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Post-Myocardial Infarction Depression

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to release.

AHRQ expects the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome comments on this evidence report. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to **epc@ahrq.gov**.

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Structured Abstract

Context: To improve outcomes of patients with myocardial infarction (MI), a number of treatments are typically recommended, including medications, revascularization procedures, behavior and lifestyle changes, and cardiac rehabilitation. Co-existent depression may influence the recovery of patients with MI in a number of important ways reviewed in this report.

Objectives: Depression is manifested by a number of symptoms, including depressed mood, diminished interest or pleasure, and low self-esteem. These symptoms may occur in patients recovering from an MI and have the potential to adversely impact recovery. In this report, we examined the evidence addressing the following questions: 1) In patients with acute MI, what is the prevalence of depression during the initial hospitalization? 2) What percentage of patients with post-MI depression continue to have depression one or more months after initial hospital discharge? 3) What is the association of post-MI depression with outcomes or with surrogate markers of cardiac risk, independent of other predictors of post-MI outcomes? 4) Do post-MI patients with depression have better outcomes with depression treatment compared to those without depression treatment? 5) What are the performance characteristics (e.g., sensitivity, specificity, reliability and predictive value) of instruments or methods that are used to screen for depression following an acute MI? 6) Does the use of cardiac treatment for patients with acute MI differ for those with and without depression?

Data Sources: The Johns Hopkins University Evidence-based Practice Center (EPC) team searched electronic databases for literature published through March 2004. The team identified additional articles by hand-searching the table of contents of 16 relevant journals for appropriate citations from October 2003 to April 2004, by querying experts, and by reviewing references in pertinent review articles identified during abstract review and in eligible articles during the article review process.

Study Selection: Paired investigators reviewed the abstracts of identified citations to select studies that addressed the questions, reported on human subjects, and were written in English. Some questions had additional eligibility criteria. During the abstract review process, emphasis was placed on identifying all articles that could have original data that might address the questions.

Data Collection and Analysis: Paired reviewers confirmed the relevance of each article to the research questions and abstracted data in a serial manner; the quality of each eligible study was assessed independently by each reviewer.

Main Results: The search identified 86 articles with original data that addressed the questions. Results were as follows: 1) The evidence indicated that the prevalence of major depression is about 20 percent in patients hospitalized for MI and that of potentially significant symptoms of depression an additional 10 to 47 percent. 2) Few studies reported the prevalence of depression in patients at the time of the hospitalization and then re-assessed those same patients at follow-

up, but the studies indicated that most patients with depression during the initial MI hospitalization remain depressed 1 to 4 months later. 3) Post-MI depression is associated with a significantly increased risk of subsequent death, and of cardiac re-admission and poor quality of life during the first year. There is limited evidence that post-MI depression is associated with surrogate markers of cardiac risk. 4) In post-MI patients with depression, psychosocial intervention improves depression but not other outcomes. In post-MI patients with depression, selective serotonin re-uptake inhibitors (SSRIs) improve depression and some surrogate markers of cardiac risk, but no studies of sufficient power address the question of whether this treatment improves survival. 5) There is insufficient data to adequately assess the performance characteristics of instruments or methods used to screen for depression during the initial MI hospitalization, but most commonly used screening instruments or rating scales have adequate sensitivities and specificities when used within 3 months after initial hospitalization. 6) Patients with post-MI depression exhibit lower adherence to prescribed medications and secondary prevention measures compared to those without depression. The literature was too limited or heterogeneous to make conclusions about whether there are significant differences in cardiac medication prescription or cardiac procedure use in post-MI patients based on the presence or absence of depression.

Conclusions: Evidence is consistent that in patients with MI, depression is common at the time of the hospitalization and persists for at least several months after hospital discharge without treatment. Post-MI depression is associated with a significantly increased risk of subsequent death, and of cardiac re-admission and poor quality of life during the first year. Strong evidence exists to indicate that both psychosocial interventions and SSRIs are effective in improving depression in MI survivors, but there is no evidence that either decreases mortality or cardiac events. Although it is not clear whether the frequency of prescription of cardiac medications or use of cardiac procedures is different based on the presence of depression, there is relatively strong evidence that those with post-MI depression have lower adherence to prescribed medications and secondary prevention measures than those without depression.

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Post-Myocardial Infarction Depression

Summary

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Introduction

Major depression is common among patients recovering from a myocardial infarction (MI).[1-5] Additionally, clinically significant depressive symptoms are present in other patients whose symptom severity or duration does not meet established criteria for a diagnosis of major depression.[5] Over the last decade, increasing evidence suggests that in addition to its effect on quality of life, post-MI depression also deserves attention because of a reported relation to increased morbidity and mortality.[5-8]

This evidence report reviews the studies that have examined depression or depressive symptoms in patients after an MI and focuses on the prevalence, clinical significance, treatment, and methods of evaluating this condition. A number of studies have evaluated various aspects of post-MI depression including prevalence,[1-4,9-27] its association with mortality, [5-10,20,28-36] and major adverse events,[25,26, 31,37-39] and treatment.[10,40-47] This report addresses the following key questions regarding post-MI depression.

1. In patients diagnosed with and hospitalized for acute MI, what is the prevalence of depression during initial hospitalization for MI? Depression was defined as symptoms of depression meeting established threshold criteria by psychiatric interview or validated questionnaire.

1a. What is the prevalence of depression during initial hospitalization for an acute MI, with and without a history of previous depression as reported by study investigators?

2. What percentage of patients with post-MI depression continue to have depression (or depressive symptoms) one or more months after initial hospital discharge?

3. What is the association of post-MI depression with outcomes independent of other predictors of post-MI outcomes? Post-MI outcomes include:
   - Clinical outcomes—total mortality, cardiac mortality, MI, resuscitated arrest, stroke, arrhythmias, and revascularization.
   - Quality of life.
   - Utilization of health care services—readmission, total hospital days, and cost of care. Potential predictors include demographic and clinical characteristics of patients that have been reported to be associated with the risk of post-MI outcomes.

3a. What is the association of post-MI depression with surrogate markers of cardiac risk independent of other predictors of post-MI outcomes? Surrogate markers of disease severity include: heart rate variability, platelet reactivity, and markers of inflammation such as C-reactive protein.

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4. Do post-MI patients with depression have better outcomes with depression treatment compared to those without depression treatment? Depression treatment includes all interventions intended to have specific impact on depression, such as antidepressants, cognitive behavioral therapy, inter-personal therapy, psychosocial support, and cardiac rehabilitation.
   4a. Do outcomes differ with or without improvement in depression for post-MI patients with depression that do receive depression treatment?
   4b. Do outcomes differ with or without improvement in depression for post-MI patients with depression that do not receive depression treatment?
5. What are the performance characteristics (e.g., sensitivity, specificity, reliability, and predictive value) of instruments or methods that are used to screen for depression (or depressive symptoms) following an acute MI?
   5a. What are the performance characteristics of instruments or methods that are used to screen for depression (or depressive symptoms) following an acute MI, during hospitalization?
   5b. What are the performance characteristics of instruments or methods that are used to screen for depression (or depressive symptoms) following an acute MI, within three months after hospitalization?
6. Does the use of cardiac treatment for patients with acute MI differ for those with and without depression? Cardiac treatment includes: revascularization (angioplasty or bypass surgery), angiotensin converting enzyme (ACE) inhibitors, beta blockers, statins, antiplatelet agents, or other treatments recommended by the American Heart Association or the American College of Cardiology.

Methods

The Johns Hopkins University Evidence-based Practice Center (EPC) assembled a team including clinicians and researchers from diverse specialties including cardiology, psychiatry, general internal medicine, and cardiac rehabilitation. The EPC team then recruited eight technical experts to provide input regarding the choice of key questions. The expert review panel consisted of a representative from the EPC's partner organization, the American Academy of Family Physicians, as well as investigators active in post-MI depression research including those from cardiology, psychiatry and psychology, nursing, cardiac rehabilitation, and representatives of private and governmental payers.

Literature Search

The EPC team performed a comprehensive search that included electronic and hand searching. In March 2004, we searched the following electronic databases: MEDLINE®, the Cochrane CENTRAL® Register of Controlled Trials (Issue 1, 2003), the Cochrane Database of Methodology Reviews (CDMR®), the Cumulative Index of Nursing and Allied Health Literature (CINAHL®), the Psychological Abstracts (PsycINFO®), and EMBASE®.

Hand searching for possibly relevant articles was performed by three techniques. First, the EPC team identified 16 journals that we thought were most likely to contain relevant studies and scanned the table of contents of each of these journals for relevant citations from October 2003 to April 2004. Second, we reviewed references cited in recent review articles for inclusion. Third we examined the reference lists of eligible articles for additional articles that might be relevant

Two members of the EPC team independently reviewed the abstracts identified by the search to exclude those that did not meet the eligibility criteria. Primary studies were eligible if they addressed one of the key questions, included original human data, were not case reports, and were written in the English language. Individual key questions had additional exclusion criteria. When two reviewers agreed that an abstract was not eligible, it was excluded from further review.

