

REVIEW TOPIC OF THE WEEK

Behavioral Cardiology

Current Advances and Future Directions



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ABSTRACT

Growing epidemiological evidence identifies key domains relevant to behavioral cardiology, including health behaviors, emotions, mental mindsets, stress management, social connectedness, and a sense of purpose. Each of these domains exists along a continuum, ranging from positive factors that promote health, to negative factors, which are pathophysiological. To date, there has been relatively little translation of this growing knowledge base into cardiology practice. Four initiatives are proposed to meet this challenge: 1) promulgating greater awareness of the potency of psychosocial risk factors; 2) overcoming a current "artificial divide" between conventional and psychosocial risk factors; 3) developing novel cost-effective interventions using Internet and mobile health applications, group-based counseling, and development of tiered-care behavioral management; and 4) in recognition that "one size does not fit all" with respect to behavioral interventions, developing specialists who can counsel patients in multidisciplinary fashion and use evidence-based approaches for promoting patient motivation and execution of health goals. (J Am Coll Cardiol 2014;64:100-10) © 2014 by the American College of Cardiology Foundation.

Various psychosocial factors, such as depression and chronic stress, have been linked to the pathogenesis of coronary heart disease (CHD) (1). In 2005, on the basis of a review of such associations, the emergence of a new field of behavioral cardiology was predicted (2). Indeed, over the last decade, studies of psychosocial risk factors for CHD have increased exponentially. Accordingly, the present review explores new knowledge regarding behavioral and psychosocial risk factors, with particular emphasis on meta-analytic studies, which were nearly nonexistent before 2005. Second, the present review addresses a particular current challenge for the field of behavioral cardiology: its translation into a clinically integrated field within cardiovascular medicine.

EPIDEMIOLOGICAL ADVANCES

Based on epidemiological data, the behavioral risk factors for CHD can be divided into five broad

categories, as summarized in [Table 1](#) and discussed in the following text.

PHYSICAL HEALTH BEHAVIORS. The association between CHD and physical inactivity, poor diet, and smoking are well established. Emerging literature also targets 2 other behavior-related factors: poor sleep and inadequate rest and relaxation. With respect to sleep, recent meta-analyses have identified insomnia (3) and duration of sleep, either long or short (4), as risk factors for CHD ([Fig. 1](#)). Longer duration of sleep could be a potential marker of depression or medical comorbidities. Shorter sleep duration may be multifactorial, including sleep that is curtailed by worry and other causes of insomnia or that is curtailed voluntarily. Interest in shorter duration of sleep has risen based on investigations linking curtailed sleep to neuroendocrine and autonomic dysfunction, inflammation, and increased appetite.

The health value of relaxation is of growing interest in light of trends toward heavier workloads, faster

pace of living, and diminished boundaries between work and leisure. On a theoretical basis, the potential benefits of relaxation are supported by a “paradigm of flexibility” that appears to be beneficial for both physiological and cognitive function (5). To date, however, epidemiological study in this arena has been relatively sparse.

EMOTIONAL DISORDERS AND NEGATIVE MENTAL MINDSETS. Depression. Studies have consistently demonstrated that depression is a potent risk factor for CHD. A series of meta-analyses has confirmed the prognostic significance of depression, the largest being an analysis of 54 studies which showed an approximately 2-fold increase in risk among community cohorts (Fig. 2), with a similar elevation noted among patients with known CHD (6).

Anxiety symptoms and syndromes. In recent years, the role of anxiety as a CHD risk factor has been clarified. Various meta-analyses have identified an increased risk associated with symptoms of anxiety in both community and patient cohorts (7,8). Other recent studies have established that CHD event risk is elevated among patients with generalized anxiety disorder (9,10), panic attacks (11), and post-traumatic stress syndrome (PTSD) (12).

Pessimism. Mental outlook is also a health determinant. The strongest example comes from studies of optimism versus pessimism (13-20). Optimism is associated with a higher experience of positive emotions, enhanced social functioning, and better recovery from myocardial infarction and cardiac procedures. Recent epidemiological studies have demonstrated that pessimism increases the risk for cardiac events, stroke, and/or all-cause mortality, whereas optimism exerts a buffering role (Table 2).

Anger and hostility. Anger and hostility have been widely studied, stemming from original interest in “type A personality,” which is a triad of hostility, impatience, and time urgency. However, a meta-analysis has found that the hazard ratio for cardiac events in association with anger and/or hostility was increased only 19% among 25 studies involving initially healthy subjects and 24% among 19 studies involving populations with CHD (21).

Chronic stress. To date, most studies of chronic stress have considered situational stressors. Work stress has been most widely studied, most commonly according to a model of “job strain” (i.e., high job demand with little latitude). In recent meta-analyses, only a 1.23-fold increase in incident CHD was found in association with job strain (22), compared with a 1.63-fold increase in mortality with unemployment (23). Marital separation and divorce are other common

stressors that increase mortality risk, and isolated epidemiological studies also suggest a relationship between marital strain and cardiovascular events.

There has been increasing interest in 2 other stressors: adverse childhood experiences and the stress associated with medical illness. Regarding childhood adversities, the Nurses’ Health Study 2, which involved a 16-year follow-up of 66,798 women (24), is the largest study to date. Nearly one-fifth reported severe childhood abuse, and this group had an approximately 1.5-fold increase in early-onset cardiovascular events. The development of medical illness is a potent stressor because of its ability to breed depression, anxiety, social isolation, and loss of self-esteem (from a lost image of good health). In addition, studies have ascertained that PTSD, most commonly identified as a war-related disorder, also can result from a variety of medical illnesses. In a meta-analysis of 24 studies, Edmondson et al. (25) found a 12% prevalence of PTSD among patients with acute coronary syndrome.

