

PREVENTIVE MEDICINE, INTEGRATIVE MEDICINE & THE HEALTH OF THE PUBLIC

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The responsibility for the content of this paper rests with the authors and does not necessarily represent the views or endorsement of the Institute of Medicine or its committees and convening bodies. The paper is one of several commissioned by the Institute of Medicine as background for the Summit on Integrative Medicine and the Health of the Public. Reflective of the varied range of issues and interpretations related to integrative medicine, the papers developed represent a broad range of perspectives.

ABSTRACT *The fields of preventive medicine and public health share the objectives of promoting general health, preventing specific diseases, and applying the concepts and techniques of epidemiology toward these goals. The purview of preventive medicine as a discipline has traditionally been described to encompass primary, secondary, and tertiary prevention levels. This paper explores the overlap and potential synergies of integrative medicine and preventive medicine in the context of these levels of prevention, acknowledging the relative deficiency of research on the effectiveness of practice-based integrative care.*

The holistic approach of integrative medicine overcomes the traditional wall of silence between complementary and alternative medicine (CAM) and conventional practice, reducing the risk of adverse interactions or gaps in care. At the level of primary prevention, an array of integrative modalities can be effective in health promotion, including lifestyle counseling, dietary guidance, stress mitigation techniques, interventions to improve sleep quality, and use of nutraceuticals and herbal supplements for health promotion. At the level of secondary prevention, stress management and nutritional supplementation can reduce risk factors for chronic disease. At the level of tertiary prevention, the full range of CAM modalities pertains to such goals as pain management, symptom control, stress relief, disease management, and risk reduction. Integrative medicine offers knowledgeable guidance to tailored therapies across the full spectrum of both conventional and CAM practice, thereby providing any given patient more options—and more opportunities for success—in the pursuit of personal health. This must be weighed against the inherent risks in making use of therapeutic practices for which the scientific evidence base is often at best incomplete.

The goal of integrative medicine should be to make the widest array of appropriate options available to patients, ultimately blurring the boundaries between conventional care and CAM. Both disciplines should be subject to rigorous scientific inquiry so that interventions that work are systematically distinguished from those that do not. The case is made that responsible use of science and responsiveness to the needs of patients that persist when the data from randomized controlled trials have been exhausted can be reconciled. Integrative medicine is a framework for this reconciliation, and practiced judiciously, offers the promise of better patient outcomes.

INTRODUCTION

Preventive Medicine

Preventive medicine encompasses both the care of individual patients, and public health practice, and as is evident in the name, focuses on the prevention of disease rather than treatment, *per se*. The fields of preventive medicine and public health share the objectives of promoting general health, preventing specific diseases, and applying the concepts and techniques of epidemiology toward these goals.

While preventive medicine seeks to enhance the lives of individuals by helping them improve their own health, public health attempts to promote health in populations through the application of organized community efforts. Although preventive medicine and public health are often discussed somewhat separately, there is a seamless continuum among the following: the practice of preventive medicine by physicians and other health professionals (clinical preventive services); the attempts of individuals and families to promote their own health and the health of loved ones; and the efforts of governments and voluntary agencies to achieve the same health goals for populations. The dividing line between preventive medicine and public health practice is thus far from distinct, as is that between prevention and treatment. The purview of preventive medicine as a discipline has traditionally been described to encompass primary, secondary, and tertiary prevention (so-called “Leavell’s levels”) (Jekel et al., 2007). Only the first of these is nominally the exclusive purview of “preventive” as opposed to other disciplines of medicine.

In the construct developed, or at least popularized, by Leavell (Leavell and Clark, 1965), all physician and other health professional activities have the goal of prevention. What is to be prevented depends on the context, and the patient’s position on the spectrum from health to disease. **Primary prevention** keeps the disease process from becoming established by eliminating causes of disease or increasing resistance to disease. **Secondary prevention** interrupts the disease process before it becomes symptomatic. **Tertiary prevention** limits the physical and social consequences of symptomatic disease.

Primary Prevention and Predisease

Primary prevention refers to health promotion, which fosters wellness in general and thus reduces the likelihood of disease, disability, and premature death in a nonspecific manner, as well as specific protection against the inception of dis-

ease. Examples of the former include the promotion of physical activity and prudent dietary practices; smoking avoidance or cessation; and the mitigation of stress. Immunization is a clear example of the latter.

Most noninfectious diseases can be seen as having an early stage, during which the causal factors will start to produce physiologic abnormalities. In atherosclerosis, for example, there may be dyslipidemia and endothelial dysfunction (Jiamsripong et al., 2008), but no overt signs of atheroma during the predisease stage. The goal of a health intervention at this time is to modify risk factors in a favorable direction. Life-modifying activities (e.g., changing to a diet low in saturated and trans fat, pursuing a consistent program of aerobic exercise, and ceasing to smoke cigarettes), are considered to be methods of primary prevention because they are aimed at keeping the pathologic process and disease inception from occurring.

Health promotion Health-promoting activities usually contribute to the prevention of a variety of diseases as well as enhancing a positive feeling of health and vitality. They consist of nonmedical interventions, such as changes in lifestyle, nutrition, and the environment. Such activities may require structural improvements in society to enable the majority of people to take part in them. Structural improvements imply societal changes that make healthful choices easier. For example, dietary modification may be difficult unless a variety of wholesome, tasty and nutrient-rich foods are available in stores at a reasonable cost. Exercise will be more difficult if bicycling or jogging is a risky activity because of automobile traffic or the threat of violence. Even more basic to health promotion is the assurance of the basic necessities of life, including freedom from poverty, environmental pollution, and assault, suggesting the ties between preventive medicine and public health. Principles of health promotion apply both to noninfectious and infectious diseases.

Specific protection When the means are available, and/or when health-promoting changes in environment, workplaces, and health-related behaviors are not fully effective, methods of specific protection against a disease may be warranted. This form of primary prevention is targeted at a specific disease or type of injury. Examples include immunization against poliomyelitis; pharmacologic treatment of hypertension to prevent subsequent end-organ damage; use of ear-protecting devices in loud working environments, such as around jet airplanes; and use of seat belts, air bags, and helmets to prevent bodily injuries in automobile and motorcycle crashes. Some measures provide specific protection while also contributing to the more general goal of health promotion. Fluoridation of water

supplies, for example, not only helps to prevent dental caries, but is also a nutritional intervention that promotes stronger bones and teeth.

Secondary Prevention and Latent Disease

Secondary prevention refers to the detection and management of presymptomatic disease, and the prevention of its progression to symptomatic disease. Screening is the dominant practice in this space, exemplified by cancer screening (e.g., mammography, colonoscopy), and cardiac risk screening (e.g., lipid testing, blood pressure screens). The margins between primary and secondary prevention can at times blur, depending on definitions used for diseases, their risks, and their antecedents. If hypertension is defined as a disease, its treatment is secondary prevention; if defined as a risk factor for coronary disease that does not yet exist, it is primary prevention.

Presymptomatic diagnosis and treatment through screening programs is referred to as secondary prevention, because it is the secondary line of defense against disease. Although it does not prevent a root cause from initiating the disease process, it may delay or obviate progression to the symptomatic stage.

Tertiary Prevention and Symptomatic Disease

Tertiary prevention refers to the treatment of symptomatic disease in an effort to prevent its progression to disability, or premature death. The overlap with treatment is self-evident, and perhaps suggests that preventive medicine has grandiose territorial ambitions. Be that as it may, there is a legitimate focus on prevention even after disease develops, such as the prevention of early cancer from metastasizing, or the prevention of coronary disease from inducing a myocardial infarction or heart failure. This domain also encompasses rehabilitation, the purpose of which is to preserve or restore functional ability, and thus prevent its degeneration. As with the other stages of prevention, the terminology here is subject to interpretation at the margins. If coronary artery disease is the disease in question, its treatment to prevent progression to myocardial infarction is tertiary prevention; if myocardial infarction is the disease, then the treatment of coronary atherosclerosis is secondary prevention. The net benefit to the patient of this endeavor pursued successfully is the same, of course, however the terminology is applied.

Disability limitation describes medical and surgical measures aimed at correcting the anatomic and physiologic components of disease in symptomatic patients. Most care provided by physicians meets this description. It may be

considered prevention because its goal is to halt the disease process and thereby prevent or limit resultant impairment or disability. An example is the surgical removal of a tumor, which may prevent the spread of disease locally or by metastasis to other sites.

Discussions about a patient's disease may provide an opportunity (a "teachable moment") to convince the patient to begin health promotion techniques designed to delay disease progression (e.g., to begin exercising and improving the diet and to stop smoking after a myocardial infarction). The use of interaction ostensibly dedicated to the treatment of established disease as an opportunity for overall health promotion begins to suggest the potential interface between integrative and preventive medicine.

Rehabilitation falls under the rubric of preventive medicine because it may mitigate the effects of disease and thereby prevent some of the social and functional disability that would otherwise occur. For example, a person who has been injured or who has suffered a stroke may be taught how to care for him/herself in the activities of daily living (e.g., feeding, bathing). This may enable him/her to avoid the adverse sequelae associated with prolonged inactivity (e.g., increasing muscle weakness).

By traditionally focusing on the diagnosis and treatment of disease, conventional medical education and practice have tended to obscure the importance, scientific basis, and clinical process of promoting the overall health of individuals. Diagnosis and treatment of disease will always be important aspects of health care, but increasing emphasis is also being placed on the preservation and enhancement of health. There are specialists who undertake research, teaching, and clinical practice in the field of preventive medicine, but prevention is no more the exclusive province of preventive medicine specialists than, for example, the care of older people is limited to geriatricians. On the contrary, prevention should be incorporated into the practice of all physicians and other health care professionals. Expanding the medical model to encompass prevention as well as treatment of active pathology shares much with the expansion of intervention modalities attendant upon the transition from conventional to integrative care models.

Integrative Medicine

Integrative medicine, a term first introduced in the mid 1990s and now clearly gaining adherents and traction, refers to the fusion—by various means, and to varying degrees—of conventional medical practice and some of the practices that fall under the complementary and alternative medicine (CAM) rubric. Integrative medicine thus offers, in theory at least, the opportunity to combine the "best" of both conventional medicine and CAM, and thereby produce better patient out-

comes, measured in terms of symptom relief, functional status, patient satisfaction, and perhaps cost-effectiveness. Integrative medicine is necessarily “holistic” in the sense that somatic, emotional, and spiritual health are considered integral to overall health (Goldstein et al., 1988). These definitions are inherently problematic; what exactly comprises spiritual health, or whether this is the appropriate realm of the physician, is debated (Luster and Hines, 2005; Scheurich, 2003). Further, holistic medicine proponents are accused of creating a forced dichotomy between holistic medicine incorporating CAM and “good conventional medicine.”

A rationale for integrative medicine depends largely on a rationale for CAM, since CAM tends to be the limiting element in efforts to advance integrative care. The health care system in the United States, and the associated reimbursement mechanisms, are closely allied to conventional medical practices. The expansion of integrative care models depends in part on establishing both a clinical and financial case for CAM in conjunction with conventional medicine.

CAM is one among the numerous designations for diverse medical practices not routinely taught in conventional medical schools (NCCAM, 2007a). Each of the terms applied to such practices is limited or objectionable in some way. *Alternative* implies both that such practices are defined by what they are not and that they are exclusive of conventional medical care. *Complementary* implies that such practices are supplemental to mainstream medicine. The inconsistency in suggesting that such practices are both alternative and complementary to conventional care has been noted (Druss and Rosenheck, 1999; Katz, 2000). There is also objection to the label as it is an intrinsically somewhat pejorative designation, denoting what it is by referring to what it is not; it is “complementary” or “alternative” to something, and that something is the conventional medical practices that predominate.

Such challenges to the nomenclature notwithstanding, CAM is the most widely used appellation, its primacy conveyed by its incorporation into the title of the National Institutes of Health National Center for Complementary and Alternative Medicine (NCCAM). NCCAM provides the following definition of the area over which its management extends:

CAM is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine. Conventional medicine is medicine as practiced by holders of MD (medical doctor) or DO (doctor of osteopathy) degrees and by their allied health professionals, such as physical therapists, psychologists, and registered nurses.

NCCAM groups CAM practices into four domains, recognizing there can be some overlap. In addition, NCCAM studies CAM whole medical systems, which cut across all domains.

1. *Whole medical systems are built upon complete systems of theory and practice. Often, these systems have evolved apart from and earlier than the conventional medical approach used in the U.S.*
2. *Mind-body medicine uses a variety of techniques designed to enhance the mind's capacity to affect bodily function and symptoms. Biologically based practices in CAM use substances found in nature, such as herbs, foods, and vitamins.*
3. *Manipulative and body-based practices in CAM are based on manipulation and/or movement of one or more parts of the body.*
4. *Energy therapies involve the use of energy fields. Biofield therapies are intended to affect energy fields that purportedly surround and penetrate the human body. Bioelectromagnetic-based therapies involve the unconventional use of electromagnetic fields, such as pulsed fields, magnetic fields, or alternating-current or direct-current fields (NCCAM, 2007a).*

This definition conveys something of the breadth of CAM, and by extension, integrative medicine, and thus begins to suggest the expansive potential overlap with preventive medicine. CAM practices encompass a broad range of approaches to health care that include whole medical systems, such as naturopathic medicine, chiropractic, homeopathy, world medical traditions such as traditional Chinese medicine and Ayurveda, as well as specific techniques, such as acupuncture, mind-body medicine, and massage. Traits widely shared by CAM approaches include an emphasis on the individualization of care, the devotion of time and attention to each patient, a reliance on or faith in the healing powers of the body, and a preference for natural remedies. Other than these prevailing characteristics, CAM is in fact an extremely heterogeneous array of practices, ranging from those well supported by scientific evidence to those that defy any plausible scientific explanation, and it is delivered by providers of widely diverse training and credentials (Katz, et al., 2003a). Some self-professed CAM practitioners have no formal training and are subject to no formal credentialing. At the other extreme, naturopathic physicians require the same 4 years of postgraduate training for their ND (Doctor of Naturopathic Medicine) degree as MDs do for theirs. The naturopathic scope of practice is regulated by the states (Houghet al., 2001).