To focus the evidence report on the studies that would be most valuable in addressing the key questions, we used the following additional eligibility criteria:

- For key question 4 we excluded studies that did not include a concurrent comparison group.
- For key question 5, we excluded studies that did not use a validated reference standard.

Review Process

Paired reviewers assessed the quality of each eligible article. Differences between the paired reviewers were resolved by face-to-face discussion. The reviewers assigned points for the quality of the studies based on information about the representativeness of the patients included in the study, the potential for bias and confounding, the description of the intervention or evaluation, the adequacy of followup, and the appropriateness of the statistical methods. The score for each category of study quality was the percentage of the total points available in each category for that study, and could range from zero to 100 percent.

One reviewer in each pair was the primary reviewer who abstracted data from the article. The second reviewer confirmed the accuracy of the first reviewer's work.

Results

Key Question 1

In patients diagnosed with and hospitalized for acute MI what is the prevalence of depression during initial hospitalization for MI?

- Twenty-five articles met criteria for inclusion in this review.[1-5,9-27,48]
- Articles were published between 1986 and 2004.
- Eight studies used a structured clinical interview,[1-3,5,10,16,17,49] and 17 used a validated questionnaire. [4,5,9,11-15,18-25,50]
- Major depression was reported in about one of every five patients hospitalized for an MI. The reported prevalence of potentially significant symptoms of depression varied widely (range 10 to 47 percent).
- In general, the reported prevalence of potentially significant symptoms of depression was higher when it was based on a Beck Depression Inventory (BDI)[5, 9,18-23,50] than when based on a Hospital Anxiety and Depression Scale (HADS)[12-15]; this may be because the BDI includes somatic symptoms that may overlap with MI symptoms, whereas the HADS does not.

Key Question 1a. What is the prevalence of depression during initial hospitalization for an acute MI, with and without a history of previous depression as reported by study investigators?

There was insufficient data to address this question.

Key Question 2

What percentage of patients with post-MI depression continues to have depression (or depressive symptoms) one or more months after initial hospital discharge?

- We found 22 articles that met criteria for inclusion in this review.[2,12,14,18-20,22,23,25,26,38,51-61]
- Nine of the 22 used a standardized clinical interview to diagnose depression.[10,26,51-57]
- Only three studies reported the prevalence of depression in patients during the MI hospitalization and then specifically re-assessed and reported the prevalence in these same patients at followup.[2,18,23]
- Based on these three studies, most patients with depression during the initial MI hospitalization continue to have depression 1 to 4 months later.

Key Question 3

What is the association of post-MI depression with outcomes independent of other predictors of post-MI outcomes?

- Sixteen studies addressed the relationship of post-MI depression and mortality.[5-10,20,28-36]
- Mortality has been assessed as early as 4 months[5] and as late as 10 years after MI.[7]
- The evidence indicates that post-MI depression is associated with a significantly increased risk of death.
- A single study indicated that post-MI depression is associated with increased cardiac re-admission in the first year after MI.[39]
- Six studies reported on cardiac events in relationship to post-MI depression.[25,26,31,37-39] The three studies reporting a positive relationship between post-MI depression and cardiac events[31,37,39] were generally larger than the three studies finding no relationship[25,26,38] suggesting that the latter may have had insufficient power to detect differences if they, in fact, were present.
- Depression during the initial hospitalization was related to poor quality of life in the first year after MI.[13,30,59,62]

Key Question 3a. What is the association of post-MI depression with surrogate markers of cardiac risk independent of other predictors of post-MI outcomes?

- Three studies examined the association of post-MI depression with heart rate variability, platelet activity, and inflammatory markers (one study for each surrogate marker).[57,63,64]
- All three studies reported surrogate markers of increased risk in patients with post-MI depression, even after adjustment for covariates.

Key Question 4

Do post-MI patients with depression have better outcomes with depression treatment compared to those without depression treatment?

- Twelve studies, 11 of which were randomized controlled trials, addressed this question.[10,40-47,65-67] The studies were published between 1991 and 2003.
- In post-MI patients with depression, psychosocial intervention improves depression but not other outcomes.[10,44]

- In post-MI patients with depression, selective serotonin reuptake inhibitors improve depression and some surrogate markers of cardiac risk, but no studies of sufficient power address the question of whether this treatment improves survival.[45,46,65,66]

Key Question 4a. Do outcomes differ with or without improvement in depression for post-MI patients with depression that do receive depression treatment?

There was insufficient data to address this question.

Key question 4b. Do outcomes differ with or without improvement in depression for post-MI patients with depression that do not receive depression treatment?

There was insufficient data to address this question.

Key Question 5

What are the performance characteristics (e.g., sensitivity, specificity, reliability, and predictive value) of instruments or methods that are used to screen for depression (or depressive symptoms) following an acute MI?

- We found six studies published between 1968 and 1988 meeting criteria to address this issue.[14,18,56,68-70]
- Of the six studies, four were from Europe,[14,56,68,70] one from Canada[18] and one from the United States.[69]
- All included studies reported exclusively on post-MI populations.
- None of the instruments reported had been normalized specifically for post-MI patients.
- The BDI tended to be more sensitive to lower levels of depressive symptoms but less sensitive to more severe depression compared to the HADS and the Symptom Checklist-90 Depression scale.

Key question 5a. What are the performance characteristics of instruments or methods that are used to screen for depression (or depressive symptoms) following an acute MI during hospitalization?

There was insufficient data to address this question.

Key question 5b. What are the performance characteristics of instruments or methods that are used to screen for depression (or depressive symptoms) following an acute MI, within three months after hospitalization?

There was insufficient data to address this question.

Key Question 6

Does the use of cardiac treatment for patients with acute MI differ for those with and without depression?

- Nine studies published between 1982 and 2004 met criteria for review on this question. [23,26,37,50,71-75]
- Four studies compared prescribed discharge medications and were inconsistent in their findings: United States and United Kingdom[50,71] studies suggested decreased prescriptions of beta-blockers and aspirin, while European[26] and Canadian[23] studies found no difference.
- Three studies compared adherence to prescribed medications and lifestyle modifications and consistently found decreased adherence among depressed patients.[71-73]
- Two studies compared use of cardiac procedures and reached divergent conclusions about the use of procedures in post-MI patients.[23,37]
- Two studies assessed completion of cardiac rehabilitation but had insufficient numbers to reach conclusions about the influence of depression on completion of rehabilitation.[74,76]

Discussion

Key Question 1

Major depression is reported in about one of every five patients hospitalized for MI. This proportion is fairly consistent among the eight studies that used a structured clinical interview to establish this diagnosis. The reported prevalence of potentially significant symptoms of depression varies more widely (range 10 to 47 percent). This wide range of reported prevalence rates appears to be due almost exclusively to differences in measurement instruments used, and even to differences in threshold criteria applied from study to study when the same instrument was used. In general, the reported prevalence of potentially significant symptoms of depression is higher when this diagnosis is based on a BDI score of 10 or higher than when it is based on a HADS score of either 8 or higher or 11 or higher. This difference may be attributed to the BDI's inclusion of somatic symptoms that may overlap with MI symptoms, whereas the HADS does not include somatic symptoms and is designed for use in hospitalized patients.

Additional studies also are needed to define the most clinically-relevant measure of depression during the initial MI hospitalization. Studies are needed to determine the clinical or demographic factors that are associated with post-MI depression.

Key Question 2

Although 22 studies reported the prevalence of depression in patients 1 month or longer after initial hospital discharge, only

three reported the prevalence of depression in patients during the MI hospitalization and then specifically reassessed and reported the prevalence of depression in these same patients at followup. These studies suggest that most patients (60 to 70 percent) with depression during the initial MI hospitalization continue to have depression (or depressive symptoms) 1 to 4 months later.

Additional studies are needed that assess depression (or depressive symptoms) in groups of patients during the initial hospitalization and at various time points after MI. Studies of patients who are reassessed for depression at multiple time points post-MI are also needed.

Key Question 3

Sixteen studies evaluated the relationship between depression, measured shortly after an acute MI, and subsequent mortality. Studies have assessed this relationship as early as 4 months post-MI and as late as 10 years post-MI. Despite the facts that various measures of depression have been used, that different subgroups of depressed patients have been evaluated, and that different post-MI survival times have been assessed, the weight of the evidence is strikingly consistent. Overall, the evidence supports the notion that post-MI depression is associated with a significantly increased risk for subsequent death, whether by cardiac or other causes. Depression appears to be associated with about a 3-fold increased risk of cardiac mortality per se based on at least three studies that addressed cardiac mortality in a total of almost 2,000 patients.[39,77,78] Depression during the initial hospitalization is associated with poor quality of life in the first year after an MI.

