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Attitudes and Cardiovascular Disease

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Abstract

Psychological attitudes are prospectively related to cardiovascular disease (CVD), but a causal relationship has not been demonstrated. Trait optimism/pessimism (positive or negative future expectation, respectively), and cynical hostility (mistrust of people), are attitudes with features of personality traits. These attitudes may affect CVD risk in several ways, by influencing an individual's 1) adoption of health behaviors, 2) maladaptive stress responding resulting in direct alteration of physiology (i.e., autonomic dysfunction, thrombosis, arrhythmias), 3) development of traditional CVD risk factors, and 4) lack of adherence to therapy in both primary and secondary prevention. More adaptive attitudes may favorably influence CVD risk at each of these critical junctures. The genetic and environmental (i.e., social, economic, racial/ethnic) determinants of attitudes have not been extensively studied. In addition, it is important to understand how some of these environmental determinants may also moderate the association between attitudes and CVD. Clinical trials to modify attitudes for CVD risk reduction (either by reducing negative attitudes or by increasing positive attitudes) are difficult to conduct, but are necessary to determine whether attitudes can indeed be modified, and if, so, to quantify any CVD-related benefits. To address these questions we present a broad, multidisciplinary research agenda utilizing mixed methods and integrating principles of epidemiology, genetics, psychophysiology, and behavioral medicine over the lifecourse (Figure 1). This overview focuses on attitudes and CVD, but has broader implications for understanding how psychological factors relate to chronic diseases of adulthood.

Keywords

attitudes; optimism; pessimism; cynical hostility; lifecourse; cardiovascular disease (CVD)

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Introduction

Over the past few decades, our understanding of the health consequences of psychological factors has broadened to include both the detrimental associations of negative psychological factors (such as depression, anxiety, anger/hostility, acute and chronic stress)(1-5) and the beneficial associations with positive factors, including positive affect and positive attitudes. (6-13) Yet in spite of years of research linking psychological factors to cardiovascular disease (CVD), data on determinants of the relationship between attitudes and CVD remain sparse. This is a critical gap in knowledge, because psychological factors, which form early in life, may influence the pathogenesis of CVD throughout the lifecourse.(14)

Most studies of attitudes and CVD have not adopted a lifecourse approach, nor were they designed to establish a causal relationship. Determining a causal relationship requires a better understanding of the complex ways in which attitudes may directly or indirectly influence CVD pathogenesis. For example, attitudes may affect CVD risk in several ways, by influencing an individual's 1) adoption of health behaviors, 2) maladaptive stress responding resulting in direct alteration of physiology (i.e., autonomic dysfunction, thrombosis, arrhythmias), 3) development of traditional CVD risk factors, and 4) lack of adherence to therapy in both primary and secondary prevention. We present in Figure 1 a novel, testable conceptual framework for examining the role of attitudes in the pathogenesis of CVD over the lifecourse. The framework integrates research questions and hypotheses from a broad range of disciplines and perspectives. *The overarching hypothesis is that attitudes, which originate in childhood and mature by early adulthood, may ultimately be responsible for a substantial portion of the burden of CVD. It is also conceivable that attitudes are important modifiable targets both for primary and secondary prevention of CVD.* Clinical biobehavioral trials, which have been difficult to conduct, are needed to test interventions to change attitudes in an attempt to reduce CVD risk.

We will first review a commonly-used definition of attitudes, and then address each domain illustrated in our research framework, including: 1) the genetic and environmental determinants of attitudes, 2) the potential mechanisms by which attitudes may affect CVD, 3) the CVD-related health outcomes (i.e., traditional CVD risk factors, subclinical disease, and clinical disease), 4) factors which may modify the observed associations between attitudes and CVD risk, and 5) research questions relating to whether attitudes can be modified for CVD risk reduction. We then conclude each section with a summary of relevant research opportunities.