Some distinctions among medical disciplines are captured in their names. Conventional medicine is often labeled as *allopathic* medicine, in which *allo* means different from and *path* refers to disease. The mainstay of allopathic therapy is to *attack* disease states with therapies that are unrelated to the condition

being treated: treating by “the other.” By analogy, this approach douses fire with water. In contrast, *homeopathic* medicine relies on treatments that supposedly induce the same or similar (*homeo*) symptoms as those being addressed, with the belief that the body will eradicate the disease by responding to minute doses of the remedy. By analogy, homeopathy espouses to fight fire with fire. Of note, the term *allopathy* was coined as a pejorative term by Samuel Hahnemann, the nineteenth-century German physician credited for founding homeopathy. *Naturopathic* medicine obviously relies on *natural* treatments in its approach to treatment and healing.

Interest in and use of CAM has remained constant in recent years (Barnes et al., 2008) after a rise in use between 1990 and 1997 (Eisenberg et al., 1998). Nearly 40 percent of the adult population and 12 percent of children have used at least one CAM therapy (Barnes et al., 2008). Visits to CAM practitioners in 1997 exceeded visits to all primary care physicians (Eisenberg et al. 1998). The majority of patients seek CAM approaches to complement rather than substitute for conventional care most often for pain and chronic musculoskeletal conditions (Barnes et al., 2008).

Particularly revealing about the popularity of CAM is the fact that the magnitude of the demand for these therapies continues despite the lack of insurance coverage for such services in most instances. Americans spent an estimated \$21.2 billion out-of-pocket for visits to alternative providers in 1997, an increase of 45 percent from 1990. The majority—58 percent—of those surveyed who used CAM did so for disease prevention, whereas 42 percent used such services for actual medical problems. The use of CAM is more prevalent among female, better-educated, higher-income populations (Barnes et al., 2008; Eisenberg et al., 1998). Although the use of CAM is greatest among people aged 50 to 59 years, use among older patients between 60 to 69 years of age is nearly the same (44.1 percent vs. 41.0 percent, respectively) (Barnes et al., 2008) and is likely to increase with the growing prevalence of chronic illnesses as populations age. The use of CAM has been found to be especially high in patients with Alzheimer’s disease, multiple sclerosis, rheumatic diseases, cancer, AIDS, back problems, anxiety, depression, headaches, head colds, and chronic pain (Barnes et al., 2004; Astin, 1998). Several of these imply the intersection of CAM and the priorities of preventive medicine.

Predictors of CAM use include poorer health status, a holistic philosophical orientation to health and life, a chronic health condition, classification in a cultural group identifiable by its commitment to environmentalism or its commitment to feminism, and an interest in spirituality and personal growth psychology (Astin, 1998). Although research findings vary somewhat, common reasons that people choose CAM include: an interest in combining conventional medicine with CAM; dissatisfaction with the ability of conventional medicine to adequately treat

chronic illnesses; a desire to avoid the harmful side effects of conventional medicine and treatments; an interest in and greater knowledge of how nutritional, emotional, and lifestyle factors affect health; and a broader focus on disease prevention and overall health (Barnes et al., 2004; Eisenberg et al., 1998; Astin, 1998).

Thus, access to CAM modalities affords patients a greater opportunity to obtain care that is consistent with their beliefs and preferences. The availability of CAM treatments may therefore be considered an important means of patient empowerment. In this way, the provision of CAM options and a patient-centered approach to care may be seen as fundamentally interrelated.

Despite the significant increase in the use of CAM over recent decades, fewer than 40 percent of alternative medicine users disclose such information to their primary care provider, which reveals an important disconnect between the preferences of patients and their willingness to share these views with their doctors (Eisenberg et al., 1993, 1998; Astin 1998; Elder et al., 1997; Feldman, 1990; McKee, 1988). This important deficiency in provider-patient communication (Elder et al., 1997; Feldman, 1990; McKee, 1988) may reflect patient dissatisfaction with the conventional medical system (Astin, 1998), distrust, or simply an accurate assessment of conventional providers' receptivity.

There is widespread reticence about (if not outright opposition to) CAM practices among conventional physicians. Those most opposed argue that CAM therapists do not have the extensive knowledge required to properly diagnose an illness, and they often cite the lack of evidence of the efficacy of CAM (Astin, 1998). The latter is the most heatedly debated among ardent proponents of evidence-based medicine, but the claim that conventional medicine is unfailingly supported by scientific evidence is invalid, thus belying evidence as a reliable discriminator between conventional practice and CAM.

A decade ago, the Office of Technology Assessment of the U.S. Congress estimated that fewer than 30 percent of the procedures currently used in mainstream medicine had been rigorously tested (Dalen, 1999). One reason why most CAM therapies are not robustly evidence based is that the majority were introduced prior to the advent of the randomized controlled clinical trial (RCT)—now the gold standard for examining clinical effectiveness. Such limitations are evident in conventional medicine as well; however, they are often overlooked because of the apparent or established effectiveness of a particular treatment. For example, the common and accepted use of antithrombotic agents for cardiovascular diseases and their complications (e.g., myocardial infarction, stroke, and pulmonary embolism) supports this contention. Three of the agents prescribed by conventional physicians for millions of patients every day—warfarin, aspirin, and heparin—were introduced prior to the era of randomized clinical trials and therefore had not been exposed to the rigorous research standards in effect today (Dalen, 1998).

Few physicians would consider these drugs unconventional treatments, despite the fact that they were not put through RCTs at the time they were introduced. Conversely, many CAM interventions are indeed supported by methodologically rigorous trials (Ornish et al., 1998; Perlman et al., 2006; Katz et al. 2003b). Disparities in evidence between conventional and CAM practices do exist—and are likely to persist—because of great discrepancies in the availability of funds to support definitive clinical trials (Tufts Center for the Study of Drug Development, 2008).

Thus, a case may be made for the responsible guidance of patients to CAM therapies both on the basis of patient interest, and in accordance with the prevailing standards of scientific evidence. Since this guidance should by no means supplant conventional treatments, a *de facto* argument for integrative medicine emerges: patients should receive expert guidance across the full expanse of available treatments and modalities that offer them the promise of better health.

The overlap of integrative medicine with preventive medicine is noteworthy. At the level of primary prevention, an array of modalities vouchsafes a meaningful contribution to health promotion. Minimally, these encompass lifestyle counseling, dietary guidance, stress mitigation techniques, interventions to improve sleep quality, and use of nutraceuticals and herbal supplements for health promotion. At the level of secondary prevention, CAM modalities such as stress management and nutrient supplements for management of high blood pressure are germane, as are interventions that facilitate use of conventional therapies for risk attenuation; the use of coenzyme Q10 to mitigate myalgia associated with statin use is an example (Marcoff and Thompson, 2007). At the level of tertiary prevention, the full range of CAM modalities pertain to such goals as pain management, symptom control, stress relief, disease management, and risk reduction. The fusion of these modalities with conventional care is integrative medicine.

To some extent, a conventional medical system that has emphasized the diagnosis and treatment of disease with ever increasing degrees of specialization has marginalized both preventive medicine, and the holistic view that is central to integrative medicine. The importance of disease prevention/health promotion is gaining increasing recognition, due in part to economic forces molding the evolution of modern health care (McGinnis et al., 2002; Hu and Reuben, 2002; Freeman et al., 2008). Integrative medicine offers the promise of more expansive means to achieve the desired ends of preventive medicine, but also imposes the challenges of assessing evidence across that broader expanse. There are, thus, pitfalls to avoid in the pursuit of promise fulfilled.

This paper explores the overlap and potential synergies of integrative medicine and preventive medicine, using the framework of Leavell's levels of prevention to lend structure and clarity to the exploration. Integrative medicine will be seen to have much potential in the areas of primary and tertiary prevention, rather

less in the middle terrain of secondary prevention. The current clinical opportunities associated with a more holistic approach to disease prevention are clear, while the need for research to better define the most effective and economical models of such care is compelling.

PHYSICAL, SOCIAL, AND ENVIRONMENTAL DETERMINANTS OF HEALTH

The rationale for a holistic perspective in medical practice is compelling, particularly in the realm of health promotion and disease prevention. Many of the underlying factors that most influence vulnerability to disease, disability, and premature death are behaviors not routinely addressed in clinical encounters. The importance of such factors (McGinnis and Foege, 1993; Mokdad et al., 2004) highlights the importance of holism that is central to integrative medicine to disease prevention efforts.

Among the influences on population and individual health are a variety of external factors; some of these have been shown to affect health and disease to a greater extent than individual aspects of health such as diet, physical activity, genetic endowment, and preventive practices. Social determinants of health identified by the Centers for Disease Control and Prevention include socioeconomic status, transportation, housing, access to services, discrimination, and social/environmental stressors (CDC, 2008).

Environmental determinants are defined as external agents that can be causally linked to change in health status. As opposed to behavioral determinants, environmental determinants are characterized as involuntary. These include air and water pollution, sunlight or the lack of it, environmental hazards, as well as impacts of global climate change. Physical, social, and environmental determinants of health are not mutually exclusive categories; there is considerable overlap (Environmental Determinants of Health, 2002).

Socioeconomic status has been shown to be a strong predictor of both individual and population health (Antonovsky, 1968; Kitagawa and Hauser, 1973). Persons at the highest levels of socioeconomic status, characterized by the most prestigious occupations, highest educational attainment, ample financial savings, and comfortable housing enjoy the longest lifespans with the highest levels of health status, by most measures (Adler and Stewart, 2007). The relative risk of premature death is 3 times higher in persons at the lowest levels of income as compared to those of middle income, while those at middle levels experience 2 times the rate of premature death as those at the highest. The prevalence of chronic disease, infectious disease, asthma, disabilities, injury, and physical inac-

tivity are all inversely correlated with socioeconomic status (Adler and Stewart, 2007).

Clearly related to socioeconomic status is the impact of race; ethnic and racial minorities tend to populate lower rungs of the socioeconomic ladder, though race in and of itself is a predictor of lower health outcomes. For example, when adjusting for other aspects of socioeconomic status, African Americans are found to have worse health outcomes, including infant mortality, than those of other racial categories, often interpreted as the impact of structural and individual racial discrimination on health. In health care settings, African Americans tend to receive less preventive services and life-saving treatments as compared to whites (Jha et al., 2003; Adler and Stewart, 2007).

Also associated with socioeconomic status in both distribution and impact on health are neighborhood factors such as availability of parks and recreation areas, stores that stock fruits and vegetables, safe streets, lighting, and access to libraries and cultural events. Directly, aspects of air, weather, and soil pollution present in neighborhoods can impose adverse health effects, such as developmental delays, and respiratory illnesses (Adler and Stewart, 2007). Other aspects of the built environment, such as availability of parks and walkways, can influence the development of asthma, obesity, hypertension, and cardiovascular disease (Adler and Stewart, 2007; Papas et al., 2007).

The inability to access adequate health care, often precipitated by lack of health insurance, is also correlated with socioeconomic status and influences individual and population health. The U.S. is the only developed nation to lack a nationalized health plan; over 45 million Americans were without health insurance in the year 2006 (Adler and Stewart, 2007). Persons without insurance tend to delay and forego health care at earlier stages of disease resulting in initial contact with the health care system at a stage of more severe disease. Furthermore, this delayed health care is often substandard when compared to the fully insured. Preventive care, including screening, is often missed resulting in a higher prevalence of infectious and chronic disease (Freeman et al., 2008).

Work-related factors, such as exposure to physical hazards and chemicals for those in blue-collar occupations and mental/social stress in white-collar occupations also influence health status. The National Academy of Social Insurance estimated the impact of work-related problems to total \$55 billion in the year 2000, directly attributable to the cost of insurance claims, work replacement, and lost productivity. Indirect costs, such as retraining, turnover, and lack of productivity in an unstable workplace are estimated to double or triple this sum (Adler and Stewart, 2007).

Though the impact of social and environmental factors cannot be overemphasized, clinical medicine has limited capacity to address them, although public health practice potentially has considerably more. Rather, these factors can be

considered as influences on health, and appropriate interventions can be tailored in response to them.

Stress and Emotional Impact on Health

Integrative medicine emphasizes the centrality of psychological stress and its impact on overall health (Snyderman and Weil, 2002). The evidence is robust and clear; psychological stress leads to poorer health outcomes—encompassing infectious and chronic disease, morbidity and mortality, developing illness, and recovery.

