

CHRONIC STRESS AND INSULIN RESISTANCE-RELATED INDICES OF CARDIOVASCULAR DISEASE RISK, PART 2: A POTENTIAL ROLE FOR MIND-BODY THERAPIES

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Cardiovascular disease (CVD) is the leading cause of death and disability in the industrialized world, and its prevalence is rapidly increasing among developing nations. The increasing global prevalence of CVD reflects in part the concurrent rise in insulin resistance, obesity, dyslipidemia, and other atherogenic changes associated with insulin resistance syndrome (IRS). Evidence suggests that chronic stress and related psychosocial factors also play an important role in the development and progression of IRS-related states and ultimately,

in the pathogenesis of CVD. Designed to address these interrelated psychological and physiological components of health, yoga and other traditional mind-body therapies may offer particular promise in both the primary and secondary prevention of CVD. In this article, we review the evidence regarding the potential benefits of specific mind-body modalities for CVD risk reduction and discuss possible mechanisms underlying these observed effects. (*Altern Ther Health Med.* 2007;13(5):44-51.)

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Chronic psychosocial stress can lead to a destructive, self-perpetuating cascade of neuroendocrine, metabolic, inflammatory, and neuropsychological changes that promote the development of insulin resistance syndrome (IRS), atherosclerosis, and ultimately, cardiovascular disease (CVD).¹ As discussed in part 1 of this article, chronic stress and related psychosocial factors can exert a powerful influence on the pathogenesis of both IRS and CVD. Given the importance of neuropsychological factors and sympathetic activation in the development of insulin-re-

sistant states and the synergistic, mutually exacerbating effects of these and other IRS-related risk factors, mind-body therapies may have considerable potential in the prevention and management of CVD. One popular mind-body therapy that may hold particular promise as a therapeutic and health promotion measure is yoga. Yoga is an ancient practice that is gaining increasing popularity in western industrialized countries for alleviating stress, enhancing well-being, and improving health and fitness.²⁻⁵ A traditional discipline of the mind, body, and spirit dating back to at least 2000 BC, yoga has been widely used in India to manage hypertension, diabetes, and other chronic insulin-resistance conditions^{4,6-15} and may offer a cost-effective intervention for people in Western populations who have or are at risk for CVD and related disorders. There is increasing evidence that even the short-term practice of yoga may reduce IRS-related risk factors for CVD and may attenuate signs, decrease complications, and improve the prognosis of those with clinical or underlying disease. Similarly, recent research suggests that certain other traditional mind-body practices such as tai chi chuan and qigong also may reduce risk for CVD and related disorders.¹⁶⁻²⁰ In the following sections, we review the evidence regarding the potential beneficial effects of specific mind-body modalities and outline possible mechanisms underlying these observed effects. The primary focus of our discussion is on yoga, which remains the most extensively studied mind-body practice with respect to effects on IRS-related indices of CVD risk.

YOGA AS A THERAPEUTIC INTERVENTION FOR THE PREVENTION AND MANAGEMENT OF CARDIOVASCULAR DISEASE

Yoga (a Sanskrit term meaning "yoke" or "union") is an ancient healing, restorative, and transformational discipline that originated in India at least 4000 years ago.^{2-4,16} Yogic teachings and philosophy are at the heart of India's 3 great religious cultures, Hinduism, Buddhism, and Jainism.²¹ Of the 7 major branches of Hindu yoga, Hatha (or forceful) yoga, Raja (Royal or classical) yoga, and Mantra yoga are perhaps the best known and most widely practiced forms. Mantra yoga, emphasizing the use of specific sounds or chants to achieve physical, mental, and spiritual transformation, has been popularized in recent decades by Maharishi Mahesh Yogi, the founder of transcendental meditation (TM).^{16,22} Raja yoga, based on the 8-limb system of meditation, contemplation, and renunciation compiled by Sage Patanjali Maharishi in the Yoga Sutras, seeks transformation and self-realization through progressive control of the mind.^{21,22} Hatha yoga, the Hindu branch of yoga most commonly practiced in the Western industrialized world, focuses on specific physical postures (*asanas*) and breath control (*pranayama*) as a path to healing and transformation. Hatha yoga also incorporates mental concentration (*dharana*), mantras or chants, meditation (*dhyana*), cleansing exercises (*kriyas*), and specific hand gestures (*mudras*).^{16,22}