Definition of Optimism/Pessimism and Cynical Hostility

Trait optimism/pessimism and cynical hostility are prospectively linked to incident CVD and total mortality. Among post-menopausal women, we found that optimism was associated with a favorable profile, and cynical hostility with an unfavorable profile, of baseline risk factors for CVD and mortality. The relationship between optimism/pessimism and cynical hostility and important health outcomes persisted even after adjustment for these baseline differences. Optimists (vs. pessimists) had a 9% lower risk of coronary heart disease and a 14% lower risk of mortality, while most (vs. least) cynical hostile women showed a trend toward increased incident coronary heart disease, as well as a 16% increased risk of mortality over eight years of follow up.(15)

Measurement of Attitudes

While there are several well-established questionnaires which capture the phenotype of optimism/pessimism and cynical hostility, this overview focuses on the Life Orientation Test-Revised(16) and the Cook Medley cynicism subscale.(17) These scales have been studied both separately and together in relation to CVD-related outcomes in men and women. The Life

Orientation Test-Revised (LOT-R)(16) measures optimism/pessimism and contains six items. Item ratings are summed to yield a total score ranging from 6 to 30 (higher scores indicating greater optimism, lower scores indicating greater pessimism). The LOT-R also features subscales for optimism (higher scores indicate higher optimism) and pessimism (higher scores indicate higher pessimism). The cynicism subscale of the Cook-Medley Questionnaire(17) contains 13 true/false items (higher scores indicate greater cynical hostility.)

Conceptual Framework for Researching Attitudes and CVD over the Life-course

I. Genetic and Environmental Determinants of Attitudes

Debate still continues over the determinants of attitudes (Figure 1, Section I). Data from the study of twins suggest that the heritability for optimism and pessimism is moderate.(18) Plomin and colleagues investigated optimism and pessimism subscores (as assessed by the subscales of the LOT-R) among pairs of monozygotic and dizygotic twins reared together and apart. Averages of heritability estimates were 24% for optimism and 29% for pessimism. Genome-wide association studies(GWAS) of neuroticism(19, 20) and other personality traits in the five-dimension model of personality (extraversion, agreeableness, conscientiousness, neuroticism, and openness)(21) have revealed that the few areas of statistically significant genotypic variation (i.e., single nucleotide polymorphisms (SNPs)) explained only a small percentage of phenotypic variation in personality. Together, these findings suggest that multiple genetic loci may each contribute a small degree to personality, and underscore the need for large sample sizes in future studies.

Environmental factors, such as aspects of the physical and social environment, may also influence attitudes. For example, our qualitative work enabled us to examine in depth the familial, cultural, and societal contributions to negative attitudes surrounding obesity and weight loss among adult women. Women reported that many of these attitudes developed during childhood.(22) Heinonen et al found that higher pessimism (LOT-R subscale) was associated with childhood socioeconomic status (SES), while higher optimism (LOT-R subscale) was associated with adult SES.(23) Gene-by-environment ($G \times E$) interactions have yielded clearer explanations of how psychological factors influence health outcomes, as in the case of greater vulnerability to depression observed among carriers of the short (s) allele of the serotonin transporter who also experienced early life adversity.(24) Further advances in behavior genetics now consider that determinants of psychological factors such as personality are best “conceptualized as dynamic systems of gene-environment interplay, p. 1485.” (25) Lifecourse studies are critical to understanding these complex interactions.

Research Opportunities—Future GWAS should not only attempt to identify SNPs associated with optimism/pessimism and cynical hostility, but must also investigate potential gene-by-environment interactions. Relevant environmental factors may include measures of socioeconomic status, education, exposure to environmental toxins (i.e., air pollution) and depressive symptoms. Both qualitative and quantitative studies are needed to investigate the relationship of physical, social and cultural environmental factors on the development of attitudes.

II. Potential Mechanisms Linking Attitudes And Health

Available data suggest that multiple mechanisms underlie the relationship between attitudes and health (Figure 1, Section II). Optimism/pessimism and cynical hostility may influence physiology directly and indirectly. Direct mechanisms include activation of stress response systems with resulting alteration of neural, cardiac, endocrine, and immune physiology, which over time may accelerate CVD pathogenesis and/or increase the risk of sudden cardiac death.

(26–31) Indirect mechanisms include the adoption and/or maintenance of health behaviors such as smoking, and adherence to medical advice and treatment regimens.(32)

Health Behaviors—Health behaviors (including smoking, diet, and physical activity) only partially explain how attitudes may influence CVD. Highly cynical and pessimistic adult individuals tend to report unhealthy behaviors such as smoking, while optimistic individuals tend to report healthy behaviors such as physical activity.(12–15) Furthermore, structural equation modeling has shown that childhood personality traits influence smoking behavior, which in turn influences adult health status.(33) This powerful methodology has not yet been extended to include links with clinical CVD outcomes.

