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Literature Reviews

# The Relationship Between Coronary Heart Disease (CHD) and Major Depressive Disorder (MDD): Key Mechanisms and the Role of Quality of Life

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## Abstract

Various trials have been conducted evaluating depression management programs for patients with Coronary Heart Disease (CHD). However, to date, the most effective way to manage this co-morbidity in the real world setting remains unclear. To better understand the past successes and failures of previous trials and subsequently develop suitable interventions that target key components of health related quality of life (HRQOL) such as mental, physical and vocational functioning, we first need to understand the mechanisms underpinning the relationship between the two conditions. This paper will draw on the key literature in this field as identified by psychiatric, medical and social sciences databases (Cochrane Central Register of Controlled Trials, PubMed, OVID, Medline) available up to January 2012, with the aim to conduct a narrative review which explores: the aetiological relationship between depression and CHD; its association with HRQOL; the relationship between CHD, depression and vocational functioning; and the impact of depression treatment on these outcomes. Key recommendations are made regarding the management of this prevalent co-morbidity in clinical settings.

*Keywords:* coronary heart disease, depression, health related quality of life, vocational functioning, mechanisms, cardiovascular disease

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## Background

### Coronary Heart Disease (CHD) and Major Depressive Disorder (MDD)

The relationship between coronary heart disease (CHD) and major depressive disorder (MDD) has been investigated extensively over recent decades, as the prevalence of both conditions has risen around the world (Murray & Lopez, 1996). Each condition remains a major contributor to the global burden of disease; CHD is the leading cause of death (World Health Organization, 2004), while MDD (defined as the presence of severely depressed mood persisting for at least two weeks) is the top-ranking cause of disability (World Health Organization, 2008). In Western countries (e.g. Australia), heart disease is the leading cause of disease burden and death, and depression is the top-ranking cause of non-fatal burden (Mathers, Vos, & Stevenson, 1999). Increasing rates of obesity and metabolic syndrome, an ageing population, sedentary lifestyles and chronic life stressors (among other factors) have all contributed to this rising trend.

While depression and heart disease commonly occur in the general population as individual conditions, the two often coexist. For example, depression is highly prevalent among individuals with CHD. This condition has been

estimated to affect one in five hospitalised myocardial infarct (MI) patients (Bush et al., 2005). This co-morbidity is particularly problematic because CHD patients with depressive symptoms are more likely to experience poorer behavioural, psychological and clinical outcomes, including increased likelihood of morbidity and mortality, compared with those who are not depressed. In MI patients, a landmark study by Frasure-Smith, Lesperance, and Talajic (1995) revealed that the presence of depression was significantly related to 18-month cardiac mortality (Frasure-Smith et al., 1995). This finding has since been corroborated; others have demonstrated that even mild to moderate depressive symptoms in post-MI populations are associated with decreased survival (Bush et al., 2001). While it may seem intuitive that individuals who have experienced a life threatening event would report negative emotions such as low mood in the ensuing recovery period, the relationship between cardiovascular disease (CVD) and depression is much more complex; the conditions may act bi-directionally rather than causally. Gaining a better understanding of the nature of these two conditions is of great importance; both in understanding the role of psychosocial factors in the relationship between CVD and depression and for the development of appropriate treatment programs if they are to effectively impact on key components of HRQOL including mental, physical and related functioning outcomes. Therefore, this paper will draw on the key literature in this field as identified by psychiatric, medical and social sciences databases (Cochrane Central Register of Controlled Trials, PubMed, OVID, Medline) available up to January 2012, with the aim to conduct a narrative review which explores: the aetiological relationship between depression and CHD; its association with HRQOL; the relationship between CHD, depression and vocational functioning; and the impact of depression treatment on these outcomes. Key recommendations are made regarding the management of this prevalent co-morbidity in clinical settings.

## Depression as a Risk Factor for CVD

While depression is a prognostic indicator for a range of outcomes in patients with existing CHD including increased risk of heart failure (May et al., 2009), suicide (Larsen, Agerbo, Christensen, Sondergaard, & Vestergaard, 2010), reduced health service utilisation (Frasure-Smith et al., 2000) and medication adherence, depression is also considered an independent risk factor for the onset of heart disease (Van der Kooy et al., 2007). The presence of depressive symptoms before the onset of a cardiac condition appears to increase the risk of cardiac fatality (Whang et al., 2009). In fact, those with a history of depression are four times more likely to have a MI than those without (Pratt et al., 1996). Indeed, there is evidence that the presence of depressed mood in the preceding hour may trigger potentially life-threatening cardiac events (Steptoe, Strike, Perkins-Porras, McEwan, & Whitehead, 2006). For example, by comparing the depressed mood of 295 Acute Coronary Syndrome (ACS) patients two hours prior to ACS symptom onset with the same period 24 hours earlier and with usual levels of depressed mood, Steptoe et al. (2006) found that the odds of ACS were 2.5 following depressed mood, and the relative risk of ACS onset following depressed mood was 4.3 compared with usual levels of mood (Steptoe et al., 2006). A meta-analysis has further demonstrated that the overall risk of depressed but otherwise healthy individuals developing heart disease is 64% higher than for those without depression (Van der Kooy et al., 2007). The bi-directional nature of this co-morbidity would suggest that depression is not purely reactionary to a life threatening cardiac event and the association is, in fact, much more complex.

While the pathways that play a role in the initiation of depression and/or in the pathogenesis of heart disease remain largely undetermined, a number of causal pathways have been proposed. A comprehension of this network is important if we are to understand the overall impact of co-morbid heart disease and depression on key aspects of functioning. In order to provide a more comprehensive review of their association, the aetiological relationships between the two conditions including hypothalamic-pituitary-adrenocortical (HPA) axis, cortisol elevation, heart

rate variability, pro-inflammatory cytokines, platelet activation, genetics, risk factor clustering, medication non-compliance, anger and anxiety, demographics and psychosocial factors will now be explored in more detail.

## Aetiological Relationships Between Depression & Heart Disease

### Hypothalamic-Pituitary-Adrenal (HPA) Axis Hyperactivity and Cortisol Elevation

There is evidence to suggest that depression elicits the same biological responses that contribute to ACS (Steptoe et al., 2006). Firstly, it should be noted that depression has traditionally been associated with hyperactivity of the hypothalamic-pituitary-adrenocortical (HPA) axis, as an extension of the 'fight or flight response.' This term was coined to explain the response of a person to threat, characterised by a discharge of the sympathetic nervous system enabling a person to either fight or flee danger ("Bodily Changes in Pain", 1929). The result is an overstimulation of the sympathetic nervous system, which increases circulating levels of adrenaline, noradrenaline and serum cortisol. This response has the potential to contribute to increased cardiovascular risk through a variety of related risk factors, including those consistent with the metabolic syndrome (high lipid levels, obesity, elevated blood pressure, insulin resistance). It is possible, however, that these physiologic responses may vary for different severities of depression. Abnormal HPA axis function resulting in hypercortisolaemia (high amounts of circulating cortisol) has been associated with severe depression. Evidence suggests that those with MDD exhibit blunted reactivity (Burke, Fernald, Gertler, & Adler, 2005), whereas this process may differ for those with milder cases of depression. It is likely that patients with less severe depression show a reduced cortisol response to stress and have low or normal ambulatory measures of cortisol (Taylor et al., 2006).

Despite these advances in knowledge, the extent to which HPA activity mediates the relationship between CHD and depression (of varying degrees) remains unclear. Disentangling this relationship by observing the effects of depression treatment on HPA activity has failed to provide clarity; this may be because altering HPA activity via psychological interventions is considered particularly difficult to achieve. For example, Taylor et al. (2009) randomised 48 depressed participants with elevated cardiovascular risk factors to a cognitive behavioural therapy (CBT) intervention or a wait list control (WLC) condition to determine whether achieving improvements in mood would ameliorate autonomic dysregulation, HPA dysfunction, typical risk factors and C-reactive protein (CRP). Traditional risk factors (such as lipids and blood pressure), CRP and psychophysiological stress tests were assessed pre- and post-treatment after six months. Results indicated that, while the CBT subjects were significantly less depressed than those assigned to the WLC (post-intervention Hamilton Rating Scale for Depression (HRSD) mean scores were 5.5 versus 15.5, respectively), no significant differences in any of the traditional risk factors or psychophysiological measures (with the exception of triglyceride levels and heart rate) were observed. Further, 20 non-depressed, age and risk-matched controls exhibited no change in the variables measured during the same time (Taylor et al., 2009). Despite limited generalisability due to the small sample, the authors concluded that alterations in mood have limited impact on HPA activity, traditional or atypical risk factors, cortisol or cardiophysiology; a finding which contradicts the conventional wisdom that depression is linked to increased cortisol levels and HPA dysfunction (Gillespie & Nemeroff, 2005). Interestingly, this study did, however, highlight the role of another key mechanism thought to underpin the relationship between heart disease and depression, Heart Rate Variability (HRV).

