Education Initiative (OEI) guidelines for weight management.

Promote prevention of weight gain:

- Calculate BMI for every patient at every visit
- Anticipate high-risk times for weight gain (perimenopausal years, times of significant life stress) and counsel patient on ways to prevent weight gain
- Follow-up visits to discuss success of weight gain prevention strategies

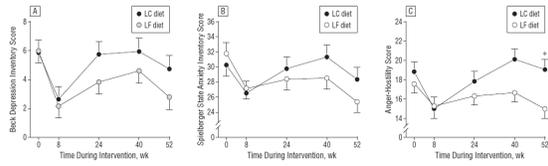
JNC 7

The pathogenesis of hypertension in different racial subgroups may differ with respect to the contributions of such factors as salt, potassium, stress, cardiovascular reactivity, body weight, nephron number, sodium handling, or hormonal systems

Exercise for depression

For the 23 trials (907 participants) comparing **exercise** with no treatment or a control intervention, the pooled SMD was -0.82 (95% CI -1.12, -0.51)

Mead GE et al. *Exercise for depression*. Cochrane Database Syst Rev. 2009;(3):CD004366.



Estimated marginal means (SEs) of mood scores before and after 8, 24, 40, and 52 weeks of energy restriction with a low-carbohydrate, high-fat (LC) diet or a high carbohydrate, low-fat (LF) diet. Beck Depression Inventory score (A), Spielberger State-Trait Anxiety Inventory score (B), and the Profile of Mood States subscales: anger-hostility (C). The asterisk indicates that the score is significantly higher compared with the LF diet (*P* < .05).

Arch Intern Med. 2009;169(20):1873-1880

Cochrane Database Syst Review

Reducing saturated fat by reducing and/or modifying dietary fat reduced the risk of cardiovascular events by 14%(RR 0.86, 95%CI 0.77 - 0.96) 24 comparisons, 65,508 participants

But not all cause mortality or cardiovascular mortality

Hooper L, Summerbell CD, Thompson R, Sills D, Roberts FG, Moore H, Davey Smith G. Reduced or modified dietary fat for preventing cardiovascular disease. Cochrane Database Syst Rev. 2011 Jul 6;(7):CD002137

Meta-analysis (2000): Effectiveness of and estimated abstinence rates for various types of counseling and behavioral therapies (n = 64 studies)

Type of counseling and behavioral therapy	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No counseling/behavioral therapy	35	1.0	11.2
Relaxation/breathing	31	1.0 (0.7-1.3)	10.8 (7.9-13.8)
Contingency contracting	22	1.0 (0.7-1.4)	11.2 (7.8-14.6)
Negative affect	8	1.2 (0.8-1.9)	13.6 (8.7-18.5)
Intratreatment social support	50	1.3 (1.1-1.6)	14.4 (12.3-16.5)
Extratreatment social support	19	1.5 (1.1-2.1)	16.2 (11.8-20.6)
Practical counseling (general problem solving/ skills training)	104	1.5 (1.3-1.8)	16.2 (14.0-18.5)

(From U.S. Department of Health and Human Services. Public Health Services: Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.)

Common elements of practical counseling (problem solving/skills training)

Practical counseling (problem solving/skills training) treatment component	Examples
Recognize danger situations – Identify events, internal states, or activities that increase the risk of smoking or relapse.	<ul style="list-style-type: none"> • Negative affect and stress • Being around other tobacco users • Drinking alcohol • Experiencing urges • Smoking cues and availability of cigarettes
Develop coping skills – Identify and practice coping or problem solving skills. Typically, these skills are intended to cope with danger situations.	<ul style="list-style-type: none"> • Learning to anticipate and avoid temptation and trigger situations • Learning cognitive strategies that will reduce negative moods • Accomplishing lifestyle changes that reduce stress, improve quality of life, and reduce exposure to smoking cues • Learning cognitive and behavioral activities to cope with smoking urges (e.g., distracting attention; changing routines)

(From U.S. Department of Health and Human Services. Public Health Services: Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline.)

1차 진료의가 만드는 임상진료지침(심뇌혈관질환 일차예방)

2. 스트레스는 심뇌혈관질환 발생과 관련이 있으므로 일차의료 의사는 스트레스가 의심되는 증상이 있을 때 스트레스 평가와 상담을 하도록 권고한다.

가슴 두근거림, 흉통, 복통 등 여러 기관에 걸친 증상이 함께 있을 때, 신체적 증상과 함께 불안, 우울 등 정서적 증상이 동반될 때이다.