Psychophysiological Processes

Autonomic Dysfunction/HPA Axis: Psychological factors have been shown to be associated with a number of measures of autonomic alterations, underscoring the relationship of optimism and cynical hostility to stress, coping, and social support. For example, compared to pessimists, optimists tend to have healthier social relationships(34) and to cope well with adversity. (35) By contrast, hostility may impair the stress-buffering effects of social support.(36) Over time, these psychophysiological processes may result in more frequent and/or sustained cardiovascular activation. For example, during ambulatory blood pressure monitoring, optimists, as compared to pessimists, display fewer episodes of stress and negative affect, as well as fewer episodes of elevated blood pressure.(27) Similarly, neural imaging studies demonstrate differential activation of brain regions among optimists, as compared to pessimists,(37) and in hostile as compared to nonhostile individuals.(38) In addition, individuals reporting positive affect and optimism have a lower cortisol awakening response (a marker of HPA axis functioning)(10–39–40).

Many studies of risk factors focus on a single measurement in time. However, it is now shown that within-individual variability in physiologic indices (such as non-dipping of blood pressure in the evening, higher nonfasting triglyceride levels, and cardiac autonomic dysfunction), may independently contribute to risk. The association of this within-individual variation with attitudes in response to environmental stressors may be an independent determinant of disease.

Inflammation and Immunosenesence: Studies have demonstrated a link between pessimism and elevated titres of inflammatory markers in combination with shorter telomeres (termed immunosenescence). (41–42) Such physiologic changes are important to CVD pathogenesis, as low grade chronic inflammation has been associated with increased insulin resistance, reduced pancreatic B-cell function, incident diabetes,(43) and overt CVD (independent of traditional CVD risk factors).(44–45) (46–47) Attitudes may also be related to the pathogenesis of CVD via alterations in thrombogenesis (i.e., platelet function, endothelial dysfunction, and activation of clotting factors).(41)

Adherence to Medical Advice: Optimists may adhere to medical advice more readily than pessimists. Tinker et al found that among post-menopausal women who were randomized to a low fat diet, optimists tended to adhere better than pessimists.(32) These findings of lower adherence among pessimists parallel research demonstrating the failure of some depressed individuals to adhere to medical advice and therapy.(48) Failure to adhere to treatment is partially mediated by health beliefs and expectations,(49) and has been described as an “unrecognized cardiac risk factor” leading to poor health outcomes and increased costs.(50) It should be noted that adherence to treatment is only as beneficial as a given treatment. In the age of “evidence-based medicine” it is often tempting to assume that the current standard of care represents the best care, which is not always the case. A classic example is the prescription of bedrest, which was widely recommended for a variety of ailments including acute

myocardial infarction, until randomized trials demonstrated the benefit of early mobilization. (51- 52) As treatments evolve, evidence clearly demonstrates the health benefits of adherence to medical advice and therapy,(53) which has become a priority for the United States and other healthcare systems.(54)

Research Opportunities: Prospective qualitative and quantitative data are needed to understand how people with certain attitudes adopt and maintain health behaviors. One important research question would be whether optimists are more likely than pessimists to change behaviors, such as quitting smoking. Understanding the psychobiological mechanisms underlying the pathogenesis of CVD may be best accomplished through a combination of laboratory and “real life” settings combining self-reported and physiologic data. In addition, future research should address how attitudes may influence adherence to treatment and the associated costs.

III. Health Outcomes

Epidemiologic evidence to date supports a relationship between attitudes and health outcomes (Figure 1, Section III). In this framework, we broadly define health outcomes to incorporate traditional CVD risk factors and subclinical and overt CVD. Traditional CVD risk factors are included here to underscore the lifecourse perspective that attitudes may lead to the development of these risk factors during early adulthood and mid-life. Figure 1 also acknowledges the potential relationship of attitudes to other chronic diseases, such as depression, cancer, and dementia, which may be influenced by many of the same processes involved in the pathogenesis of CVD.

CVD Risk Factors—Because most studies of attitudes and CVD have been conducted in older adults, less is known about how attitudes influence the development of CVD risk factors. For example, the association between depressive symptoms, life stress and the metabolic syndrome was only recently understood to be prospective. (55- 56) Hostility has been shown to predict incident hypertension among young adults. This relationship followed a dose-response increase with increasing quantiles of hostility, and was independent of other psychosocial factors. The most (vs. least) hostile adults demonstrated an 84% increased risk of incident hypertension over 15 years of follow up.(57)

Subclinical and Clinical CVD—Attitudes have also been prospectively related to subclinical and clinical CVD. In healthy middle aged women, hostility has been linked to accelerated carotid intima medial thickness (IMT) progression, and optimism to slower rates of IMT progression.(28- 29) Hostility also predicts coronary artery calcification in young adults.(58) These findings provide indirect evidence of a causal relationship between attitudes and subclinical CVD. The considerable evidence for an association between attitudes and overt clinical CVD outcomes has been discussed earlier. Much of the data has focused on coronary heart disease and mortality, with less emphasis on peripheral vascular disease or cerebrovascular disease.