### Decreased Heart Rate Variability

HRV has been defined as the varying time interval between heart beats. Decreased HRV has previously been associated with a heightened risk of mortality (Dekker et al., 2000). More specifically, along with other alterations of the Autonomic Nervous System (ANS), it has long been considered a fundamental mechanism linking heart

disease and major depression. Changes in the ANS, such as heart rate variability, are commonly linked with cardiac function (Musselman, Evans, & Nemeroff, 1998). It is also well established that depression can impact the autonomic control of the cardiovascular system, thereby impeding cardiac functioning. Typically, depressed patients have been found to experience elevated resting heart rate, even when adjusting for confounding factors such as medication usage. In a review, Carney and Freedland (2009) identified higher resting heart rate as a common feature of both CHD patients with depression, and medically well patients with depression. The mechanism linking the two conditions has been identified as excessive sympathetic activity (or, alternatively, reduced parasympathetic nervous system activity) found in depressed patients, which can promote myocardial ischaemia or other related cardiac conditions. However, research in support of this remains inconsistent. Findings from the Heart and Soul study, comprising a sample of 873 outpatients with stable CHD found little evidence of an association between depression and HRV, leading the authors to question HRV as the fundamental mechanism linking depression and CVD (Gehi, Mangano, Pipkin, Browner, & Whooley, 2005). Several limitations have been associated with this study, however, including its cross-sectional design.

Others have examined the effects of depression treatment on cardiovascular outcomes as another means by which to explore the role of HRV. Studies evaluating the use of psychological interventions in patients with high CVD risk (Carney et al., 2000; Taylor et al., 2009) have demonstrated some benefits; depression treatment can effectively reduce HRV in this population. However, meta-analyses and other studies have revealed that, in spite of the benefits, the effects of psychological therapy do not translate to reduced cardiovascular mortality or morbidity (Rees, Bennett, West, Smith, & Ebrahim, 2004).

**Elevated Plasma Levels of Pro-Inflammatory Cytokines Leading to Atherosclerosis**

Another mechanism thought to be associated with CHD and depression is inflammation. Inflammatory changes are common characteristics of both heart disease and depression. The underlying inflammatory component of ACS is atherosclerosis- the build up of plaque in the arteries. This inflammatory component is also a physiological characteristic associated with depression. For example, patients with depression have been found to exhibit elevated inflammatory markers, including interleukin-6 (IL-6) and CRP (a non-specific measure of inflammation). Moreover, IL-6 and CRP are significant predictors of various outcomes in patients with ACS (Hartford et al., 2007) and other inflammatory conditions (e.g. stroke (Muir, Weir, Alwan, Squire, & Lees, 1999)). Circulating IL-6 induces the release of CRP, as well as other inflammatory markers, making IL-6 a strong independent marker of increased mortality in those with unstable Coronary Artery Disease (CAD) (Lindmark, Diderholm, Wallentin, & Siegbahn, 2001). Interestingly, the presence of high levels of CRP has also been found in non-depressed patients at risk of CVD, as well as in depressed samples without known CVD. A meta-analysis has demonstrated that both CRP and IL-6 are positively associated with depression (CRP: Standardised mean difference (SMD) = 0.15, 95% CI = 0.10,0.21; IL-6: SMD = 0.25, 95% CI = 0.18,0.31, indicating a high level of significance). Sub-group analyses revealed similar results both in clinical and community samples (Howren, Lamkin, & Suls, 2009).

In cardiac patients with co-morbid depression, the association with IL-6 and CRP is complex. Patients with severe post-ACS depressive symptoms exhibit higher levels of CRP and IL-6 than those with mild symptoms. In fact, it has been estimated that patients with the most severe depression record CRP levels > 50% higher than patients in the middle and lowest range (Miller, Freedland, Duntley, & Carney, 2005). It has been argued that such trends are responsible for the effect of atherosclerosis on ACS. As cortisol is responsible for suppressing pro-inflammatory cytokines, the hypo-pituitary response to stress exhibited by these patients is subsequently inadequate, making individuals with depression more susceptible to, or less equipped to respond to stress. A review by von Känel,

Mills, Fainman, & Dimsdale, (2001) highlighted the common pathophysiologic characteristics of depression and stress reactivity. In addition to elevated plasma levels, other common features include increased blood pressure, heart rate, arousal mobilisation of energy stores and elevated risk of ventricular fibrillation. Recently, evidence has emerged suggesting that increased inflammation explains only a small proportion of the relationship between heart disease and depression (Davidson et al., 2009). This is supported by earlier data from the Heart and Soul study which suggest that inflammation is unlikely to explain the adverse CVD outcomes linked to depression in those with heart disease (Whooley et al., 2007). These findings have led researchers to focus on other possible mechanisms linking depression and heart disease such as platelet activation and hypercoagulability.

### Platelet Activation and Hypercoagulability

Increased platelet activation is another common physiological feature of both ACS and depression. There is evidence that depression is associated with increased platelet activation (Morel-Kopp et al., 2009), leading to thrombus formation, vascular damage and an increased risk of a cardiac event. Enhanced platelet reactions are often the result of psychologic stress, and a common characteristic of MI. In a 2001 review comprising 68 articles, von Känel et al. (2001) found that pro-coagulant responses to stressors induced blood clotting (hypercoagulability) in patients with atherosclerosis but not in healthy subjects. More specifically, the authors found that chronic psychosocial stressors, namely job strain and those associated with low socioeconomic status, were found to be related to a hypercoagulable state, which may be responsible for, or contribute to, a depressed state and/or atherosclerosis (von Känel et al., 2001) (the role of demographic and psychosocial factors in the relationship between heart disease and depression will be discussed in further detail later in the review).

However, evidence from large scale studies (e.g. the Heart and Soul study (Gehi et al., 2010)) has challenged the idea that increased platelet activation, a previously putative mechanism, is the underlying mechanism linking depression to CVD. Using a cross-sectional design, Gehi and colleagues (2010) assessed platelet activation in 104 patients with stable CHD ($n$ = 58 with a current episode of major depression and $n$ = 46 without past or current major depression). Platelet activation was measured by plasma concentrations of platelet factor 4 (PF4) and beta-thromboglobulin (β-TG), and by urinary concentrations of 11-dehydro-thromboxane B2 (TBXB2). The authors found no differences in mean levels of PF4, B-TG or TBXB2 in patients with and without major depression, even after adjusting for covariates such as medication and aspirin usage, age, and smoking. The authors concluded that the association between depression and cardiovascular disease is not attributable to platelet activation among patients with stable CHD (Gehi et al., 2010).

### Genetic Factors and Predispositions

It is known that genetic predisposition plays a role in the initiation of depression and in the pathogenesis of heart disease, either independently or via interactions with extraneous factors. First, there is strong evidence that depression has a hereditary component. For example, in the largest sample to date, a Swedish national twin study found that lifetime MDD was heritable (Kendler, Gatz, Gardner, & Pedersen, 2006); first-degree relatives of individuals with MDD were two to three times more likely to develop depression when compared with the first-degree relatives of controls. The mechanism underlying a potential 'depression gene' is thought to be associated with genetic variation related to endothelial dysfunction. Endothelial dysfunction is predictive of depressive symptoms and has been proposed as another mechanism contributing to depression among cardiac patients (McCaffery et al., 2009). Animal models have demonstrated that deficits in endothelial function are associated with recent stress exposure, which persist even after stressful stimuli have been eliminated (Williams, Kaplan, & Manuck, 1993). The role of endothelial dysfunction in the relationship between CVD and depression has been associated with

cytokine release. This is either as a result of, or a contributor to, various disease processes, such as those which occur in hypertension, hypercholesterolaemia or diabetes as well as from environmental factors, such as smoking. These findings highlight the multi-factorial nature of the association between depression and CVD.

### Inter-Relationships Among Psychophysiological Factors

Indeed, it is recognised that, due to the complexity of the two conditions, it is unlikely that any single physiological mechanism can explain their relationship. Rather, it is likely that these mechanisms are inter-related (Grippo & Johnson, 2009). De Jonge et al. (2010) argues that the aetiological relationship between depression and CVD is "best described as a complex system, consisting of many distinct but inter-related and inter-dependent components linked through multiple interconnections and feedback loops" (de Jonge et al., 2010). As examples, serotonin has been identified as a catalyst in platelet activation that leads to atherosclerosis, HPA activity which, due to elevated cortisol levels, can result in immune system changes, and the inflammatory nature of atherosclerosis can, itself, promote decreases in central serotonin.

There is also evidence that key lifestyle factors, such as diet, sedentary lifestyles and alcohol, can precipitate depression, heart disease or both. The influence of such biobehavioural factors will now be explored.

## Factors Mediating the Relationship Between Depression and Heart Disease

### Risk Factor Clustering

The presence of depression and its symptoms, including anhedonia (characterised by apathy and lack of pleasure), helplessness and hopelessness, can inhibit the primary prevention behaviours associated with CVD. That is, individuals with depression may be more likely to report risk factor behaviours that contribute to CHD onset, such as smoking and high alcohol consumption. Hughes, Hatsukami, Mitchell, and Dahlgren (1986) found that the prevalence of smoking was higher in those with mental disorders than in the general population, a finding which has also been observed for alcohol use (Sullivan, Fiellin, & O'Connor, 2005). While there is good evidence that alcohol use can precede the onset of MDD (Hasin & Grant, 2002), individuals with existing depression may use alcohol as a form of self-medication. In fact, depression has been found to act as a mediator between stress and excess alcohol (Camatta & Nagoshi, 1995). Interestingly, alcohol consumption has been closely associated with other risk factors for heart disease such as smoking and dietary habits, particularly in depressed populations. While there is evidence of risk factor clustering in the general population, clustering is more common among people with depression (Verger, Lions, & Ventelou, 2009). Other studies have demonstrated that depression affects other key primary and secondary prevention behaviours such as physical activity. Not only are those experiencing depression as a sole condition more likely to be sedentary than those without, but there is evidence that for cardiac patients, depression impedes exercise regimes after a coronary event (Roshanaei-Moghaddam, Katon, & Russo, 2009). A recent review evaluating 11 studies (representing 20,000 cardiac patients) found post-MI depressive symptoms to be a significant risk factor for a sedentary lifestyle or poor compliance to a physical activity program (Roshanaei-Moghaddam, Katon, & Russo, 2009).