Higher levels of acute and chronic stress are associated with depressed immune function resulting in greater frequency of infectious disease (Brosschot et al., 1994; Lutgendorf and Costanzo, 2003). Furthermore, wound healing is compromised in highly stressed individuals (Christian et al., 2006). Perceived stress decreases as income and socioeconomic status increases (Adler and Stewart, 2007). Chronic stress and depression are associated with type 2 diabetes, cardiovascular disease, and stroke, mediated through hypothalamic-pituitary-adrenal (HPA) axis dysfunction resulting in abnormal cortisol levels (Rosmond and Bjorntorp, 2000). HPA axis dysfunction is also associated with visceral and abdominal obesity (Nieuwenhuizen and Rutters, 2008; Pasquali et al., 2006).

Those who have suffered from childhood abuse have greater odds of self-destructive health behaviors in the future, including smoking, severe obesity, lack of physical activity, increased depression, and suicidal attempts (Whitfield, 1998). Childhood abuse is associated with higher levels of the inflammatory marker C-reactive protein (Danese et al., 2007, 2008), increasing the risk of cardiovascular disease (Ridker and Silvertown, 2008), type 2 diabetes, and certain cancers (Nanri et al., 2007). Rape (Ciccone et al., 2005) and sexual abuse (Boisset-Pioro et al., 1995) are associated with the development of fibromyalgia, while childhood abuse predicts more severe forms of fibromyalgia (McBeth et al., 1999).

Personality and disposition also predict health-related outcomes. Higher levels of anger are associated with worse cardiac outcomes, including a 2- to 3-fold increase in the risk of development of angina, acute myocardial infarction, or sudden cardiac death, with evidence for a dose-response relationship (Kawachi et al., 1996; Chang et al., 2002). The “disease prone personality” includes anger, hostility, anxiety, and depression and has been shown to predict, with varying degrees of association, a variety of chronic disease, including cardiovascular disease, asthma, peptic ulcer, and arthritis include (Friedman and Booth-Kewley, 1987).

Psychological states can also be beneficial; the presence of “positive emotions” has been shown to predict better health and health outcomes (Ryff et al., 2004). Optimistic patients have reduced all-cause mortality as compared to

nonoptimists; mostly related to the prevention of cardiovascular mortality (Giltay et al., 2004). Personality aspects such as commitment to self, an attitude of concern for the environment, a sense of meaningfulness, and an internal locus of control are all associated with decreased illness in high-stress environments (Kobasa, 1979).

Intimate relationships, close friendships, and sense of community all predict more favorable health outcomes in a variety of conditions, from development of the common cold to cancer survivorship. Those with a sense of belonging and intimacy have more pronounced recovery from myocardial infarction, surgery, and cancer (Ornish 1998).

Integrative medicine offers a framework that incorporates psycho-emotional factors as integral to overall health. These factors are routinely overlooked in conventional clinical practice and conventional medical education (Roter et al., 1995; Kligler et al., 2004; Abbo et al., 2008; Teutsch, 2003). Thus, integrative medicine offers a means to enhance the practice and modify the goals of preventive medicine through patient-centered, holistic care incorporating mind-body therapies.

INTEGRATIVE MEDICINE ACROSS THE PREVENTION SPECTRUM

Integrative medicine has the potential to reduce morbidity and mortality by various means, particularly through a strong emphasis on prevention and behavior change, as well as considering stress reduction an integral part of treatment. As behavioral and lifestyle choices account for the majority of premature mortality in the U.S., targeting these areas can potentially provide the greatest benefit.

In the year 2000, the leading cause of death in the U.S. was tobacco use, which resulted in some 435,000 deaths, or 18.1 percent of total deaths. Closely following was diet and lack of physical activity resulting in 365,000 deaths (15.2 percent of total). Other behaviors resulting in substantial premature deaths include alcohol consumption, firearm accidents, sexual behavior, and illicit drugs (Mokdad et al., 2004).

In the following sections, we discuss the potential for integrative medicine across the prevention spectrum. Much of the data exist in the preventive medicine literature, distinct from the integrative or CAM literature. By and large, the efficacy of integrative medicine in health promotion or disease prevention has not been tested; data derived from direct tests of integrative care models are not available. There is, however, a clear case to be made for the importance of a holistic approach to health, and for the opportunities provided by integrative care to adopt that holistic approach through the incorporation of CAM therapies and providers.

Thus, a persuasive argument for the melding of integrative and preventive care may be constructed by stringing together data that are available. In the following sections, we will distinguish between research data and informed speculation, both of which subtend the basic argument.

Integrative Medicine In Primary Prevention

Primary prevention keeps the disease process from becoming established by eliminating causes of disease or by increasing resistance to disease. Health promotion through promotion of healthy lifestyle, nutrition, and environment is emphasized (Jekel et al., 2007).

Among the means to promote lifestyle change is modeling healthy behavior, notably diet and physical activity. Physicians that practice healthy behaviors tend to emphasize these behaviors in patient care; consequently, patients of these physicians generally receive stronger, more pronounced, and more specific advice regarding lifestyle change. Physicians who exercise regularly are more likely to counsel their patients to do so; nonsmokers are more likely to emphasize the risks of smoking (Frank and Kunovich-Frieze, 1995). Furthermore, physicians who tend to emphasize healthy habits in their patients often feel that they should be role models in healthy lifestyle habits (Maheux et al., 1989).

A number of CAM organizations and professions encourage members to model healthy lifestyle behaviors including the American Holistic Medical Association (Goldstein et al., 1988) and the American Association of Naturopathic Physicians (Hough et al., 2001). Among some CAM professional educational institutions, a culture of wellness exists, where healthy food choices are readily (if not exclusively) available and faculty model healthy behaviors.

Furthermore, a number of CAM whole systems consider dietary habits and therapeutic nutrition as a cornerstone of health, namely Traditional Chinese Medicine (Kaptchuk, 2000), Ayurveda (NCCAM, 2008; Chopra and Doiphode, 2002), and naturopathy (Hough et al., 2001; NCCAM, 2007b). Many of their recommendations are consistent with current mainstream dietary recommendations for chronic disease prevention; though some traditional recommendations conflict. Nevertheless, the emphasis of food as a primary basis of health conforms well to the objectives of primary prevention.

Novel approaches to addiction and smoking cessation also have the potential to improve public health. The most salient example is of a simple acupuncture protocol, initially incorporated in a substance abuse program to replace methadone treatment at Lincoln Hospital in New York City (Faass, 2001). This approach has now expanded to over 1,500 clinical locations nationally, and is

associated with a formal training program for health care professionals (Margolin et al., 2005). Other CAM approaches used for treating addictions include mind-body therapies, yoga, and herbal products (Sood et al., 2006), though scant data exist regarding the efficacy of these interventions.

Certain lifestyle aspects, namely digestive function and sleep, both impact risk of acute and chronic disease and are generally more emphasized by integrative and CAM practitioners than conventional primary care providers (Hough et al., 2001; Weil, 2000). The consumption of dietary fiber is associated with reductions in risk for cardiovascular disease (Retelny et al., 2008), certain cancers (Mulholland et al., 2008; Anand et al., 2008), reduced body weight (van Dam and Seidell, 2007), and lower all-cause mortality (Papanikolaou and Fulgoni, 2008). Dietary fiber consumption is also associated with reduced intestinal transit time (Hillemeier, 1995) and improved bowel function. This is synonymous with “digestive health” that is emphasized in a number of CAM systems, including functional medicine (Jones, 2008), Ayurveda (Chopra and Doiphode, 2002; NCCAM, 2008), naturopathy (Hough et al., 2001; NCCAM, 2007b), and traditional Chinese medicine (Kaptchuk 2000).

Chronic sleep deprivation is associated with hypertension, myocardial infarction, heart failure, stroke, obesity, psychiatric problems, attention deficit disorder, mental impairment, fetal and childhood growth retardation, accidental injury, and overall poor quality of life (Melamed and Oksenberg, 2002; Leger, 1994). In animal models, sleep deprivation has been shown to increase aggression, impair cognitive function, as well as impact neural cytokine levels, oxidative stress markers, and brain glycogen levels (McEwen, 2007). Abnormally short or long sleep duration is associated with metabolic syndrome (Hall et al., 2008), a prediabetic state. Short sleep duration is associated with abdominal obesity, elevated fasting glucose, and hypertriglyceridemia, all components of the metabolic syndrome. Short sleep duration is also associated with obesity, most likely mediated by a disruption of appetite control, resulting in reduced levels of the satiety factor leptin and increasing the hunger-promoting hormone ghrelin (Schmid et al., 2008).

Integrative medicine tends to emphasize the importance of restful sleep; integrative clinical encounters often discuss sleep quality in the context of health promotion and disease prevention (Rakel, 2007). A number of CAM therapies are commonly used to treat sleep disturbances including melatonin, valerian, yoga, meditation, acupuncture, and tai chi. Most have been shown to be safe with preliminary evidence of efficacy (Gooneratne, 2008; Winbush et al., 2007; Buscemi et al., 2004). The adverse effects of poor sleep habits can also be mitigated with positive social relationships (Friedman et al., 2005), emphasized in holistic medicine (Ornish, 1998).

The emphasis on emotional and psychological well being as an integral aspect of health in most traditional medical systems and many CAM approaches also

adds to the potential value of integrative medicine in primary prevention (Rakel, 2007). The mainstreaming of a number of concepts of mind-body medicine reflects the quality and quantity of scientific studies supporting the basic suppositions of internal harmony and balance in traditional systems of medicine. A number of formalized training programs in mind-body medicine have flourished in academic medical centers in the past few decades (MGH, 2008; Shapiro et al., 2008).

Based on the wide array of therapies available and preliminary evidence of safety and efficacy, there is immense potential for integrative medicine in primary prevention. However, no research has been conducted on integrative medicine practices or practitioners on the uptake of, adherence to, or outcomes of preventive care. Claims that the appropriate and proactive use of integrative medicine services will result in public health benefits as well as overall cost savings are premature. Many barriers exist to foundational and critical research in this arena; lack of funding (NCCAM, 2005; Tufts Center for the Study of Drug Development, 2008) being paramount. Well-constructed outcomes research on whole-practice systems already operational in the integrative medicine arena are clearly warranted. Initial emphasis should be placed on integrative medicine models that stress evidence-based care, and where credentialing and training are most stringent, including naturopathic medicine, acupuncture, chiropractic, nutritional and herbal medicine, mind-body interventions, and therapeutic massage (Katz and Ali, 2008). While the overlap between integrative medicine and primary preventive practices is both clear and compelling, the degree to which integrative care models can advance the objectives of primary prevention remains to be formally proved.

Secondary Prevention and Integrative Medicine

Secondary prevention interrupts the disease process before it becomes symptomatic. Screening, case finding, and appropriate treatment are secondary prevention interventions (Jekel et al., 2007).

The U.S. Preventive Services Task Force (USPSTF), first convened by the U.S. Public Health Service in 1984, and since 1998 sponsored by the Agency for Healthcare Research and Quality (AHRQ), analyzes and assesses the evidence for preventive interventions, including screening, counseling, and preventive medication (AHRQ, 2008). The USPSTF recommendations (see Table 1) are considered the gold standard in preventive medicine.

TABLE 1 Examples of USPSTF Screening Recommendations

Condition	Recommendation	Grade*
Breast cancer	Screening mammography, with or without clinical breast examination (CBE), every 1-2 years for women aged 40 and older	B
Colorectal cancer	Screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy, or colonoscopy, in adults, beginning at age 50 years and continuing until age 75 years.	A
Hypertension	Screening for high blood pressure in adults aged 18 and older.	A
Hepatitis B Virus	Screening for hepatitis B virus (HBV) infection in pregnant women at their first prenatal visit	A
Type II diabetes	Screening for type 2 diabetes in asymptomatic adults with sustained blood pressure (either treated or untreated) greater than 135/80 mm Hg.	B
Glaucoma	Insufficient evidence to recommend for or against screening adults for glaucoma.	I
COPD	Recommends against screening adults for chronic obstructive pulmonary disease (COPD) using spirometry.	D

NOTES: *Definitions of USPSTF Grades*

A. The USPSTF recommends the service. There is high certainty that the net benefit is substantial.

B. The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.

C. The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is at least moderate certainty that the net benefit is small.

D. The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.

I The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

SOURCE: AHRQ, 2008

Integrative medicine has the potential to improve rates of screening and uptake of preventive services through an emphasis on a strong therapeutic alliance, prevention, teaching, and holistic care (Snyderman and Weil, 2002). Nationally, screening rates for preventive services are considerably lower than ideal (Maciosek et al., 2006); much of the blame can be placed on lack of emphasis and training in health promotion and disease prevention as well as the burdens of a health care system that constrains primary care visits to an average of 30 minutes annually (Bindman et al., 2007). Abbreviated primary care encounters, coupled with barriers to access, tend to compromise continuity of care as well. Furthermore, a substantial proportion of patients seeking integrative medicine or CAM tend to be skeptical of preventive interventions, especially vaccination (Benin et al., 2006; Stokley et al., 2008). Promotion of preventive interventions by integra-

tive practitioners demonstrating a sympathetic understanding of patients' concerns could improve uptake rates.