나쁜 스트레스: 영향



2007년 정신건강의 날 행사 스트레스 불안 증폭, 대한신경정신의학회 편

Psychological distress measured by the GHQ-12 and mortality: A prospective population-based study_10year survival

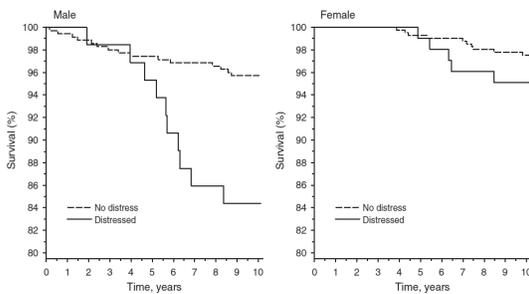


Figure 1. Kaplan-Meier estimates of non-distressed (GHQ 0-3) and distressed (GHQ 4-12) participants, divided by gender. Scandinavian Journal of Public Health, 2011; 39: 577-581

3. 환자에게 직접 물어서 스트레스를 평가한다. 스트레스 증상이 의심되는 경우 이와 관련된 사건이 있었는지 파악한다. 직장 및 가족 내 스트레스가 있는지 확인한다. 환자 본인이 스트레스를 인지하지 못하면 의사가 증상과 사건에 대해 구체적으로 묻고 시간적 선후 관계를 봐서 파악한다.

- Open ended question
- 짧은 진료 시간에 최대한 간단히
- 여러 번 진료에서 문제 파악하도록
- 직장, 가정 내 스트레스, 우울, 불안 증상

Turner J, Raphael B. MJA practice essentials. 6. Stress management and counselling in primary care. Med J Aust. 1997 Nov 17;167(10):547-51.

질문

- 당신의 문제가 뭐라고 생각하나요?
- 스트레스가 있는 사람에게서 당신과 유사한 증상을 많이 봤어요. 혹시 당신에게 어떤 일이 있었나요?
- 당신 가족에게는 스트레스가 없었나요? 혹시 당신에게 감당하기 어려운 일이 있었나요?

4. 스트레스가 심혈관질환을 악화시키는 요인으로 작용할 수 있음을 환자에게 설명한다.

5. 일차의료의사는 환자가 호소하는 스트레스를 적극적 청취하도록 권고한다. 짧은 시간이어도 적극적 상담 기법을 활용하여 상담하면 환자의 스트레스를 줄일 수 있다.

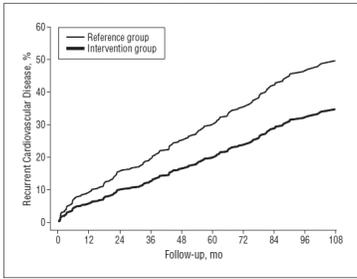
의사가 스트레스에 관심을 가지고 상담을 하면 일반적 진료보다 우울, 불안 등 증상이 감소한다.

Table 3 Odds-ratios for mortality and morbidity outcomes: psychological treatment vs. usual care

Sub-analysis	Follow-up	Mortality			Morbidity					
		K	N	OR (CI, 95%)	K	N	OR (CI, 95%)			
All studies	≤ 2 years	23	9856	0.72 (0.56-0.94)	34.0 (0.06)	22	7831	0.84 (0.70-1.02)	41.9 (0.021)	
	> 2 years	6	4727	0.89 (0.69-1.14)	39.4 (0.14)	6	5872	0.57 (0.37-0.86)	71.5 (0.004)	
Gender	Women	≤ 2 years	4	1190	1.01 (0.46-2.23)	58.8 (0.06)	4	1121	0.88 (0.67-1.15)	0.0 (0.61)
	> 2 years	2	1557	1.30 (0.95-1.79)	25.0 (0.25)	1	1084	1.01 (0.80-1.29)	0.0 (1.00)	
	Men	≤ 2 years	6	2042	0.73 (0.51-1.05)	17.5 (0.30)	4	2023	0.84 (0.64-1.11)	32.2 (0.19)
	> 2 years	3	2761	0.83 (0.67-1.03)	0.0 (0.94)	3	1914	0.82 (0.68-0.99)	2.0 (0.36)	
Total/Overall	≤ 2 years	10	3232	0.77 (0.56-1.07)	49.7 (0.46)	10	3144	0.86 (0.71-1.04)	2.0 (0.18)	
	> 2 years	5	4318	0.96 (0.80-1.15)	46.8 (0.02)	
Treatment initiation	≤ 2 months post-event	14	8522	0.87 (0.66-1.15)	37.5 (0.08)	11	6432	0.80 (0.61-1.04)	62.5 (0.003)	
	> 2 months post-event	5	4527	0.95 (0.75-1.20)	31.1 (0.21)	4	5616	0.63 (0.39-1.03)	73.6 (0.010)	
	> 2 months post-event ^b	6	639	0.28 (0.12-0.70)	0.0 (0.98)	7	659	0.94 (0.61-1.46)	0.0 (0.64)	
Distress reduced ^a	Yes ^a	≤ 2 years	3	754	0.46 (0.28-0.75)	0.0 (0.53)	3	687	0.79 (0.57-1.08)	0.0 (0.38)
	No ^a	≤ 2 years	4	603	0.67 (0.27-1.65)	0.0 (0.71)	
Depression reduced ^d	Yes ^d	≤ 2 years	3	1071	1.03 (0.78-1.36)	0.0 (0.65)	4	1274	0.93 (0.74-1.18)	0.0 (0.51)
	No ^d	≤ 2 years	6	4173	1.04 (0.79-1.37)	2.0 (0.40)	5	3946	0.92 (0.76-1.12)	0.0 (0.49)