There is mounting evidence that yoga may be effective in the prevention and management of CVD and other chronic disorders related to IRS. In uncontrolled Indian studies of adults with hypertension^{14,23} and/or diabetes,^{8,14,22,24} yoga practice alone^{22,24} or in combination with other therapies^{8,14,22} was associated with a markedly reduced need for medication relative to baseline. In controlled studies of adults with hypertension,²⁵⁻²⁸ risk factors for CVD,²⁹ and/or coronary artery disease,³⁰ similar reductions in medication requirements have been reported among those completing a yoga-based intervention as compared to controls receiving enhanced usual care,^{25,27,29} usual care plus a diet and exercise program,³⁰ or placebo therapy.²⁸ Controlled studies in Indian,¹⁵ British,²⁹ and American^{31,32} populations also suggest that yoga-based programs may decrease signs, reduce complications, and enhance the prognosis of active disease. In a randomized controlled trial (RCT) of Indian men with coronary artery disease (CAD), those enrolled in a 12-month comprehensive yoga program demonstrated retardation of coronary atherosclerosis, increased regression and decreased progression of vascular lesions, and reduced anginal episodes as compared to usual care controls.¹⁵ Another non-randomized controlled study of CAD patients reported similar findings.³⁰ Likewise, in an RCT of American elderly, those completing a 1-year comprehensive yoga-based program showed a decline in carotid intimal media thickness, an index of carotid atherosclerosis, relative to those receiving usual care or a comprehensive lifestyle intervention program.³¹ This observed decline was significantly correlated with program adherence, suggesting a direct relationship between the practice of this program and atherosclerotic change. An RCT of African Americans with CVD yielded similar results.³²

Moreover, the clinical benefits observed following yoga-based programs may persist long-term. For example, in a 4-year follow-up of hypertensive adults, Patel et al found that those who had participated in an 8-week, comprehensive yoga relaxation program were less likely to experience CVD-related complications, a serious coronary event, or ischemia.²⁹

Yoga may improve physiological and anthropometric indices of cardiovascular risk as well.¹⁶ For example, as detailed in our recent comprehensive review,¹⁶ studies in India offer evidence that yoga-based programs may enhance glucose tolerance and reduce glycemia in both healthy adults³³ and in those with diabetes^{8,22,24,34,35} or cardiovascular disorders.^{14,30} Controlled investigations in India,^{15,30,36,37} Europe,^{26,29,38,39} and Thailand⁴⁰ have reported improvement in lipid profiles following yoga-based interventions in healthy subjects^{36,38} and patients with CVD,^{15,30,40} hypertension,²⁶ or other CVD risk factors.^{29,37,39} Observed changes included reductions in triglycerides,^{15,37,40} total cholesterol,^{15,26,30,36-39} and low-density lipoprotein (LDL)^{15,30,37,38} relative to control values. Likewise, controlled studies from at least 7 countries offer evidence that yoga-based programs can reduce body weight,^{15,30,37,38,40-43} improve body composition,^{42,44} and reduce blood pressure^{26-29,31,32,39,43,45-51} in healthy subjects^{31,36,41,42,46-49} and adults with CVD,^{15,30,32,40} hypertension,^{11,25-28,32,43,45,50-53} and/or other CVD risk factors.^{29,37,39}

Recent studies of Indian^{14,34,54,55} and Thai populations⁴⁰ suggest that yoga may decrease oxidative stress in healthy adults^{54,55} and in adults with hypertension,¹⁴ CAD,⁴⁰ or type II diabetes.^{22,34} Limited data in healthy Indian⁵⁶ and German adults³⁸ also suggest that yoga practice may improve coagulation profiles. Investigations of Indian,^{11,49,57-63} European,^{38,39,64,65} American,³¹ and Japanese populations⁶⁶ indicate that yoga can reduce sympathetic activation^{11,14,38,39,49,51,57-60,67} and accelerate cardiovascular recovery^{11,61-66} in healthy adults^{38,49,57-59,61-66} and adults with hypertension^{11,14,39,51,60} or epilepsy.⁶⁷