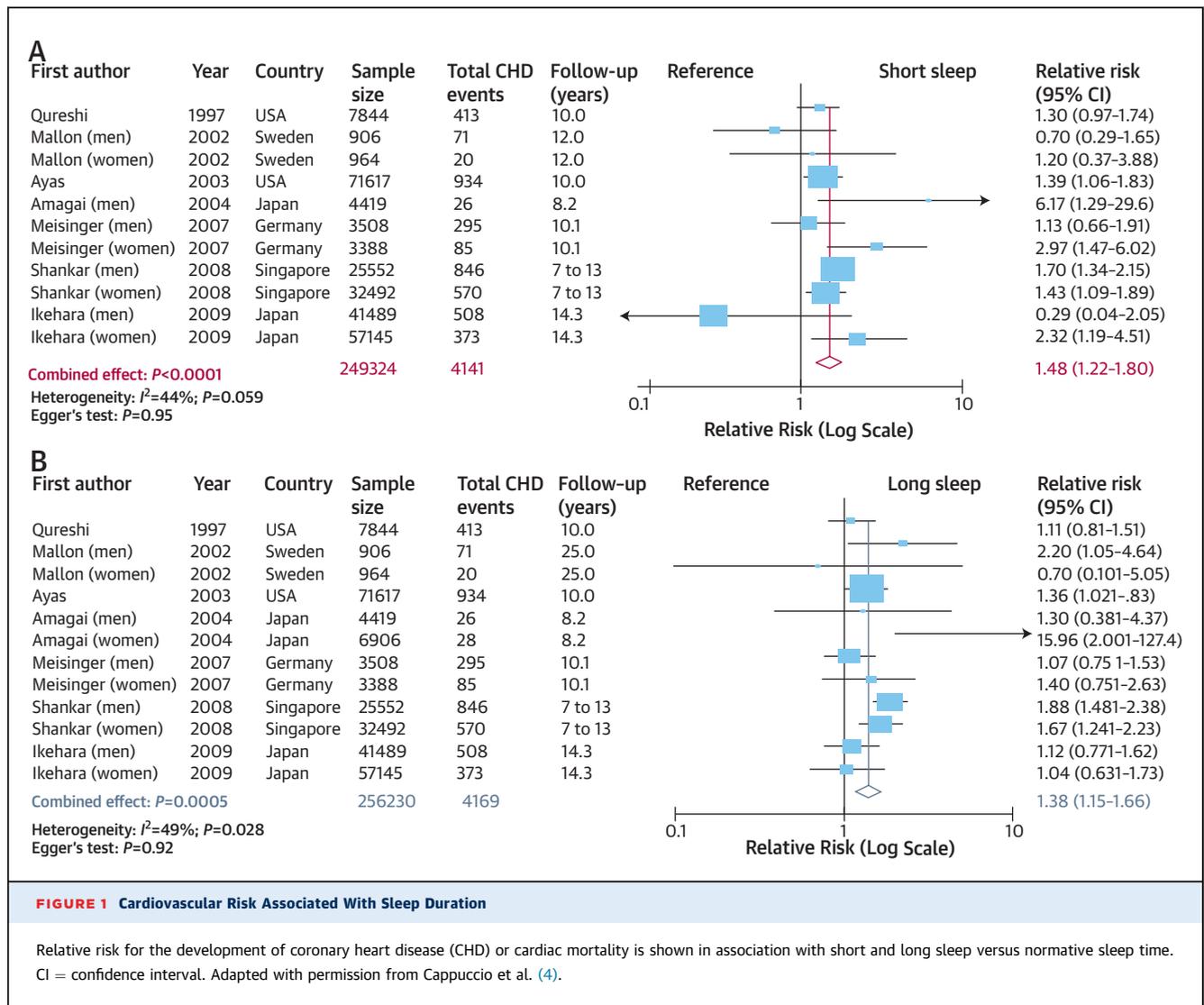
Notably, one’s *perceived* sense of stress also may be an important health determinant. One important study by Keller et al. (26) evaluated 28,753 subjects both for their level of perceived stress and for their perception of whether their stress was impairing their health. Increased mortality in association with stress was limited only to those who self-appraised

**ABBREVIATIONS
 AND ACRONYMS**

- CHD** = coronary heart disease
- PTSD** = post-traumatic stress disorder

TABLE 1 Behavioral Risk Factors Associated With CHD

A. Physical health behaviors
1. Physical inactivity
2. Poor diet and obesity
3. Smoking
4. Poor or inadequate sleep
5. Inadequate rest and relaxation
B. Negative emotions and mental mindsets
1. Depressive symptoms
2. Anxiety
3. Pessimism
4. Anger and hostility
C. Chronic stress
1. Situational stressors
• Work stress
• Marital stress
• Social stressors
• Caregiver strain
• Childhood and adult abuse
• Medical illness
2. Perceived stress
D. Social isolation and poor social support
E. Lack of sense of purpose
CHD = coronary heart disease.



their risk as harmful to their health. A complementary study by Jamieson et al. (27) suggests that instructing subjects to perceive their stress symptoms in a positive functional manner can lead to improved cognitive and cardiovascular responses to stress. Combined, these data suggest a need for more research into the subjective perception of stress and how its modification can affect health outcomes.

SOCIAL ISOLATION AND POOR SOCIAL SUPPORT. Epidemiological studies have consistently established that small social networks, poor functional support, loneliness, and/or a sense of poor emotional support increase the risk for cardiac events (1,2). As with other psychosocial risk factors, a gradient relationship has been noted between the degree of reduced social support and the likelihood of adverse cardiac events. The role of various social factors was

assessed in a recent meta-analysis of 148 studies (28). A combined measure of positive social integration was associated with a nearly 2-fold increase in survival.

LACK OF SENSE OF PURPOSE. Observational studies indicate that having a strong sense of life purpose is a core component of positive well-being, whereas a lack of life purpose is associated with boredom, increased risk for developing depression, and diminished resilience during stress. Although only scant study has evaluated the pathophysiological sequelae of a low sense of purpose, substantial recent study has demonstrated an increased mortality risk associated with a low sense of purpose (Table 3) (29-36). For instance, in a study involving 43,391 subjects followed for 7 years, the adjusted hazard ratio for all-cause mortality among those