In addition to increasing screening rates and utilization of preventive services, integrative medicine has the potential to modify secondary prevention efforts for chronic diseases with strong diet and lifestyle associations, namely cardiovascular disease, diabetes, and certain cancers. Many CAM therapies have demonstrated preliminary efficacy in treating early disease or risk factors such as improving lipid profiles (Nies et al., 2006), reducing inflammation (Rakel and Rindfleisch, 2005), controlling serum glucose (Yeh et al., 2003), and reducing blood pressure (Yeh et al., 2006; Ali et al., Bracken, 2007). By using these in combination with comprehensive lifestyle change, mind-body medicine interventions, and USPSTF recommendations with a strong therapeutic alliance, the potential to improve outcomes rationally follows. In certain instances, an integrative approach can be used to enhance adherence with conventional therapies, such as use of the following:

- Nutritional supplement coenzyme Q10 to reduce statin-induced myopathy (Marcoff and Thompson, 2007) and anthracycline-induced cardiotoxicity (Conklin, 2005),
- Probiotics to reduce antibiotic-associated diarrhea (McFarland, 2006; Johnston et al., 2007),
- Licorice and its derivatives to potentiate the effects of cortisone (Teelucksingh et al., 1990) and reduce nonsteroidal anti-inflammatory drug (NSAID)-associated gastropathy (Russell et al., 1984), and
- Glutamine to reduce adverse effects of chemotherapy, including mucositis, neuropathy, diarrhea, and cardiotoxicity (Savarese et al., 2003).

Tertiary Prevention and Integrative Medicine

Tertiary prevention limits the physical and social consequences of symptomatic disease. Disability limitation and rehabilitation are tertiary prevention interventions (Jekel et al., 2007).

The goals of tertiary prevention are advanced when symptoms are controlled, disease progression is forestalled, and/or functional capacity is preserved, restored, or optimized. Among the strengths of integrative medicine practitioners are symptom control—even when disease etiology and pathophysiology are vague—and an emphasis on the diverse factors that influence quality of life. The overlap of integrative medicine with preventive medicine is thus especially noteworthy in the realm of tertiary prevention.

Conditions characterized by medically unexplained symptoms, also known as somatoform disorders, including chronic fatigue syndrome, irritable bowel syn-

drome, fibromyalgia, chronic Lyme disease, and chronic unexplained pain (Hatcher and Arroll, 2008), are often complicated by concurrent psychological distress and strong emotions (McEwen, 2007). Conventional care for patients suffering from these conditions is often frustrating, usually resulting in extensive and expensive diagnostic workups and significant iatrogenic complication rates (Smith et al., 2003; Ring et al., 2005). Furthermore, the psycho-emotional disturbances that are prevalent in this population (Ring et al., 2005) may be invoked to explain symptoms, but are often overlooked in efforts to alleviate them.

Patients with medically unexplained symptoms comprise a significant proportion of outpatient care; at least 13 percent of outpatient visits are attributable to medically unexplained symptoms (Ring et al., 2005; van der Weijden et al., 2003). Patients with these conditions often seek out CAM therapies and providers (Barnes et al., 2008; Lind et al., 2007; Vlieger et al., 2008). Integrative medicine offers a patient-centered approach, providing treatment options outside of the mainstream that have demonstrated some efficacy in the treatment of medically unexplained symptoms (Sarac and Gur, 2006; Jones et al., 2007). Furthermore, the holistic nature of integrative care with a mind-body emphasis often results in treatment plans incorporating psychological and somatic therapies (Rakel, 2007; Goldstein et al., 1988).

A number of comprehensive nutritional and lifestyle programs have demonstrated efficacy in tertiary prevention efforts. While some elements of such programs have now arguably been conventionalized, such as basic dietary guidance, the blending of lifestyle, medication, supplements, and mind-body intervention is certainly suggestive, if not diagnostic, of integrative care.

The Diabetes Prevention Program, incorporating a heart-healthy diet with regular exercise and lifestyle coaching demonstrated that a lifestyle approach can double the efficacy of pharmacotherapy in the prevention of type 2 diabetes in patients at high risk (Knowler et al., 2002). The Lyon Diet Heart Study demonstrated that a Mediterranean-style diet reduced coronary heart disease recurrence by 50 to 70 percent (Kris-Etherton et al., 2001), while Jenkins' Dietary Portfolio has been shown to be as efficacious as low-dose statins in the reduction of LDL cholesterol and C-reactive protein (Jenkins et al., 2006). The Ornish Lifestyle Heart Program includes a low-fat vegetarian diet coupled with yoga, meditation, exercise, and smoking cessation has been shown to reverse coronary atherosclerosis (Pischke et al., 2008; Ornish et al., 1990). Clinical and cost-effectiveness of this program is currently being assessed (see Box 1). A combination of lifestyle change, fish oil, and red yeast rice demonstrated efficacy comparable to simvastatin in reducing LDL cholesterol, and stronger effects in reducing triglycerides and weight (Becker et al., 2008). As noted, elements of these programs are in many cases now mainstream and not exclusively in the province of integrative medicine. However, integrative medicine strongly emphasizes and

promotes nutritional approaches to chronic disease (Rakel, 2007; Goldstein et al., 1988) and the comprehensive lifestyle approach of these interventions (Bindman et al., 2007). Thus, integrative medicine is potentially a vehicle to carry such practices into a larger proportion of patient encounters.

Integrative therapies for the treatment of chronic disease can improve functionality, reduce morbidity, improve quality of life, and directly influence disease processes. The quality of evidence for CAM therapies is mixed for treating chronic conditions with significant public health impact (NCCDPHP 2008). Nutritional supplements such as fish oil (Hartweg et al., 2008), chromium (Balk et al., 2007), alpha-lipoic acid (Singh and Jialal, 2008), herbal medicines (Bradley et al., 2007), and mind-body techniques (Kligler, 2004) have been used to treat type 2 diabetes mellitus. Hyperlipidemia can be treated with therapeutic diets consisting of functional foods (Becker et al., 2008; Jenkins et al., 2006), nutritional supplements, and herbal medicines (Nies et al., 2006). Manual therapies such as

BOX 1

The Ornish Lifestyle Heart Program incorporates aspects of care that fall under NCCAM's domains (NCCAM, 2007a), such as yoga and meditation. Other aspects are clearly mainstream, such as a heart-healthy diet. Nevertheless, this program, consisting of a low-fat whole foods vegetarian diet, aerobic exercise, stress management training, smoking cessation, and group psychosocial support has demonstrated regression of coronary atherosclerosis (Ornish et al., 1998), reduction of prostate cancer progression (Ornish et al., 2005) with concomitant changes in gene expression (Ornish et al., 2008a), and increased telomerase activity (Ornish et al. 2008b). This promising research demonstrates that intensive lifestyle changes can modify genetic markers of aging, potentially expanding the realm of prevention efforts towards influencing genetic susceptibility to disease and blurring the lines between genetic and environmental determinants of health.

The Lifestyle Modification Program Demonstration is a trial designed to test the benefit and cost-effectiveness of this program for reversing heart disease along with the Cardiac Wellness Extended Program designed by Dr. Herbert Benson of the Mind Body Medical Institute. The Benson program consists of supervised exercise, individual nutritional counseling, and a comprehensive stress management program, including relaxation response training.

Program effectiveness, feasibility, and cost-savings are being compared to conventional cardiac rehabilitation services for Medicare beneficiaries age 65 or older with moderate to severe coronary artery disease. This project follows 3,600 Medicare enrollees with recent history of myocardial infarction, coronary artery bypass graft surgery, percutaneous revascularization procedures, stable angina, or matched controls. Subjects received three months of training and support in both the Benson and Ornish programs, consisting of dietary change, stress reduction, exercise, and group therapy followed by nine months of less intense therapy. Demonstration sites providing the Ornish program receive 80 percent of \$5,650 or \$4,520 per person. Sites offering the Benson program receive 80 percent of \$4,800 or \$3,840 per person.

Preliminary data analysis revealed that both programs achieve modest improvements in total cholesterol, LDL, triglycerides, body-mass index, and blood pressure (Stason et al., 2005).

massage can be useful for osteoarthritis (Perlman et al., 2006), as well as acupuncture (Berman et al., 2004), nutritional, and herbal supplements (Ernst, 2006). An anti-inflammatory diet (Adam et al., 2003), nutritional supplements, manual therapies, and other CAM therapies have shown promise in the management of rheumatoid arthritis (Rakel, 2007).

The public health impact of obesity and its related sequelae is unparalleled in the U.S., while the prevalence is quickly rising throughout the rest of the world (Kelly et al., 2008). Over two-thirds of the U.S. adult population—some 130 million people—is overweight or obese (Ogden et al., 2006). Obesity increases all-cause mortality (Calle et al., 1999), as well as risk of hypertension, Hypercholesterolemia, and type II diabetes mellitus (Must et al., 1999). Obese persons have a lower overall life expectancy compared to the nonobese (Peeters et al., 2003). Over 300,000 deaths per year are attributable to obesity (Mokdad et al., 2004); the impact so great on populations that it reverses the 200-year trend of increasing life expectancy (Olshansky et al., 2005). Competing dietary strategies for weight loss have been proposed demonstrating varying levels of efficacy (Dansinger et al., 2005; Bravata et al., 2003; Shai et al., 2008). It is generally believed that a multifaceted approach is optimal including dietary, lifestyle, and environmental interventions (Poston and Foreyt, 2000). Integrative medicine has the potential to add to obesity prevention and control efforts by emphasizing nutrition, stress reduction, and exercise (Bradley and Oberg, 2006), though specific CAM therapies used for weight loss remain largely untested (Cherniack, 2008).

Exercise-based cardiac rehabilitation programs are an example of a tertiary prevention program with demonstrated efficacy for patients with coronary heart disease. Cardiac rehabilitation programs reduce all-cause and cardiac mortality and improve left ventricular ejection fraction (Giannuzzi et al., 1997), total cholesterol, triglycerides, and systolic blood pressure (Taylor et al., 2004). Depressed patients experience higher levels of mortality following cardiac events; those who complete rehabilitation programs improve both in depressive symptoms and the related increase risk of mortality (Milani and Lavie, 2007). One trial demonstrated improvements comparable to exercise training in depressive symptoms, endothelial function, and ejection fraction with stress management programs in patients with ischemic heart disease (Blumenthal et al., 2005), though the additive effects have not been studied. It is thought that much of the benefits of cardiac rehabilitation arise through improvements in blood pressure, lipid profile, endothelial function, and inflammation (Milani et al., 2004). A diverse array of integrative therapies can assist with these mediators (Rakel, 2007); it follows that cardiac rehabilitation efforts may be bolstered through standard exercise training, coupled with integrative mainstays of mind-body therapies, anti-inflammatory diets (Adam et al., 2003), and prudent use of nutritional and herbal supplements (Harris et al., 2008). Research in this area is particularly warranted.

BOX 2

A male veterinarian in his mid 40s presented with persistent abdominal pain for ten years following an exploratory laparotomy. The pain, attributed to surgical adhesions, had been assessed and treated by general surgeons, anesthesiologists, neurologists, and at least one specialized pain center. The pain persisted, and the patient managed it with short acting narcotics taken daily.

When evaluated from a slightly more holistic perspective, the importance of sleep deprivation to the patient's pain became clear. He was placed on long-acting narcotics that did not wear off in a shorter than normal sleep cycle, and he slept through the night for the first time in years. His pain subsided considerably.

A course of acupuncture was initiated, and over a span of 2 months the narcotic dose was tapered. After 8 weeks, the patient was off narcotics and pain free, both for the first time in years. A course of homeopathy followed acupuncture, and is used to this day for maintenance. At last contact, the patient was pain free for 3 years using homeopathy only, following 10 years of unremitting pain prior to his encounter with integrative care. He continues to practice veterinary medicine.

Other rehabilitation programs—injury and stroke recovery—may benefit from integrative therapies that improve functionality, from pain control using acupuncture and massage, postsurgical and other types of wound healing enhanced with nutritional supplementation and herbal medicine (Rahm and Labovitz, 2007; Leach, 2004), to increased energy through use of adaptogenic herbs (Rakel, 2007).

Finally, tertiary prevention strategies deployed in an integrative manner may be a prerequisite to primary prevention. For example, patients with ineffectively managed chronic pain creating a barrier to physical activity can begin to benefit from simple preventive lifestyle measures that can, in turn, help prevent other chronic disease. Both obesity and chronic pain share a multifactoral etiology with no simple solutions, necessitating a holistic therapeutic approach. It is estimated that 70 million persons in the U.S. suffer from chronic pain (Rosenblum et al., 2003) costing between \$15,000-\$24,000 per patient annually when taking into account lost wages and social support (Latham and Davis, 1994). Pain is the most common chief complaint in patients visiting primary care physicians (Sullivan et al., 1991). Conventional therapies such as NSAIDs, opioids, and antidepressants are not always effective, and may result in dependence and/or adverse effects (Benyamin et al., 2008).

Limited data exist to support the idea of improved pain control with a combination of conventional and CAM therapies, though CAM and integrative practitioners claim particular success in this area. CAM therapies for pain control vary in demonstrated efficacy, spanning mind-body therapies such as meditation and biofeedback (Morone and Greco, 2007), to acupuncture, yoga, hypnosis, chiropractic, nutritional interventions (Ali et al., 2009), herbal medicines, massage (Perlman et al., 2006), or combinations thereof (Little et al., 2008). The judicious combination of a myriad of CAM techniques with pharmacotherapy is in the

realm of integrative medicine, where an understanding of evidence-based, diverse treatment options is coupled with a patient-centered, holistic orientation can increase the likelihood of safe and effective treatment.