Other Chronic Diseases—Many of the mechanisms proposed to explain CVD outcomes (health behaviors, biological processes, and adherence factors) may be applicable to other chronic health outcomes. For example, evidence suggests that psychological factors such as “distress-prone personalities” may affect the risk of incident cancer, recurrence, and cancer-related death.(5) In our own work in post-menopausal women, attitudes were associated with cancer-related mortality. Among African-Americans, optimistic (vs. pessimistic) women had a 44% lower risk of dying from cancer. Conversely, the most (vs. least) cynical hostile women showed a 23% higher risk of cancer-related death.(15) Finally, optimism has been prospectively associated with decreased incidence of depression in older adults.(59)

Research Opportunities—More research is needed on how attitudes may influence development of additional CVD risk factors such as diabetes, hypercholesterolemia, and obesity, as well as other measures of subclinical CVD. Epidemiologic studies across the lifecourse are ideally suited to investigate how attitudes affect the multiple steps from CVD risk factors to clinical CVD. Lifecourse studies will also support investigation of possible causal links between attitudes and other chronic illnesses.

IV. Socioeconomic and Racial/ethnic/cultural Factors as Potential Effect Modifiers

Race/ethnicity appears to moderate the relationship between psychological factors and health outcomes. The cultural context in which racial and ethnic constructs exist and are influenced by socioeconomic factors make it easier to understand how cynical attitudes toward others may be both realistic and adaptive in some minority groups with a long history of exposure to discrimination. While hostile or pessimistic cognitions may be an appropriate coping response to an individual's external reality,(60) there appears to be a physiological cost to such responses.(61–63)

Recently, we observed differences in the association of attitudes and health outcomes between African-American and white post-menopausal women.(15) At baseline, the prevalence of pessimism and cynical hostility was higher in African American as compared to white women. Over eight years of follow up, optimism and cynical hostility were associated with larger effects for total and cancer-related mortality in African-American women. However, the study sample was limited by few highly cynical, hostile white women. As noted above, overt clinical disease and mortality may be influenced heavily by health behaviors, which are themselves influenced by racial and ethnic differences. For example, we found that the cultural origins of negative attitudes surrounding obesity and weight loss experiences differed among African-American and white obese women.(22)

Research Opportunities—Physiological reactions to mental phenomena, such as hostile cognitions, may be more pronounced in African-American or minority individuals relative to whites, thus leading to greater amplitude or longer time course of physiologic responding, which over time facilitates greater disease burden. Psychophysiologic studies of attitudes and stress reactivity across racial/ethnic groups are needed to test this hypothesis. The lifecourse perspective is critical to understand the degree to which socioeconomic, racial/ethnic, and cultural factors shape the relationship between attitudes and health outcomes over time.

V. Conclusion and Future Research Directions

We have presented a research framework (Figure 1) for examining the role of attitudes in the pathogenesis of CVD over the lifecourse, and have proposed a number of research opportunities. Three central questions emerge from this framework: 1) Can attitudes be altered to reduce CVD risk, and if so, how? 2) Should interventions target positive or negative attitudes? 3) When is the optimal time to intervene? To effectively address these questions, lifecourse studies, clinical trials, and psychophysiologic studies should proceed in parallel.

Optimism and hostility, like other psychological factors, may be modifiable with cognitive behavioral therapy.(64, 65) Prior bio-behavioral studies have demonstrated success in treating psychological processes such as Type A behaviors(66) and mental stress(67, 68) with resulting improvements in cardiovascular health, but other bio-behavioral studies of depression and social support(69, 70) did not demonstrate clear improvements. Further research is needed to identify therapies to alter attitudes, and to determine which populations may maximally benefit. These studies urge a broader definition of “behavioral interventions”-- to not only target behaviors, but also the attitudes and beliefs which often precede them and which may either sabotage or facilitate successful long term behavior change.(49)

Clinically, it is important to understand if adopting less negative attitudes (e.g., becoming less pessimistic) leads to greater risk reduction than adopting more positive ones. Knowing this will allow interventions to be tailored appropriately. Finally, it is unclear when the delivery of interventions to change attitudes may be most effective. For example, are attitudes malleable only up to a certain point in early adulthood? Or would adults who have already suffered CVD events be more receptive to change their attitudes?

