

Approximately 20% of older adults with cardiovascular disease (CVD) experience significant depression. Further, in a pattern consistent with the general adult population, women with CVD have double the rates of depression compared to men. Among older men and women with CVD, depression is associated with poorer cardiac outcomes, although patterns of depressive symptoms appear to differ between men and women. Treatment approaches include traditional modalities, namely psychotherapy and pharmacotherapy. Additional recommendations involve emphasizing adherence to prescribed medical and behavioural health regimens, fostering social support, and increasing referrals to cardiac rehabilitation programs as medically appropriate.

**Key words:** depression, gender differences, cardiovascular disease, myocardial infarction, mortality

## Cardiovascular Disease and Depression in Older Men and Women

Adrienne H. Kovacs, PhD, CPsych, Behaviour Cardiology, Division of Cardiology, University Health Network, Toronto, ON.

### Introduction

Cardiovascular disease (CVD) is most accurately conceptualized as a disease with a biopsychosocial impact. An understanding of the experience of living with CVD is incomplete without consideration of psychosocial factors and the complex interaction among psychological, social, and biomedical variables. Depression is the psychological factor that has received the greatest attention, both as a potential antecedent and correlate of CVD.

It is important to distinguish between “depression” and “depressive symptoms.” Many studies identify “depression” with self-report measure of depressive symptoms, such as the Beck Depression Inventory (BDI). This approach is contrasted with a diagnosis of a mood disorder (e.g., major depressive disorder), which typically requires a formal diagnostic interview. The methodological approach to defining depression is important because incidence rates may differ as a function of the assessment method. In a comprehensive review of studies investigating the incidence of post-MI depression, Thombs and colleagues<sup>1</sup> found that major depression was identified in approximately 20% of individuals in studies that employed a structured interview methodology but ranged between 8% and 31% using various self-report measures, including the BDI. For many individuals with CVD, depressive symptoms represent an understandable transient reaction to an unexpected negative cardiac diagnosis or event, such as a myocardial infarction (MI). For a sizeable minority, how-

ever, post-MI depressive symptoms are of a duration and severity consistent with a major depressive disorder. In fact, approximately 20% of individuals experience significant post-MI depression.<sup>1</sup>

An age of 65 or older, living alone, and being female are known risk factors for depression among post-MI individuals.<sup>2,3</sup> Further, it is important to consider possible gender differences in order to enhance our understanding of the link between CVD and depression.

### Gender Differences in Rates of Depression among Adults with CVD

Irrespective of cardiac disease, the rate of depression is twice as high among females compared to males.<sup>4</sup> This consistent finding likely reflects an interaction of biological and environmental influences. This difference in the rate of depression between men and women is also observed among adults with CVD. Specifically, women are approximately twice as likely to experience post-MI depression as men.<sup>3,5</sup>

The patterns of post-MI depression, however, may differ between men and women. For example, Bjerkeset and colleagues<sup>6</sup> found that women had greater risk of depressive symptoms during the first two years post-MI, followed by reduced risk. Conversely, men's risk of depressive symptoms increased after the two-year period. The authors suggested that “women tend toward an initial and time-limited psychological reaction and adaptation to the event,” whereas “men seem less able to cope with the long-term consequences of the MI.”<sup>6</sup>

**Table 1:** Strategies to Maximize Psychosocial and Biomedical Outcomes for Older Adults with Cardiovascular Disease

Proactively discuss the increased likelihood of depressive symptoms among older adults with CVD; anticipate higher rates among women.

Inquire about pre-CVD depression, a risk factor for post-MI depression.

Identify mental health professionals in the community to refer depressed patients who are motivated and able to pursue treatment.

Consider antidepressant medication for depressed patients favourable to a pharmacological approach.

Discuss the importance of adherence to prescribed medication regimens and heart-healthy lifestyle recommendations (for optimal physical and psychological outcomes).

Inquire about the individual's marital status and social support; discuss options for increased social interaction.

Discuss the physical and mental health benefit of physical activity and consider a referral to cardiac rehabilitation; problem-solve barriers to regular exercise.