DISCUSSION

With patients increasingly interested in CAM and conventional practitioners often uninformed and/or reticent, a system of unintegrated or, worse, disintegrated health care prevails in the U.S. Many conventional physicians actively discourage the use of CAM wholesale, without considering the differences in modalities or practitioners—or the potential value of CAM treatments. Practitioners of CAM may be just as apt to discourage the use of conventional medicine, citing its reliance on dangerous drugs and invasive procedures, its failure to respect the healing powers of nature, and its lack of compassion and patient-centeredness. There is real danger here of patients toppling into the divide, with attendant squandering of the potential for disease prevention and health promotion. The case study in Box 3 illustrates this threat.

BOX 3

A 72 year-old male with occasional chest pain and no prior medical history was referred by a primary care provider to a cardiologist, who recommended cardiac catheterization. Reticent about conventional medical care, the patient decided to seek alternative care instead. Doing so raised the prospect that a potentially life-threatening coronary condition might not be evaluated and treated as warranted.

Instead, the patient's nephew—a PhD in psychology—brought him to an integrative medicine center, where the roles and value of both conventional and CAM treatments are recognized. Evaluation by an internist suggested the chest pain had a low prior probability of being cardiac, and was clearly not unstable. A nuclear stress test was proposed to the patient as a less invasive alternative to cardiac catheterization, and the patient accepted the recommendation. The cardiologist was contacted, the case discussed, and consensus achieved. The nuclear stress test was normal, and the patient was successfully treated for noncardiac chest pain. His cardiac risk factors were evaluated and managed with lifestyle, and he remained under the care of his PCP, with cardiology follow-up as warranted.

The patient and his nephew subsequently acknowledged that had the option of integrative care not been available, the patient would likely have abandoned conventional care for CAM, even at the risk of his life. The case, of course, would be that much more compelling had the chest pain proven to be of cardiac origin, but it might well have, and the next case certainly could.

Patients under such conditions are left in a precarious position:

- Those seeking both conventional care and CAM are likely to receive conflicting advice and lack the expertise required to achieve a prudent reconciliation;
- Those choosing to follow both sets of advice may be subject to dangerous interactions that neither half of the fractured care system knows about;
- Those avoiding a possible conflict by limiting their selection to just one medical discipline may be losing important benefits offered by others, with resultant deficiencies in care, and potential for disease prevention.

The patient with a chronic health problem for which conventional treatment is ineffective may be left to search among a wide array of therapies, with no place to go for expert guidance that considers all of the options. The costs of such possibly aimless care are likely to be high in both human suffering and dollars (Katz and Ali, 2008), with patients choosing therapies that may be futile, potentially causing them to lose hope, causing insurers in turn to continue resisting including CAM modalities among covered benefits. There is thus a compelling case for the enlightened practice of integrative medicine on the basis of both clinical and financial grounds.

Even as CAM in the U.S. health care system is known to be widely popular among the public (Barnes et al., 2008), resistance to the proliferation of CAM among conventionally trained practitioners persists (Angell and Kassirer, 1998; Marcus, 2002; Sampson, 2001). Health insurers, although uncertain as to the potential costs and benefits, are subject to increasing pressures to reimburse for various CAM practices (Pelletier and Astin, 2002; Pelletier et al., 1999). These tensions and incompatibilities constitute a challenge and a threat to patient-centered, holistic approaches to care, and to the goals and objectives of preventive medicine.

Patient empowerment is one of the dominant principles and trends in modern health care, but there are others. The popularity of CAM is itself an important trend, as is interest in natural therapies and holism. The importance of evidence as the basis for therapies and decisions is an increasingly salient feature in medical education and practice. Finally, the advent of managed care has resulted in increasing attention to the cost-effectiveness of medical interventions.

The confluence of these trends represents the context in which CAM and conventional medicine must coexist. An increasing emphasis on prevention as a cornerstone of health policy merely adds to the urgency and promise of reconciling these trends, and to the costs of failure to do so.

The reconciliation of evidence-based and patient-centered care begins by recognizing that, as Green (2006) points out, evidence-based practice cries out for

practice-based evidence. Conventionally, the pinnacle of evidence in research is the multi-center, randomized controlled trial, or a meta-analysis of such trials. But the pinnacle of evidence in practice is simply what happens to the patient. If a therapy decisively supported by evidence from multiple clinical trials fails to alleviate symptoms or arrest disease progression, or produces adverse rather than beneficial effects, in a given patient, the therapy does not work for the patient in question. That might be called an anecdote, but another appellation is just as apt: it is a fact.

Similarly, when a therapeutic modality that lacks the strong support of definitive clinical trials alleviates symptoms or arrests disease progression in a patient in whom the tried and true has failed, it, too, is a fact. This fact, when it occurs, reminds us of the distinction between deficient evidence, and evidence of deficiency.

An appreciation for the nature of practice-based evidence encourages the reconciliation of responsible use of science, with responsiveness to the needs of patients that often persist as clinical trial data run out. The Clinical Utility of Research Evidence Construct, in Table 2 below, highlights the practical, and practice-oriented, implications of this interface.

This framework suggests that clinical application of “evidence” depends on 5 considerations: the relative safety of a given intervention; the relative effectiveness; the quality and quantity of the supporting evidence; the availability of other treatment options for the condition; and patient preferences. When treatment approaches are unsafe, ineffective, poorly supported by science, less effective than other options, and not the uniquely compatible with patient preference, they should never be used. When a treatment is safe, effective, supported decisively by science, better than any other therapeutic option, and preferred by a patient, it

TABLE 2 The CURE (Clinical Utility of Research Evidence) Construct

Safety	Efficacy	Science	Other therapeutic options	Patient preference	Utilization frequency of treatment in question
High	High	Decisive	None that is superior	Prefers recommended approach	Always
Probable	Possible	Unclear	None / few	Anything that will work	Often
Low	Low	Absent / opposed	Many that are superior	Anything that will work	Never

should always be used. The challenges, and the contributions of integrative medicine, reside in between, such as when the approaches supported by the best science have all been tried, and have all failed. What is left to try is a treatment that is apparently safe, possibly effective, desired by the patient, but not definitively supported by the available research evidence. This construct highlights the overlap of integrative medicine and preventive medicine as well: integrative medicine broadens the array of treatment options available to fulfill the objectives of preventive medicine described in the text.

Perhaps the ultimate expression of integrative care is when practitioners from both CAM and conventional medicine make their recommendations available to patients, who can then choose, with expert guidance and support, from a wider array of options. This removes barriers and ensures continuity of care between conventional medicine and CAM—an idealized “seamless interface.” Although few and far between thus far, such models do exist, and they appear likely to proliferate.

The advantages of integrative care, in which diverse practitioners collaborate, are compelling. The traditional wall of silence between CAM and conventional practice is overcome, thereby avoiding the risk of adverse interactions or gaps in care. Interaction in the care of a patient can help practitioners learn about one another in a manner conducive to more productive collaborations over time. Rather than relying on the limited expertise in all of medicine that any one individual can attain, physicians can take a collaborative approach to care, which provides the patient with access to practitioners who have complementary knowledge and expertise. Because training, credentials, and legitimacy of practice vary widely across the expanse of CAM, and because proficiency varies among conventionally trained physicians, direct communication among practitioners can also help patients identify the most competent, credible, and suitable providers.

As the term CAM refers to any therapy or provider outside the mainstream, any modicum of efficacy or legitimacy satisfies this label. The CAM disciplines with the most promise of successful integration into conventional medicine are those with tangible standards. Specifically, those that have accredited training programs, national certification, standardized education, and government regulation and licensure. Of the myriad CAM degrees available, the distinctly licensed fields are acupuncture, chiropractic, midwifery, massage therapy, and naturopathic medicine (see Table 3).

TABLE 3 Licensed CAM Professions

Profession	Designation	Degree	Training	Regulation	Credentialing body
Acupuncture and Oriental Medicine	L.Ac. (Licensed Acupuncturist)	Masters	2-4 years	43 states	National Certification Commission for Acupuncture and Oriental Medicine (NCCAOM)
Chiropractic	D.C. (Doctor of Chiropractic)	Doctorate	4 years	50 states	Federation of Chiropractic Licensing Boards
Midwifery	C.P.M. (Certified Professional Midwife)	variable	variable	Licensed or certified in 22 states	North American Registry of Midwives (NARM)
Massage therapy	None	None	500-1000 hours	Regulated in 39 states	National Certification Board for Therapeutic Massage and Bodywork (NCBTMB)
Naturopathic Medicine	N.D. (Doctor of Naturopathic Medicine)	Doctorate	4 years	Licensed in 15 states	North American Board of Naturopathic Examiners (NABNE)

To date, the outpatient setting, where patient autonomy is far greater and regulation of practice is less strict, is where CAM has flourished. With few but noteworthy exceptions, such as the cardiac surgery program at Columbia Presbyterian Medical Center (Okvat et al., 2002; Oz, 2004) and cancer service at Beth Israel Hospital (Hartocollis, 2008), both in New York City, as well as Abbott Northwest Hospital (Institute for Health and Healing, 2007) in Minneapolis, the inpatient setting has been largely inhospitable to CAM, and consequently integrative medicine, thus far. Hospital care is particularly dominated by concerns for evidence-based practice, as well as the stipulations of insurers. Despite this, hospitals are increasingly tempted to address the public's interest in CAM by making some of the most clearly benign therapies, such as massage, available (Hemphill and Kemp, 2000). Such gestures may enhance patient satisfaction at low cost.

As one example of an integrative care model that embraces these principles, the Integrative Medicine Center (IMC) at Griffin Hospital in Derby, Connecticut, offers outpatient care that is fully consensus based (Katz et al., 2003a; McCloud, 2008). The IMC is codirected by a conventional physician and a naturopathic physician. Patients, either self- or physician-referred, are evaluated sequentially by a conventionally trained medical provider and by a naturopathic physician. Each such evaluation terminates with a consensus conference, in which the providers from both disciplines review the array of treatment options with the patient.

The IMC is supported by a panel of CAM providers throughout the state of Connecticut, to whom patients may be referred for specialized therapies. Among the services the IMC provides is an evaluation of the credentials and practice history of these practitioners, thereby helping patients find the most reputable practitioners. Other models of integrative medicine around the country have addressed integration in a variety of ways, but the true potential of integrative care to enhance patient outcomes, satisfaction, and/or the cost-effectiveness of care is as yet unclear. This will remain the case until research funds are specifically dedicated to the testing of models of care, and their impact on symptoms, disease progression, functional capacity, patient satisfaction, and costs of care.

The case for integrative medicine at this juncture in the evolution of health care is persuasive, and perhaps nowhere more so than in the zone of overlap with preventive medicine, summarized in Table 4. Given the public's clear and growing interest in CAM, a system of care that fails to address CAM simply cannot be truly patient-centered. Patient empowerment and autonomy, however, should not be at the expense of science and evidence, and thus wholesale endorsement of CAM in conventional medical institutions is equally inappropriate.

The ultimate goal of integrative medicine should be to make the widest array of appropriate options available to patients. Appropriateness should be predicated on fundamental considerations that pertain equally to conventional and CAM practice: treatment safety and treatment effectiveness. Treatment safety and treatment effectiveness must, in turn, be interpreted in light of the available evidence.

TABLE 4 The interface of integrative medicine with the levels of preventive medicine, and the potential benefits.

Level of Prevention	Disease prevention objectives	Representative integrative medicine modalities	Potential advantages
Primary	Health promotion; preventing the inception of disease	Dietary counseling; nutraceutical use; stress management; etc.	Greater patient engagement in self-care, more effective and widespread primary prevention
Secondary	Treatment of pre-symptomatic disease	Diet; nutraceuticals; etc.	Enhanced patient compliance; reduced reliance on pharmacotherapy
Tertiary	Control of disease progression; symptom management	Acupuncture; massage; stress management; nutraceuticals; etc.	Enhanced symptom control; enhanced satisfaction; improved function

The ultimate goal in the evolution of integrative care should be the blurring of boundaries between conventional care and CAM. Both disciplines should be subject to rigorous scientific inquiry so that interventions that work are systematically distinguished from those that do not (Vickers, 2001). Safety should not be assumed in either case but should similarly be derived from rigorous evaluation.

Although the importance of scientific evidence in modern medicine is indisputable, its application is often questionable. Evidence simply does not exist to indicate the best treatments for many chronic conditions and syndromes. Under such circumstances, practitioners who choose to view evidence rigidly may have nothing to offer their patients but an apology (Katz, 2000). Where strong evidence in support of a particular therapy exists, that therapy should be recommended in preference to others. The less clear it is as to which might be the “right” treatment choice, the more important it is to work down a hierarchy of evidence, considering safety, effectiveness, alternatives, the evidence supporting each (see Table 2). For many conditions, such as chronic fatigue syndrome or fibromyalgia, a definitive therapy does not exist, and the best available treatments are those likely to be safe—and possibly effective. Access to CAM modalities greatly broadens patient options at this end of the evidence hierarchy, where options are generally most needed. It should be noted, as well, that a therapy a patient is unwilling to use is ineffective, regardless of conclusions reached in RCTs.

Any effort to expand the applications of integrative medicine should proceed from the more evidence based modalities to the less, and from the outpatient to the inpatient setting. There are challenges to overcome in reconciling four prominent themes in modern health care: patient autonomy; reliance on scientific evidence; cost-effectiveness; and an emphasis on prevention. Any effort to do so at present will itself be hindered by a relative lack of pertinent evidence. This evidence should demonstrate efficacy and practicality; research priorities should include outcomes research and cost-effectiveness studies on existing models of integrative medicine.