In summary, attitudes may represent a largely untapped avenue to prevent and treat CVD. Decades after the introduction of the biopsychosocial model,⁽⁷¹⁾ these attitudes (49) have yet to be integrated into prevention and treatment efforts. Our framework proposes to determine if such integration will ultimately ameliorate the vast public health burden of CVD.

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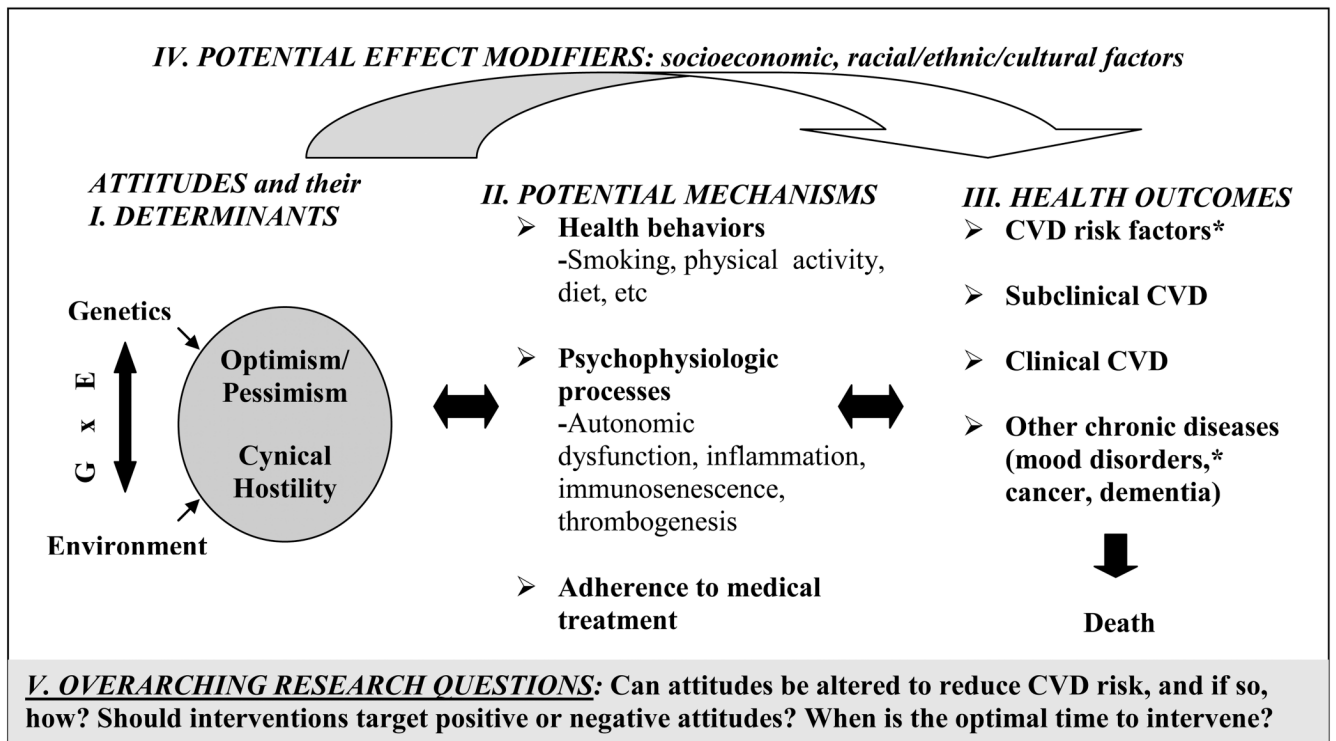


Figure 1.
Conceptual Model for Ongoing Research into Attitudes and Health over the Life-course

- *Note that some factors, such as traditional CVD risk factors and mood disorders (e.g., depression), are included under “Health Outcomes” but may also be in the causal pathway between attitudes and disease.
- Bidirectional arrows between sections underscore the potential for bidirectional relationships between attitudes, intermediate factors, and clinical disease.