During the first year after MI, depression during the initial MI hospitalization has been found to be inversely related to physical quality of life, social quality of life of women, sexual activity and satisfaction among men, return to work of employed men, and to physical, psychological, and social health and function. Limitations of the above mentioned studies included the variety of diagnostic instruments used to assess depression; the lack of agreement on what aspects of quality of life are of greatest import or how to measure included studies; the degree to which potential confounders were adequately considered; and the absence of data in early post-MI time points.

Additional studies are needed to determine the major cause(s) of mortality among depressed post-MI patients. Additional studies also are needed to determine whether patients with depression are at higher risk for malignant arrhythmias than comparable post-MI patients without depression.

Key question 3a. A small amount of evidence suggests that post-MI patients with depression have alterations in autonomic function as reflected by decreased heart rate variability, increased platelet activity, and increased levels of soluble adhesion molecule 4. These studies suggest that the risk associated with post-MI depression could be transmitted by multiple biological pathways.

Additional studies are needed to elucidate the mechanism(s) responsible for increased mortality in patients with post-MI depression. Particular emphasis should be placed on surrogate markers which have been previously associated with increased risk without regard to depression, including markers for sudden death including heart rate variability, T-wave alternans, etc, and inflammatory markers including C-reactive protein, interleukins, adhesion molecules and others. Studies are needed that evaluate the hemostatic and platelet function of patients with post-MI depression. Future studies also should address whether responses to commonly used antiplatelet agents differ among post-MI patients with versus without depression.

Key Question 4

No studies of sufficient power have yet been performed that directly address the question as to whether treatment with antidepressants improves survival in depressed patients after an MI. Some evidence suggests that selective serotonin reuptake inhibitor antidepressants have beneficial effects on surrogate markers of post-MI risk (e.g., heart rate variability, aortic time velocity integral). There is evidence that both psychosocial intervention and selective serotonin reuptake inhibitor antidepressants improve depression in post-MI patients. However, the possibility of increases in rare adverse events cannot be excluded.

Studies are needed to determine whether patients with depression who are treated for depression, especially with highly effective drugs, differ in outcomes from patients who are not treated. Future studies should also determine whether treatment for depression per se or resolution of depression is associated with different outcomes.

Key Question 5

There are insufficient data to allow an adequate assessment of the performance characteristics of instruments or methods used to screen for depression during the initial MI hospitalization. The very low positive predictive values of these screening instruments (generally in the 25 to 50 percent range) may be acceptable clinically if followed by a more thorough assessment of those who screen positive; however, the low positive predictive values are particularly problematic if used to detect relationships to outcome variables in the research setting. When compared with the HADS and Symptom Checklist-90

Depression scale, the BDI tends to diagnose less significant symptoms of depression at higher rates. It may be less effective in accurately diagnosing major depression.

Additional studies are needed to determine the performance characteristics of instruments or methods used to screen for depression (or depressive symptoms) during the initial MI hospitalization. Studies are needed in post-MI patients that examine the ability for depression screening instruments or methods to distinguish symptoms of depression from symptoms attributable to the MI, to poor physical health, or to the hospitalization itself.

Key Question 6

It remains unclear whether there are significant differences in cardiac medications prescribed to post-MI patients based on the presence or absence of depression. Three studies evaluated adherence to prescribed medications and secondary prevention measures in post-MI patients and consistently found lower adherence in those with depression than those without depression. Two good-quality studies, using different methods, came to diverse conclusions about whether the frequency with which cardiac procedures are used varies between post-MI patients with depression and those without depression.

Additional large studies are needed to examine whether the use of diagnostic and therapeutic procedures differs between depressed and non-depressed post-MI patients. Future studies should also address whether potential differences in procedures are due to differences in provider recommendation or to differences in patient acceptance. Further studies are needed to determine whether the treatment prescribed to post-MI patients with depression differs from those without depression. Future studies should address whether the non-pharmacologic interventions (including diet, exercise and cardiac rehabilitation) recommended to post-MI patients differ between those patients with and without post-MI depression. Future studies should examine the adherence behavior of post-MI patients and evaluate measures that could improve adherence to recommended treatment.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and Quality (AHRQ) by The Johns Hopkins University Evidence-based Practice Center under Contract No. 290-02-0018. It is expected to be available in spring 2005. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 123, *Post-Myocardial Infarction Depression*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

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Chapter 1: Introduction

Overview of Post-Myocardial Infarction Depression

Myocardial infarction (MI) is the leading cause of death in this country.[1] The prognosis of patients with MI depends on the extent, location, and type of infarct.[2]

In an effort to improve outcomes of patients with MI, a number of treatments are typically recommended, including medications, revascularization procedures, behavior and lifestyle changes, and cardiac rehabilitation. Co-existent depression may influence the recovery of patients with MI in a number of important ways reviewed in this report.

Depression is manifested by a number of symptoms including depressed mood, diminished interest or pleasure in all or almost all, activities, low self-esteem, sleep disturbance, changes in appetite, loss of energy, difficulty concentrating, psychomotor retardation or agitation, and suicidal ideation. Depression is common among patients recovering from am MI. Approximately one in six patients with an MI experience major depression and at least twice as many as that have significant symptoms of depression soon after the event.[3, 4] Although minor mood disturbance is likely to resolve spontaneously after an MI, major depression is more persistent.[5] Many studies have found that depression is an independent risk factor for increased mortality among patients recovering from an MI. This increased risk appears to be present even by 4 months or earlier after hospital discharge,[6] and the relation between depression and risk has been reported to be graded and "dose-dependent", with more severe depression associated with greater mortality risk.[6] Despite these findings, depression in patients recovering from an MI is often unrecognized, as it is in other medical populations.[7] Of note, only recently have MI treatment guidelines begun to call for the screening for post-MI depression.[8] This practice is in sharp contrast to the manner in which many other risk factors for increased morbidity and mortality are handled; for example, screening for diabetes mellitus or for reduced left ventricular ejection fraction (LVEF) are routinely performed as part of the standard care of patients hospitalized for an MI.

Conceptual Framework

No mechanism has yet been defined that links depression after MI with the observed higher morbidity and mortality. However, a number of plausible mechanisms have been proposed. These putative mechanisms fall into two broad categories, “behavioral” (either patient or provider/health system) or “biological”. “Behavioral” mechanisms include: (1) a greater prevalence of noncompliance on the part of the patient, and (2) a failure of providers to offer important cardiac treatments as often as those patients without depression. “Biological” mechanisms include: (1) an increased risk of sudden cardiac death, possibly indicated by decreased heart rate variability (HRV) (2) increased platelet activation and thrombosis, and (3) increased activation of the systemic inflammatory response. These mechanisms are likely to act in some combination as indicated in the conceptual framework shown in Figure 1.

Prevalence of Post-MI Depression

Depression has been reported to occur in a significant percentage of patients suffering from acute MI.[3,6,9,10] However, the prevalence of post-MI depression may vary considerably by patient population and the instruments used to make the assessment. This evidence report reviews in detail the studies reporting the prevalence of depression among patients who had an acute MI.

Depression and Risk of Coronary Heart Disease

The development of coronary artery disease (CAD) involves the interplay of many factors. Some of these risk factors are well established: hypercholesterolemia, hypertension, diabetes, smoking, age, and genetic factors including sex. Management of these classic risk factors now forms the basis of current management recommendations for individuals at risk for coronary heart disease (CHD) events.[11] Epidemiologic studies also have found an association between clinical depression or depressive symptoms and increased risk of developing future symptomatic CAD, MI, and cardiac mortality.[12-19] Recent prospective studies have confirmed this association. In a study of 1,190 male medical students followed for up to 40 years, there was a 12 percent cumulative incidence of depression.[20] A history of depression carried a two-fold greater risk of developing symptomatic CAD or MI. In the Cardiovascular Health Study 4,493 Americans without evident coronary disease at baseline were followed for 6 years.[21] Depressive symptoms had a significant association with mortality, and an independent association with developing CAD and mortality, even after adjustment for other established coronary risk factors.

Possible Mechanisms Linking Post-MI Depression and Adverse Outcomes

Many potential mechanisms have been proposed as plausible links between depression and higher rates of mortality after MI. Increased mortality has been detected as early as 4 months and as late as 10 years after MI among patients with depression at the time of hospitalization for MI.[6,9-22] Although no mechanism for the observed higher mortality has been established, suicide does not appear to play a role. Thus, there has been a search for other mechanisms by which post-MI depression could have a large adverse impact on survival within the first few months and extending for at least a decade. It is notable that not all studies of depressed post-MI patients have found an increase in mortality.[23]

Figure 1 illustrates pathways by which depression could produce an early and sustained increase in post-MI mortality. In particular, increased thrombosis or arrhythmogenesis could directly cause higher mortality. Although numerous studies have reported an increased risk of sudden death with post-MI depression,[24] one study failed to find an increased rate of non-fatal MI over 5 years of follow-up.[25] Increased rates of non-fatal as well as fatal MI might be expected if a thrombotic mechanism were the prime mediator of increased risk. Taken together, these observations tend to favor an arrhythmic mechanism.