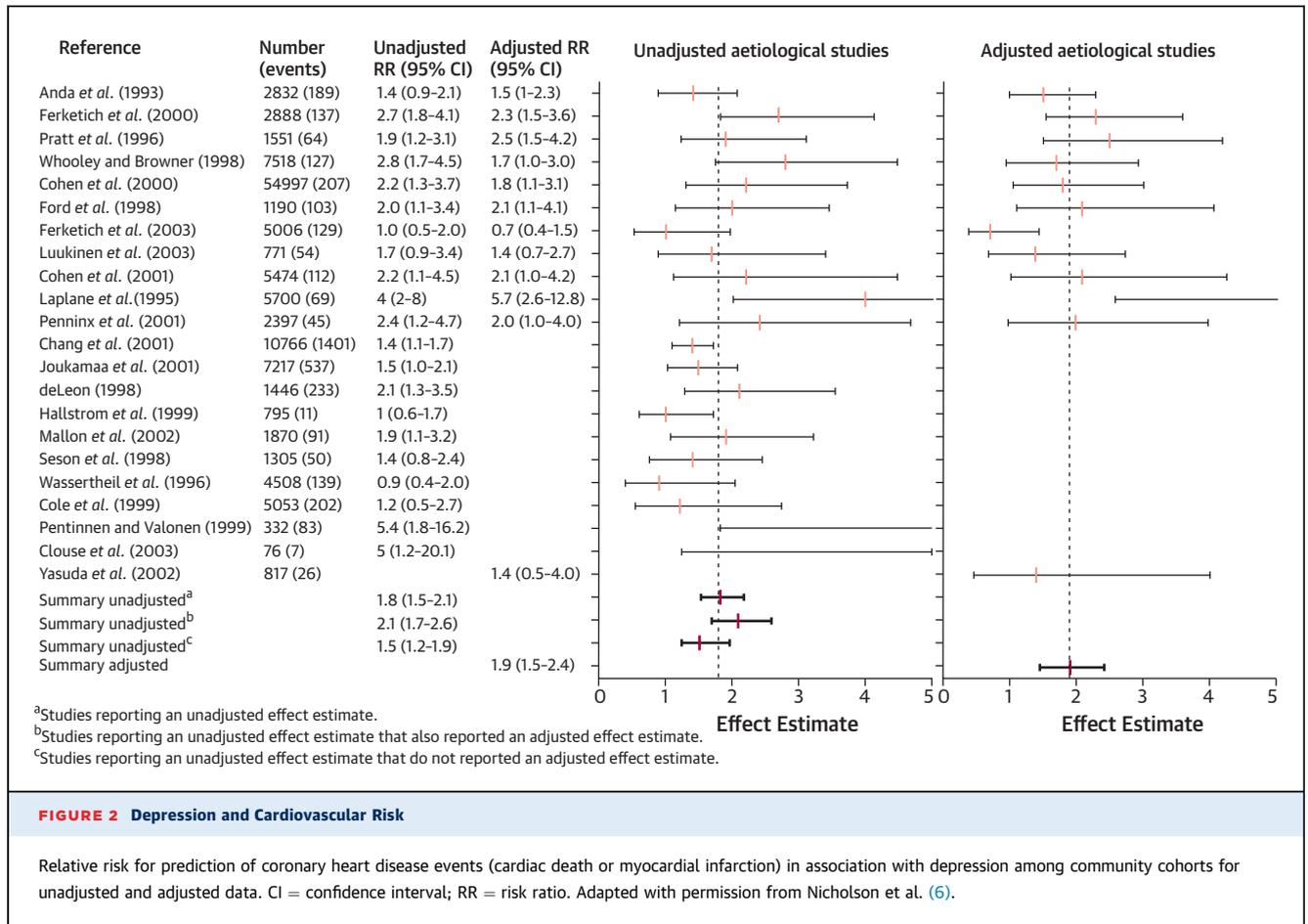


FIGURE 2 Depression and Cardiovascular Risk

Relative risk for prediction of coronary heart disease events (cardiac death or myocardial infarction) in association with depression among community cohorts for unadjusted and adjusted data. CI = confidence interval; RR = risk ratio. Adapted with permission from Nicholson et al. (6).

reporting a low versus high sense of life purpose was 1.5 (95% confidence interval [CI]: 1.3 to 1.7) (Fig. 3) (31).

POSITIVE PSYCHOSOCIAL FUNCTIONING. As with physical behaviors, each domain of psychosocial risk can be considered along a spectrum, ranging from positive to negative (Fig. 4). Negative psychosocial factors promote illness by fostering negative health behaviors and by their direct pathophysiological effects. These effects can vary according to the type of psychosocial stress, but as a group they include induction of autonomic dysfunction, heightened cardiovascular reactivity, insulin resistance, central obesity, increased risk for hypertension, endothelial and platelet dysfunction, and unfavorable alterations in brain plasticity and cognitive function (1,2). By contrast, positive psychosocial factors are associated with more healthy behaviors and promote favorable physiologic effects, including enhanced immune, endothelial, and autonomic function (37,38). Further, positive psychosocial functioning helps promote vitality (i.e., an innate sense of energy), which in turn

produces an increased sense of well-being, better goal pursuit, and enhanced resilience (1,15). The importance of positive psychosocial function is supported by a meta-analysis of 35 studies demonstrating increased longevity in association with positive emotions (39).

TABLE 2 Optimism and Pessimism as Predictors of Clinical Outcomes

First Author (Ref. #)	Year	n	Follow-Up (yrs)	Endpoints	Adjusted RR (95% CI)*
Pessimism as a risk factor					
Brummet et al. (13)	2006	6,958	40.0	ACM	1.42 (1.13-1.77)
Grossbart et al. (14)	2009	7,216	32.0	ACM	1.32 (1.13-1.77)
Optimism as a buffer					
Kubzansky et al. (15)	2004	1,306	10.0	MI/CV death	0.44 (0.26-0.74)
Giltay et al. (16)	2004	941	9.1	CV death	0.27 (0.12-0.57)
Giltay et al. (17)	2006	554	15.0	CV death	0.45 (0.29-0.68)
Tindle et al. (18)	2009	97,253	8.0	CV death	0.76 (0.64-0.90)
Nabi et al. (19)	2010	23,216	7.0	Stroke	0.52 (0.29-0.93)
Kim et al. (20)	2011	6,044	2.0	Stroke	0.90 (0.84-0.97)†

*Risk ratios are primarily for first versus third tertile or fourth quartile. †For each unit increase in optimism. ACM = all-cause mortality; CI = confidence interval; CV = cardiovascular; RR = risk ratio; MI = myocardial infarction.