More recently, diet has been identified as a key factor that may mediate the relationship between depression and CVD. Not only are low levels of Omega-3 fatty acids – derived from foods such as fish – associated with increased risk of CHD and high prevalence mental disorders like anxiety, but case-control studies have demonstrated that low Omega-3 levels are related to depression levels after a recent cardiac event (Frasure-Smith, Lesperance, & Julien, 2004). Conversely, CAD patients experiencing depression have been shown to report higher levels of

Polyunsaturated Fatty acids (PUFAs), compared with non-depressed patients. While the protective effects of Omega-3 result from its anti-inflammatory properties (de Jonge et al., 2010), evidence of the full effects of PUFAs remains conflicted. Large scale, international studies have also found no association between depression and Omega-3 deficiencies (Hakkarainen et al., 2004). Despite this, there remains some long standing evidence of the benefits of Omega-3 fatty acids on CVD-related risk factors including reducing blood pressure (Appel, Miller, Seidler, & Whelton, 1993) and triglycerides.

Additionally, the association between depressive symptoms and high risk behaviour related to alcohol, smoking, physical activity and diet may precipitate other medical conditions, such as diabetes mellitus (Dunbar et al., 2008), overweight and obesity, hypertension, and hypercholesterolaemia, all associated with the onset of heart disease. Indeed, the inextricable link between depression, heart disease and lifestyle factors suggests that a multi-faceted approach may be required when developing appropriate depression management or secondary prevention interventions in this patient population.

Evidently, lifestyle as a mediating factor in the relationship between depression and heart disease affects both primary CVD prevention activities, as well as secondary prevention behaviours. Important components of the latter, adherence to cardiac rehabilitation programs and medication regimes can often be compromised by the presence of depression after a heart event, increasing the risk of recurrent CVD events.

### Noncompliance With Cardiac Rehabilitation and Medical Regimens

The World Health Organisation (WHO) considers cardiac rehabilitation "an integral component in the overall management of patients with CVD" (World Health Organization Expert Committee, 1964). While it is recommended that patients who are hospitalised with heart disease as an index admission are referred to early outpatient rehabilitation (Thomas et al., 2007), evidence suggests that patients experiencing depression post-discharge are less likely to complete a cardiac rehabilitation program compared with their non-depressed counterparts (Roblin, Diseker, Orenstein, Wilder, & Eley, 2004), increasing the likelihood of a recurrent CVD event. For these patients, increased attrition levels may be due to the cognitive and/or somatic symptoms of depression including hopelessness, reduced motivation, social exclusion, fatigue and helplessness. In any case, noncompliance to rehabilitation and medical regimes in this population has been identified as "a formidable problem impacting on the failure of risk-reduction therapies, on patient morbidity, and on health care costs" (Burke, Dunbar-Jacob, & Hill, 1997). The presence of depression, has been specifically linked with the under-utilisation of appropriate health services (Frasure-Smith et al., 2000) and poorer self-care, specifically in relation to medication adherence. Kronish and others (2006) found that patients with persistent post-ACS depression differ significantly in their level of adherence to medications prescribed for their cardiac condition, compared with those who did not exhibit depression in hospital (Kronish, et al., 2006). Interestingly, the presence of other negative emotions, such as anxiety, in cardiac patients has recently been shown to be associated with better medication adherence (De Jong et al., 2011). The relationship between depression, anxiety and CVD will now be discussed.

### Anxiety and Anger

Similarly to depression, there appears to be a bi-directional, rather than purely causal, relationship between anxiety and CVD. Anxiety is both highly prevalent in patients with existing CHD (Serber, Todaro, Tilkemeier, & Niaura, 2009) and has been shown to independently predict subsequent CVD events over decades (Janszky, Ahnve, Lundberg, & Hemmingsson, 2010). Anxiety is thought to produce an activation of inflammation, coagulation and fibrinolysis (Geiser et al., 2008), common characteristics of CVD. Given that anxiety and depression often

occur co-morbidly, it is possible that anxiety may mediate the relationship between depression and CVD, or conversely that depression may mediate the relationship between anxiety and CVD. Frasure-Smith and Lesperance have demonstrated substantial overlap in MDD and generalised anxiety disorder (GAD) in patients with stable CAD, concluding that both are associated with prospective coronary events (Frasure-Smith & Lesperance, 2008). These findings have led some to argue that clinically meaningful distinctions of distress in CAD patients need to be considered (de Jonge & Ormel, 2008), if this relationship is to be truly understood, and should be considered in the development of treatment programs for this population.

Further, the role of personality traits, hostility and anger, have been identified as having the potential to alter one's susceptibility to CHD onset. Chida and Steptoe (2009) conducted one of the first quantitative systematic reviews in this area, and found that anger and hostility were significantly correlated with poorer prognosis in CHD patients. If appropriate treatment programs are to be provided for patients after a heart event, the role of negative mood and traits, as well as other psychosocial factors, may need to be taken into consideration.

### Demographic Factors

Depression has been significantly associated with social isolation (Finkelstein, O'Connor, & Friedmann, 2001), chronic life stressors (Kessler, 1997) and maladaptive coping style in both cardiac (Allman, Berry, & Nasir, 2009) and other populations (Benson et al., 2010). It is well established that these factors can be mediated by demographic variables such as gender, social economic status (SES) and income, and have also been linked to cardiovascular risk. For example, a gradient exists between SES and depression risk among individuals with chronic disease (e.g. diabetes (Golden et al., 2007)). This trend has also been observed for those with established CHD; those reporting CHD and low SES are more likely to report depression (Mendes de Leon, 1992). Those belonging to a lower SES may have accentuated cardiac risk factors simply because of their location within the SES hierarchy. Indeed, those belonging to a lower SES bracket are more likely to suffer adverse cardiovascular events than those reporting high SES (Vieweg, Dougherty, & Bernardo, 1998). Additionally, low SES, which can translate to poorer standards of living (for example, less exposure to important resources, fresh and healthy foods, safe exercising environments) can act synergistically with other cardiac risk factors such as overweight and obesity, hyperlipidaemia or hypertension, to accelerate the course of atherosclerosis (Vieweg, Dougherty, & Bernardo, 1998).

### Psychosocial Factors

In a similar manner, psychosocial variables like social isolation and low levels of emotional support have been related to both depression and CHD. Social isolation may adversely affect the origin, course, and outcome of heart disease (King, 1997). Evidence indicates that low social support confers a risk of 1.5 to 2.0 in both healthy individuals and in CHD populations (Lett et al., 2005). This relationship is thought to share the same risk factor pathways as the relationship between SES and onset of CHD. Moreover, recent evidence indicates that the impact of social support on mortality is comparable with other well established risk factors for mortality like smoking (Holt-Lunstad, Smith, & Layton, 2010).

The way in which one perceives their own physical and mental health functioning – their health related quality of life (HRQOL) – is another psychosocial variable that can provide important insights about the relationship between depression and heart disease. Depression is closely linked to HRQOL. In fact, depression has been identified as the single most important, independent predictor of HRQOL (Lane, Carroll, Ring, Beevers, & Lip, 2001) in cardiac populations. The concept of HRQOL has been developed and defined as 'the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient' (Schipper, Clinch, & Olweny, 1996). A concept

traditionally encompassing physical functioning, mental health, social relationships, and happiness or global satisfaction, HRQOL has become of increasing importance in the context of disease populations for several reasons. It is considered both a determinant in the course and onset of some diseases (e.g. diabetes (Tapp, O'Neil, Shaw, Zimmet, & Oldenburg, 2010)) and is considered by some, a significant endpoint for evaluating the impact of a disease or treatment.

The concept of measuring HRQOL, however, is contentious. It has been argued that a quantitative instrument to measure, by its very nature, a qualitative concept is an insufficient means by which to gauge an individual's HRQOL status. In addition to the issue of subjectivity versus objectivity, there is contention surrounding HRQOL as a function-based or satisfaction-based measure. For example, HRQOL measures may be used to assess patients' satisfaction with care or the effects of therapy, or alternatively to assess one's functional status as a result of illness. In spite of these assertions, the importance of investigating the role of HRQOL in disease populations is becoming increasingly apparent. In fact, HRQOL can be predictive of clinical outcomes in patients with chronic disease. Functional components have been used to predict survival and rehospitalisation in chronic disease populations (Osman, Godden, Friend, Legge, & Douglas, 1997). Moreover, HRQOL is of increasing importance in the context of health economics as its derivative can often be used to capture Quality Adjusted Life Years (QALYs), a measure of disease burden encapsulating both quality and quantity of life lived.

The relationship between HRQOL, depression and CHD is a complex one. For example, while it is clear that some depressive symptoms such as hopelessness, sadness and anhedonia impact poorly on self-rated health status and thereby HRQOL status (Ruo et al., 2003), components of HRQOL, like impaired functioning, can also intensify depression. An example of this is that loss of mental and physical functionality is a strong mediator in the association between depression and chronic disease. Those with depression possess a 34% greater attributable risk of functional limitation (95% CI: 24.8-42.7) (Dunlop, Lyons, Manheim, Song, & Chang, 2004). The effect of depression is such that symptoms impact cardiac functioning; depressive symptoms can diminish the functional benefits of interventions aimed at improving cardiac functioning (e.g. Coronary Artery Bypass Grafting (CABG) surgery (Mallik et al., 2005)).