Arrhythmias

In support of an arrhythmic mechanism are the observations that patients with coronary disease and depression have lower HRV than age- and sex-matched patients with coronary disease who are not depressed.[26] The finding of low HRV indicates abnormally high sympathetic tone with or without abnormally low parasympathetic neurological input to the heart, and it may be the link between post-MI depression and an apparently increased risk of sudden death. Individuals with post-MI depression have higher rates of ventricular ectopy than do those without depression.[27] An interaction between depressive symptoms and ventricular ectopy has also been reported, with an odds ratio of 29 for 18-month cardiac mortality in comparisons between post-MI patients with depression and premature ventricular contractions (PVCs) of at least 10 per hour and post-MI patients without either of these characteristics.[9]

Hemostasis

Alterations in hemostasis are also plausible links between depression and post-MI adverse events. Individuals with depression have evidence of increased platelet activation. The neurobiology of depression involves alteration in serotonin receptors and transport pathways.[28,29] The platelets of individuals with depression have alterations in receptors, including the serotonin 5 hydroxy-tryptamine (serotonin 5-HT2) receptor, that result in increased levels of activation.[30,31,32]

Inflammation

The onset and progression of atherosclerosis is strongly associated with vascular inflammation characterized by increased levels of inflammatory mediators such as interleukin 1(IL-1) and interleukin 6 (IL-6), tumor necrosis factor, and C-reactive protein (CRP).[33] In particular, the acute phase reactant CRP has emerged as a significant predictor of increased risk.[34] In populations without evident coronary disease, elevated CRP levels predict higher risk for developing an acute coronary syndrome (ACS). In those who have experienced an acute MI, higher levels of CRP are associated with poorer prognosis.[35,36] Major depression also has been associated with elevated CRP levels particularly in men.[37] Thus, adverse cardiac outcomes and depression could be linked through pathways with CRP or other markers.

Quality of Life

Depression in medical illness is associated with a marked decrease in quality of life (QOL) and an increase in utilization of health care resources.[38,39] Among post-MI patients the presence of depression may be a powerful predictor of QOL.[40]

Other Possible Mechanisms

There are certainly other mechanisms not already mentioned that may link depression with increased morbidity and mortality post-MI. Depression has been associated with increased activity of the sympathetic nervous system.[41] In addition to its relationship to increased myocardial ischemia and arrhythmia, sympathetic nervous system activity may also result in higher blood pressure, insulin resistance, and an increased susceptibility to infection.[42] Depression has also been associated with deficiencies of omega-3 fatty acids and with elevated homocysteine levels which may increase the burden or cardiovascular disease,[43] and thereby adversely affect post-MI outcome.

Response to Treatment for Depression

Several trials have now evaluated pharmacologic and non-pharmacologic treatment of depressive symptoms in post-MI patients.[44-50] However, these trials have had inconsistent results or insufficient power to detect significant differences. Consequently, no consensus exists regarding the efficacy of various treatment options for patients with post-MI depression.

Patient Adherence and Provider Bias

Depression is a risk factor for non-adherence to treatment in many medical conditions.[51] Thus, it is important to determine the extent to which depression is associated with non adherence to recommended cardiac treatment in patients who have had an acute MI. As indicated in Figure 1, depression may well contribute to post-MI patients' difficulty in adhering to prescribed medications, accepting recommended procedures, and completing cardiac rehabilitation. Figure 1 also indicates that provider bias may play a role in keeping patients from receiving treatments that otherwise might be recommended after an MI. It is possible that health care providers are less likely to recommend some types of treatment for post-MI patients with depression than for those without depression. Indeed, some studies have found that patients with depression received a different level of medical treatment than those without depression.[52]

Screening and Diagnostic Approaches

In their recently released recommendation for depression screening,[53,54] the U.S. Preventive Services Task Force (USPSTF) points out that depressive disorders are common, chronic, and costly. The prevalence of depression is high, with community-based surveys indicating prevalence rates of 1.8 to 3.3 percent for depression within the last month and lifetime prevalence rates of 4.9 to 17.1 percent.[55] Depressive illness is projected to be the second leading cause of disability worldwide in 2020.[56] More than a decade ago, the economic burden of depression in the United States was estimated at approximately $44 billion, with $24 billion of that attributable to excess absenteeism of depressed workers and reductions in their productive capacity while at work during episodes of illness.[57] The USPSTF supports screening adults for depression in clinical practices that have systems in place to assure accurate diagnosis, effective

treatment, and follow-up.[53] Although several reports address the ideal screening and diagnostic instruments for the detection of depression in general medical patients, little is known about the ideal method for diagnosing depression in patients in the post-MI period. What are the sensitivity and specificity of methods that could be used to screen for depression in post-MI patients? Do the accuracy and reliability of screening methods depend on the time of the evaluation relative to the diagnosis of an acute MI? Since post-MI depression has been associated with adverse outcomes, it is particularly important to have answers to these types of questions.

Therapeutic Approaches

A number of therapeutic approaches have been advocated for patients with post-MI depression, including cardiac rehabilitation, social support, cognitive behavior therapy, and antidepressants. Two recent large studies examined the safety and efficacy of treating depression in patients recovering from an MI. In the Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) study, the effects of a psychosocial intervention on cardiac outcomes was examined in post-MI patients who were either depressed or had low perceived social support, or both.[58] The Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) examined the safety and efficacy of antidepressant therapy with a selective serotonin reuptake inhibitor (SSRI) in patients who recently experienced an acute MI.[59] Although several types of antidepressant drugs might be considered in patients recovering from an MI, the tricyclic antidepressants usually are avoided because of their tendency to increase resting heart rate, produce orthostatic hypotension, and alter intracardiac conduction and the susceptibility to ventricular arrhythmias.[60] The SSRI antidepressants do not appear to have important cardiac side effects when administered to patients soon after an acute MI.[59]

Chapter 2: Methods

The American Academy of Family Physicians (AAFP) requested an evidence report to synthesize the available evidence on depression and post-MI depression, with an overall goal of using the report in supporting the development of evidence based clinical practice guidelines. The Johns Hopkins University Evidence-based Practice Center (EPC) was awarded this contract in December 2003. The EPC established a team and work plan to develop the evidence report. The project consisted of recruiting technical experts, formulating and refining the specific questions, performing a comprehensive literature search, summarizing the state of the literature, constructing evidence tables, and submitting the report for peer review.

Recruitment of Experts and Peer Reviewers

At the beginning of the project, we recruited a panel of eight external technical experts (see Appendix A[*]) from national and international communities to give us input on key steps including the selection and refinement of questions to be examined. This panel of experts included a representative from our partner organization (the AAFP), as well as other respected experts from the fields of psychiatry, psychology, rehabilitation, and cardiology. This panel of experts provided feedback on the key questions and was asked to review the draft report.

Target Population

Our review focused on studies of adults (male and female), including members of any racial/ethnic population, who had suffered an acute MI. The main targeted users of the review are clinical leaders of health care quality improvement efforts and clinicians, including family physicians, internists, cardiologists, psychiatrists, and psychologists.

Identifying the Key Questions

The AAFP provided the EPC its original list of questions. We revised the questions on the basis of preliminary literature searches. The panel of technical experts reviewed the draft questions and ranked each question according to importance, amount of available evidence, and clarity. We collected the responses from the experts and revised the questions as suggested.

Key Questions

The EPC team sought evidence to address the following key questions:

1. In patients diagnosed with and hospitalized for acute MI, what is the prevalence of depression during initial hospitalization for MI?

[*] **Note:** Appendixes and Evidence Tables cited in this report are provided electronically at http://www.ahrq.gov/clinic/tp/mideprtp.htm.

- We defined depression as symptoms meeting established clinical threshold criteria for depression as measured by validated questionnaires or standardized psychiatric interviews.

1a. What is the prevalence of depression during initial hospitalization for an acute MI, with or without a history of previous depression, as reported by study investigators?

2. What percentage of patients with post-MI depression continues to have depression (or depressive symptoms) 1 month or longer after initial hospital discharge?

3. What is the association of post-MI depression with outcomes independent of other predictors of post-MI outcomes?

- Post-MI outcomes include (1) clinical outcomes—total mortality, cardiac mortality, MI, resuscitated arrest, stroke, arrhythmias, and revascularization, (2) QOL, and (3) utilization of health care services—readmission, total hospital days, and cost of care.
- Potential predictors include demographic and clinical characteristics of patients that have been reported to be associated with the risk of post-MI outcomes.