### The Impact of Depression on Mortality of Men and Women with CVD

An increased risk of cardiac mortality among depressed individuals with CVD has been observed in both men and women.<sup>5,7</sup> In their prospective study, Frasure-Smith and colleagues administered the BDI to evaluate depressive symptoms in hospitalized MI patients.<sup>5</sup> Logistic regression was performed in order to predict one-year cardiac mortality from BDI scores. Results indicated that the rates of cardiac death were significantly higher in both men and women with elevated BDI scores (i.e., scores of 10 or greater) with an odds ratio of 3.29 for women and 3.05 for men, suggesting that the rate of cardiac mortality was three times higher among depressed adults. Similarly, Grace and colleagues examined the impact of elevated BDI scores on five-year all-cause mortality in 750 older adults (mean age of 62 years) who had been hospitalized for an MI or unstable angina.<sup>7</sup> After adjusting for a number of factors, including disease severity, they concluded that depressive symptomatology at the time of hospital admission was a significant predictor of five-year mortality. Increased mortality among adults with CVD is not limited to the post-MI

experience. For example, elevated depression in adults who undergo coronary artery bypass graft surgery is also associated with poorer cardiac outcomes.<sup>8</sup>

The results of two meta-analyses published in 2004 support the contention that depression is associated with poorer cardiac outcome. In one meta-analysis, it was determined that, among CVD patients at least two years after diagnosis, the mortality risk of depressed individuals was more than double that of nondepressed individuals.<sup>9</sup> In a second meta-analysis, it was concluded that the risk of mortality among depressed individuals post-MI was 2 to 2.5 times higher than nondepressed individuals.<sup>10</sup> Proposed mechanisms for the link between depression and increased cardiac mortality include behavioural factors (e.g., nonadherence to heart-healthy lifestyle recommendations) and physiological pathways (e.g., lowered heart rate variability and altered inflammatory responses).

The data, however, are not unequivocal, and it is possible that the link between depressive symptoms and cardiac mortality is decreasing over time. In one systematic review, the authors concluded that more recent studies were less

likely to show a relationship between post-MI depression and mortality.<sup>11</sup> A recent prospective study of 494 individuals with MI found that those with elevated post-MI depression were more likely to experience a cardiovascular event during the 2.5-year follow-up period, although the impact of depression was less than in earlier studies.<sup>12</sup> It will be interesting to follow the future wave of research studies to determine whether the relationship between depressive symptoms and cardiac outcomes is weakening over time, perhaps as a reflection of increasing clinical attention to the impact of depressive symptoms on quality of life and cardiac mortality.

Empirical investigation of depressive symptoms among older adults with CVD is generally supportive of a link with cardiac mortality. Romanelli and colleagues<sup>13</sup> studied the incidence of depression in post-MI patients who were 65 years of age and older. The risk of dying was 27% among depressed older adults and 7% among nondepressed older adults. Among post-MI patients 65 and older, increased mortality has been observed even with minimal symptoms of depression.<sup>2</sup>