TABLE 3 Sense of Purpose as a Predictor of All-Cause Mortality

First Author (Ref. #)	Year	n	Follow-Up	Endpoint	Adjusted RR (95% CI)
Low purpose as a risk factor					
Okamoto et al. (29)	2004	784	6.0	ACM	2.24 (1.17-4.26)
Gruenewald et al. (30)	2007	1,189	7.0	ACM	3.13 (1.43-6.84)
Sone et al. (31)	2008	43,391	7.0	ACM	1.50 (1.30-1.70)
High purpose as a buffer					
Koizumi et al. (32)	2008	1,306 men 1,653 women	13.3	ACM	0.62 (0.46-0.86) 0.74 (0.45-1.22)
Boyle et al. (33)	2009	1,238	2.7	ACM	0.60 (0.42-0.87)
Tanno et al. (34)	2009	30,155 men 43,117 women	12.5 12.5	ACM	0.85 (0.80-0.90) 0.93 (0.86-1.00)
Kim et al. (35)	2013	1,546 CAD patients	2.0	MI	0.73 (0.57-0.93)
Kim et al. (36)	2013	6,739	4.0	Stroke	0.78 (0.67-0.91)

CAD = coronary artery disease; other abbreviations as in Table 2.

These observations raise the need for future epidemiological research that examines how an unfavorable stimulus in one behavioral or psychosocial domain may be offset by favorable changes in other domains. An arena in which this complexity is amply evident is in the interaction between physical fitness and psychosocial risk. Physical fitness reduces heart rate, blood pressure, and cortisol responses to psychosocial stress (40), buffers the relationship between depression and inflammation (41), and decreases the likelihood of impaired glucose metabolism in response to chronic stress (42).

Thus, future epidemiological studies should seek to further investigate the synergistic interactions between positive and negative psychosocial risk factors. A fruitful area for investigation in this regard may be

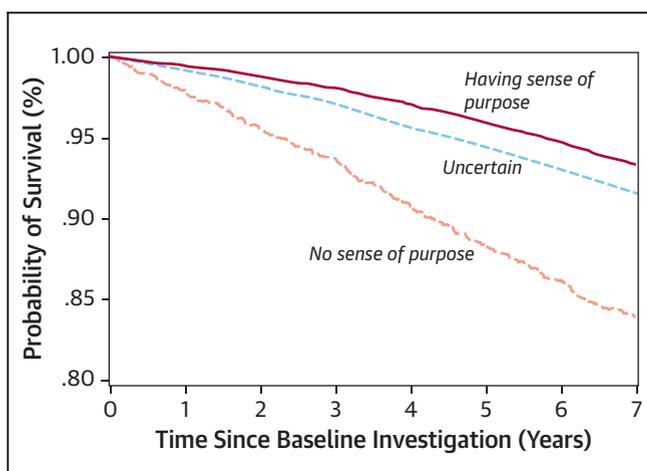


FIGURE 3 Sense of Purpose and Mortality Risk

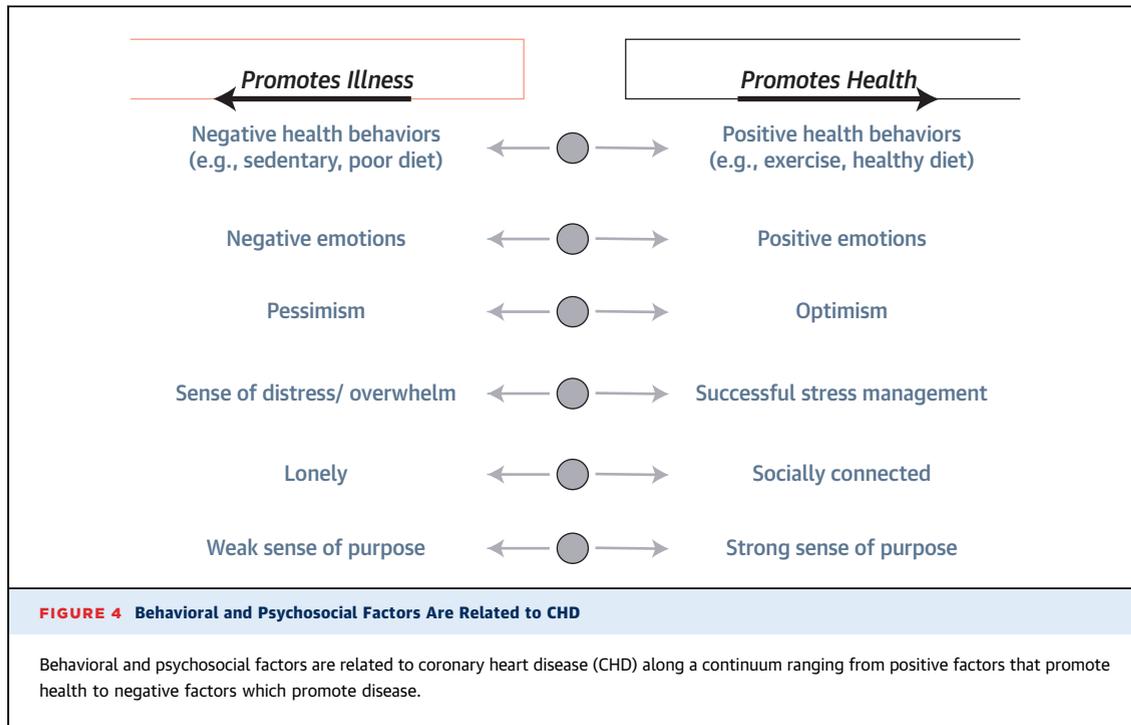
Kaplan Meier curve of all-cause mortality associated with a high, uncertain, and low sense of life purpose. Adapted with permission from Sone et al. (31).

to look at the interaction between a chronic stressor and the sense of meaning associated with that stressor. Specifically, implicit in the basic human need for purpose is a desire to take on life challenges (“good” stress). “Bad” or “toxic” stress is stress that becomes overwhelming, uncontrollable, or non-meaningful. This concept might help explain an interesting U-shaped relationship between the magnitude of experiential stress and clinical outcomes, as shown in a recent longitudinal study (Fig. 5) (43). Caregiver strain may represent an example of an arena where the interplay between a strong stressor and the meaning attached to the care giving influences clinical outcomes (44). Potentially, the meaning attached to work stress could also be an important modifier of clinical risk.