3a. What is the association of post-MI depression with surrogate markers of cardiac risk independent of other predictors of post-MI outcomes?

- Surrogate markers of disease severity include HRV, platelet reactivity, and markers of inflammation such as CRP.

4. Do post-MI patients with depression have better outcomes with depression treatment than do those without such treatment?

- We defined depression treatment as including all interventions intended to have specific impact on depression, such as antidepressants, cognitive behavioral therapy, interpersonal therapy, psychosocial support, and cardiac rehabilitation.

4a. Do outcomes differ with or without improvement in depression for post-MI patients with depression who do receive depression treatment?

4b. Do outcomes differ with or without improvement in depression for post-MI patients with depression who do not receive depression treatment?

5. What are the performance characteristics (e.g., sensitivity, specificity, reliability, and predictive value) of instruments or methods that are used to screen for depression (or depressive symptoms) after an acute MI?

5a. What are the performance characteristics of instruments or methods that are used to screen for depression (or depressive symptoms) after an acute MI, during hospitalization?

5b. What are the performance characteristics of instruments or methods that are used to screen for depression (or depressive symptoms) after an acute MI, within 3 months after hospitalization?

6. Does the use of cardiac treatment for patients with acute MI differ for those with and those without depression?

- Cardiac treatment includes revascularization (angioplasty or bypass surgery), angiotensin converting enzyme (ACE) inhibitors, beta blockers, statins, antiplatelet agents, or other treatments recommended by the American Heart Association or the American College of Cardiology.

Analytic Framework

We used our conceptual framework (see Figure 1) to guide the analysis of our questions, based on the relationships between MI, depression, various risk factors, pertinent treatment options, and subsequent clinical events.

Literature Search Methods

Searching the literature included the steps of identifying reference sources, formulating a search strategy for each source, and executing and documenting each search.

Sources

Our comprehensive search plan included electronic and hand searching. In March 2004, we searched the following electronic databases: MEDLINE®, the Cochrane CENTRAL Register of Controlled Trials (Issue 1, 2003), the Cochrane Database of Methodology Reviews (CDMR), the Cumulative Index of Nursing and Allied Health Literature (CINAHL®), the Psychological Abstracts (PsycINFO®), and EMBASE®.

Hand searching for possibly relevant citations took several forms. First, the EPC team identified 16 journals that we thought were most likely to contain relevant studies (see Appendix B). We scanned the tables of contents of these journals for relevant citations from October 2003 to April 2004.

For the second form of hand searching, we used ProCite®, a reference management software, to create a database of reference material identified through an electronic search for relevant guidelines and reviews, through discussions with experts, and through the article review process. We also reviewed the references in pertinent recent review articles that were identified during the abstract review process.

Finally, we examined the reference lists of eligible articles to identify any other potentially relevant articles. This task was performed by the second reviewer as part of the article review process (see description of article review process below).

Search Terms and Strategies

Search strategies, specific to each database, were designed to maximize sensitivity. Initially, we developed a core strategy for MEDLINE, accessed via PubMed®, based on an analysis of the Medical Subject Headings (MeSH) and text words of key articles identified a priori. The

PubMed strategy formed the basis for the strategies developed for the other electronic databases (see Appendix C).

Organization and Tracking of the Literature

We downloaded electronic search results into the citation management database ProCite. (ProCite, ISI Research Soft, Berkeley, CA) The software's duplication check was used to eliminate citations already retrieved. We used the ProCite software to store and track the searching strategies and sources used to retrieve each citation. This software was also useful during the abstract review process to track the reviewed abstracts.

Title Review

After the search strategies were completed and the citations downloaded into ProCite, two reviewers independently scanned the titles. During this scan, reviewers looked for article titles that clearly were irrelevant to the study questions. If both reviewers agreed, on the basis of the title, that an article was irrelevant, it was excluded from further consideration. Once a citation was selected for deletion, a note was made in the ProCite database deleting the citation from further review.

Abstract Review

Specific inclusion and exclusion criteria were applied at each of the levels of review, with criteria becoming more stringent as the process moved from database searches, to the review of titles, to the review of abstracts, and to the review of articles. After identifying a title as potentially relevant, two team members independently reviewed the abstract of the citation, and articles were included or excluded from the article review on this basis. Also at this step, abstracts were flagged according to their relevance to a key question. To be excluded at this stage, both reviewers had to agree that an abstract was ineligible. Discrepancies were discussed during weekly face-to-face meetings.

Inclusion and Exclusion Criteria

During the abstract review process, emphasis was placed on identifying all articles that could have original data pertinent to the questions. As previously described, a representative of the AAFP was consulted during the development of inclusion and exclusion criteria. In evaluating titles and abstracts, the following criteria were used to exclude articles from further consideration: (1) not in English, (2) no human data, (3) no original data, and (4) meeting abstract (no full article for review).

We also had two question-specific exclusion criteria. For key question 4, we excluded studies that did not have a concurrent comparison group. For key question 5, we excluded studies that did not have a validated reference standard for diagnosing depression.

Abstract Review Process

The EPC team used an abstract review form for this stage of the process that was similar to abstract forms used in other EPC projects. The form was designed to address our specific questions and the eligibility criteria appropriate for this project (see Appendix D). Each abstract was circulated to two members of the EPC team who independently reviewed the abstract both for eligibility and applicability to specific key questions. For those articles deemed ineligible, the reviewers selected a reason for exclusion. When a citation contained no abstract, or when the reviewers could not determine from the abstract if the citation met eligibility criteria, a full copy of the article was obtained for review. Investigators met face-to-face to adjudicate disagreements about the eligibility of abstracts.

Article Review

The purpose of the article review was to confirm the relevance of each article to the research questions, to determine methodological characteristics pertaining to study quality, and to collect evidence that addressed the research questions. The study team reviewed each article identified as being eligible during the abstract review process. The abstraction forms for the article review process were filled out in a serial manner. Two study team members worked on each article. The first reviewer had the task of filling out the quality and content abstraction forms. The secondary reviewer performed an independent assessment of the quality of each study, and then checked the information recorded by the primary reviewer on the content abstraction form. We used face-to-face meetings to adjudicate differences between the reviewers on the quality and content forms. We did not mask author and journal names because previous work has shown that masking does not make a significant difference during the data abstraction.[61]

Qualitative and Quantitative Data Abstraction

The study team developed content review forms and a quality review form for use in this project. The forms were pilot tested and revised before use. Because of the different types of questions, the team had a general content review form (See Appendix E), and five separate question-specific content review forms (see Appendix E): one addressing key questions 1 and 2, and one each for key questions 3, 4, 5, and 6. To make sure that all articles met eligibility criteria, the general content review form began with a check of the eligibility criteria (see Abstract Review, above). For key question 4, the team limited the review to studies with a comparison group, and for key question 5, the studies were limited to studies using a validated reference standard.

The quality assessment form included items about study quality in the following categories: representativeness of study population, bias and confounding, description of therapy and management, description of assessment protocols, test or instrument interpretation, outcome and follow-up, statistical analysis, and conflict of interest (see Appendix E).

Evidence Tables

For each key question, the EPC team created a set of evidence tables. Each set of tables contained basic information about study aims and eligibility criteria, selected characteristics of study participants, assessments of study quality, and results most pertinent to the key question.

Grading of the Evidence

After all articles were reviewed, we graded the evidence supporting each question on the basis of its quantity, quality, and consistency. Our evidence-grading scheme followed the approach recommended by the International GRADE Working Group.[62] In terms of quantity of evidence for each question, we determined the number of studies and the total number of patients studied. We assessed the quality and consistency of evidence on each key question based on the criteria recommended by the Grade Working Group that applies to the questions (see Appendix F for details).

Peer Review

Throughout the project, feedback was sought from the technical experts through formal and ad hoc requests for guidance. A draft of the completed report was sent to the technical experts, as well as to the partner (AAFP), Agency for Healthcare Research and Quality (AHRQ) and other peer reviewers. Substantive comments were catalogued and entered into a database. Revisions were made to the evidence report as warranted, and a summary of the comments and their disposition was submitted to AHRQ with the final report.

Chapter 3: Results

Literature Search and Abstract Review

The literature search process identified 3,770 unique citations potentially relevant to key questions for which the EPC team evaluated primary literature (see Figure 2). Fifteen duplicate citations were found and excluded. During the title review process 2,597 citations were excluded because they did not appear to pertain to the subject. At abstract review 825 citations were found not to meet the criteria for inclusion. Abstracts were excluded for the following reasons: the article was not in English; did not include human data; did not have original data; or was a meeting abstract (hence no full article available for review). For articles related to only key question 4, the team excluded studies that did not have a concurrent comparison study; for key question 5, the team excluded articles without a validated reference model.