Despite such evidence, surprisingly, the role of HRQOL in populations with co-morbid depression and heart disease remains under-researched (Haas, 2006). Traditionally, research exploring the impact of depression or depression treatment in cardiac populations has focused predominantly on clinical outcomes. The emerging rationale for an increased focus on HRQOL as both a risk factor and an outcome in this area of research, is two-fold. First, investigating the role of HRQOL in cardiac populations has the potential to shed light on the relationship between depression and CVD, where there remains a deficit in our knowledge. Just as treating depression in CVD populations has not been shown to improve CVD-related outcomes or survival (Berkman et al., 2003), neither can it be assumed that treating depression will alter HRQOL status. Recently, it has been argued: "As investigators move forward in attempting to unravel the intriguing relation between depression and coronary disease, it will be important to include quality of life indicators as outcomes of interest" (Haas, 2006). Second, if we are to use our existing understanding of this relationship, with the view to improve patient outcomes, a distinction needs to be made between enhancing quality and quantity of life, which begins with the inclusion of HRQOL indicators. For example, Rumsfeld and Ho (2005) argue for the prioritisation of HRQOL in cardiac research, because for coronary patients, HRQOL outcomes are as important as any potential survival outcomes. Of survival gain, they argue that the benefits are "limited to specific patient subsets and many patients express a desire for quality of life equal to or greater than their desire

for quantity of life" (Rumsfeld & Ho, 2005). The complex relationship between depression, CHD and HRQOL will now be explored in more detail.

## The Relationship Between Depression and Mental and Physical Functioning (HRQOL) in Cardiac Populations

Traditionally, assessing clinical endpoints such as survival and recurrent CVD events has been considered paramount for monitoring both the recovery of cardiac patients and the effectiveness of rehabilitation interventions, including health coaching and depression management programs. Increasingly, HRQOL outcomes have become of interest in cardiac populations, particularly over the past five years, as evidence has emerged to link clinical and HRQOL outcomes, and to expose the detrimental impact of depression on HRQOL (both in cardiac and other medically ill populations (Gaynes, Burns, Tweed, & Erickson, 2002)). For example, physical parameters such as body mass index (BMI) and obesity, as well as psychological conditions such as depression and anxiety directly relate to HRQOL status in medically ill patients (Katz, McHorney, & Atkinson, 2000). In fact, HRQOL has been found to be more strongly and directly related to symptoms of depression than physical components like BMI (Fabricatore, 2005). Similarly in cardiac populations, while clinical parameters like heart failure severity have been found to impair the physical domain of HRQOL, depression significantly impairs both the psychological and physical domains of HRQOL (Faller et al., 2009; Müller-Tasch et al., 2007). Additionally, timing of depression onset in relation to a coronary event can impact upon self-rated mental health (O'Neil, Williams, Stevenson, Oldenburg, Berk, & Sanderson, 2012). 'Early' depression (assessed at an average of six days post-MI) can impact HRQOL long after a cardiac event (Lane, Carroll, Ring, Beevers, & Lip, 2001). It has therefore been concluded that depression is the best predictor of HRQOL in MI populations, and can remain detrimental to HRQOL for the ensuing year, or even longer (Drory, Kravetz, & Hirschberger, 2002).

### The Effects of Depression Treatment on HRQOL of Cardiac Patients

Few studies have evaluated the impact of depression treatment on HRQOL outcomes of MI patients. Through the implementation of the Bypassing the Blues study, Rollman et al. (2009) developed one of the first studies in this area to use HRQOL as a primary endpoint in their evaluation of a telephone-delivered, stepped, collaborative care program to treat depression in CABG patients. Briefly, this depression treatment intervention was proven efficacious in improving mental HRQOL outcomes, as measured by SF-36. No significant differences in physical HRQOL were observed between groups. A recent meta-analysis comprising five studies including the Bypassing the Blues study, provided further evidence of the benefits of depression treatment on mental HRQOL outcomes (O'Neil, Sanderson, Oldenburg, & Taylor, 2011). The authors demonstrated the overall benefits of depression treatment on mental HRQOL in cardiac patients after 6 months (standardized mean difference: -0.29) compared with comparator conditions (placebo/usual care). Significant yet modest effects on physical HRQOL outcomes were also observed (standardized mean difference: -0.14).

Given that changes in depression and HRQOL appear to be synchronous (Atalay et al., 2010; Caruso et al., 2010), it may seem intuitive that alterations in depressive symptoms would lead to subsequent improvements in mental HRQOL. However, further research into the role of HRQOL is required in cardiac populations, not only to corroborate the findings of Rollman et al. (2009), but to identify a depression treatment program most effective for impacting all areas of HRQOL, including physical functioning. While observational studies (Ormel, Oldehinkel, Brilman, vanden Brink, & Leenstra, 1994) have demonstrated an association between alterations in depressive symptoms

and changes in physical functioning status, this relationship is complex. It appears that the link between improved depression and reduced functioning may not contain a direct causal link, rather it is more likely to be bi-directional. As previously discussed, depression could either be the cause or the consequence of reduced functioning or disability (Simon et al., 1998).

### The Effects of Lifestyle Interventions on HRQOL of Cardiac Patients

Depressive symptoms such as declining motivation, apathy and hopelessness have also been linked to increased risk-factor clustering such as reduced physical activity levels, unhealthy dietary patterns, smoking and alcohol (Verger, Lions, & Ventelou, 2009). These behaviours can debilitate physical functioning and also act as mediators in the onset of other medical conditions. Obesity, hyperlipidaemia, hypertension, diabetes, liver disease and cancers may manifest as a result of risk-factor clustering, or the depression itself. In fact, depression is a modifiable risk factor for diabetes (Molife, 2010). This can thereby impact one's physical functioning and level of disability. Physical activity interventions have been found to significantly improve physical HRQOL in medically ill patients, for example, a recent study of cancer survivors evaluated the impact of a strength training program, which demonstrated an effect size of 0.54 on physical HRQOL (De Backer et al., 2007). In cardiac patients, physical HRQOL benefits have been observed, attributable to an educational intervention (Strömberg & Mårtensson, 2003).

In cardiac patients with depression, the anticipated benefits of combining a lifestyle modification intervention targeting physical functioning with depression treatment that targets mental health functioning become apparent. For patients with both depression and a medical illness, Gaynes, Burns, Tweed, and Erickson (2002) recommend "adopting a multidimensional approach to HRQOL rather than treating it unidimensionally". To date, the effectiveness of such a program in cardiac populations is unknown. The benefits of treatment have the potential to go beyond mental and physical functioning to improve other important recovery outcomes, including vocational functioning.

## The Relationship Between Heart Disease, Depression and Vocational Functioning

### Work Resumption

The relationship between depression, heart disease and employment is equally complex. After a cardiac event, depression may act as a barrier to work resumption, or conversely may manifest as a by-product of functional restrictions (e.g. exercise, employment). Specifically, long absences from the workforce after a cardiac event may exacerbate depressive symptoms through feelings of social isolation, reduced productivity or stimulation. Equally, returning to everyday activities like work in the post-MI period may promote feelings of self-worth, self-esteem, social connectivity and productivity.

Evidence suggests that the majority of patients will resume work after a cardiac event (Söderman, Lisspers, & Sundin, 2003). However, those experiencing depression will be slower and less likely to return to work (Schleifer & Macari-Hinson, 1989), and more likely to experience social problems than their non-depressed peers. These longer absences from the workplace could be further exacerbated by a range of other variables including cognitive factors (e.g. illness perceptions, attitudes to work, values), demographic factors (such as age, location) and environmental factors (e.g. family life, job content and stress (physical and emotional)). The role of depression in work resumption after a cardiac event, however, is more complex than this, when considering that depression appears to be present in a significant proportion of cardiac patients prior to their coronary event. It has been reported in one study that 44% of CAD patients have a prior history of diagnostically defined Major Depression, however the exact figure and the precise sequence of onset of the conditions, remains unclear (Freedland, Carney, Lustman,

Rich, & Jaffe, 1992). Since authoritative bodies have identified depression and other psychosocial factors (e.g. stress) as risk factors for heart disease, occupational research in chronic disease populations has become of increasing interest (Bunker et al., 2003). For example, employment factors such as decision latitude, job strain, high effort-reward imbalance and psychological demands have all been identified as predicting CHD morbidity and mortality (Schnall, Landsbergis, & Baker, 1994). In cardiac patients, workplace productivity (including physical, psychological and social functioning of an individual while at work (Ellis, Eagle, Kline-Rogers, & Erickson, 2005)) is a useful measure by which a patient's recovery can be determined. Employment status has also been recognised as an index of the success of rehabilitation efforts (Steger & Chrisholm, 1977), because both physiological and psychological factors influence vocational outcomes, and both are key components of cardiac rehabilitation. Yet, measuring work resumption alone does not capture productivity once back in the workplace.

### Work Performance

Post-MI, patients may be prone to absenteeism (work days lost as a result of illness), presenteeism (attending work while sick at reduced productivity), and lower retention rates. Subjectively, almost one third of cardiac patients feel that their MI has decreased their work performance and output one year after the event (Currell, Urquhart, Wainwright, & Lewis, 2000). In Western countries such as Australia, CHD and depression are the most common conditions related to unemployment (Bishop & Philips, 2009). Moreover, the work-related burden of comorbid depression and CVD at the population level has been demonstrated (O'Neil, Williams, Stevenson, Oldenburg, & Sanderson, 2012).