FUTURE DIRECTIONS IN CLINICAL MANAGEMENT

Whereas epidemiological and pathophysiological study in behavioral cardiology is now quite advanced, clinical translation of this field is still in its relative infancy. To date, there is no clear consensus on what interventions may work best. Initial large behavioral trials produced conflicting results (2), but potential behavioral interventions have become more tailored, sophisticated, and multidimensional, with an increasing evidence base to support their use in cardiac practice. How best to integrate these approaches into practical delivery of care, however, constitute a major challenge. Four initiatives that could help meet this challenge are addressed here:

A CALL TO ACTION. A greater recognition of the importance of psychosocial risk factors must be promulgated. Various lines of evidence underscore this risk. First, comparison of large studies or meta-analyses demonstrates nearly comparable levels of risk between some conventional and psychosocial risk factors (Table 4) (45-51). Second, psychosocial risk factors tend to cluster, often leading to compounded risk, as may occur when anxiety and depression are both present. Third, a strong dose-response relationship has been demonstrated for most psychosocial risk factors, with evidence that adverse clinical effects may begin to occur with even minor levels of distress. This is illustrated by a meta-analysis of 10 large, community-based cohort studies that each assessed psychological distress by the 12-item General Health Questionnaire (GHQ-12) (51). Even minor elevations in GHQ-12 scores were associated with a 25% increase in cardiac mortality (Fig. 6). Fourth, the risk associated with psychosocial risk factors is generally adjusted for behavioral risk



factors, but stimulation of adverse health behaviors is a key causative mechanism by which psychosocial factors increase clinical risk.

ADDRESSING THE “ARTIFICIAL DIVIDE”. Two health behaviors, physical activity and diet or weight management, are commonly grouped with “conventional” risk factor management for CHD. Clinically, however, these behaviors are commonly separated from other behavioral and psychosocial risk factors. Overcoming this divide could lead to the development of more integrated, effective behavioral interventions. For instance, there is growing interest in using exercise as medical therapy for depressive symptoms. This interest is supported by increasing epidemiological data (52), as well as by prospective randomized trials that have found exercise training to be comparable to the effects of antidepressant medication (53) (Fig. 7). In addition, as demonstrated by Win et al. (54), characterizing patients by both depressive symptoms and exercise may optimize risk stratification and help identify patient cohorts with the highest need for behavioral interventions (Fig. 8).

Just as the use of exercise may help treat psychosocial risk factors, the converse is also true. This potential is best understood according to a 3-component model of behavioral goal pursuit (Fig. 9). Motivating patients to pursue health behaviors is critical for

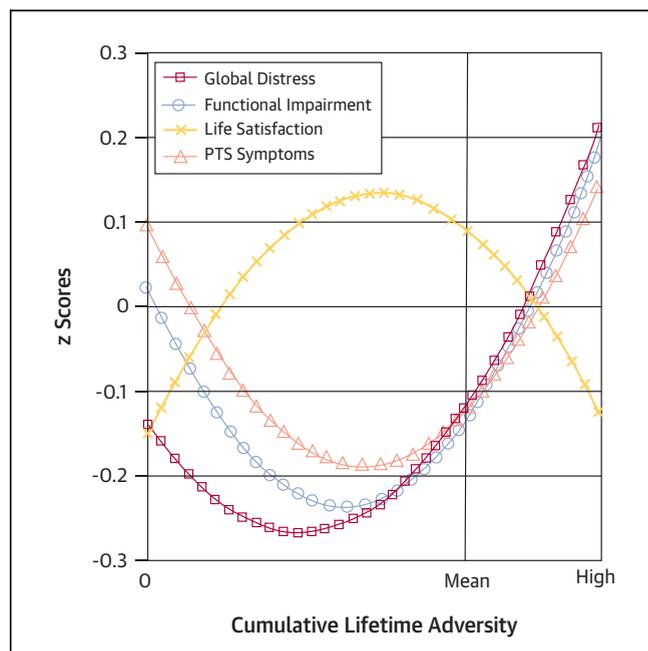


FIGURE 5 Quadratic Relationship Between Cumulative Adversity and Well-Being

Results for 4 measures are shown: global distress, functional impairment, life satisfaction, and post-traumatic stress (PTS) symptoms, as assessed among 2,398 persons reporting lifetime exposure to negative events. Some exposure versus no exposure to stress predicted lower distress and higher life satisfaction. Adapted with permission from Seery et al. (43).

TABLE 4 Risk Factors for CHD-Related Outcomes Associated With Clinical Parameters, Behavioral Risk Factors in Large Studies, or Meta-Analyses

Parameters	First Author (Ref. #)	n	Endpoint	Adjusted Risk Estimates (95% CI)*
Conventional CHD risk factors				
Smoking	Jha (45)	88,496 men†	ACM	2.80 (2.40-3.10)
Passive smoking	He (46)	637,814	CVD/MI	1.25 (1.17-1.32)
Elevated Non-HDL-C	RFC (47)	302,430	CVD	1.50 (1.39-1.61)
Diabetes mellitus	Emerging	820,900	Vascular deaths	2.32 (2.11-2.56)
Low fitness	Kodama (49)	102,980	CHD/CVD	1.56 (1.39-1.79)
BMI 30-34.9 kg/m ²	Berrington de Gonzalez (50)	1,460,000	ACM	1.44 (1.38-1.50)
Psychosocial CHD risk factors				
Insomnia	Sofi (3)	122,501	CHD/CVD	1.45 (1.29-1.62)
Short sleep	Cappuccio (4)	474,684	CHD/CVD	1.48 (1.22-1.80)
Depression	Nicholson (6)	146,538	CVD/MI	1.90 (1.49-2.52)
Anxiety	Roest (7)	67,187	CVD	1.48 (1.14-1.92)
Psychological distress (GHQ >6)	Russ (51)	68,222	CVD	1.72 (1.44-2.06)
Anger	Chida (21)	67,187	CHD/CVD	1.19 (1.05-1.35)
Positive social integration	Holt-Lunstad (28)	309,849	ACM	1.91 (1.63-2.23)‡