Articles Eligible for Review

Following the abstract review process 318 articles were found to be eligible. Of these, 128 were tagged for key question 1 and 2; 56 were tagged for question 3; 54 were tagged for question 4; 12 for question 5; and 13 for question 6. Added together the total number of articles pertaining to key questions exceeded the actual number of articles reviewed because some articles were identified as relevant for more than one key question.

Key Questions 1 and 2

Question 1. In patients diagnosed with and hospitalized for acute MI, what is the prevalence of depression during initial hospitalization for MI?

Question 1a. What is the prevalence of depression during initial hospitalization for MI in patients with or without a known history of depression as reported by study investigators?

Question 2. What percentage of patients with post-MI depression continue to have depression (or depressive symptoms) 1 month or longer after initial hospital discharge?

Introduction

Most studies that examined the prevalence of depression after MI examined patients at the time of the initial hospitalization and at various times after discharge. Because question 2 refers to the percentage of patients who continue to have depression after hospital discharge, these two questions are interrelated, and therefore questions 1 and 2 are combined for the purposes of this report.

Important technical and methodological issues should be clarified before examining this review. First, depression is defined and addressed differently from study to study. For the

Note: Appendixes and Evidence Tables cited in this report are provided electronically at http://www.ahrq.gov/clinic/tp/mideprtp.htm.

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purposes of this review, we have defined *depression* as "symptoms meeting established clinical threshold criteria for depression as measured by validated questionnaires or standardized psychiatric interviews." It must be noted, however, that the manner in which "clinical threshold criteria" is interpreted varies considerably across studies. For example, one study used a score of 8 or higher on the depression subscale of the Hospital Anxiety and Depression Scale (HADS) to report a prevalence of "clinically significant levels of depression",[63] whereas another used a cutoff of 11 to denote "clinical levels of depression".[64] Three other studies referred to a score in the 8 to 10 range as "possibly clinically significant" or "borderline" depression and a score of 11 or higher as "probably clinically significant" depression.[65-67] This review found similar variability in threshold criteria and designation when other screening instruments were used. Wherever possible, this has been specifically noted given that prevalence data may become confusing when "depression" is characterized according to different threshold criteria. In addition, although the definition of *depression* for the purposes of this review includes measurements by validated questionnaires and standardized interviews, the former typically measure symptoms of depression whereas the latter typically use a version of the Diagnostic and Statistical Manual (DSM) to establish a diagnosis of major or minor depression or dysthymia. Again, wherever possible, this is noted in the report. Finally, it should be noted that the screening instruments typically used for depression are referred to in this report as "validated questionnaires or rating scales." Some validation evidence is available for all of these, but the quality varies and no systematic validation has been carried out in patient populations with recent MI. Indeed, question 5 of this report addresses the performance characteristics of instruments or methods used to screen for depression after an acute MI.

Question 2 asks specifically about the percentage of patients with post-MI depression who continue to have depression (or depressive symptoms) 1 month or longer after initial hospital discharge. To address this question, a study must provide data on the prevalence of depression during the initial hospitalization and then reassess those patients with depression after hospital discharge and specifically indicate the prevalence of depression at follow-up in those patients initially depressed. Whereas data are provided in the tables (Appendix G Evidence Tables 2.1, 2.2, 2.3, 2.4) from studies that report prevalence data only at follow-up (i.e., no data were available on the prevalence of depression during the hospitalization), these studies do not specifically address question 2 and therefore are handled separately in this report. To specifically address question 2, a study would have to report the prevalence of depression at follow-up in those patients depressed during the hospitalization. Several studies reported prevalence data at hospitalization and follow-up, but did not report the prevalence of depression after discharge among the group initially depressed; these studies also are handled separately in this report.

Results of Literature Search

After the final article review, 51 articles were eligible pertaining to question 1. Of these, 22 were studies reporting data that were also reported in at least one other study. For example, some investigators reported the prevalence of in-hospital depression and outcome at 6 months. In another study by the same investigators, the prevalence of in-hospital depression was again reported but with a 12-month outcome. In such instances, only one article was considered eligible for question 1. After these 22 articles were excluded, 5 others were excluded because the

prevalence of depression was determined by using a non-standard screening instrument for which no validation was provided. This left 25 articles for question 1.

After article review, 30 articles were eligible pertaining to question 2. One of these was excluded as duplicative, and six others were excluded because the prevalence of depression was determined by using a non-standard screening instrument for which no validation was provided. One study was excluded because the follow-up data were collected 2 weeks after discharge rather than the minimum 1 month after discharge that was required for this question. This left 22 articles for question 2. Of these 22 articles, seven reported prevalence data both at hospitalization and follow-up. However, only three of these separately reported prevalence data at follow-up for those depressed during hospitalization. The other four articles and the 15 that reported only follow-up data are reported separately because they did not directly address question 2.

Characteristics of Studies

Tables are presented separately for questions 1 and 2 (see Tables 1 and 2, and Appendix G). In Evidence Table 1 and 2 (Appendix G) for each question we have summarized the study aims, number of subjects included, and study quality scores for the 24 studies for question 1 and the 22 studies for question 2. The articles were published between 1986 and 2004.

Of the 25 articles for question 1, eight used a standardized clinical interview for the diagnosis of depression (e.g., Structured Clinical Interview or the Diagnostic Interview Schedule).[58,68-74] One of these[72] interviewed patients within a month of their MI, but the exact timing of the assessment relative to the hospitalization is unclear, and so data from this study are not included in summary tabulations. Seventeen used one or more validated questionnaires or rating scales such as the Beck Depression Inventory (BDI),[25,74-81] Hamilton Rating Scale for Depression (HAMD),[78,82] HADS,[63-67] Montgomery and Asberg Depression Rating Scale,[83] or Symptom Check List-90 (SCL-90) Depression Subscale.[84]

Of the 22 articles for question 2, nine used a standardized clinical interview for the diagnosis of depression.[10,69,85-91] Seventeen used one or more validated questionnaires or rating scales such as the BDI,[10,75,76,78,80,81,88,89,92] HAMD,[10,78,93] Zung Depression Rating Scale (ZDS),[94,95] HADS,[10,64,66,88,89] or SCL-90 Depression Subscale.[10,84,88,89,96]

Quality of Studies

As shown in Appendix G Table 1.3, the number of eligible studies on question 1 with scores greater than 50 percent for given study quality categories were as follows: 18 for representativeness of the study population, none for description of therapy and management, 20 for description of the assessment protocol, nine for reporting of outcomes and follow-up, and four for statistical analyses. Only 13 studies reported information about potential conflicts of interest. As indicated in Appendix G Table 2.3, the number of eligible studies on question 2 with scores greater than 50 percent for the following study quality categories were 18 for representativeness of the study population, only one for description of therapy and management, 14 for description of the assessment protocol, 12 for reporting of outcomes and follow-up, and four for statistical analyses. Only nine of these studies reported information about potential conflicts of interest.

Results of Studies

Question 1. In patients diagnosed with and hospitalized for acute MI, what is the prevalence of depression during initial hospitalization for MI? (Table 1)

Table 1.1(Appendix G) describes the patient populations and prevalence of depression during the initial MI hospitalization. Table 1.2 (Appendix G) describes the patient populations and prevalence of depression 1 month or longer after hospital discharge.

Of the 25 articles for question 1, seven included fewer than 100 subjects,[63,64,68,73,75,76,80] and 17 studied more than 100 individuals.[25,58,65-67,69-72,77-79,81-84,97] The range of subjects studied was 37 to 2,481 patients. Thirteen studies were from the United States and/or Canada,[25,58,68-72,74-76,78,80,82] and 12 studies were from Europe.[63-67,73,77,79,80,83,84,97] The mean age of study subjects ranged from 52 to 67 years. Sex was reported in all but two studies; men alone were studied in three reports and the remainder reported depression prevalence from a population mix of men and women. Only three of 25 studies reported race;[58,70,78] in these three, non-whites made up 33 to 38 percent of the sample. Nine studies reported the prevalence of individual cardiac risk factors[25,58,67,68,71,74,77,80,84]; whereas one study reported the aggregate number of cardiac risk factors in the population.[76] Killip class and/or LVEF was reported in seven studies.[25,69-71,73,74,81] All studies reported depression prevalence data from MI survivors alone or from a study sample in which prevalence data from MI survivors were reported separately.

Although in question 1a the prevalence of depression in patients with a history of depression (as reported by study investigators) was to be addressed, only two studies reported history of depression,[71,78] and none provided separate prevalence data for this segment of the sample. Therefore, there is insufficient evidence to answer this question.

The prevalence of depression ranged from 17 to 27 percent in the seven studies that used a Structured Clinical Interview for DSM IV (SCID) to establish the diagnosis. The largest of these studies, the ENRICHD study,[58] which examined 2,481 patients, reported a prevalence of 20 percent with major depression.