Of further importance, is that depression can predict the work outcomes of CHD patients (O'Neil, Sanderson, & Oldenburg, 2010). This is of particular relevance as MI survival rates and length of working lives are increasing; indicators of productivity have been identified as "essential in this era of increased attention to resource utilization" (Milani, Lavie, & Cassidy, 1996). The association between depression and the work performance of cardiac patients has been of much interest in light of epidemiologic and other studies (Stewart, Ricci, Chee, Hahn, & Morganstein, 2003; Whooley et al., 2002); depression has been shown to predict poor work outcomes in other chronic disease cohorts (e.g. diabetes) (Von Korff et al., 2005). The current evidence base indicates that depression, disease severity and age may all act as determinants of work performance (Ellis, Eagle, Kline-Rogers, & Erickson, 2005). Epidemiological data have also revealed the long term impact of chronic depression on work outcomes; longitudinal (Druss, Schlesinger, & Allen, 2001), community (Broadhead, Blazer, George, & Tse, 1990) and primary care (Spitzer, 1995) mental health surveys have reinforced that the presence of chronic depression is correlated with persistent work related impairments. Therefore, there has been much interest in developing efficacious, as well as cost-effective approaches to treating depression in psychiatric populations in order to enhance vocational outcomes.

### The Impact of Depression Treatment on Vocational Outcomes of Cardiac Patients

Studies evaluating the key work outcomes of depressed, medically healthy patients have provided promising results; strong links have been identified between enhanced wellbeing and work performance. In fact, it has been argued that mood can improve synchronously with work productivity (Aikens, Kroenke, Nease, Klinkman, & Sen, 2008; WHO, 2001), reduce absenteeism (Keyes & Grzywacz, 2005; Pelled & Xin, 1999) and predict sound job performance (Cropanzano & Wright, 1999).

Others have found no effect; Simon et al. (1998) argue that depression treatment does not translate to direct vocational benefits. The authors did, however, discuss the temporal nature of depression and functioning when

discussing this null finding. They propose a possible delay in visible improvements in occupational functioning compared with depressive symptoms, and subsequently, argue that sustained remission of depression may be necessary to achieve good occupational outcome (Simon et al., 1998). In other words, although depression treatment has the potential to improve work outcomes, the relationship does not appear to be immediately synchronous. Rather, programs designed to treat depression with the view to enhance work productivity and performance may require evidence of long term sustainability if the effect of an intervention is to go beyond altering depression. Of the existing depression treatment programs that have been evaluated in cardiac populations, few, if any, have evaluated the impact on vocational outcomes. Given the relationship between depression, CHD and work, it is likely that treating depression in cardiac patients would improve vocational functioning either directly or as a by-product of enhancing mood outcomes. While there is limited evidence from clinical trials to support this, such an intervention could be personally, clinically and economically advantageous.

## Conclusion

The relationship between depression and CHD is well established. The two conditions often co-exist and there remains compelling evidence that individuals who report this co-morbidity experience a range of poorer outcomes, including worse HRQOL and work outcomes. The biological mechanisms underpinning the relationship between the two conditions were reviewed to provide a context for the role of psychosocial factors, such as HRQOL. While it is clear that key components of HRQOL – mental and physical health functioning – can partially mediate the relationship between depression and CHD, there is much about this relationship that remains unclear. Understanding the burden of co-morbid depression and CVD on HRQOL and work outcomes, as well as the prognostic role of depression after a cardiac event, is crucial for the development of targeted interventions to improve key functioning outcomes of cardiac patients experiencing depression. Evidently, more research regarding suitable treatment approaches is required in this area: "It would be expected that treating depression and anxiety would lead to improved quality of life and reduction in days of restricted activity and days missed from work [in cardiac patients]. This remains to be demonstrated in a clinical trial, however" (Dickens et al., 2006). While a shortcoming of this review is that it is narrative and not systematic, therefore may be subject to bias, the evidence presented in this paper shows some support for depression treatment impacting mental HRQOL and lifestyle interventions, like exercise, benefiting physical HRQOL few programs have applied a multi-faceted approach to treating co-morbid depression in cardiac populations. Combining a depression management program with a lifestyle intervention using a targeted approach, could result in overall HRQOL benefits and subsequently enhance vocational functioning.

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The author declares no competing interests.

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## References

Aikens, J. E., Kroenke, K., Nease, D. E., Jr, Klinkman, M. S., & Sen, A. (2008). Trajectories of improvement for six depression-related outcomes. *General Hospital Psychiatry, 30*(1), 26-31. doi:10.1016/j.genhosppsych.2007.10.003

Allman, E., Berry, D., & Nasir, L. (2009). Depression and coping in heart failure patients: A review of the literature. *The Journal of Cardiovascular Nursing, 24*(2), 106-117.

Appel, L. J., Miller, E. R., III, Seidler, A. J., & Whelton, P. K. (1993). Does supplementation of diet with 'fish oil' reduce blood pressure? A meta-analysis of controlled clinical trials. *Archives of Internal Medicine, 153*(12), 1429-1438. doi:10.1001/archinte.1993.00410120017003

Atalay, H., Solak, Y., Biyik, M., Biyik, Z., Yeksan, M., Uguz, F., . . . Turk, S. (2010). Sertraline treatment is associated with an improvement in depression and health-related quality of life in chronic peritoneal dialysis patients. *International Urology and Nephrology, 42*(2), 527-536. doi:10.1007/s11255-009-9686-y

Bishop, K., & Philips, A. (2009). *Chronic disease and participation in work* (AIHW Report PHE 109). Canberra: Australian Institute of Health and Welfare.

Benson, S., Hahn, S., Tan, S., Janssen, O. E., Schedlowski, M., & Elsenbruch, S. (2010). Maladaptive coping with illness in women with polycystic ovary syndrome. *Journal of Obstetric, Gynecologic, and Neonatal Nursing, 39*, 37-45. doi:10.1111/j.1552-6909.2009.01086.x

Berkman, L. F., Blumenthal, J., Burg, M., Carney, R. M., Catellier, D., Cowan, M. J., . . . Schneiderman, N. (2003). Effects of treating depression and low perceived social support on clinical events after myocardial infarction: The Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial. *Journal of the American Medical Association, 289*(23), 3106-3116. doi:10.1001/jama.289.23.3106

Bodily changes in pain, hunger, fear and rage [Book Review]. (1929). *Archives of Internal Medicine, 44*(6), 908.

Broadhead, W. E., Blazer, D. G., George, L. K., & Tse, C. K. (1990). Depression, disability days, and days lost from work in a prospective epidemiologic survey. *Journal of the American Medical Association, 264*(19), 2524-2528. doi:10.1001/jama.1990.03450190056028

Bunker, S. J., Colquhoun, D. M., Esler, M. D., Hickie, I. B., Hunt, D., Jelinek, M., & Tonkin, A. M. (2003). “Stress” and coronary heart disease: Psychosocial risk factors. *The Medical Journal of Australia, 178*, 272-276.

Burke, H. M., Fernald, L. C., Gertler, P. J., & Adler, N. E. (2005). Depressive symptoms are associated with blunted cortisol stress responses in very low-income women. *Psychosomatic Medicine, 67*(2), 211-216. doi:10.1097/01.psy.0000156939.89050.28

Burke, L. E., Dunbar-Jacob, J. M., & Hill, M. N. (1997). Compliance with cardiovascular disease prevention strategies: A review of the research. *Annals of Behavioral Medicine, 19*(3), 239-263. doi:10.1007/BF02892289

Bush, D. E., Ziegelstein, R. C., Patel, U. V., Thombs, B. D., Ford, D. E., Fauerbach, J. A., … Bass, E. B. (2005). *Post-myocardial infarction depression* (Evidence Report/Technology Assessment No. 123). Retrieved from AHRQ website: http://archive.ahrq.gov/downloads/pub/evidence/pdf/postmidep/midep.pdf

Bush, D. E., Ziegelstein, R. C., Tayback, M., Richter, D., Stevens, S., Zahalsky, H., & Fauerbach, J. A. (2001). Even minimal symptoms of depression increase mortality risk after acute myocardial infarction. *The American Journal of Cardiology, 88*, 337-341. doi:10.1016/S0002-9149(01)01675-7

Camatta, C. D., & Nagoshi, C. T. (1995). Stress, depression, irrational beliefs, and alcohol use and problems in a college student sample. *Alcoholism: Clinical and Experimental Research, 19*(1), 142-146. doi:10.1111/j.1530-0277.1995.tb01482.x

Carney, R. M., & Freedland, K. E. (2009). Depression and heart rate variability in patients with coronary heart disease. *Cleveland Clinic Journal of Medicine, 76*, (Suppl. 2), S13-S17. doi:10.3949/ccjm.76.s2.03

Carney, R. M., Freedland, K. E., Stein, P. K., Skala, J. A., Hoffman, P., & Jaffe, A. S. (2000). Change in heart rate and heart rate variability during treatment for depression in patients with coronary heart disease. *Psychosomatic Medicine, 62*(5), 639-647.

Caruso, R., Rossi, A., Barraco, A., Quail, D., & Grassi, L. (2010). The Factors Influencing Depression Endpoints Research (FINDER) study: Final results of Italian patients with depression. *Annals of General Psychiatry, 9*(1), Article 33.