*Risk estimates are varied, ranging from temporally adjusted hazard ratios to specific odds and/or relative risks at a particular point in time. †Adjusted risk in 113,752 women was 3.0 (95% CI: 2.7 to 3.3). ‡Improvement in odds of survival with social integration.
BMI = body mass index; CHD = incidence of coronary heart disease; CI = confidence interval; CVD = cardiovascular death; GHQ = General Health Questionnaire; HDL-C = high-density lipoprotein cholesterol; RFC = Risk Factor Collaboration.

improving these behaviors and can be promoted in part by supporting patients' autonomy (i.e., helping patients to identify their own reasons and preferences for goal pursuit and execution), enhancing self-efficacy (e.g., setting goals according to patients' beliefs about what they can achieve), using financial or other incentives, inspirational stories, and motivational interviewing. However, spurring motivation is frequently not sufficient. In fact, in a meta-analysis of 622 studies, motivation accounted for only 28% of the variance in goal pursuit (55). The remainder was largely the result of failure to execute or maintain goals over time.

Various techniques can be applied to promote goal execution, including the following: helping patients identify highly specific, measurable goals; commitment to verbal review and introspection on goals on a regular basis; promotion of patient self-monitoring (e.g., use of pedometers to promote exercise); application of time management techniques; and use of simple psychological techniques, such as implementation intentions, in which patients are asked to identify an external cue to serve as a stimulus to initiate a behavioral practice (56). A meta-analysis of 94 studies showed that the use of implementation intentions has a moderate to large effect in inducing successful goal pursuit (57). Mental contrasting is

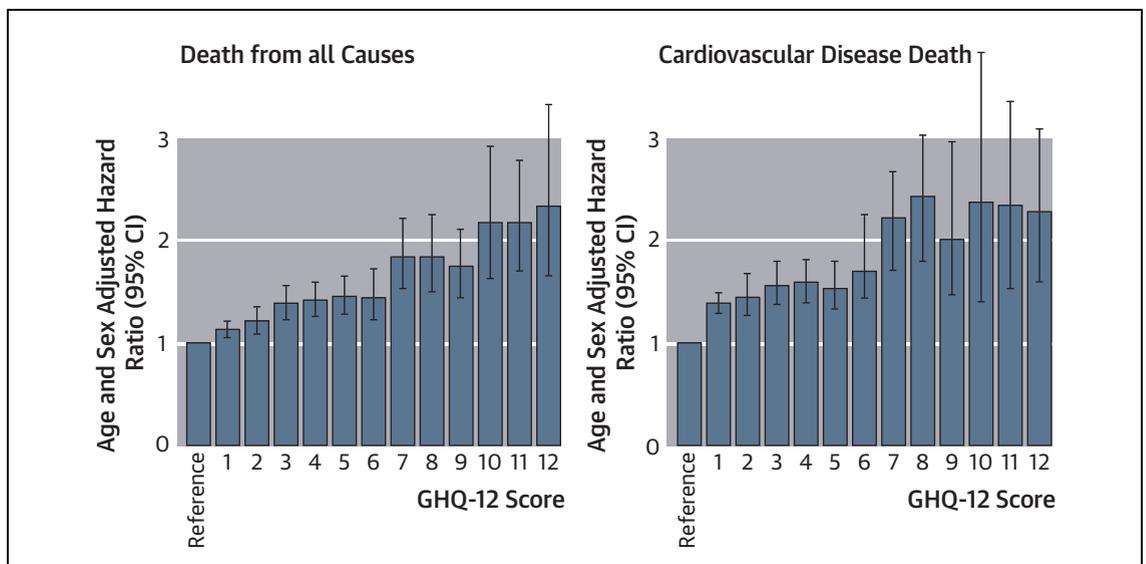


FIGURE 6 Risk Associated With Psychological Distress in a Participant Pooled Analysis of 10 Prospective Studies

Even mild elevations in 12-item General Health Questionnaire (GHQ-12) scores were associated with elevated all-cause and cardiac mortality. CI = confidence interval. Adapted with permission from Russ et al. (51).

another new technique that can promote behavioral pursuit (58).

With respect to goal maintenance, 2 principal pillars are the provision of feedback and social support. In addition, contingency planning (i.e., prospective identification of a minimal base of action in the presence of stress), application of techniques to support stress management (i.e., teaching coping skills), and energy management (i.e., better sleep hygiene) can help foster goal maintenance. Techniques also can be combined, such as the use of obligation intentions, which combine social support with implementation intentions (Fig. 10).

COST-EFFECTIVE INNOVATIONS IN BEHAVIORAL INTERVENTIONS. Health delivery systems are currently constrained with respect to providing the types of tools needed to assist patients in the inherent challenge of changing health behaviors. This challenge is compounded by current economic constraints that necessitate the development of inexpensive interventions. One way to achieve this mission is to capitalize on the capability of the Internet and mobile phone applications to support patient education and engagement, by making health information more readily available, inspirational, and personally relevant; by providing more varied, frequent, and tailored patient counseling; and by delivering computer-generated feedback regarding behavioral and self-monitoring efforts.

A second method is the development of tailored group programs to provide patients with practical behavioral information and techniques regarding diet, exercise, sleep hygiene, rest, relaxation, stress management, and time management practices. The use of groups can be inspirational, provide social support, and complement one-on-one counseling and Web-based interventions.

A third component is development of a tiered (or “stepped”) model for behavioral health care. One 3-tiered model would have physicians serve as the first tier, responsible for triage of patients for behavioral risk and provision of brief counseling. The second tier would involve physician referral of patients to behavioral intervention programs designed to provide integrated intervention across the wide domains of behavioral factors. The third tier would involve the referral of patients to behavioral specialists when depression, anxiety, stress, or other psychosocial issues mandate.