Odds-ratios < 1 indicate a reduction in mortality/morbidity due to psychological treatment.
 K, number of studies included in analysis; N, sample size; OR, odds ratio; P, level of significance; CI, confidence interval; I², homogeneity of variance statistic; ellipse, insufficient data to complete analysis.
^aNo data for > 2 years.
 Linden W, Phillips MJ, Leclerc J. Psychological treatment of cardiac patients: a meta-analysis. Eur Heart J. 2007 Dec;28(24):2972-84. Epub 2007 Nov 5

Randomized Controlled Trial of Cognitive Behavioral Therapy vs Standard Treatment to Prevent Recurrent Cardiovascular Events



Cumulative first recurrent fatal and nonfatal cardiovascular events during 9 years (108 months) from baseline, adjusted for the influence of age, sex, marital status, education, smoking habits, comorbidity (number of previous acute myocardial infarctions, angina pectoris, hyperlipidemia, hypertension, heart failure, diabetes mellitus, asthma/chronic obstructive pulmonary disease, and stroke), peripheral artery disease, and 2-year mean systolic blood pressure, serum cholesterol, and serum triglyceride level, and scores for vital exhaustion, coping ability resources, and credence in the future, by treatment group.

Arch Intern Med. 2011;171(2):134-140

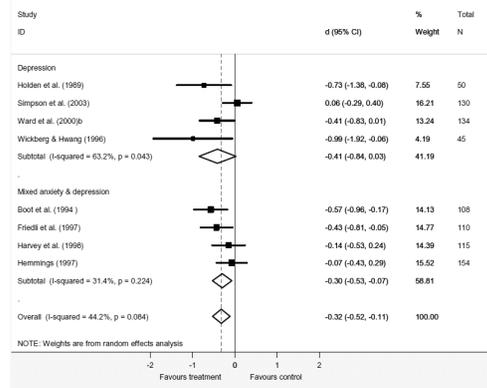
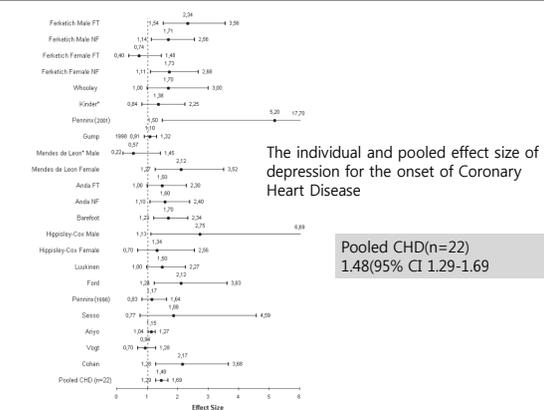


Figure 3 Brief counselling versus usual general practitioner care, sub-grouped by diagnosis

BCape J, Whittington C, Buszewicz M, Wallace P, Underwood L. Brief psychological therapies for anxiety and depression in primary care: meta-analysis and meta-regression. BMC Med. 2010 Jun 25;8:38. Review.

6. 스트레스와 함께 우울, 불안 등 정동장애가 있는지 확인하도록 권고한다.



Van der Kooy K et al. Depression and the risk for cardiovascular diseases: systematic review and meta analysis. Int J Geriatr Psychiatry. 2007;22(7):613-26.

Depressive mood

- Beck Depression Inventory(BDI)
- Zung's SDS

불안증

- STAI(State-trait anxiety inventory)
- Beck Anxiety Inventory(BAI)
- Zung Anxiety Scale (ZAS) questionnaires

7. 스트레스가 높은 환자의 순응도를 높이는 방법(간호사의 전화상담, 작은 목표 설정 등)을 사용하여 권고한다.