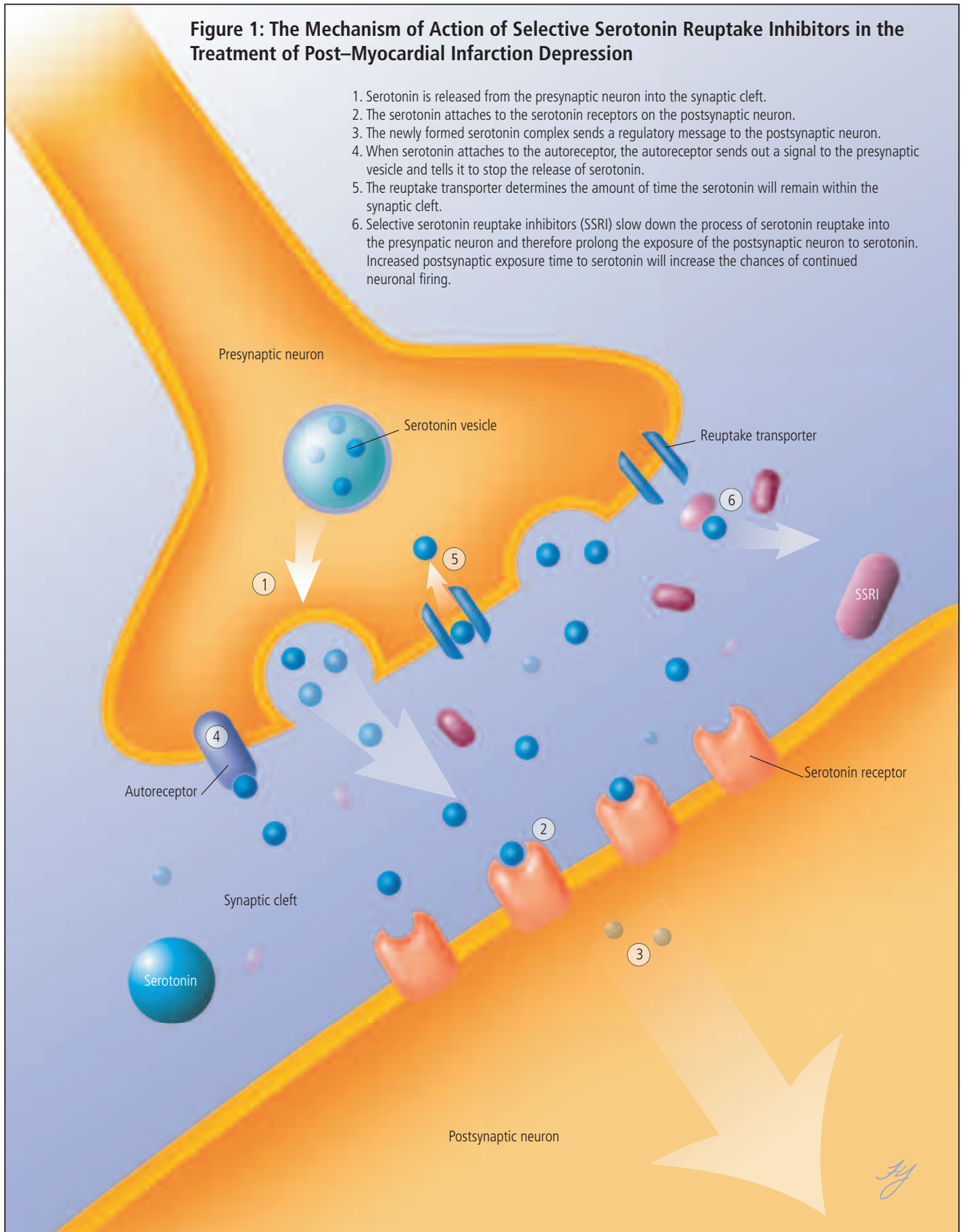
Any conclusions regarding the interaction between depressive symptoms, cardiac outcomes, and gender are preliminary. The results of a study of older Finnish adults suggest that depression may be a predictive factor for total and cardiac mortality among older women with CVD but not among older men.<sup>14</sup> Frasure-Smith and colleagues<sup>5</sup> found that although the rate of depression was higher among women than men, there was not a higher mortality rate among women. There appear to be different correlates of depression among men and women post-MI. One team of researchers found that men were more likely to be depressed if they lived alone and were unmarried, whereas depressive symptoms among women were lower if they lived alone and were unmarried.<sup>5</sup>

### Implications for Treatment

An interdisciplinary working group of health professionals and researchers

**Figure 1: The Mechanism of Action of Selective Serotonin Reuptake Inhibitors in the Treatment of Post-Myocardial Infarction Depression**

1. Serotonin is released from the presynaptic neuron into the synaptic cleft.
2. The serotonin attaches to the serotonin receptors on the postsynaptic neuron.
3. The newly formed serotonin complex sends a regulatory message to the postsynaptic neuron.
4. When serotonin attaches to the autoreceptor, the autoreceptor sends out a signal to the presynaptic vesicle and tells it to stop the release of serotonin.
5. The reuptake transporter determines the amount of time the serotonin will remain within the synaptic cleft.
6. Selective serotonin reuptake inhibitors (SSRI) slow down the process of serotonin reuptake into the presynaptic neuron and therefore prolong the exposure of the postsynaptic neuron to serotonin. Increased postsynaptic exposure time to serotonin will increase the chances of continued neuronal firing.



### Key Points

Approximately 20% of individuals experience significant depression subsequent to myocardial infarction (MI).

Known risk factors for depression include being of age 65 or older, living alone, and being female.

Women are approximately twice as likely to experience post-MI depression as men.

Several studies have produced data that support the contention that depression is associated with poorer cardiac outcome; however, data are not unequivocal.

Proposed mechanisms for the link between depression and increased cardiac mortality include behavioural factors (e.g., nonadherence to a heart-healthy lifestyle) and physiological pathways (e.g., lowered heart rate variability and altered inflammatory responses).