But even in the absence of evidence, it is clear that none of the goals of health care are served by a failure to treat symptoms adequately, engage patients in a therapeutic alliance, control disease progression, or produce satisfaction. The simple and compelling argument for integrative care is that as impressive as are the bounds of modern medical science and knowledge, they encompass far less terrain than patient need. We simply do not manage to make all of our patients better. Integrative care will not achieve universal success either, but it does expand the array of options, and thereby promises to increase the total ratio of successes to failures. Those successes may be reasonably, and constructively, catalogued across the stages of prevention.

RECOMMENDATIONS ON HOW THIS CAN MOVE FORWARD

1. Funding for outcomes research on integrative medicine *models of care* should be increased.
 - observational and interventional
 - emphasis on whole systems and whole person approaches
2. Research must be increased on the ability to assist in and adhere to life-style change in patients utilizing integrative medicine.
3. Research should compare differing models of integrative care in terms of optimizing outcomes and cost, as well as comparing integrative medicine models with standard care.
4. Clinical trials of integrative medicine should be conducted on outcomes with high public health significance.
5. A standardized definition of integrative medicine should be developed that is both specific and inclusive of different practice types.
 - this will also entail defining what is *not* integrative care.
6. Besides research focusing on standard biomarkers, other “holistic” outcomes should be studied: quality of life, functionality, and financial impact (including absenteeism and presenteeism).
7. The case can and should be made in medical education that respect for evidence and responsiveness to the needs of patients are complementary priorities.
8. Exposure to integrative practice should be routine in medical education.

QUESTIONS WE SHOULD BE ADDRESSING DURING SUMMIT

- *How do we define integrative care in practice – is it a philosophy or a concrete set of structures?*
- *What defines an integrative medicine practitioner?*
- *What populations can best potentially benefit from integrative medicine?*
- *How do we address barriers to widespread implementation of integrative medicine?*
- *Is there enough evidence or rationale for widespread implementation of integrative medicine?*
- *Is integrative medicine a fad?*
- *Will the ideals of integrative medicine render integrative care obsolete? (i.e. when “good medicine” becomes the norm)*

REFERENCES

- Abbo, E. D., Q. Zhang, M. Zelder, and E. S. Huang. 2008. The Increasing Number of Clinical Items Addressed During the Time of Adult Primary Care Visits. *J Gen Intern Med*.
- Adam, O., C. Beringer, T. Kless, C. Lemmen, A. Adam, M. Wiseman, P. Adam, R. Klimmek, and W. Forth. 2003. Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis. *Rheumatol Int* 23 (1):27-36.
- Adler, NE, and J Stewart. 2007. Reaching for a Healthier Life: Facts on Socioeconomic Status and Health in the U.S. . In *The John D. and Catherine T. Macarthur Foundation Research Network on Socioeconomic Status and Health*.
- AHRQ. 2008. *Guide to Clinical Preventive Services*. U.S. Preventive Services Task Force 2008 [cited December 16 2008]. Available from <http://www.ahrq.gov/clinic/cps3dix.htm>.
- Ali, A, VY Njike, V Northrup, AB Sabina, A-l Williams, LS Liberti, AI Perlman, H Adelson, and DL Katz. 2009 (In Press). Intravenous Micronutrient Therapy (Myers' Cocktail) for Fibromyalgia: A Placebo-controlled Pilot Study. *Journal of Alternative and Complementary Medicine*.
- Ali, A., D. L. Katz, and M. B. Bracken. 2007. Mind-body practices for hypertension: Systematic review and meta-analysis. Paper read at APHA, at Washington, DC.
- Anand, P., A. B. Kunnumakkara, C. Sundaram, K. B. Harikumar, S. T. Tharakan, O. S. Lai, B. Sung, and B. B. Aggarwal. 2008. Cancer is a preventable disease that requires major lifestyle changes. *Pharm Res* 25 (9):2097-116.
- Angell, M., and J. P. Kassirer. 1998. Alternative medicine--the risks of untested and unregulated remedies. *N Engl J Med* 339 (12):839-41.
- Antonovsky, A. 1968. Social class and the major cardiovascular diseases. *J Chronic Dis* 21 (2):65-106.
- Astin, J. A. 1998. Why patients use alternative medicine: results of a national study. *JAMA* 279 (19):1548-53.
- Balk, E. M., A. Tatsioni, A. H. Lichtenstein, J. Lau, and A. G. Pittas. 2007. Effect of chromium supplementation on glucose metabolism and lipids: a systematic review of randomized controlled trials. *Diabetes Care* 30 (8):2154-63.
- Barnes, P. M., E. Powell-Griner, K. McFann, and R. L. Nahin. 2004. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data* (343):1-19.
- Barnes, PM, B Bloom, and R Nahin. 2008. Complementary and Alternative Medicine Use Among Adults and Children: United States, 2007.

- Becker, D. J., R. Y. Gordon, P. B. Morris, J. Yorko, Y. J. Gordon, M. Li, and N. Iqbal. 2008. Simvastatin vs therapeutic lifestyle changes and supplements: randomized primary prevention trial. *Mayo Clin Proc* 83 (7):758-64.
- Benin, A. L., D. J. Wisler-Scher, E. Colson, E. D. Shapiro, and E. S. Holmboe. 2006. Qualitative analysis of mothers' decision-making about vaccines for infants: the importance of trust. *Pediatrics* 117 (5):1532-41.
- Benyamin, R., A. M. Trescot, S. Datta, R. Buenaventura, R. Adlaka, N. Sehgal, S. E. Glaser, and R. Vallejo. 2008. Opioid complications and side effects. *Pain Physician* 11 (2 Suppl):S105-20.
- Berman, B. M., L. Lao, P. Langenberg, W. L. Lee, A. M. Gilpin, and M. C. Hochberg. 2004. Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 141 (12):901-10.
- Bindman, A. B., C. B. Forrest, H. Britt, P. Crampton, and A. Majeed. 2007. Diagnostic scope of and exposure to primary care physicians in Australia, New Zealand, and the United States: cross sectional analysis of results from three national surveys. *BMJ* 334 (7606):1261.
- Blumenthal, J. A., A. Sherwood, M. A. Babyak, L. L. Watkins, R. Waugh, A. Georgiades, S. L. Bacon, J. Hayano, R. E. Coleman, and A. Hinderliter. 2005. Effects of exercise and stress management training on markers of cardiovascular risk in patients with ischemic heart disease: a randomized controlled trial. *JAMA* 293 (13):1626-34.
- Boisset-Pioro, M. H., J. M. Esdaile, and M. A. Fitzcharles. 1995. Sexual and physical abuse in women with fibromyalgia syndrome. *Arthritis Rheum* 38 (2):235-41.
- Bradley, R., and E. B. Oberg. 2006. Naturopathic medicine and type 2 diabetes: a retrospective analysis from an academic clinic. *Altern Med Rev* 11 (1):30-9.
- Bradley, R., E. B. Oberg, C. Calabrese, and L. J. Standish. 2007. Algorithm for complementary and alternative medicine practice and research in type 2 diabetes. *J Altern Complement Med* 13 (1):159-75.
- Bravata, D. M., L. Sanders, J. Huang, H. M. Krumholz, I. Olkin, and C. D. Gardner. 2003. Efficacy and safety of low-carbohydrate diets: a systematic review. *JAMA* 289 (14):1837-50.
- Brosschot, J. F., R. J. Benschop, G. L. Godaert, M. Olf, M. De Smet, C. J. Heijnen, and R. E. Ballieux. 1994. Influence of life stress on immunological reactivity to mild psychological stress. *Psychosom Med* 56 (3):216-24.
- Buscemi, N., B. Vandermeer, R. Pandya, N. Hooton, L. Tjosvold, L. Hartling, G. Baker, S. Vohra, and T. Klassen. 2004. Melatonin for treatment of sleep disorders. *Evid Rep Technol Assess (Summ)* (108):1-7.

- Calle, E. E., M. J. Thun, J. M. Petrelli, C. Rodriguez, and C. W. Heath, Jr. 1999. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 341 (15):1097-105.
- CDC. 2008. *Social Determinants of Disparities in Health 2008* [cited November 20 2008]. Available from <http://www.cdc.gov/sdoh/>.
- Chang, P. P., D. E. Ford, L. A. Meoni, N. Y. Wang, and M. J. Klag. 2002. Anger in young men and subsequent premature cardiovascular disease: the precursors study. *Arch Intern Med* 162 (8):901-6.
- Cherniack, E. P. 2008. Potential applications for alternative medicine to treat obesity in an aging population. *Altern Med Rev* 13 (1):34-42.
- Chopra, A., and V. V. Doiphode. 2002. Ayurvedic medicine. Core concept, therapeutic principles, and current relevance. *Med Clin North Am* 86 (1):75-89, vii.
- Christian, L. M., J. E. Graham, D. A. Padgett, R. Glaser, and J. K. Kiecolt-Glaser. 2006. Stress and wound healing. *Neuroimmunomodulation* 13 (5-6):337-46.
- Ciccone, D. S., D. K. Elliott, H. K. Chandler, S. Nayak, and K. G. Raphael. 2005. Sexual and physical abuse in women with fibromyalgia syndrome: a test of the trauma hypothesis. *Clin J Pain* 21 (5):378-86.
- Conklin, K. A. 2005. Coenzyme q10 for prevention of anthracycline-induced cardiotoxicity. *Integr Cancer Ther* 4 (2):110-30.
- Dalen, J. E. 1998. "Conventional" and "unconventional" medicine: can they be integrated? *Arch Intern Med* 158 (20):2179-81.
- Dalen, JE. 1999. Is integrative medicine the medicine of the future? A debate between Arnold S. Relman, MD, and Andrew Weil, MD. *Arch Intern Med* 159 (18):2122-6.
- Danese, A., T. E. Moffitt, C. M. Pariante, A. Ambler, R. Poulton, and A. Caspi. 2008. Elevated inflammation levels in depressed adults with a history of childhood maltreatment. *Arch Gen Psychiatry* 65 (4):409-15.
- Danese, A., C. M. Pariante, A. Caspi, A. Taylor, and R. Poulton. 2007. Childhood maltreatment predicts adult inflammation in a life-course study. *Proc Natl Acad Sci U S A* 104 (4):1319-24.
- Dansinger, M. L., J. A. Gleason, J. L. Griffith, H. P. Selker, and E. J. Schaefer. 2005. Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 293 (1):43-53.
- Druss, B. G., and R. A. Rosenheck. 1999. Association between use of unconventional therapies and conventional medical services. *JAMA* 282 (7):651-6.
- Eisenberg, D. M., R. C. Kessler, C. Foster, F. E. Norlock, D. R. Calkins, and T. L. Delbanco. 1993. Unconventional medicine in the United States. Prevalence, costs, and patterns of use. *N Engl J Med* 328 (4):246-52.

- Eisenberg, David M., Roger B. Davis, Susan L. Ettner, Scott Appel, Sonja Wilkey, Maria Van Rompay, and Ronald C. Kessler. 1998. Trends in Alternative Medicine Use in the United States, 1990-1997: Results of a Follow-up National Survey. *JAMA* 280 (18):1569-1575.
- Elder, N. C., A. Gillcrist, and R. Minz. 1997. Use of alternative health care by family practice patients. *Arch Fam Med* 6 (2):181-4.
- Environmental Determinants of Health. 2002. In *Encyclopedia of Public Health*, edited by L. Breslow. New York: MacMillan Publishing Co.
- Ernst, E. 2006. Complementary or alternative therapies for osteoarthritis. *Nat Clin Pract Rheumatol* 2 (2):74-80.
- Faass, Nancy. 2001. *Integrating Complementary Medicine into Health Systems*: Jones and Bartlett Publishers, Inc.
- Feldman, M. K. 1990. Patients who seek unorthodox medical treatment. *Minn Med* 73 (6):19-25.
- Frank, E., and T. Kunovich-Frieze. 1995. Physicians' prevention counseling behaviors: current status and future directions. *Prev Med* 24 (6):543-5.
- Freeman, J. D., S. Kadiyala, J. F. Bell, and D. P. Martin. 2008. The causal effect of health insurance on utilization and outcomes in adults: a systematic review of US studies. *Med Care* 46 (10):1023-32.
- Friedman, E. M., M. S. Hayney, G. D. Love, H. L. Urry, M. A. Rosenkranz, R. J. Davidson, B. H. Singer, and C. D. Ryff. 2005. Social relationships, sleep quality, and interleukin-6 in aging women. *Proc Natl Acad Sci U S A* 102 (51):18757-62.
- Friedman, H. S., and S. Booth-Kewley. 1987. The "disease-prone personality". A meta-analytic view of the construct. *Am Psychol* 42 (6):539-55.
- Giannuzzi, P., P. L. Temporelli, U. Corra, M. Gattone, A. Giordano, and L. Tavazzi. 1997. Attenuation of unfavorable remodeling by exercise training in postinfarction patients with left ventricular dysfunction: results of the Exercise in Left Ventricular Dysfunction (ELVD) trial. *Circulation* 96 (6):1790-7.
- Giltay, E. J., J. M. Geleijnse, F. G. Zitman, T. Hoekstra, and E. G. Schouten. 2004. Dispositional optimism and all-cause and cardiovascular mortality in a prospective cohort of elderly dutch men and women. *Arch Gen Psychiatry* 61 (11):1126-35.
- Goldstein, M. S., C. Sutherland, D. T. Jaffe, and J. Wilson. 1988. Holistic physicians and family practitioners: similarities, differences and implications for health policy. *Soc Sci Med* 26 (8):853-61.
- Gooneratne, N. S. 2008. Complementary and alternative medicine for sleep disturbances in older adults. *Clin Geriatr Med* 24 (1):121-38, viii.
- Green, L. W. 2006. Public health asks of systems science: to advance our evidence-based practice, can you help us get more practice-based evidence? *Am J Public Health* 96 (3):406-9.