In addition, a growing body of research suggests that yoga therapy can relieve stress and reduce psychological morbidity. For example, yoga has been reported to decrease reactivity to stressors,⁶⁸ enhance stress-related coping,^{69,70} reduce symptoms of depression,^{47,71-74} and anxiety,^{6,47,69-71,75} and decrease anger, tension, and fatigue.⁷¹ Similarly, yoga has been shown to enhance psychological well-being,^{6,14,47,68-71,76} reduce sleep disturbance,⁷⁷ improve cognitive function,^{6,47,78} and enhance quality of life.¹⁴

YOGA AND INDICES OF CARDIOVASCULAR RISK: POSSIBLE UNDERLYING MECHANISMS

As reviewed above, chronic psychosocial stress has been linked to the development of psychological and associated cognitive dysfunction in both animal models and human populations,⁷⁹⁻⁸² an association thought to be mediated by dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and sympathoadrenal system.^{83,84} There is growing evidence that these negative affective states, in turn, increase risk for visceral obesity,^{85,86} hypertension,⁸⁷⁻⁸⁹ insulin resistance,⁹⁰⁻⁹² and other features of IRS,⁹²⁻⁹⁴ as well as for CVD^{89,95-100} and diabetes.¹⁰¹ In addition, negative emotional states and responses, once entrenched,

may themselves operate as profound sources of psychogenic stress, contributing to chronic HPA axis activation and aversive neural programming. A vicious cycle is thus initiated that results in progressive emotional, cognitive, structural, and physiologic impairment and culminates in the development and progression of CVD. By alleviating stress, improving mood, and promoting positive downstream effects on the functional and physiological indices of CVD risk, yoga may help to break this destructive cycle and foster new pathways that support health and well-being.

There is increasing evidence that even short-term practice of yoga can reduce both psychological and physiological risk factors for CVD and may attenuate signs, reduce complications, and improve the prognosis of clinical disease.¹⁶ Although the mechanisms underlying the observed beneficial effects of yoga therapy on cardiovascular risk profiles remain speculative, the observed changes likely occur through at least 2 pathways. First, by reducing the activation and reactivity of the sympathoadrenal system and the HPA axis and promoting feelings of well-being, yoga may alleviate the effects of stress and foster multiple positive effects on neuroendocrine status, metabolic function, and related inflammatory responses (Figure 1). Second, by directly stimulating the vagus nerve, yoga may enhance parasympathetic output and thereby shift the autonomic nervous system balance from primarily sympathetic to parasympathetic, leading to positive changes in cardiac-vagal function, in mood and energy state, and in related neuroendocrine, metabolic, and inflammatory responses (Figure 2).

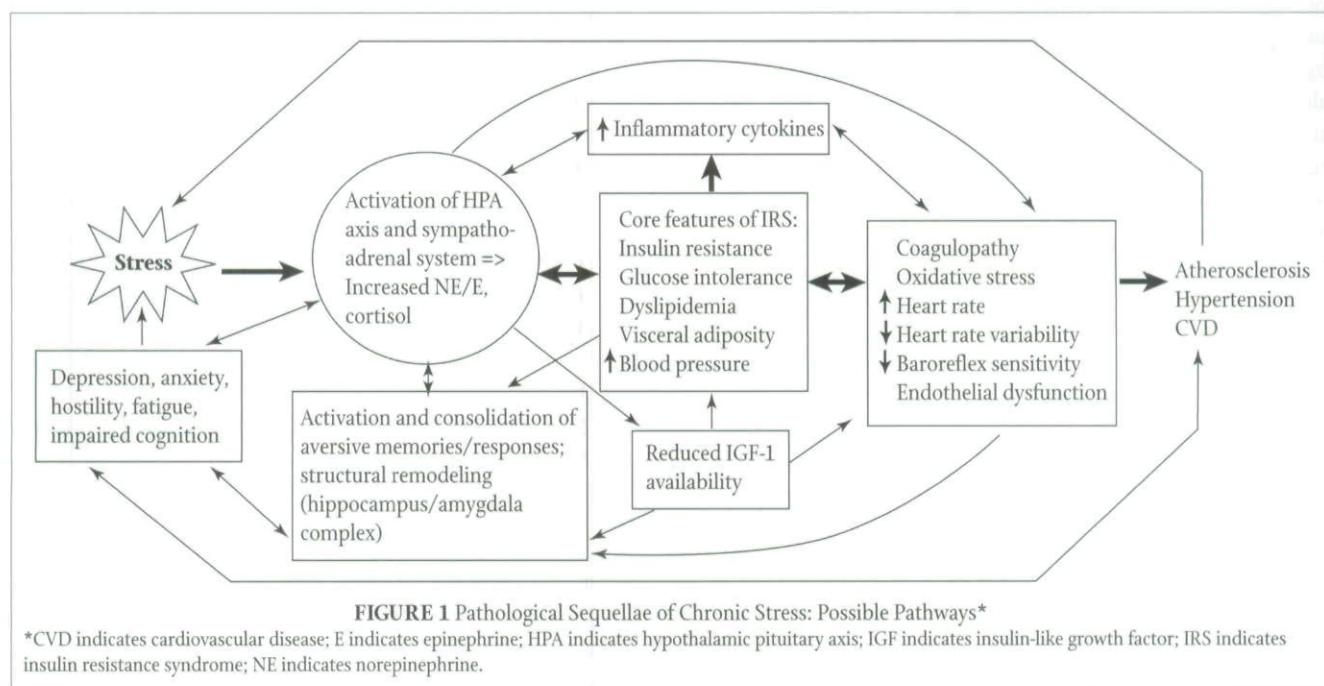
Stabilizing Hypothalamic-Pituitary-Adrenal Axis and Sympathoadrenal Activity