- Psychosocial problem → nonadherence
- Multidisciplinary approach
- multiple approaches and diverse strategies

Miller NH, Hill M, Kottke T, Ockene IS. The multilevel compliance challenge: recommendations for a call to action. A statement for healthcare professionals. *Circulation*. 1997 Feb 18;95(4):1085-90.

1. Use clear and effective communication, including making recommendations that are as specific and simple as possible.
2. Schedule follow-up visits to check adherence, especially during the early practice phase, as opposed to the later, more ingrained habit phase.
3. Provide a motivating rationale for the patient's treatment regimen, with consideration of explanations that befit the patient's health literacy.
4. Follow oral suggestions with written ones to reinforce the cardiologist's message and aid memory and concentration.
5. Begin with "micro" goals for patients who are resistant to behavior change or who have fewer available personal resources.
6. Help patients establish realistic goals and expectations.
7. Involve patients in tailoring behavioral suggestions rather than dictating change.
8. Suggest activities that are commensurate with patients' abilities and that provide positive feedback (factors that tend to promote a sense of pleasure).
9. Openly and candidly explore potential patient barriers to adherence (such as lack of personal motivation, time, family support, facilities, or knowledge; fears; job, home or other pressures; and cultural issues) and assist patients with problem-solving and developing strategies (e.g., self-monitoring approaches, written agreements, and relapse prevention) at the time of recommendations.
10. Refer patients with poor structural or functional social support to programs or activities that will enhance adherence by providing social support.

Rozanski A. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. *J Am Coll Cardiol*. 2005;45(5):637-51.

Reference

- 1) Harkness E, Macdonald W, Valderas J, Coventry P, Gask L, Bower P. Identifying psychosocial interventions that improve both physical and mental health in patients with diabetes: a systematic review and meta-analysis. *Diabetes Care*. 2010;33(4):926-30.
- 2) American Diabetes Association. Executive summary: standards of medical care in diabetes. 2011. *Diabetes Care*. 2011;34 Suppl 1:S4-10.
- 3) Benson H, Rosner BA, Marzetta BR, et al. Decreased blood pressure in pharmacologically treated hypertensive patients who regularly elicited the relaxation response. *Lancet* 1974;1:289-291.
- 4) Leserman J, Stuart EM, Mamish ME, Benson H. The efficacy of the relaxation response in preparing for cardiac surgery. *Behav Med*. 1989;15(3):111-7.
- 5) Schneider RH, Alexander CN, Staggers F, et al. A randomized controlled trial of stress reduction in African Americans treated for hypertension for over one year. *Am J Hypertens*. 2005;18(1):88-98.
- 6) From U.S. Department of Health and Human Services. Public Health Services: Treating Tobacco Use and Dependence: 2008 Update. *Clinical Practice Guideline*
- 7) Kozak AT, Fought A. Beyond alcohol and drug addiction. Does the negative trait, of low distress tolerance have an association with overeating? *Appetite*. 2011 ;26.
- 8) Ashbridge M, Payne E, Cartwright J, Mann R. Driving under the influence of alcohol: examining ethno-specific rates and the mediating effects of psychological distress and harmful and problematic drinking. *Accid Anal Prev*. 2010 ;42(4):1408-15.
- 9) Turner J, Raphael B. MIA practice essentials. 6. Stress management and counselling in primary care. *Med J Aust*. 1997 ;167(10):547-51.
- 10) Rozanski A, Blumenthal JA, Davidson KW, Saab PG, Kubzansky L. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice: the emerging field of behavioral cardiology. *J Am Coll Cardiol*. 2005 ;45(5):637-51.
- 11) Bower P, Knowles S, Coventry PA, Rowland N. Counselling for mental health and psychosocial problems in primary care. *Cochrane Database Syst Rev*. 2011 ;9:CD001025.
- 12) Hooper L, Summerbell CD, Thompson R, Sills D, Roberts FG, Moore H, Davey Smith G. Reduced or modified dietary fat for preventing cardiovascular disease. *Cochrane Database Syst Rev*. 2011;(7):CD002137
- 13) Strikworth GD et al. Long-term effects of a very low-carbohydrate diet and a low-fat diet on mood and cognitive function. *Arch Intern Med*. 2009;169(20):1873-80.
- 14) Van der Kooy K, van Hout H, Marwijk H, Marten H, Stehouwer C, Beekman A. Depression and the risk for cardiovascular diseases: systematic review and meta analysis. *Int J Geriatr Psychiatry*. 2007;22(7):613-26.
- 15) Meijer A, Conradi HJ, Bos EH, Thoms BD, van Melle JP, de Jonge P. Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis of 25 years of research. *Gen Hosp Psychiatry*. 2011 ;33(5):203-16.