In the 17 studies that used a validated questionnaire or rating scale, 10 to 47 percent of patients had symptoms of depression considered above a clinical threshold criterion. Of the nine studies that used the original version of the BDI, five used a cutoff score of 10 or higher.[25,74,77,78,80,81] The prevalence of at least mild to moderate symptoms of depression using a cutoff of 10 or higher on the BDI was 21 to 37 percent. In the four studies that used a HADS cutoff score of 8 or higher,[63,65-67] the prevalence of possible clinical depression was 11 to 18 percent. In the four studies that used a HADS cutoff score of 11 or higher,[64-67] the prevalence of probable clinical depression was 6 to 13 percent.

In summary, the prevalence of major depression during the initial MI hospitalization is fairly consistent across studies. Based on these studies, about one of every five patients has major depression during the initial MI hospitalization. By contrast, the prevalence of different levels of depressive symptoms varies more widely across studies assessed by questionnaire or rating scale. Variation in screening instruments used, as well as variation in cutoff criteria within instruments, may account for the difference. It is impossible given current research on the assessment of depression in MI patients to compare "possible clinical depression" based on a HADS depression subscale with "at least mild-to-moderate symptoms of depression" based on a BDI. In general,

the prevalence of symptoms of depression that meet standard threshold criteria on the BDI (10 or higher) is greater than that using the HADS (either 8 or higher or 11 or higher) in patients during the initial MI hospitalization. For example, the two studies in this report that included the most patients used the BDI for 870 patients, reporting a prevalence of 32 percent[25] and the HADS for 688 patients, reporting prevalences of 18 percent and 10 percent depending on the cutoff.[64] This is consistent with the prevalence ranges for all studies using these two instruments as noted above. This discrepancy is not surprising in that the BDI includes somatic symptoms that may overlap with MI symptoms in hospitalized patients, whereas the HADS is designed for use in hospitalized patients and does not include somatic symptoms.

As summarized in Evidence Grade Table 1, we concluded that the overall body of evidence on question 1 merited a medium quantity of evidence and reasonable quality of evidence despite the presence of some inconsistencies in the evidence.

Question 2. What percentage of patients with post-MI depression continue to have depression (or depressive symptoms) 1 month or longer after initial hospital discharge? (Table 2)

The three studies that specifically addressed question 2 were from North America and reported data on 52 patients (mean age 51 years; 90 percent male),[75] 335 patients (mean age 64 years; 64 percent male),[69] and 550 patients (mean age 60 years; 79 percent male).[81] None of these studies reported race, only one reported on cardiac risk factors,[81] and two reported Killip class and/or LVEF.[69,81]

Nineteen of the studies reported the prevalence of depression at least 1 month after hospital discharge, but they did not address question 2 specifically. Of these studies, eight included fewer than 100 subjects,[64,76,80,84-86,93,94] and 11 studied more than 100 individuals.[10,66,87-92,95,96,98] The range of study subjects was from 32 to 1,042 patients. Six studies were from the United States and/or Canada,[76,87,88,91,93,96] 12 studies were from Europe,[10,64,66,80,84-86,89,90,92,94,98] and one was from Asia.[95] The mean age of study subjects ranged from 50 to 67 years. Men alone were studied in four reports,[84-86,94] and the remainder reported depression prevalence from a gender-mixed population. Only three of 19 studies reported race.[90,92,93] Three studies reported information on only one cardiac risk factor,[85,87,96] six studies reported information on multiple cardiac risk factors,[84,89,91,92,95,98] and one study reported the average number of risk factors per study subject.[76] Killip class and/or LVEF was reported in five studies.[87,88,91,92,95] Two studies included patients without MI,[85,91] but in both of these studies, more than 80 percent of the patients were MI survivors. The other 17 studies reported depression prevalence data from MI survivors alone or from a study sample in which prevalence data from MI survivors were reported separately.

Three studies reported prevalence data at follow-up for those depressed during the initial MI hospitalization and therefore specifically addressed question 2. These studies reported follow-up data at 30 days after MI,[81] 6 to 8 weeks after MI,[75] and 3 to 4 months after MI.[69] A study by Davis and Jensen[75] used the BDI to assess 52 patients during the initial hospitalization and again at follow-up. Of the five patients who were assessed as "clinically depressed" during the hospitalization (BDI of 13 or higher), three (60 percent) were still depressed 6 to 8 weeks later when the same BDI cutoff was used. Schleifer et al.[68] studied 335 patients during the initial MI hospitalization and reported both in-hospital and follow-up data in 190 patients. Of these 190 patients, 30 had major depression (15.8 percent) and 51 had minor depression (26.8 percent) according to a SCID performed during the initial hospitalization. Of the 30 patients with major depression at baseline, 11 (36.7 percent) still had major depression 3 to 4 months later and

another 11 (36.7 percent) had minor depression. The total number of patients with either major or minor depression at follow-up was therefore 73.3 percent of those with major depression at baseline. Of the 51 patients with minor depression during the initial MI hospitalization, eight (15.7 percent) had major depression at follow-up and another 11 (21.6 percent) had minor depression. The total number of patients with either major or minor depression at follow-up was 37.3 percent of those with minor depression at baseline. Lauzon et al.[81] used the BDI to evaluate 550 patients during the initial MI hospitalization. They reported a prevalence of clinically significant depressive symptoms (BDI of 10 or higher) as 34.7 percent at baseline. Of these 550 patients, 466 were re-evaluated using a BDI 30 days later. These authors reported that of patients depressed at baseline, 70 percent continued to be depressed at 30 days; the breakdown of patients with and without depression in those lost to follow-up was not reported. In these three studies, the majority of patients with clinically significant depression during the initial MI hospitalization remained depressed when assessed 1 to 4 months later.

As summarized in Evidence Grade Table 1, we concluded that the overall body of evidence on question 2 merited a medium quantity of evidence and reasonable quality of evidence despite the presence of some inconsistencies in the evidence (see Appendix F).

Key Question 3

Question 3. What is the association of various measures of depression with outcomes in patients with acute MI, independent of other known predictors of post-MI outcomes?

Question 3a. What is the association of various measures of depression with surrogate markers of cardiac risk in patients with acute MI, independent of known predictors of post-MI outcomes?

Introduction

A number of studies have reported that depression after an MI is associated with increased mortality and poorer outcomes on a variety of psychosocial and health-related variables. However, not all of these studies accounted for the potential role of confounding factors that might have influenced these observations, including cardiovascular disease severity, socioeconomic factors, psychological variables, and psychiatric conditions apart from depression. To better understand the role of depression per se in predicting negative outcomes after an acute MI, we reviewed the English language literature for articles that evaluated the relationship between depression in days to weeks following an acute MI and a variety of health and psychosocial outcome measures.

We also reviewed the literature for articles that examined the relation between post-MI depression and surrogate markers of cardiac risk that might be associated with adverse outcomes—e.g., increased ventricular arrhythmias, reduced HRV, higher levels of inflammatory markers, and abnormal platelet function.

Results of Literature Search

After final article review, there were 33 articles that reported on 27 different patient cohorts addressing question 3 or 3a. Thirty articles were eligible for question 3. Of these, 16 articles

reported data on survival.[6,22-25,40,58,74,77,99-105] Four of these articles were by Frasure-Smith and colleagues reported on the same cohort of patients or a subset at different times or with somewhat different analyses.[25,101 102,105] Similarly, Lane et al. reported on a single patient cohort at three different times.[23,40,77] Also, one included article was from the ENRICHD study[58] and reported cardiac events in depressed patients who received and did not receive a psychosocial intervention. Another study compared a subsample of patients from ENRICHD with depression to a population of patients who had neither depression nor low perceived social support.[74] This study[74] and the ENRICHD study[58] were considered separate studies and reported as such in this review. Thus, we found 11 independent studies with data on survival. Six studies reported data on cardiac events.[24,52,84,89,95,106] Data on sudden cardiac death from one study[24] were included in both the survival and cardiac events categories. Twelve articles from 11 independent studies reported data on QOL.[6,23,40,63,65,67,93,107-111] Two of these articles reported data from the same study on different outcomes related to QOL.[107,109] Three of the studies that reported data on QOL also reported data on survival.[6,23,40] Three studies, published between 2001 and 2004, reported data for question 3a.[91,112,113] Articles meeting criteria for inclusion in the review of this key question are shown in Tables 3, 4, 5, 6 and Appendix G (Evidence Tables 3.1, 3.2, 3.3 and 3.4).

Characteristics of Studies

Tables are presented separately for each type of outcome addressed in question 3 and for question 3a (see Tables 3, 4, 5, 6 and Appendix G). In the first Evidence Table (Appendix G) for each type of outcome, we have summarized the study aims, design, setting, geographical area, and time period of data collection for the studies. The articles related to question 3 were published between 1990 and 2004, which included studies published from 1990 to 2003 for survival, from 1999 to 2004 for cardiac events, and from 1994 to 2003 for QOL. The studies with data relevant to question 3a were published between 2001 and 2004.