As mentioned above, yoga appears to have widespread beneficial effects on both psychological and physiological indices of cardio-

vascular risk. These effects likely occur in part via the stabilization of HPA axis and sympathoadrenal activity. The attendant reduction in catecholamines and cortisol, decline in cardiovascular reactivity, enhancement of mood and well-being, and alleviation of perceived stress may result in positive downstream effects on metabolic and hemodynamic profiles.

Several studies have demonstrated pronounced changes in markers of sympathetic activation within a single yoga session,^{57,58,66,102,103} suggesting an immediate beneficial effect. Other clinical trials have documented beneficial alterations in baseline measurements following as few as 3 to 8 sessions of yoga training^{45,46} when compared to baseline^{11,14,60,104,105} or to controls receiving usual care,^{39,51,67} a restful, non-yoga intervention,⁴⁹ sham yoga,⁶⁷ or no intervention.³⁸ Observed changes have included reductions in cortisol^{66,104,105} and catecholamine levels,^{11,14,38,67} renin-angiotensin activity,^{11,39,51} and basal skin conductance,^{14,49,57,60,67} indicating progressive attenuation of sympathoadrenal activation.¹¹ Numerous controlled trials also have reported a decline in heart rate^{38,47,49,52,57-59,61,102,103,106} and blood pressure^{26,28,30,38,39,43,45-49,51} compared to engagement in a relaxing, non-yogic activity^{45,57-59,102,103} and/or controls receiving usual care,^{26,27,30,39,46,51,52} an aerobic exercise program,^{48,49,106} placebo therapy,³⁸ or no intervention.^{38,43,47,49,61}

Several studies suggest that yoga practice also can reduce cardiovascular reactivity to stress,^{44,47,107,110} a factor strongly associated with insulin resistance^{111,112} and a major independent predictor of hypertension, stroke, myocardial infarction, and cardiovascular mortality.¹¹³ For example, studies in healthy,^{44,47,107,108} hypertensive,¹⁰⁹ and asthmatic patients¹¹⁰ have shown significant reductions in blood pressure and heart rate responses to cold pressor,¹⁰⁹ hand grip,¹¹⁰ and other stress tests^{44,47,107,108} after as few as 7 days of yoga training¹¹⁰ when compared to baseline^{44,110} or controls receiving non-yogic exercise,¹⁰⁷ usual care,¹⁰⁹ or no intervention.^{47,108}