- Hall, M. H., M. F. Muldoon, J. R. Jennings, D. J. Buysse, J. D. Flory, and S. B. Manuck. 2008. Self-reported sleep duration is associated with the metabolic syndrome in midlife adults. *Sleep* 31 (5):635-43.
- Harris, W. S., M. Miller, A. P. Tighe, M. H. Davidson, and E. J. Schaefer. 2008. Omega-3 fatty acids and coronary heart disease risk: clinical and mechanistic perspectives. *Atherosclerosis* 197 (1):12-24.
- Hartocollis, A. 2008. In One Section of Beth Israel Hospital, Some Patients Are Saying 'Om,' Not 'Ah' *New York Times*, October 29, 2008 A31.
- Hartweg, J., R. Perera, V. Montori, S. Dinneen, H. A. Neil, and A. Farmer. 2008. Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus. *Cochrane Database Syst Rev* (1):CD003205.
- Hatcher, S., and B. Arroll. 2008. Assessment and management of medically unexplained symptoms. *BMJ* 336 (7653):1124-8.
- Hemphill, L., and J. Kemp. 2000. Implementing a therapeutic massage program in a tertiary and ambulatory care VA setting: the healing power of touch. *Nurs Clin North Am* 35 (2):489-97.
- Hillemeier, C. 1995. An overview of the effects of dietary fiber on gastrointestinal transit. *Pediatrics* 96 (5 Pt 2):997-9.
- Hough, HJ, C Dower, and EH O'Neil. 2001. Profile of a Profession: Naturopathic Practice. San Francisco: University of California, San Francisco, Centre for the Health Professions.
- Hu, P., and D. B. Reuben. 2002. Effects of managed care on the length of time that elderly patients spend with physicians during ambulatory visits: National Ambulatory Medical Care Survey. *Med Care* 40 (7):606-13.
- Institute for Health and Healing. 2007. Overview and outcomes Report 2007. Minneapolis, MN: Abbott Northwestern Hospital.
- Jekel, JF, DL Katz, JG Elmore, and DMG Wild. 2007. *Epidemiology, Biostatistics, and Preventive Medicine*. 3 ed: W.B. Saunders Company.
- Jenkins, D. J., C. W. Kendall, D. A. Faulkner, T. Nguyen, T. Kemp, A. Marchie, J. M. Wong, R. de Souza, A. Emam, E. Vidgen, E. A. Trautwein, K. G. Lapsley, C. Holmes, R. G. Josse, L. A. Leiter, P. W. Connelly, and W. Singer. 2006. Assessment of the longer-term effects of a dietary portfolio of cholesterol-lowering foods in hypercholesterolemia. *Am J Clin Nutr* 83 (3):582-91.
- Jha, A. K., P. D. Varosy, A. M. Kanaya, D. B. Hunninghake, M. A. Hlatky, D. D. Waters, C. D. Furberg, and M. G. Shlipak. 2003. Differences in medical care and disease outcomes among black and white women with heart disease. *Circulation* 108 (9):1089-94.
- Jiamsripong, P., M. Mookadam, T. Honda, B. K. Khandheria, and F. Mookadam. 2008. The metabolic syndrome and cardiovascular disease: Part I. *Prev Cardiol* 11 (3):155-61.

- Johnston, B. C., A. L. Supina, M. Ospina, and S. Vohra. 2007. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database Syst Rev* (2):CD004827.
- Jones, D. 2008. A look at the Institute for Functional Medicine with David Jones, MD. Interviewed by Mark A Hyman. *Altern Ther Health Med* 14 (1):10-1.
- Jones, J. F., E. M. Maloney, R. S. Boneva, A. B. Jones, and W. C. Reeves. 2007. Complementary and alternative medical therapy utilization by people with chronic fatiguing illnesses in the United States. *BMC Complement Altern Med* 7:12.
- Kaptchuk, TJ. 2000. *The Web That Has No Weaver : Understanding Chinese Medicine*. 2 ed: McGraw-Hill.
- Katz, D. L. 2000. Conventional medical care and unconventional therapies. *JAMA* 283 (1):56; author reply 57.
- Katz, D. L., and A. Ali. 2008. Integrating Complementary & Alternative Practices into Conventional Care. In *Putting Patients First: Designing and Practicing Patient-Centered Care*, edited by S. B. Frampton and P. A. Charmel. San Francisco, CA: Jossey-Bass Publishers, Inc.
- Katz, David L., Alyse Behrman Sabina, Christine Girard, Harry Adelson, Lauren Schiller-Liberti, and Anna-leila Williams. 2003a. Teaching Evidence-Based Integrative Medicine: Description of a Model Programme. *Evidence-Based Integrative Medicine* 1 (1):77-82.
- Katz, D. L., A. L. Williams, C. Girard, J. Goodman, B. Comerford, A. Behrman, and M. B. Bracken. 2003b. The evidence base for complementary and alternative medicine: methods of Evidence Mapping with application to CAM. *Altern Ther Health Med* 9 (4):22-30.
- Kawachi, I., D. Sparrow, A. Spiro, 3rd, P. Vokonas, and S. T. Weiss. 1996. A prospective study of anger and coronary heart disease. The Normative Aging Study. *Circulation* 94 (9):2090-5.
- Kelly, T., W. Yang, C. S. Chen, K. Reynolds, and J. He. 2008. Global burden of obesity in 2005 and projections to 2030. *Int J Obes (Lond)* 32 (9):1431-7.
- Kitagawa, EM, and PM Hauser. 1973. *Differential Mortality in the United States: A Study in Socioeconomic Epidemiology*. Cambridge: Harvard Univ Press.
- Kligler, B. 2004. The role of the optimal healing environment in the care of patients with diabetes mellitus type II. *J Altern Complement Med* 10 Suppl 1:S223-9.
- Kligler, B., V. Maizes, S. Schachter, C. M. Park, T. Gaudet, R. Benn, R. Lee, and R. N. Remen. 2004. Core competencies in integrative medicine for medical school curricula: a proposal. *Acad Med* 79 (6):521-31.
- Knowler, W. C., E. Barrett-Connor, S. E. Fowler, R. F. Hamman, J. M. Lachin, E. A. Walker, and D. M. Nathan. 2002. Reduction in the incidence of type 2

- diabetes with lifestyle intervention or metformin. *N Engl J Med* 346 (6):393-403.
- Kobasa, S. C. 1979. Stressful life events, personality, and health: an inquiry into hardiness. *J Pers Soc Psychol* 37 (1):1-11.
- Kris-Etherton, P., R. H. Eckel, B. V. Howard, S. St Jeor, and T. L. Bazzarre. 2001. AHA Science Advisory: Lyon Diet Heart Study. Benefits of a Mediterranean-style, National Cholesterol Education Program/American Heart Association Step I Dietary Pattern on Cardiovascular Disease. *Circulation* 103 (13):1823-5.
- Latham, J., and B. D. Davis. 1994. The socioeconomic impact of chronic pain. *Disabil Rehabil* 16 (1):39-44.
- Leach, M. J. 2004. A critical review of natural therapies in wound management. *Ostomy Wound Manage* 50 (2):36-40, 42, 44-6 passim.
- Leavell, HR, and EG Clark. 1965. *Preventive Medicine for the Doctor in His Community*. 3 ed. New York: McGraw-Hill Book Company.
- Leger, D. 1994. The cost of sleep-related accidents: a report for the National Commission on Sleep Disorders Research. *Sleep* 17 (1):84-93.
- Lind, B. K., W. E. Lafferty, P. T. Tyree, P. K. Diehr, and D. E. Grembowski. 2007. Use of complementary and alternative medicine providers by fibromyalgia patients under insurance coverage. *Arthritis Rheum* 57 (1):71-6.
- Little, P., G. Lewith, F. Webley, M. Evans, A. Beattie, K. Middleton, J. Barnett, K. Ballard, F. Oxford, P. Smith, L. Yardley, S. Hollinghurst, and D. Sharp. 2008. Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain. *BMJ* 337:a884.
- Luster, L., and B. Hines. 2005. Debate question: should physicians incorporate spirituality into the care of patients? *South Med J* 98 (12):1242.
- Lutgendorf, S. K., and E. S. Costanzo. 2003. Psychoneuroimmunology and health psychology: an integrative model. *Brain Behav Immun* 17 (4):225-32.
- Maciosek, M. V., A. B. Coffield, N. M. Edwards, T. J. Flottemesch, M. J. Goodman, and L. I. Solberg. 2006. Priorities among effective clinical preventive services: results of a systematic review and analysis. *Am J Prev Med* 31 (1):52-61.
- Maheux, B., R. Pineault, J. Lambert, F. Beland, and M. Berthiaume. 1989. Factors influencing physicians' preventive practices. *Am J Prev Med* 5 (4):201-6.
- Marcoff, L., and P. D. Thompson. 2007. The role of coenzyme Q10 in statin-associated myopathy: a systematic review. *J Am Coll Cardiol* 49 (23):2231-7.
- Marcus, D. M. 2002. Integrative medicine is a trojan horse. *Arch Intern Med* 162 (20):2381-3; author reply 2383.
- Margolin, A., S. K. Avants, and R. Arnold. 2005. Acupuncture and spirituality-focused group therapy for the treatment of HIV-positive drug users: a preliminary study. *J Psychoactive Drugs* 37 (4):385-90.

- McBeth, J., G. J. Macfarlane, S. Benjamin, S. Morris, and A. J. Silman. 1999. The association between tender points, psychological distress, and adverse childhood experiences: a community-based study. *Arthritis Rheum* 42 (7):1397-404.
- McCloud, A. 2008. Connecticut's Integrative Medicine Center Offers a New Conventional Medicine Model: An Interview With David L. Katz, MD, MPH, FACPM, FACP, and Ather Ali, ND, MPH *Integrative Medicine: A Clinician's Journal* 7 (1):34-37.
- McEwen, B. S. 2007. Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiol Rev* 87 (3):873-904.
- McFarland, L. V. 2006. Meta-analysis of probiotics for the prevention of antibiotic associated diarrhea and the treatment of *Clostridium difficile* disease. *Am J Gastroenterol* 101 (4):812-22.
- McGinnis, J. M., and W. H. Foege. 1993. Actual causes of death in the United States. *JAMA* 270 (18):2207-12.
- McGinnis, J. M., P. Williams-Russo, and J. R. Knickman. 2002. The case for more active policy attention to health promotion. *Health Aff (Millwood)* 21 (2):78-93.
- McKee, J. 1988. Holistic health and the critique of Western medicine. *Soc Sci Med* 26 (8):775-84.
- Melamed, S., and A. Oksenberg. 2002. Excessive daytime sleepiness and risk of occupational injuries in non-shift daytime workers. *Sleep* 25 (3):315-22.
- MGH. *Benson-Henry Institute for Mind-Body Medicine* 2008. Available from http://www.mbmi.org/health_professionals/Training.asp.
- Milani, R. V., and C. J. Lavie. 2007. Impact of cardiac rehabilitation on depression and its associated mortality. *Am J Med* 120 (9):799-806.
- Milani, R. V., C. J. Lavie, and M. R. Mehra. 2004. Reduction in C-reactive protein through cardiac rehabilitation and exercise training. *J Am Coll Cardiol* 43 (6):1056-61.
- Mokdad, A. H., J. S. Marks, D. F. Stroup, and J. L. Gerberding. 2004. Actual causes of death in the United States, 2000. *JAMA* 291 (10):1238-45.
- Morone, N. E., and C. M. Greco. 2007. Mind-body interventions for chronic pain in older adults: a structured review. *Pain Med* 8 (4):359-75.
- Mulholland, H. G., M. M. Cantwell, L. A. Anderson, B. T. Johnston, R. G. Watson, S. J. Murphy, H. R. Ferguson, J. McGuigan, J. V. Reynolds, H. Comber, and L. J. Murray. 2008. Glycemic index, carbohydrate and fiber intakes and risk of reflux esophagitis, Barrett's esophagus, and esophageal adenocarcinoma. *Cancer Causes Control*.
- Must, A., J. Spadano, E. H. Coakley, A. E. Field, G. Colditz, and W. H. Dietz. 1999. The disease burden associated with overweight and obesity. *JAMA* 282 (16):1523-9.