Health practitioners working with older adults with CVD should emphasize adherence to prescribed medical and behavioural health regimens; encourage physical activity and refer patients to cardiac rehabilitation programs when medically appropriate; and address the affected individual's level of social support.

assembled in 2004 to discuss the assessment and treatment of depression among individuals with CVD.<sup>15</sup> The group's report emphasized that randomized clinical trials are necessary to determine whether effective treatment for depression among individuals with CVD might improve both psychosocial and biomedical outcomes. Unfortunately, data from two large randomized trials<sup>16,17</sup> do not offer strong support for this expectation that management of depressive symptoms might reduce cardiac mortality. The absence of a strong and consistent link between depressive symptom reduction and improved cardiac outcome does not imply that we should reduce our focus on depressive symptoms. Researchers remain committed to commencing randomized controlled trials evaluating the efficacy and safety of psychotherapeutic and pharmacological approaches to treating depression in adults with CVD. Strategies to maximize psychosocial and biomedical outcomes among CVD patients are predicted in Table 1.

There is undertreatment of mental health concerns among post-MI patients with elevated depression scores.<sup>5</sup> Screening for depression in cardiac settings has been recommended<sup>7</sup> but would likely only be beneficial in settings in which there are available resources to follow positive screens with an accurate diagno-

sis as well as to provide effective treatment and follow-up.<sup>18</sup>

Depression may be treated with psychotherapy, pharmacotherapy, or a combination of both. Selection of the treatment approach(es) depends upon a number of factors including language and patient preferences, availability of mental health providers, and financial considerations. The aforementioned working group on the assessment and treatment of depression in patients with cardiovascular disease<sup>15</sup> concluded that selective serotonin reuptake inhibitors (SSRIs) have an improved safety profile for individuals with CVD compared to tricyclics and monoamine oxidase inhibitors (SSRI mechanism of action is represented in Figure 1). Treatments proven effective for depression among individuals who do not have CVD (SSRIs, psychotherapy, and a combined pharmacological-psychotherapeutic approach) are likely to be effective at treating depression in those with CVD.<sup>15</sup> Gorman<sup>4</sup> reminds readers of the ongoing debate as to whether women and men respond differently to antidepressant medications. The duration of treatment can range from relatively brief to longer-term, and typically reflects a number of factors including treatment modality, response to treatment, and whether an individual experienced pre-CVD depression.

Older adults and women are two identified subgroups at greater risk for elevated depressive symptoms following a cardiac event.<sup>2,3</sup> Therefore, health care professionals are strongly encouraged to pay particular attention to older and/or female cardiac patients. In addition to traditional approaches to mental health (i.e., psychotherapy, pharmacotherapy), health practitioners working with older adults with CVD are encouraged to consider the following three factors to maximize biopsychosocial outcomes: one, emphasizing adherence to prescribed medical and behavioural health regimens; two, encouraging physical activity and considering referrals to cardiac rehabilitation programs (when medically appropriate); and three, addressing social support.

### Adherence

The results of a meta-analysis conducted in 2000 suggest that depressed individuals are three times more likely to be non-adherent with medical treatment.<sup>19</sup> Among post-MI patients 65 years and older, depression has been associated with poorer adherence to prescribed medications and heart-healthy lifestyle behaviours, such as diet and exercise.<sup>13</sup> For this reason, it has been hypothesized that strategies to improve adherence might positively alter cardiac outlook among depressed older adults post-MI.<sup>13</sup>

### Physical Activity

Exercise can be an effective strategy to improve mood. For this reason, cardiac rehabilitation may assist with both physical and psychological recovery from a cardiac event. Research has indicated that older men and women experience physical and psychological benefits from cardiac rehabilitation.<sup>20,21</sup> Unfortunately, women are less likely to participate in cardiac rehabilitation programs<sup>20</sup> and depressed women are more likely to drop out of cardiac rehabilitation programs.<sup>22</sup>


### Social Support

Social support and social isolation have been highlighted for their effect on depression among older adults with CVD.<sup>23</sup> Compared to males, female post-



MI patients report lower levels of social support.<sup>24</sup> Perceived social support appears to buffer the impact of depression on cardiac mortality, such that higher social support is associated with a weaker relationship between depressive symptoms and mortality.<sup>25</sup> Living alone is a risk factor for post-MI symptoms of depression,<sup>3</sup> and women are typically widowed before men. Therefore, encouragement of strategies that enhance the social support networks of older adults, and particularly women (e.g., social gatherings, peer support groups), is recommended.

## Conclusion

It is worth re-emphasizing that 20% of adults with CVD experience significant depression, which is in turn linked to poorer cardiac outcomes. Risk factors for depression among this medical population include older age and being female. Therefore, older adults with CVD, particularly older women, represent a particularly vulnerable group. When contemplating treatment strategies, health care providers are encouraged to consider traditional approaches (psychotherapy and pharmacotherapy) in addition to maximizing adherence to medical recommendations, physical activity, and social support. 