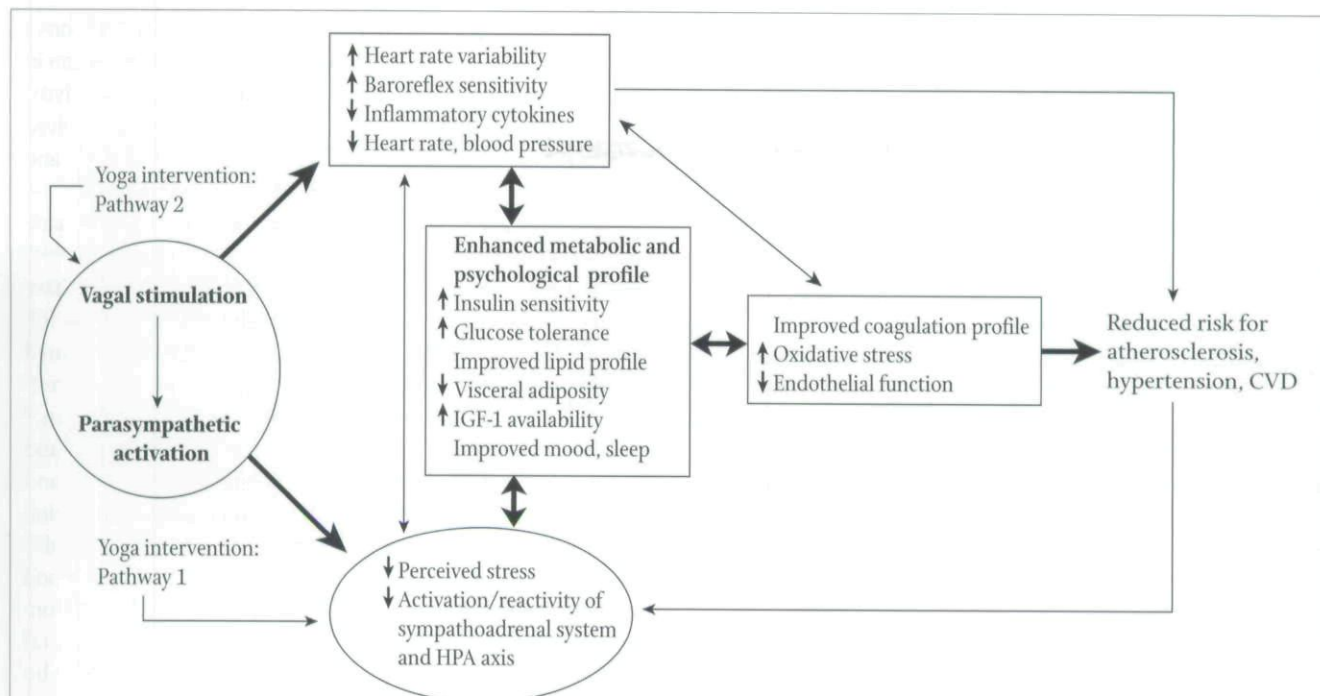


FIGURE 2 Hypothesized Pathways By Which Yoga Intervention May Enhance Cardiovascular Risk Profiles*

*CVD indicates cardiovascular disease; HPA indicates hypothalamic pituitary axis; IGF indicates insulin-like growth factor.

In addition, numerous studies have demonstrated beneficial effects of yoga practice on psychological status and response to stress. Even short-term yoga training has been reported to enhance psychological well-being and decrease reactivity to stressors. For example, several studies have demonstrated significant improvements in mood^{68,102,114} and reductions in fatigue,^{115,116} psychological distress,¹¹⁶ emotional reactivity,⁶⁸ irritability,⁶⁸ hostility,⁶⁸ and other symptoms of depression and anxiety^{75,117} following a single 30- to 60-minute yoga session. Likewise, other studies have documented significant improvement in psychological functioning after yoga-based interventions ranging in duration from only 3^{118,119} to 30 days.^{77,120-122} Reported changes include reduction in depression,^{118-120,122,123} anxiety,^{45,118,122,123} perceived stress,⁷⁷ and fatigue¹²⁰ and improvement in sleep, psychological well-being, and self-esteem.⁷⁷ These effects on psychological reactivity and well-being are thought to reflect reduced sympathetic arousal and normalization of the HPA system.⁸³

Vagal Stimulation and Parasympathetic Activation

The vagus nerve, the 10th cranial nerve, is a conduit for parasympathetic outflow regulating autonomic functions in the thorax and abdomen,^{124,125} including heart rate, blood pressure, and gastric acid secretion;^{124,125} it innervates the heart, lungs, and several visceral organs, including the liver, kidney, pancreas, and gastrointestinal tract.^{124,126} The vagus nerve also projects to and receives input from a wide array of autonomic, reticular, and limbic structures of the brain.¹²⁵