ONE SIZE DOES NOT FIT ALL. At the core of such proposed tiered care are the design and function of behavioral intervention programs. Optimally, these programs should address 2 key goals. First, to

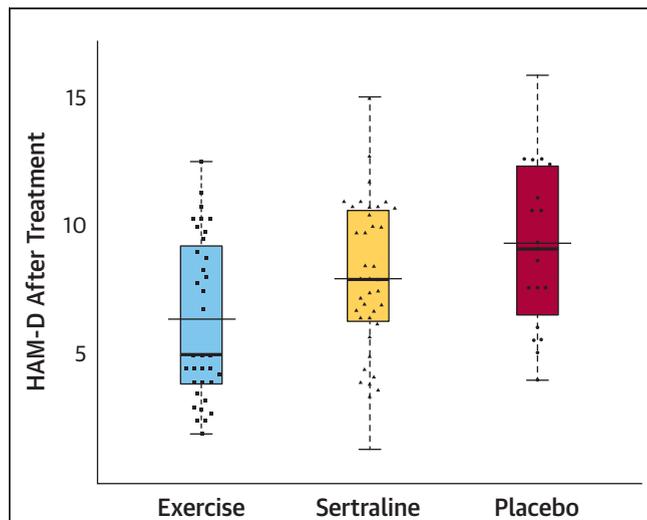


FIGURE 7 Reduction of HAM-D in 3 Treatment Groups

Comparison of reduction following randomization of patients with coronary heart disease to aerobic exercise, sertraline, or placebo. Both exercise and sertraline resulted in larger reductions than placebo. Adapted with permission from Blumenthal et al. (53). HAM-D = Hamilton Depression Rating.

address the difficulty in fostering behavioral change, programs should be comprehensive. Currently, many types of behavioral intervention programs tend to reside in their own silos, including exercise training programs, nutritional counseling services, weight

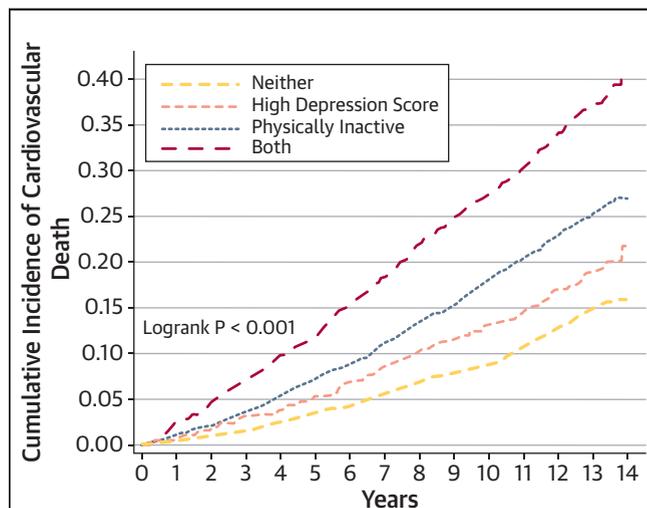
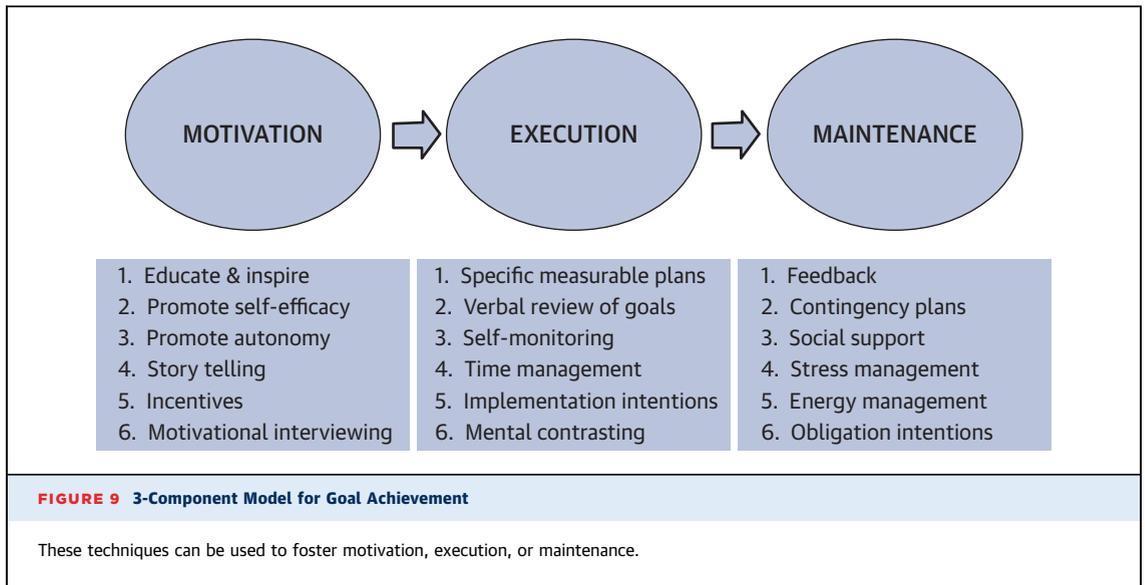


FIGURE 8 Cumulative Incidence of Cardiovascular Death in the Cardiovascular Health Study

Patients are grouped according to presence or absence of physical activity and the presence or absence of depression. Adapted with permission from Win et al. (54).



loss programs, and sleep centers. Psychological interventions also tend to be highly fractionated.

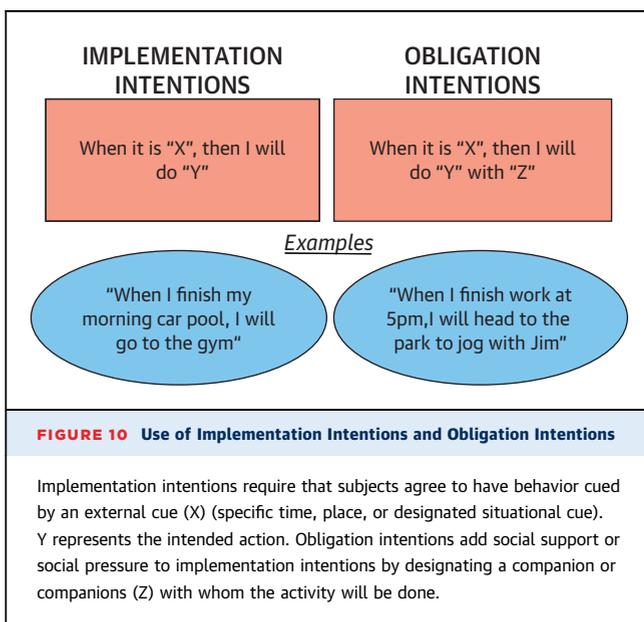
Second, although the treatment of most CHD risk factors is guideline driven, a high degree of flexibility and clinical judgment is required for the treatment of behavioral risk factors. To illustrate, consider the hypothetical example of John F., a 56 year-old busy midlevel executive of a company that is downsizing. John presents to his physician with nonanginal chest pain that, following testing, is identified as functional. Because John has gained weight and is highly sedentary, his physician establishes exercise and weight loss as health goals. A brief psychosocial