Chida, Y., & Steptoe, A. (2009). The association of anger and hostility with future coronary heart disease: A meta-analytic review of prospective evidence. *Journal of the American College of Cardiology, 53*(11), 936-946. doi:10.1016/j.jacc.2008.11.044

Cropanzano, R., & Wright, T. A. (1999). A 5-year study of change in the relationship between well-being and job performance. *Consulting Psychology Journal, 51*(4), 252-265. doi:10.1037/1061-4087.51.4.252

Currell, R., Urquhart, C., Wainwright, P., & Lewis, R. (2000). Telemedicine versus face to face patient care: Effects on professional practice and health care outcomes. *Cochrane Database of Systematic Reviews,* Article CD002098. doi:10.1002/14651858.CD002098

Davidson, K. W., Schwartz, J. E., Kirkland, S. A., Mostofsky, E., Fink, D., Guernsey, D., & Shimbo, D. (2009). Relation of inflammation to depression and incident coronary heart disease (from the Canadian Nova Scotia Health Survey [NSHS95] Prospective Population Study). *The American Journal of Cardiology, 103*(6), 755-761. doi:10.1016/j.amjcard.2008.11.035

De Backer, I. C., Van Breda, E., Vreugdenhil, A., Nijziel, M. R., Kester, A. D., & Schep, G. (2007). High-intensity strength training improves quality of life in cancer survivors. *Acta Oncologica, 46*, 1143-1151. doi:10.1080/02841860701418838

De Jong, M. J., Chung, M. L., Wu, J.-R., Riegel, B., Rayens, M. K., & Moser, D. K. (2011). Linkages between anxiety and outcomes in heart failure. *Heart & Lung, 40*(5), 393-404. doi:10.1016/j.hrtlng.2011.02.002

de Jonge, P., & Ormel, J. (2008). Heterogeneity of patients with coronary artery disease and distress and the need to identify relevant subtypes. *Archives of General Psychiatry, 65*, 851-852. doi:10.1001/archpsyc.65.7.851

de Jonge, P., Rosmalen, J. G. M., Kema, I. P., Doornbos, B., van Melle, J. P., Pouwer, F., & Kupper, N. (2010). Psychophysiological biomarkers explaining the association between depression and prognosis in coronary artery patients: A critical review of the literature. *Neuroscience and Biobehavioral Reviews, 35*(1), 84-90. doi:10.1016/j.neubiorev.2009.11.025

Dekker, J. M., Crow, R. S., Folsom, A. R., Hannan, P. J., Liao, D., Swenne, C. A., & Shouten, E. G. (2000). Low heart rate variability in a 2-minute rhythm strip predicts risk of coronary heart disease and mortality from several causes: The ARIC study. *Circulation, 102*(11), 1239-1244. doi:10.1161/01.CIR.102.11.1239

Dickens, C. M., McGowan, L., Percival, C., Tomenson, B., Cotter, L., Heagerty, A., & Creed, F. H. (2006). Contribution of depression and anxiety to impaired health-related quality of life following first myocardial infarction. *The British Journal of Psychiatry, 189*(4), 367-372. doi:10.1192/bjp.bp.105.018234

Drory, Y., Kravetz, S., & Hirschberger, G. (2002). Long-term mental health of men after a first acute myocardial infarction. *Archives of Physical Medicine and Rehabilitation, 83*(3), 352-359. doi:10.1053/apmr.2002.30616

Druss, B. G., Schlesinger, M., & Allen, H. M., Jr. (2001). Depressive symptoms, satisfaction with health care, and 2-year work outcomes in an employed population. *The American Journal of Psychiatry, 158*(5), 731-734. doi:10.1176/appi.ajp.158.5.731

Dunbar, J. A., Reddy, P., Davis-Lameloise, N., Philpot, B., Laatikainen, T., Kilkkinen, A., . . . Janus, E. D. (2008). Depression: An important comorbidity with metabolic syndrome in a general population. *Diabetes Care, 31*(12), 2368-2373. doi:10.2337/dc08-0175

Dunlop, D. D., Lyons, J. S., Manheim, L. M., Song, J., & Chang, R. W. (2004). Arthritis and heart disease as risk factors for major depression: The role of functional limitation. *Medical Care, 42*(6), 502-511. doi:10.1097/01.mlr.0000127997.51128.81

Ellis, J. J., Eagle, K. A., Kline-Rogers, E. M., & Erickson, S. R. (2005). Perceived work performance of patients who experienced an acute coronary syndrome event. *Cardiology, 104*(3), 120-126. doi:10.1159/000087410

Fabricatore, A. N. (2005). Health-related quality of life and symptoms of depression in extremely obese persons seeking bariatric surgery. *Obesity Surgery, 15*(3), 304-309. doi:10.1381/0960892053576578

Faller, H., Störk, S., Schuler, M., Schowalter, M., Steinbüchel, T., Ertl, G., & Angermann, C. E. (2009). Depression and disease severity as predictors of health-related quality of life in patients with chronic heart failure: A structural equation modeling approach. *Journal of Cardiac Failure, 15*, 286-292. doi:10.1016/j.cardfail.2008.10.022

Finkelstein, J., O'Connor, G., & Friedmann, R. H. (2001). Development and implementation of the Home Asthma Telemonitoring (HAT) system to facilitate asthma self-care. In V. L. Patel, R. Rogers, & R. Haux (Eds.), *MEDINFO 2001* (Vol. 84, pp. 810–814). Amsterdam: IOS Press.

Frasure-Smith, N., & Lesperance, F. (2008). Depression and anxiety as predictors of 2-year cardiac events in patients with stable coronary artery disease. *Archives of General Psychiatry, 65*(1), 62-71. doi:10.1001/archgenpsychiatry.2007.4

Frasure-Smith, N., Lespérance, F., Gravel, G., Masson, A., Juneau, M., Talajic, M., & Bourassa, M. G. (2000). Depression and health-care costs during the first year following myocardial infarction. *Journal of Psychosomatic Research, 48*(4-5), 471-478. doi:10.1016/S0022-3999(99)00088-4

Frasure-Smith, N., Lesperance, F., & Julien, P. (2004). Major depression is associated with lower omega-3 fatty acid levels in patients with recent acute coronary syndromes. *Biological Psychiatry, 55*(9), 891-896. doi:10.1016/j.biopsych.2004.01.021

Frasure-Smith, N., Lesperance, F., & Talajic, M. (1995). Depression and 18-month prognosis after myocardial infarction. *Circulation, 91*, 999-1005. doi:10.1161/01.CIR.91.4.999

Freedland, K. E., Carney, R. M., Lustman, P. J., Rich, M. W., & Jaffe, A. S. (1992). Major depression in coronary artery disease patients with vs. without a prior history of depression. *Psychosomatic Medicine, 54*, 416-421.

Gaynes, B. N., Burns, B. J., Tweed, D. L., & Erickson, P. (2002). Depression and health-related quality of life. *The Journal of Nervous and Mental Disease, 190*(12), 799-806. doi:10.1097/00005053-200212000-00001

Gehi, A., Mangano, D., Pipkin, S., Browner, W. S., & Whooley, M. A. (2005). Depression and heart rate variability in patients with stable coronary heart disease: Findings from the Heart and Soul Study. *Archives of General Psychiatry, 62*(6), 661-666. doi:10.1001/archpsyc.62.6.661

Gehi, A., Musselman, D., Otte, C., Royster, E., Ali, S., & Whooley, M. (2010). Depression and platelet activation in outpatients with stable coronary heart disease: Findings from the Heart and Soul Study. *Psychiatry Research, 175*(3), 200-204. doi:10.1016/j.psychres.2009.01.010

Geiser, F., Meier, C., Wegener, I., Imbierowicz, K., Conrad, R., Liedtke, R., . . . Harbrecht, U. (2008). Association between anxiety and factors of coagulation and fibrinolysis. *Psychotherapy and Psychosomatics, 77*, 377-383. doi:10.1159/000151518

Gillespie, C. F., & Nemeroff, C. B. (2005). Hypercortisolemia and depression. *Psychosomatic Medicine, 67*, (Suppl. 1), S26-S28. doi:10.1097/01.psy.0000163456.22154.d2

Golden, S. H., Lee, H. B., Schreiner, P. J., Roux, A. D., Fitzpatrick, A. L., Szklo, M., & Lyketsos, C. (2007). Depression and type 2 diabetes mellitus: The multiethnic study of atherosclerosis. *Psychosomatic Medicine, 69*(6), 529-536. doi:10.1097/PSY.0b013e3180f61c5c

Grippo, A. J., & Johnson, A. K. (2009). Stress, depression and cardiovascular dysregulation: A review of neurobiological mechanisms and the integration of research from preclinical disease models. *Stress (Amsterdam, Netherlands), 12*, 1-21. doi:10.1080/10253890802046281

Haas, D. C. (2006). Depression and disability in coronary patients: Time to focus on quality of life as an end point. *Heart, 92*, 8-10. doi:10.1136/hrt.2005.066035

Hakkarainen, R., Partonen, T., Haukka, J., Virtamo, J., Albanes, D., & Lonnqvist, J. (2004). Is low dietary intake of omega-3 fatty acids associated with depression? *The American Journal of Psychiatry, 161*(3), 567-569. doi:10.1176/appi.ajp.161.3.567

Hartford, M., Wiklund, O., Hultén, L. M., Persson, A., Karlsson, T., Herlitz, J., & Caidahl, K. (2007). C-reactive protein, interleukin-6, secretory phospholipase $A_2$ group IIA and intercellular adhesion molecule-1 in the prediction of late outcome events after acute coronary syndromes. *Journal of Internal Medicine, 262*(5), 526-536. doi:10.1111/j.1365-2796.2007.01862.x

Hasin, D. S., & Grant, B. F. (2002). Major depression in 6050 former drinkers: Association with past alcohol dependence. *Archives of General Psychiatry, 59*(9), 794-800. doi:10.1001/archpsyc.59.9.794

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: A meta-analytic review. *PLoS Medicine, 7*(7), e1000316. doi:10.1371/journal.pmed.1000316

Howren, M. B., Lamkin, D. M., & Suls, J. (2009). Associations of depression with C-reactive protein, IL-1, and IL-6: A meta-analysis. *Psychosomatic Medicine, 71*(2), 171-186. doi:10.1097/PSY.0b013e3181907c1b

Hughes, J. R., Hatsukami, D. K., Mitchell, J. E., & Dahlgren, L. A. (1986). Prevalence of smoking among psychiatric outpatients. *The American Journal of Psychiatry, 143*(8), 993-997.