Vagal stimulation triggers a series of autonomic responses that may buffer the effects of chronic stress and help restore sym-

pathovagal balance. For example, vagal stimulation slows heart rate, reduces blood pressure, induces gastric motility, dilates arterioles, and constricts the pupils.¹²⁷ Stimulation of the vagus nerve also suppresses inflammation and activates the cholinergic anti-inflammatory pathway, which inhibits synthesis of TNF- α , reduces TNF- α serum concentrations, and inhibits TNF- α activity, leading to a reduction in proinflammatory cytokines.¹²⁷⁻¹³⁰ This anti-inflammatory effect, in turn, leads to reduced HPA axis and sympathoadrenal activation and related positive, downstream changes. Vagal stimulation also increases heart rate variability (HRV) and baroreflex sensitivity, measures widely used as indicators of autonomic activity in the heart.¹³¹⁻¹³⁴ The cardiovagal baroreflex plays an important role in modulating heart rate and blood pressure.^{135,136} HRV is the cyclic variation in the beat-to-beat interval (duration between successive heart beats) that results from the tonic firing of cardiac-vagal efferents, originating in the medulla.^{133,134} High HRV and baroreflex sensitivity are generally considered to indicate cardiovagal adaptability and sympathovagal balance,¹³⁴ allowing greater responsiveness and sensitivity to changing environmental demands.

Yoga breathing exercises and postures have immediate beneficial effects on heart rate variability and baroreflex sensitivity.^{11,59,64,65} These effects are thought to reflect direct stimulation of the vagal nerve.^{11,64} The observed reductions in heart rate and blood pressure that occur during yoga practice^{58,59,68,102} or following short-term (2-day to 6-week) yoga interventions^{28,44,46,49,52,58,65,109,137} may also, in part, reflect vagal stimulation and consequent improved cardiovagal function. Yoga-based interventions also have been associated with accelerated cardiovascular recovery time from stress as

compared to non-yoga resting poses¹⁰³ or controls receiving usual care¹⁰⁹ or no intervention.¹⁰⁸ Cardiovascular recovery from stress is a marker of vagal rebound that has likewise been strongly associated with CVD risk.¹³⁸

OTHER MIND-BODY THERAPIES AND CVD RISK

While yoga remains the most extensively studied mind-body therapy with respect to effects on IRS-related indices of cardiovascular risk, a growing body of research suggests that other traditional mind-body modalities, such as tai chi and qigong, may also have promise for the prevention and management of CVD. Qigong, a major branch of traditional Chinese medicine,¹³⁹ combines meditation and controlled breathing with precise physical movements and postures.^{139,140} Developed more than 2500 years ago in China, qigong has been used throughout history by emperors to achieve health and longevity, by monks to attain peace and inner clarity, and by martial artists to increase inner strength and power.^{139,140,141}

Tai chi is an ancient Chinese martial art derived from qigong that traces its roots back to at least the seventh century AD.¹⁴² Tai chi is widely thought to have originated as a formal discipline in the 13th century with the teachings of the legendary Taoist monk, Zhang San Feng.^{142,143} While there are now multiple styles of tai chi (chen, yang, old wu, wu, and sun), all combine deep diaphragmatic breathing with specific postures that are performed in a continuous, dance-like series of slow, graceful movements.^{19,142,144-146} Due to its characteristic slow pace, gentle movements, and low impact, tai chi is particularly attractive as a practice for older adults. Both qigong and tai chi are practiced widely in China to promote physical, mental, and spiritual health; to improve balance and flexibility; and to enhance memory and concentration.^{17,20} Like yoga, tai chi and qigong are gaining popularity in Western industrialized nations for their purported beneficial effects on psychological well-being, quality of life, health, and fitness.^{19,144-146}

Studies from several countries suggest that tai chi and qigong also may be helpful in reducing risk for CVD and CVD-related complications. For example, investigations of both healthy and chronically ill adults suggest that these practices may lower blood pressure,^{18,19,139,141,147-151} reduce sympathetic reactivity,^{139,140,148,150} and enhance cardiorespiratory function.^{19,152,153} Limited data suggest that the practice of tai chi and qigong may have beneficial effects on lipid profiles,^{147,150,154} and studies of diabetic adults in Japan have reported reductions in post-prandial glucose,¹⁵⁵ glycated hemoglobin,¹⁵⁶ and C-peptide¹⁵⁶ following qigong practice.