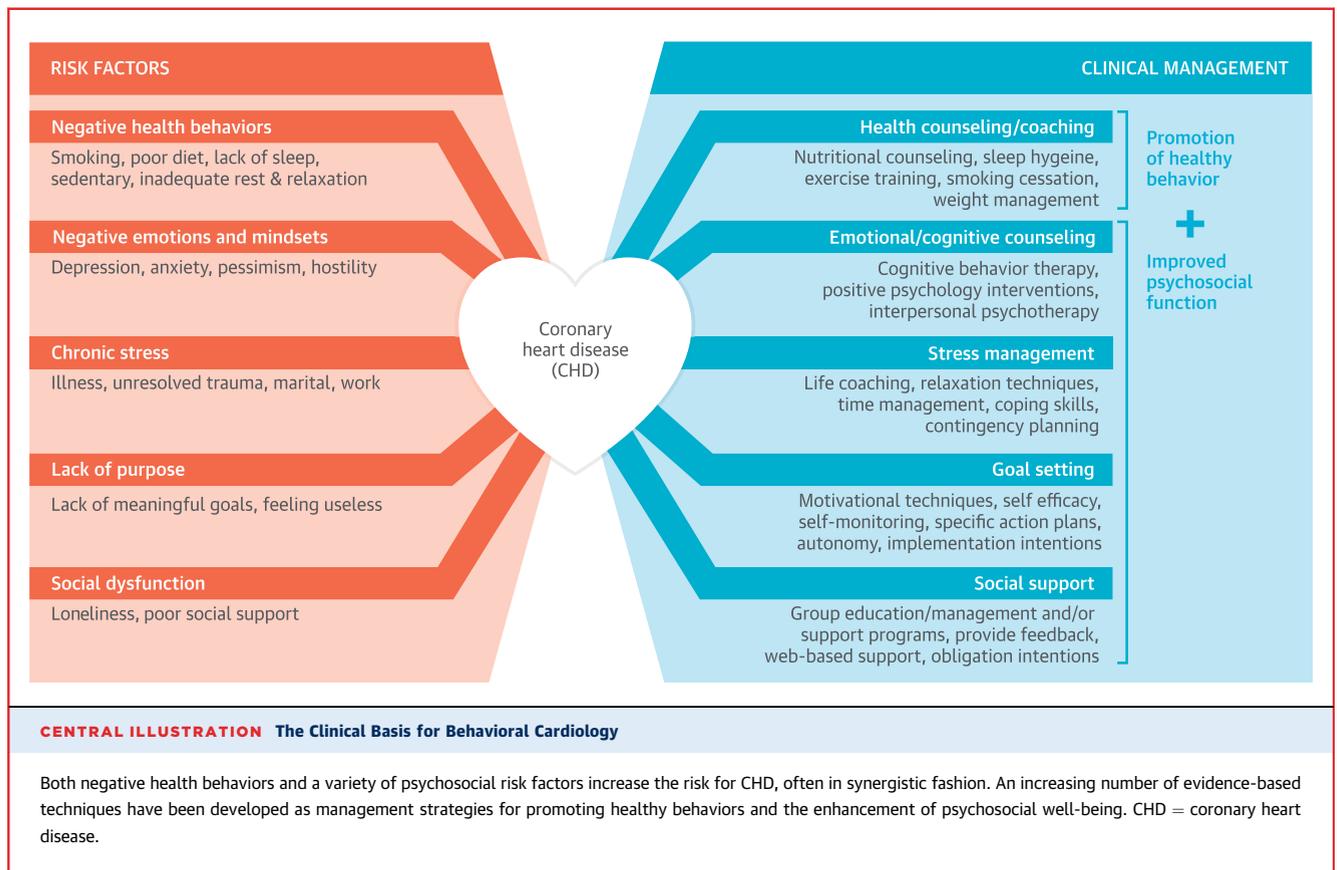
review reveals that John goes to sleep too late as a result of work pressure, has mild insomnia, and feels a bit down and pessimistic about his work situation, which he believes is thwarting his sense of purpose. John is also socializing less. Thus, John’s work situation has led to dysfunction in each of the behavioral domains (Fig. 4).

What, then, is the optimal first behavioral intervention for assisting John? In the behavioral domain, “one size does not fit all.” Life circumstances, current habits, personal preferences, motivation, and coping skills, for instance, may dictate varied alternatives to initiating a specific behavioral intervention for John. Rather, the “art” of optimizing behavioral intervention is based on clinical judgment that is derived from an experience base in providing coordinated, integrated care. Whereas many professionals are currently trained to provide specialized expertise in such areas as fitness instruction, dietary counseling, sleep hygiene, rest and relaxation techniques, and psychological counseling, few are trained in integrating these services. The development of such expertise would aid the growth of behavioral cardiology as a new, distinct subspecialty within cardiology.

CONCLUSIONS

Epidemiological studies over the last decade demonstrate generally strong dose-response relationships between an expanding number of psychosocial risk factors and CHD. Increasing data also indicate that positive psychosocial functioning serves to improve health. To date, however, there has been relatively little translation of these findings into cardiac practice. The application of evidence-based approaches





toward promoting patient motivation and goal execution, innovative applications of technology, group-based interventions, and the development of a tiered behavioral care delivery system are needed to help behavioral cardiology develop into a mature field (Central Illustration). The need for this maturation is highlighted by the general challenge of eliciting behavioral change in cardiac practice, as well as societal trends that may now be making this challenge

more difficult, including trends toward a faster pace of living, increasing job and time stress, reduced sleep, increasing obesity, and declining physical activity.

REPRINT REQUESTS AND CORRESPONDENCE:

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