Janszky, I., Ahnve, S., Lundberg, I., & Hemmingsson, T. (2010). Early-onset depression, anxiety, and risk of subsequent coronary heart disease: 37-year follow-up of 49, 321 young Swedish men. *Journal of the American College of Cardiology, 56*(1), 31-37. doi:10.1016/j.jacc.2010.03.033

Katz, D. A., McHorney, C. A., & Atkinson, R. L. (2000). Impact of obesity on health-related quality of life in patients with chronic illness. *Journal of General Internal Medicine, 15*(11), 789-796. doi:10.1046/j.1525-1497.2000.90906.x

Kendler, K. S., Gatz, M., Gardner, C. O., & Pedersen, N. L. (2006). A Swedish national twin study of lifetime major depression. *The American Journal of Psychiatry, 163*(1), 109-114. doi:10.1176/appi.ajp.163.1.109

Kessler, R. C. (1997). The effects of stressful life events on depression. *Annual Review of Psychology, 48*(1), 191-214. doi:10.1146/annurev.psych.48.1.191

Keyes, C. L. M., & Grzywacz, J. G. (2005). Health as a complete state: The added value in work performance and healthcare costs. *Journal of Occupational and Environmental Medicine, 47*(5), 523-532. doi:10.1097/01.jom.0000161737.21198.3a

King, K. B. (1997). Psychologic and social aspects of cardiovascular disease. *Annals of Behavioral Medicine, 19*(3), 264-270. doi:10.1007/BF02892290

Kronish, I. M., Rieckmann, N., Halm, E. A., Shimbo, D., Vorchheimer, D., Haas, D. C., & Davidson, K. W. (2006). Persistent depression affects adherence to secondary prevention behaviors after acute coronary syndromes. *Journal of General Internal Medicine, 21*(11), 1178-1183. doi:10.1111/j.1525-1497.2006.00586.x

Lane, D., Carroll, D., Ring, C., Beevers, D. G., & Lip, G. Y. H. (2001). Mortality and quality of life 12 months after myocardial infarction: Effects of depression and anxiety. *Psychosomatic Medicine, 63*(2), 221-230.

Larsen, K. K., Agerbo, E., Christensen, B., Sondergaard, J., & Vestergaard, M. (2010). Myocardial infarction and risk of suicide: A population-based case-control study. *Circulation, 122*, 2388-2393. doi:10.1161/CIRCULATIONAHA.110.956136

Lett, H. S., Blumenthal, J. A., Babyak, M. A., Strauman, T. J., Robins, C., & Sherwood, A. (2005). Social support and coronary heart disease: Epidemiologic evidence and implications for treatment. *Psychosomatic Medicine, 67*(6), 869-878. doi:10.1097/01.psy.0000188393.73571.0a

Lindmark, E., Diderholm, E., Wallentin, L., & Siegbahn, A. (2001). Relationship between interleukin 6 and mortality in patients with unstable coronary artery disease. *Journal of the American Medical Association, 286*(17), 2107-2113. doi:10.1001/jama.286.17.2107

Mallik, S., Krumholz, H. M., Lin, Z. Q., Kasl, S. V., Mattera, J. A., Roumains, S. A., & Vaccarino, V. (2005). Patients with depressive symptoms have lower health status benefits after coronary artery bypass surgery. *Circulation, 111*(3), 271-277. doi:10.1161/01.CIR.0000152102.29293.D7

Mathers, C., Vos, T., & Stevenson, C. (1999). *The burden of disease and injury in Australia* (AIWH Report PHE 17). Canberra: Australian Institute of Health and Welfare.

May, H. T., Horne, B. D., Carlquist, J. F., Sheng, X., Joy, E., & Catinella, A. P. (2009). Depression after coronary artery disease is associated with heart failure. *Journal of the American College of Cardiology, 53*(16), 1440-1447. doi:10.1016/j.jacc.2009.01.036

McCaffery, J. M., Duan, Q. L., Frasure-Smith, N., Barhdadi, A., Lespérance, F., Théroux, P., . . . Dubé, M.-P. (2009). Genetic predictors of depressive symptoms in cardiac patients. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics, 150B*(3), 381-388. doi:10.1002/ajmg.b.30824

Mendes de Leon, C. F. (1992). Anger and impatience/irritability in patients of low socioeconomic status with acute coronary heart disease. *Journal of Behavioral Medicine, 15*(3), 273-284. doi:10.1007/BF00845356

Milani, R. V., Lavie, C. J., & Cassidy, M. M. (1996). Effects of cardiac rehabilitation and exercise training programs on depression in patients after major coronary events. *American Heart Journal, 132*(4), 726-732. doi:10.1016/S0002-8703(96)90304-X

Miller, G. E., Freedland, K. E., Duntley, S., & Carney, R. M. (2005). Relation of depressive symptoms to C-reactive protein and pathogen burden (cytomegalovirus, herpes simplex virus, Epstein-Barr virus) in patients with earlier acute coronary syndromes. *The American Journal of Cardiology, 95*(3), 317-321. doi:10.1016/j.amjcard.2004.09.026

Molife, C. (2010). Is depression a modifiable risk factor for diabetes burden? *Journal of Primary Care & Community Health, 1*(1), 55-61. doi:10.1177/2150131909359633

Morel-Kopp, M. C., McLean, L., Chen, Q., Tofler, G. H., Tennant, C., Maddison, V., & Ward, C. M. (2009). The association of depression with platelet activation: Evidence for a treatment effect. *Journal of Thrombosis and Haemostasis, 7*(4), 573-581. doi:10.1111/j.1538-7836.2009.03278.x

Muir, K. W., Weir, C. J., Alwan, W., Squire, I. B., & Lees, K. R. (1999). C-reactive protein and outcome after ischemic stroke. *Stroke, 30*(5), 981-985. doi:10.1161/01.STR.30.5.981

Müller-Tasch, T., Peters-Klimm, F., Schellberg, D., Holzapfel, N., Barth, A., Jünger, J., . . . Herzog, W. (2007). Depression is a major determinant of quality of life in patients with chronic systolic heart failure in general practice. *Journal of Cardiac Failure, 13*, 818-824. doi:10.1016/j.cardfail.2007.07.008

Murray, C. J. L., & Lopez, A. D. (1996). *The global burden of disease: A comprehensive assessment of mortality and disability from disease, injuries, and risk factors in 1990 and projected to 2020.* Cambridge, MA: Harvard University Press.

Musselman, D. L., Evans, D. L., & Nemeroff, C. B. (1998). The relationship of depression to cardiovascular disease: Epidemiology, biology, and treatment. *Archives of General Psychiatry, 55*(7), 580-592. doi:10.1001/archpsyc.55.7.580

O'Neil, A., Sanderson, K., & Oldenburg, B. (2010). Depression as a predictor of work resumption following myocardial infarction (MI): A review of recent research evidence. *Health and Quality of Life Outcomes, 8*(1), Article 95. doi:10.1186/1477-7525-8-95

O'Neil, A., Sanderson, K., Oldenburg, B., & Taylor, C. B. (2011). Impact of depression treatment on mental and physical health-related quality of life of cardiac patients: A meta-analysis. *Journal of Cardiopulmonary Rehabilitation and Prevention, 31*(3), 146-156.

O'Neil, A., Williams, E. D., Stevenson, C. E., Oldenburg, B., Berk, M., & Sanderson, K. (2012). Co-morbid cardiovascular disease and depression: Sequence of disease onset is linked to mental but not physical self-rated health: Results from a cross-sectional, population-based study. *Social Psychiatry and Psychiatric Epidemiology, 47*, 1145-1151. doi:10.1007/s00127-011-0421-5

O'Neil, A., Williams, E. D., Stevenson, C. E., Oldenburg, B., & Sanderson, K. (2012). Co-morbid depression is associated with poor work outcomes in persons with cardiovascular disease (CVD): A large, nationally representative survey in the Australian population. *BMC Public Health, 12*, Article 47.