- Nanri, A., M. A. Moore, and S. Kono. 2007. Impact of C-reactive protein on disease risk and its relation to dietary factors. *Asian Pac J Cancer Prev* 8 (2):167-77.
- NCCAM (National Center for Complementary & Alternative Medicine). 2005. Expanding horizons of health care: Strategic plan 2005-2009. edited by N. I. o. Health. Bethesda, MD.
- NCCAM. 2007a. What is CAM? <http://nccam.nih.gov/health/whatiscam>.
- NCCAM. 2007b. An Introduction to Naturopathy. <http://nccam.nih.gov/health/naturopathy>.
- NCCAM 2008. Ayurvedic Medicine: An Introduction.
- NCCDPHP. 2008. *Chronic Disease Overview* 2008 [cited December 16 2008]. Available from <http://www.cdc.gov/NCCDPHP/overview.htm>.
- Nies, L. K., A. A. Cymbala, S. L. Kasten, D. G. Lamprecht, and K. L. Olson. 2006. Complementary and alternative therapies for the management of dyslipidemia. *Ann Pharmacother* 40 (11):1984-92.
- Nieuwenhuizen, A. G., and F. Rutters. 2008. The hypothalamic-pituitary-adrenal-axis in the regulation of energy balance. *Physiol Behav* 94 (2):169-77.
- Ogden, C. L., M. D. Carroll, L. R. Curtin, M. A. McDowell, C. J. Tabak, and K. M. Flegal. 2006. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA* 295 (13):1549-55.
- Okvat, H. A., M. C. Oz, W. Ting, and P. B. Namerow. 2002. Massage therapy for patients undergoing cardiac catheterization. *Altern Ther Health Med* 8 (3):68-70, 72, 74-5.
- Olshansky, S. J., D. J. Passaro, R. C. Hershov, J. Layden, B. A. Carnes, J. Brody, L. Hayflick, R. N. Butler, D. B. Allison, and D. S. Ludwig. 2005. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med* 352 (11):1138-45.
- Ornish, D. 1998. *Love and Survival: The Scientific Basis for the Healing Power of Intimacy*: HarperCollins.
- Ornish, D., S. E. Brown, L. W. Scherwitz, J. H. Billings, W. T. Armstrong, T. A. Ports, S. M. McLanahan, R. L. Kirkeeide, R. J. Brand, and K. L. Gould. 1990. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. *Lancet* 336 (8708):129-33.
- Ornish, D., M. J. Magbanua, G. Weidner, V. Weinberg, C. Kemp, C. Green, M. D. Mattie, R. Marlin, J. Simko, K. Shinohara, C. M. Haqq, and P. R. Carroll. 2008a. Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. *Proc Natl Acad Sci U S A* 105 (24):8369-74.
- Ornish, D., J. Lin, J. Daubenmier, G. Weidner, E. Epel, C. Kemp, M. J. Magbanua, R. Marlin, L. Yglecias, P. R. Carroll, and E. H. Blackburn. 2008b.

- Increased telomerase activity and comprehensive lifestyle changes: a pilot study. *Lancet Oncol* 9 (11):1048-57.
- Ornish, D., L. W. Scherwitz, J. H. Billings, S. E. Brown, K. L. Gould, T. A. Merritt, S. Sparler, W. T. Armstrong, T. A. Ports, R. L. Kirkeeide, C. Hogeboom, and R. J. Brand. 1998. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 280 (23):2001-7.
- Ornish, D., G. Weidner, W. R. Fair, R. Marlin, E. B. Pettengill, C. J. Raisin, S. Dunn-Emke, L. Crutchfield, F. N. Jacobs, R. J. Barnard, W. J. Aronson, P. McCormac, D. J. McKnight, J. D. Fein, A. M. Dnistrian, J. Weinstein, T. H. Ngo, N. R. Mendell, and P. R. Carroll. 2005. Intensive lifestyle changes may affect the progression of prostate cancer. *J Urol* 174 (3):1065-9; discussion 1069-70.
- Oz, M. 2004. Emerging role of integrative medicine in cardiovascular disease. *Cardiol Rev* 12 (2):120-3.
- Papanikolaou, Y., and V. L. Fulgoni, 3rd. 2008. Bean consumption is associated with greater nutrient intake, reduced systolic blood pressure, lower body weight, and a smaller waist circumference in adults: results from the National Health and Nutrition Examination Survey 1999-2002. *J Am Coll Nutr* 27 (5):569-76.
- Papas, M. A., A. J. Alberg, R. Ewing, K. J. Helzlsouer, T. L. Gary, and A. C. Klassen. 2007. The built environment and obesity. *Epidemiol Rev* 29:129-43.
- Pasquali, R., V. Vicennati, M. Cacciari, and U. Pagotto. 2006. The hypothalamic-pituitary-adrenal axis activity in obesity and the metabolic syndrome. *Ann NY Acad Sci* 1083:111-28.
- Peeters, A., J. J. Barendregt, F. Willekens, J. P. Mackenbach, A. Al Mamun, and L. Bonneux. 2003. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Intern Med* 138 (1):24-32.
- Pelletier, K. R., and J. A. Astin. 2002. Integration and reimbursement of complementary and alternative medicine by managed care and insurance providers: 2000 update and cohort analysis. *Altern Ther Health Med* 8 (1):38-9, 42, 44 passim.
- Pelletier, K. R., J. A. Astin, and W. L. Haskell. 1999. Current trends in the integration and reimbursement of complementary and alternative medicine by managed care organizations (MCOs) and insurance providers: 1998 update and cohort analysis. *Am J Health Promot* 14 (2):125-33.
- Perlman, A. I., A. Sabina, A. L. Williams, V. Y. Njike, and D. L. Katz. 2006. Massage therapy for osteoarthritis of the knee: a randomized controlled trial. *Arch Intern Med* 166 (22):2533-8.
- Pischke, C. R., L. Scherwitz, G. Weidner, and D. Ornish. 2008. Long-term effects of lifestyle changes on well-being and cardiac variables among coronary heart disease patients. *Health Psychol* 27 (5):584-92.

- Poston, W. S., 2nd, and J. P. Foreyt. 2000. Successful management of the obese patient. *Am Fam Physician* 61 (12):3615-22.
- Rahm, D. H., and J. M. Labovitz. 2007. Perioperative nutrition and the use of nutritional supplements. *Clin Podiatr Med Surg* 24 (2):245-59.
- Rakel, D. P., and A. Rindfleisch. 2005. Inflammation: nutritional, botanical, and mind-body influences. *South Med J* 98 (3):303-10.
- Rakel, David, ed. 2007. *Integrative Medicine*. 2 ed: Saunders.
- Retelny, V. S., A. Neuendorf, and J. L. Roth. 2008. Nutrition protocols for the prevention of cardiovascular disease. *Nutr Clin Pract* 23 (5):468-76.
- Ridker, P. M., and J. D. Silvertown. 2008. Inflammation, C-reactive protein, and atherothrombosis. *J Periodontol* 79 (8 Suppl):1544-51.
- Ring, A., C. F. Dowrick, G. M. Humphris, J. Davies, and P. Salmon. 2005. The somatising effect of clinical consultation: what patients and doctors say and do not say when patients present medically unexplained physical symptoms. *Soc Sci Med* 61 (7):1505-15.
- Rosenblum, A., H. Joseph, C. Fong, S. Kipnis, C. Cleland, and R. K. Portenoy. 2003. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. *JAMA* 289 (18):2370-8.
- Rosmond, R., and P. Bjorntorp. 2000. The hypothalamic-pituitary-adrenal axis activity as a predictor of cardiovascular disease, type 2 diabetes and stroke. *J Intern Med* 247 (2):188-97.
- Roter, D. L., J. A. Hall, D. E. Kern, L. R. Barker, K. A. Cole, and R. P. Roca. 1995. Improving physicians' interviewing skills and reducing patients' emotional distress. A randomized clinical trial. *Arch Intern Med* 155 (17):1877-84.
- Russell, R. I., R. J. Morgan, and L. M. Nelson. 1984. Studies on the protective effect of deglycyrrhised liquorice against aspirin (ASA) and ASA plus bile acid-induced gastric mucosal damage, and ASA absorption in rats. *Scand J Gastroenterol Suppl* 92:97-100.
- Ryff, C. D., B. H. Singer, and G. Dienberg Love. 2004. Positive health: connecting well-being with biology. *Philos Trans R Soc Lond B Biol Sci* 359 (1449):1383-94.
- Sampson, W. 2001. Dancing with a dream: the folly of pursuing alternative medicine. *Acad Med* 76 (4):301-3.
- Sarac, A. J., and A. Gur. 2006. Complementary and alternative medical therapies in fibromyalgia. *Curr Pharm Des* 12 (1):47-57.
- Savarese, D. M., G. Savy, L. Vahdat, P. E. Wischmeyer, and B. Corey. 2003. Prevention of chemotherapy and radiation toxicity with glutamine. *Cancer Treat Rev* 29 (6):501-13.

- Scheurich, N. 2003. Reconsidering spirituality and medicine. *Acad Med* 78 (4):356-60.
- Schmid, S. M., M. Hallschmid, K. Jauch-Chara, J. Born, and B. Schultes. 2008. A single night of sleep deprivation increases ghrelin levels and feelings of hunger in normal-weight healthy men. *J Sleep Res* 17 (3):331-4.
- Shai, I., D. Schwarzfuchs, Y. Henkin, D. R. Shahar, S. Witkow, I. Greenberg, R. Golan, D. Fraser, A. Bolotin, H. Vardi, O. Tangi-Rozental, R. Zuk-Ramot, B. Sarusi, D. Brickner, Z. Schwartz, E. Sheiner, R. Marko, E. Katorza, J. Thiery, G. M. Fiedler, M. Bluher, M. Stumvoll, and M. J. Stampfer. 2008. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *N Engl J Med* 359 (3):229-41.
- Shapiro, S. L., D. Oman, C. E. Thoresen, T. G. Plante, and T. Flinders. 2008. Cultivating mindfulness: effects on well-being. *J Clin Psychol* 64 (7):840-62.
- Singh, U., and I. Jialal. 2008. Alpha-lipoic acid supplementation and diabetes. *Nutr Rev* 66 (11):646-57.
- Smith, R. C., C. Lein, C. Collins, J. S. Lyles, B. Given, F. C. Dwamena, J. Coffey, A. Hodges, J. C. Gardiner, J. Goddeeris, and C. W. Given. 2003. Treating patients with medically unexplained symptoms in primary care. *J Gen Intern Med* 18 (6):478-89.
- Snyderman, R., and A. T. Weil. 2002. Integrative medicine: bringing medicine back to its roots. *Arch Intern Med* 162 (4):395-7.
- Sood, A., J. O. Ebbert, R. Sood, and S. R. Stevens. 2006. Complementary treatments for tobacco cessation: a survey. *Nicotine Tob Res* 8 (6):767-71.
- Stason, W, DS Shepard, S Fournier, GK Strickler, G Ritter, and J Suaya. 2005. Effects of the Medicare Lifestyle Modification Program Demonstration (LMPD) on Risk Factors and Quality of Life in Patients with Coronary Heart Disease. Paper read at AcademyHealth Meeting, at Boston, MA.
- Stokley, S., K. A. Cullen, A. Kennedy, and B. H. Bardenheier. 2008. Adult vaccination coverage levels among users of complementary/alternative medicine - results from the 2002 National Health Interview Survey (NHIS). *BMC Complement Altern Med* 8:6.
- Sullivan, M. D., J. A. Turner, and J. Romano. 1991. Chronic pain in primary care. Identification and management of psychosocial factors. *J Fam Pract* 32 (2):193-9.
- Taylor, R. S., A. Brown, S. Ebrahim, J. Jolliffe, H. Noorani, K. Rees, B. Skidmore, J. A. Stone, D. R. Thompson, and N. Oldridge. 2004. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 116 (10):682-92.

- Teelucksingh, S., A. D. Mackie, D. Burt, M. A. McIntyre, L. Brett, and C. R. Edwards. 1990. Potentiation of hydrocortisone activity in skin by glycyrrhetic acid. *Lancet* 335 (8697):1060-3.
- Teutsch, C. 2003. Patient-doctor communication. *Med Clin North Am* 87 (5):1115-45.
- Tufts Center for the Study of Drug Development. 2008. Outlook 2008. Boston: Tufts University.
- van Dam, R. M., and J. C. Seidell. 2007. Carbohydrate intake and obesity. *Eur J Clin Nutr* 61 Suppl 1:S75-99.
- van der Weijden, T., M. van Velsen, G. J. Dinant, C. M. van Hasselt, and R. Grol. 2003. Unexplained complaints in general practice: prevalence, patients' expectations, and professionals' test-ordering behavior. *Med Decis Making* 23 (3):226-31.
- Vickers, A. J. 2001. Message to complementary and alternative medicine: evidence is a better friend than power. *BMC Complement Altern Med* 1:1.
- Vlioger, A. M., M. Blink, E. Tromp, and M. A. Benninga. 2008. Use of complementary and alternative medicine by pediatric patients with functional and organic gastrointestinal diseases: results from a multicenter survey. *Pediatrics* 122 (2):e446-51.
- Weil, A. 2000. The significance of integrative medicine for the future of medical education. *Am J Med* 108 (5):441-3.
- Whitfield, C. L. 1998. Adverse childhood experiences and trauma. *Am J Prev Med* 14 (4):361-4.
- Winbush, N. Y., C. R. Gross, and M. J. Kreitzer. 2007. The effects of mindfulness-based stress reduction on sleep disturbance: a systematic review. *Explore (NY)* 3 (6):585-91.
- Yeh, G. Y., R. B. Davis, and R. S. Phillips. 2006. Use of complementary therapies in patients with cardiovascular disease. *Am J Cardiol* 98 (5):673-80.
- Yeh, G. Y., D. M. Eisenberg, T. J. Kaptchuk, and R. S. Phillips. 2003. Systematic review of herbs and dietary supplements for glycemic control in diabetes. *Diabetes Care* 26 (4):1277-94.