Tai chi and qigong may reduce certain psychosocial risk factors for CVD as well. For example, studies of healthy adults and adults with chronic conditions have reported that tai chi and qigong decrease anxiety^{19,144,154,157} and depression,^{19,144,150,157-159} improve mood,^{19,144,157} and alleviate anger, fatigue, and tension.^{144,157} Similarly, several investigations offer evidence that tai chi and qigong may reduce perceived stress,^{19,160} enhance stress-related coping,¹⁵⁷ and improve psychological well-being.^{19,144,145,157-159,161}

While the mechanisms underlying the observed effects of these practices on CVD risk remain unknown, the changes may occur via pathways similar to those proposed in Figure 2.

LOGISTICAL ADVANTAGES OF TRADITIONAL MIND-BODY THERAPIES AND CURRENT LIMITATIONS IN THE LITERATURE

In addition to the numerous reported health benefits, yoga and other traditional mind-body disciplines have many practical advantages as therapeutic intervention and health-promotion measures. They are relatively easy to learn and are economical and non-invasive therapies with few side effects.^{2,4,16,17,20} Requiring minimal equipment and professional personnel, yoga, tai chi, and other similar mind-body practices can be relatively easy and inexpensive to maintain, with several studies indicating excellent long-term compliance.^{15-17,20,162} Yoga, qigong, and tai chi are all low-speed, low-impact forms of exercise that can generally be practiced safely by individuals who are elderly, ill, or unfit^{2,4,16,17,19,20,144,147,159,163} and are therefore appropriate for use in a broad range of populations. Mind-body therapies are increasingly incorporated into exercise prescriptions for clinical populations, as they enhance balance and flexibility, which complement strength and cardiovascular conditioning.¹⁶⁴ Group practice of these ancient disciplines also can provide a source of social support, a factor strongly and inversely associated with CVD risk,^{97,165} and may aid in improving health-related attitudes and lifestyle choices, in part by enhancing psychological well-being,¹⁶⁵ and in this way play an important role in CVD prevention and health promotion.¹⁶⁵ Showing promise as a means of reducing psychological morbidity and promoting psychological well-being, as well as preventing and managing cardiovascular disease and related chronic insulin resistance conditions, these mind-body therapies may offer a cost-effective intervention in at-risk populations.

However, while the findings detailed above suggest that yoga, tai chi, and other mind-body therapies have considerable therapeutic potential, rigorous, controlled studies investigating the effects of these practices on CVD risk factors or related clinical endpoints remain few, especially in Western populations.^{4,16,18-20,145,147,159} Additionally, interpretation of many existing studies is limited by small sample sizes, lack of appropriate control groups, inadequate description of methods, selection bias, lack of randomization, failure to adjust for lifestyle characteristics, inadequacies in statistical analysis and presentation, exposure to multiple interventions, or other methodological problems.^{16,18-20} Potential long-term effects of yoga and other mind-body therapies remain little explored, and the mechanisms underlying the reported benefits associated with these disciplines are still poorly understood. In addition, the large variation in the nature, duration, intensity, and delivery methods of the interventions used makes calculation of effect sizes and comparisons across studies difficult. Publication bias also may play a role in the selective reporting of positive results,¹⁶⁶ particularly in non-Western countries, where these disciplines are more widely accepted and more likely to be incorporated into medical treatment. Clearly, additional high-quality randomized controlled trials are needed (1) to confirm the reported beneficial

effects of yoga, tai chi, qigong, and other promising mind-body therapies on CVD risk and clinical outcomes, especially in Western populations; (2) to further investigate the potential long-term benefits of these therapies; and (3) to elucidate possible underlying mechanisms of disease prevention.

CONCLUSION

Yoga and other mind-body therapies may offer promise for the primary and secondary prevention of IRS and CVD. Available evidence suggests that these therapies may attenuate insulin resistance and related physiological risk factors for CVD, improve mood and well-being, reduce sympathetic activation, and enhance cardiovascular function. In so doing, mind-body therapies may buffer the effects of chronic stress, help restore sympathovagal balance, and compensate for adverse systemic changes related to CVD. However, additional rigorous studies are needed to confirm existing findings, elucidate the specific mechanisms of protection against CVD, and investigate long-term effects on cardiovascular health.

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