Ormel, J., Oldehinkel, T., Brilman, E., vanden Brink, W., & Leenstra, A. S. (1994). Outcome of anxiety and depression in general health care: A three-wave 3.5-year study of psychopathology, disability and life stress. *European Neuropsychopharmacology, 4*(3), 168-169. doi:10.1016/0924-977X(94)90015-9

Osman, I. M., Godden, D. J., Friend, J. A., Legge, J. S., & Douglas, J. G. (1997). Quality of life and hospital re-admission in patients with chronic obstructive pulmonary disease. *Thorax, 52*(1), 67-71. doi:10.1136/thx.52.1.67

Pelled, L. H., & Xin, K. R. (1999). Down and out: An investigation of the relationship between mood and employee withdrawal behavior. *Journal of Management, 25*(6), 875-895. doi:10.1177/014920639902500605

Pratt, L. A., Ford, D. E., Crum, R. M., Armenian, H. K., Gallo, J. J., & Eaton, W. W. (1996). Depression, psychotropic medication, and risk of myocardial infarction: Prospective data from the Baltimore ECA follow-up. *Circulation, 94*(12), 3123-3129. doi:10.1161/01.CIR.94.12.3123

Rees, K., Bennett, P., West, R., Smith, G. D., & Ebrahim, S. (2004). Psychological interventions for coronary heart disease. *Cochrane Database of Systematic Reviews, 2004*(2), Article CD002902. doi:10.1002/14651858.CD002902.pub2

Roblin, D., Diseker, R. A., III, Orenstein, D., Wilder, M., & Eley, M. (2004). Delivery of outpatient cardiac rehabilitation in a managed care organization. *Journal of Cardiopulmonary Rehabilitation and Prevention, 24*, 157-164. doi:10.1097/00008483-200405000-00004

Rollman, B. L., Belnap, B. H., LeMenager, M. S., Mazumdar, S., Houck, P. R., Counihan, P. J., . . . Reynolds, C. F. (2009). Telephone-delivered collaborative care for treating post-CABG depression: A randomized controlled trial. *Journal of the American Medical Association, 302*, 2095-2103. doi:10.1001/jama.2009.1670

Roshanaei-Moghaddam, B., Katon, W., & Russo, J. (2009). The longitudinal effects of depression on physical activity. *General Hospital Psychiatry, 31*(4), 306-315. doi:10.1016/j.genhosppsych.2009.04.002

Rumsfeld, J. S., & Ho, P. M. (2005). Depression and cardiovascular disease: A call for recognition. *Circulation, 111*(3), 250-253. doi:10.1161/01.CIR.0000154573.62822.89

Ruo, B., Rumsfeld, J. S., Hlatky, M. A., Liu, H., Browner, W. S., & Whooley, M. A. (2003). Depressive symptoms and health-related quality of life: The heart and soul study. *Journal of the American Medical Association, 290*(2), 215-221. doi:10.1001/jama.290.2.215

Schipper, H., Clinch, J. J., & Olweny, C. L. M. (1996). *Quality of life studies: Definitions and conceptual issues.* New York: Lippincott-Raven.

Schleifer, S. J., & Macari-Hinson, M. M. (1989). The nature and course of depression following myocardial infarction. *Archives of Internal Medicine, 149*(8), 1785-1789. doi:10.1001/archinte.1989.00390080059014

Schnall, P. L., Landsbergis, P. A., & Baker, D. (1994). Job strain and cardiovascular disease. *Annual Review of Public Health, 15*(1), 381-411. doi:10.1146/annurev.pu.15.050194.002121

Serber, E. R., Todaro, J. F., Tilkemeier, P. L., & Niaura, R. (2009). Prevalence and characteristics of multiple psychiatric disorders in cardiac rehabilitation patients. *Journal of Cardiopulmonary Rehabilitation and Prevention, 29*(3), 161-168.

Simon, G. E., Katon, W., Rutter, C., VonKorff, M., Lin, E., Robinson, P., . . . Russo, J. (1998). Impact of improved depression treatment in primary care on daily functioning and disability. *Psychological Medicine, 28*(3), 693-701. doi:10.1017/S0033291798006588

Söderman, E., Lisspers, J., & Sundin, Ö. (2003). Depression as a predictor of return to work in patients with coronary artery disease. *Social Science & Medicine, 56*(1), 193-202. doi:10.1016/S0277-9536(02)00024-2

Spitzer, R. L. (1995). Health-related quality of life in primary care patients with mental disorders: Results from the PRIME-MD 1000 study. *Journal of the American Medical Association, 274*(19), 1511-1517. doi:10.1001/jama.1995.03530190025030

Steger, H. G., & Chrisholm, S. (1977). Predicting adjustment of heart patients with the cardiac adjustment scale. *Journal of Clinical Psychology, 33*(3), 735-739. doi:10.1002/1097-4679(197707)33:3<735::AID-JCLP2270330327>3.0.CO;2-M

Steptoe, A., Strike, P. C., Perkins-Porras, L., McEwan, J. R., & Whitehead, D. L. (2006). Acute depressed mood as a trigger of acute coronary syndromes. *Biological Psychiatry, 60*(8), 837-842. doi:10.1016/j.biopsych.2006.03.041

Stewart, W. F., Ricci, J. A., Chee, E., Hahn, S. R., & Morganstein, D. (2003). Cost of lost productive work time among US workers with depression. *Journal of the American Medical Association, 289*, 3135-3144. doi:10.1001/jama.289.23.3135

Strömberg, A., & Mårtensson, J. (2003). Gender differences in patients with heart failure. *European Journal of Cardiovascular Nursing, 2*, 7-18. doi:10.1016/S1474-5151(03)00002-1

Sullivan, L. E., Fiellin, D. A., & O'Connor, P. G. (2005). The prevalence and impact of alcohol problems in major depression: A systematic review. *The American Journal of Medicine, 118*(4), 330-341. doi:10.1016/j.amjmed.2005.01.007

Tapp, R. J., O'Neil, A., Shaw, J. E., Zimmet, P. Z., & Oldenburg, B. F. (2010). Is there a link between components of health-related functioning and incident impaired glucose metabolism and type 2 diabetes? *Diabetes Care, 33*(4), 757-762. doi:10.2337/dc09-1107

Taylor, C. B., Conrad, A., Wilhelm, F. H., Strachoswksi, D., Khaylis, A., Neri, E., . . . Spiegel, D. (2009). Does improving mood in depressed patients alter factors that may affect cardiovascular disease risk? *Journal of Psychiatric Research, 43*(16), 1246-1252. doi:10.1016/j.jpsychires.2009.05.006

Taylor, C. B., Conrad, A., Wilhelm, F. H., Neri, E., DeLorenzo, A., Kramer, M. A., . . . Spiegel, D. (2006). Psychophysiological and cortisol responses to psychological stress in depressed and nondepressed older men and women with elevated cardiovascular disease risk. *Psychosomatic Medicine, 68*(4), 538-546. doi:10.1097/01.psy.0000222372.16274.92

Thomas, R. J., King, M., Lui, K., Oldridge, N., Piña, I. L., Spertus, J., . . . Whitman, G. R. (2007). AACVPR/ACC/AHA 2007 performance measures on cardiac rehabilitation for referral to and delivery of cardiac rehabilitation/secondary prevention services. *Circulation, 116*(14), 1611-1642. doi:10.1161/CIRCULATIONAHA.107.185734

Van der Kooy, K., van Hout, H., Marwijk, H., Marten, H., Stehouwer, C., & Beekman, A. (2007). Depression and the risk for cardiovascular diseases: Systematic review and meta analysis. *International Journal of Geriatric Psychiatry, 22*(7), 613-626. doi:10.1002/gps.1723

Verger, P., Lions, C., & Ventelou, B. (2009). Is depression associated with health risk-related behaviour clusters in adults? *European Journal of Public Health, 19*(6), 618-624. doi:10.1093/eurpub/ckp057

Vieweg, W. V. R., Dougherty, L. M., & Bernardo, N. L. (1998). Mental stress and the cardiovascular system part VI: Chronic mental stress and cardiovascular disease: Psychosocial factors. *Medical Update for Psychiatrists, 3*(3), 82-85. doi:10.1016/S1082-7579(98)00005-3

von Känel, R., Mills, P. J., Fainman, C., & Dimsdale, J. E. (2001). Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: A biobehavioral pathway to coronary artery disease? *Psychosomatic Medicine, 63*(4), 531-544.

Von Korff, M., Katon, W., Lin, E. H. B., Simon, G., Ciechanowski, P., Ludman, E., . . . Young, B. (2005). Work disability among individuals with diabetes. *Diabetes Care, 28*(6), 1326-1332. doi:10.2337/diacare.28.6.1326

Whang, W., Kubzansky, L. D., Kawachi, I., Rexrode, K. M., Kroenke, C. H., Glynn, R. J., . . . Albert, C. M. (2009). Depression and risk of sudden cardiac death and coronary heart disease in women: Results from the nurses' health study. *Journal of the American College of Cardiology, 53*(11), 950-958. doi:10.1016/j.jacc.2008.10.060

Whooley, M. A., Caska, C. M., Hendrickson, B. E., Rourke, M. A., Ho, J., & Ali, S. (2007). Depression and inflammation in patients with coronary heart disease: Findings from the Heart and Soul Study. *Biological Psychiatry, 62*(4), 314-320. doi:10.1016/j.biopsych.2006.10.016

Whooley, M. A., Kiefe, C. I., Chesney, M. A., Markovitz, J. H., Matthews, K., & Hulley, S. B. (2002). Depressive symptoms, unemployment, and loss of income. *Archives of Internal Medicine, 162*, 2614-2620. doi:10.1001/archinte.162.22.2614

Williams, J. K., Kaplan, J. R., & Manuck, S. B. (1993). Effects of psychosocial stress on endothelium-mediated dilation of atherosclerotic arteries in cynomolgus monkeys. *The Journal of Clinical Investigation, 92*(4), 1819-1823. doi:10.1172/JCI116772

World Health Organization. (2001). *World Health Report 2001: Mental health: New understanding, new hope*. Geneva: Author.

World Health Organization. (2004). *The Atlas of heart disease and stroke*. Geneva: World Health Organisation.

World Health Organization. (2008). *The global burden of disease 2004 update*. Geneva: World Health Organisation.

World Health Organization Expert Committee. (1964). *Rehabilitation of patients with cardiovascular disease: Report of a WHO expert committee* (WHO Technical Report Series, 270). Geneva: World Health Organization.

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