No competing financial interests declared.

## References

- Thombs BD, Bass EB, Ford DE, et al. Prevalence of depression in survivors of acute myocardial infarction: review of the evidence. *J Gen Intern Med* 2006;21:30–8.
- Bush DE, Ziegelstein RC, Tayback M, et al. Even minimal symptoms of depression increase mortality risk after acute myocardial infarction. *Am J Cardiol* 2001;88:337–41.
- Spijkerman TA, van den Brink RHS, Jansen JHC, et al. Who is at risk of post-MI depressive symptoms? *J Psychosom Res* 2005;58:425–32.
- Gorman JM. Gender differences in depression and response to psychotropic medication. *Gend Med* 2006;3:93–109.
- Frasure-Smith N, Lesperance F, Juneau M, et al. Gender, depression, and one-year prognosis after myocardial infarction. *Psychosom Med* 1999;61:26–37.
- Bjerkese O, Nordahl HM, Mykletun A, et al. Anxiety and depression following myocardial infarction: gender differences in a 5-year prospective study. *J Psychosom Res* 2005;58:153–61.
- Grace SL, Abbey SE, Kapral MK, et al. Effect of depression on five-year mortality after an acute coronary syndrome. *Am J Cardiol* 2005;96:1179–85.
- Burg MM, Benedetto MC, Rosenberg R, et al. Presurgical depression predicts medical morbidity 6 months after coronary artery bypass graft surgery. *Psychosom Med* 2003;65:111–18.
- Barth J, Schumacher M, Herrmann-Lingen C. Depression as a risk factor for mortality in patients with coronary heart disease: a meta-analysis. *Psychosom Med* 2004;66:802–13.
- van Melle JP, de Jonge P, Spijkerman TA, et al. Prognostic association of depression following myocardial infarction with mortality and cardiovascular events: a meta-analysis. *Psychosom Med* 2004;66:814–22.
- Sorensen C, Friis-Hasche E, Haghfelt T, et al. Postmyocardial infarction in relation to depression: a systematic critical review. *Psychother Psychosom* 2005;74:69–80.
- Spijkerman TA, van den Brink RHS, May JF, et al. Decreased impact of post-myocardial infarction depression on cardiac prognosis? *J Psychosom Res* 2006;61:493–99.
- Romanelli JR, Fauerbach JA, Bush DE, et al. The significance of depression in older adults after myocardial infarction. *J Am Geriatr Soc* 2002;50:817–22.
- Sirkka-Liisa K. Depression and coronary heart mortality in older coronary heart disease patients. *Int J Geriatr Psychiatry* 2004;19:804–5.
- Davidson KW, Kupfer DJ, Bigger JT, et al. Assessment and treatment of depression in patients with cardiovascular disease: National Heart, Lung, and Blood Institute Working Group report. *Ann Behav Med* 2006;32:121–6.
- Berkman LF, Blumenthal J, Burg M, et al. Effects of treating depression and low perceived social support on clinical events after myocardial infarction: The Enhancing Recovery in Coronary Heart Disease Patients (ENRICH) Randomized Trial. *JAMA* 2003;289:3106–16.
- Glassman AH, O'Connor CM, Califf RM, et al. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002;299:701–9.
- United States Preventative Services Task Force. Screening for depression: recommendations and rationale. *Ann Intern Med* 2002;136:760–4.
- DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000;24:2101–7.
- Ades PA, Waldmann ML, Polk DM, et al. Referral patterns and exercise response in the rehabilitation of female coronary patients aged greater than or equal to 62 years. *Am J Cardiol* 1992;69:1422–5.
- Lavie CJ, Milani R. Benefits of cardiac rehabilitation in the elderly. *Chest* 2004;126:1010–12.
- Sanderson BK, Bittner V. Women in cardiac rehabilitation: outcomes and identifying risk for dropout. *Am Heart J* 2005;150:1052–8.
- Arthur HM. Depression, isolation, social support, and cardiovascular disease in older adults. *J Cardiovasc Nurs* 2006;21:52–7.
- Mendes de Leon CF, Dilillo V, Czajkowski S, et al. Psychosocial characteristics after acute myocardial infarction: the ENRICH pilot study. Enhancing recovery in coronary heart disease. *J Cardiopulm Rehabil* 2001;21:353–61.
- Frasure-Smith N, Lesperance F, Gravel G, et al. Social support, depression, and mortality during the first year after myocardial infarction. *Circulation* 2000;101:1919–24.