Tables 3 and Appendix G (Evidence Tables 3.1A, 3.2A, 3.3A and 3.4A) describe subject populations included in the 17 studies that assessed the relation of post-MI depression to survival. All studies were prospective, and evaluated the potential relation of depression (or depressed mood), assessed at a single point in time shortly after MI, to survival at various time points thereafter (4 months,[40,74] 6 months,[100,101] 1 year, 1½ years, 2 years, 3 years, 5 years, and 10 years). Some studies only reported data on cardiac mortality[6,40,100,102,105] or sudden cardiac death, whereas others reported death from all causes.[23,25,40,58,74,77,101,103-105] Some of the studies[114] did not distinguish between depressed and nondepressed groups, but instead reported the association between depressed mood, as a continuous variable, and death. One study[58] evaluated the influence of psychosocial treatment for depression on cardiac death in patients with post-MI depression.

Among the six studies that reported data on cardiac events (Table 4), there were three prospective cohort studies, two retrospective cohort studies, and one randomized clinical trial. All 11 independent studies with QOL outcome data were prospective cohort studies (Table 5). All three studies related to surrogate markers of cardiac risk were prospective cohort studies (Table 6).

Of the 12 articles that addressed QOL, the number of subjects ranged from 62[110] to 347.[65] One study was from the United States,[93] seven from Europe,[23, 6, 40, 63, 65, 67, 111] three from the Middle East,[107,109,110] and one from Asia.[108] The patient's sex was reported in all studies; men

alone were studied in three reports, women alone in one report, and the remaining studies reported on QOL outcome in a gender-mixed population.

As shown in Table 3a-1, the three studies that evaluated a surrogate marker of cardiac risk in patients with or without post-MI depression each evaluated a different marker. One study evaluated HRV,[112] another assessed levels of platelet-derived substances as a surrogate maker for platelet activity,[113] and another evaluated inflammatory markers.[91]

Quality of Studies on Depression and Survival

As summarized in Evidence Table 3.3A in Appendix G, the numbers of studies that had scores greater than 50 percent in the study quality categories were as follows: 12 for representativeness of the study population, zero for description of therapy and management, nine for description of the assessment protocol, 12 for reporting of outcomes and follow-up, and 13 for statistical analyses. Only eight studies reported information on potential conflicts of interest.

Quality of Studies on Depression and Cardiac Events

As summarized in Evidence Table 3.3B in Appendix G, the numbers of studies on cardiac events that had scores greater than 50 percent in the study quality categories were as follows: four for representativeness of the study population, one for description of therapy and management, one for description of the assessment protocol, three for reporting of outcomes and follow-up, and four for statistical analyses. Only three studies reported information on potential conflicts of interest.

Quality of Studies on Depression and Quality of Life

As summarized in Evidence Table 3.3C in Appendix G, the numbers of studies on QOL that had scores greater than 50 percent in the study quality categories were as follows: eight for representativeness of the study population, zero for description of therapy and management, six for description of the assessment protocol, nine for reporting of outcomes and follow-up, and nine for statistical analyses. Only six studies reported information on potential conflicts of interest.

Quality of Studies on Depression and Surrogate Markers of Cardiac Risk

As shown in Evidence Table 3a.3 in Appendix G of the three studies meeting eligibility criteria for question 3a, the following numbers of studies had scores of at least 50 percent for the given criteria: one for representativeness of the study population, one for description of therapy, two for reporting outcomes and follow-up, three for description of assessment protocol and statistical analysis, and one for conflict of interest disclosure.

Results of Studies on Depression and Survival

Two studies assessed the relation between post-MI depression and mortality 4 months after MI[40,101] and differed in their conclusions (See Table 3 and Evidence Table 3.4A in Appendix G). In particular, one article reported that baseline depression, as measured using the BDI, was unrelated to 4-month survival.[40] In contrast, the other study[101] found depression (BDI score greater than or equal to 10) to be an independent predictor of mortality 4 months later. Further, this study found that higher levels of depression were associated with an increased risk for death, and that even subthreshold levels of depression (BDI scores of 4 to 9) were associated with an increased risk for death in these patients.

Two studies evaluated the relationship between post-MI depression and death 6 months after an MI. One study[101] found depression, as measured using the National Institute of Mental Health Diagnostic Interview Schedule (DIS), to be an independent predictor for mortality, while adjusting for a variety of relevant covariates (see Evidence Table 3-4). All deaths in this population were secondary to cardiac events. The second study[100] used non-English-language standard diagnostic instruments for measuring depression, and divided patients into low, medium, and high levels of major depression symptoms. These authors found that high levels of post-MI depression were predictive of cardiac mortality, even when accounting for other potential covariates (see Evidence Table 3.4A in Appendix G).

Four studies assessed mortality rates in post-MI depressed patients 1 year after the index event. One of these studies[102] involved patients that were included in two other studies covered in this evidence report.[25,115] In addition to assessing the potential relation of depression to mortality, this study evaluated the potential influence of the person's sex on mortality in these patients. The study's major conclusion was that depression, which was a predictor of death at 3 months, remained a significant risk factor for death 1 year after MI. Gender did not appear to influence this risk, which was largely independent of other post-MI risks for death. A second study[114] assessed depression on a continuous scale using the BDI and found that increased depression scores predicted mortality, after statistical adjustment for known cardiac risk factors. Another study,[23] which appears at odds with this conclusion, found that depression, measured using the BDI, did not predict either cardiac or all-cause mortality after MI.

Four studies evaluated patients approximately 1½-3 years after an MI.[12,24,58,77] Two studies involved a subgroup of patients in the ENRICHD trial who have been described elsewhere in this evidence report. The ENRICHD study[58] evaluated the influence of treatment with cognitive behavioral therapy (and, when indicated, an SSRI) on post-MI patients with depression or low perceived social support. Depression was assessed using the DIS. At 29 months of follow-up, there were no differences in survival in the treated versus the untreated patients, nor were there differences in survival between patients in the depressed and low perceived social support groups. A substudy of ENRICHD[74] compared depressed and nondepressed patients and found that depression was an independent risk factor for death after an acute MI, but the effect did not appear until nearly a year after the index event.

Two other studies reported on the 3- to 4-year survival of post-MI patients who had been evaluated for depression at the time of their index event. One study[24] evaluated the risk of sudden cardiac death 4 years after an MI and found that increased depressive symptoms (BDI score greater than or equal to 10) during the initial MI hospitalization were associated with a more than two-fold increase in mortality 4 years later. In contrast to these findings, another study[77] found that a BDI score of at least 10 after an MI did not predict survival 3 years after. Although the patients in these two trials were similar in age (63 years) and gender (75-82 percent) male the patient populations of the two studies differed significantly. The study of

Irvine et al[24] was performed in post-MI patients with frequent PVCs. Depression was assessed 2 to 4 weeks after the index MI. In this study the overall two-year mortality was 9.4 percent (63/671) with a cardiac mortality of 7.5 percent 50/671 and among those with cardiac deaths 68 percent (34/50) were sudden. In contrast, in the study of Lane et al[77] depression was assessed during the index hospitalization. The overall mortality was 13 (38/288) with a cardiac mortality of 11 percent (33/288). However, of the cardiac deaths only 9 percent were sudden (3/33) and accordingly many more deaths were due to recurrent ischemic events 60 percent (20/33) or heart failure 30 percent (10/33). Authors of both of these studies[24,77] hypothesized that somatic symptoms of depression and/or disease severity may be more predictive of death than is depression per se.

Three studies,[6,25,105] compared mortality rates in depressed patients versus non depressed patients 5 years after an acute MI. In one study,[6] patients were considered depressed when they scored in the upper tertile on a measure of depression. Symptoms of depression were not associated with an increased mortality risk, 5 years later. A second study,[25] conducted in a cohort of patients that had been previously evaluated 1 year post-MI,[102] found that post-MI depression was more closely linked to mortality 5 years after MI than 1 year after MI. Another study by the same group of researchers[105] assessed the relation of depression, anxiety, and general health in post-MI patients to mortality 5 years after the index event. They concluded that an unidentified, but unique, aspect of depression predicts long-term cardiac mortality post-MI.

A single study[102] reported on mortality in depressed post-MI patients 10 years after the index event. As with most of the studies that assessed the relationship between depression and mortality at earlier time points, this study found that death following MI was positively and independently associated with depressed mood, as measured by the ZDS.

As summarized in Evidence Grade Table 2, we concluded that the overall body of evidence on question 3, looking at survival as an outcome, merited a medium quantity of evidence and high quality of evidence (see Appendix F).

Results of Studies on Depression and Cardiac Events

Six studies reported data on cardiac events, as shown in Evidence Table 3.4B in Appendix G. Irvine and colleagues[24] evaluated 671 patients within 6 to 45 days of acute MI who participated in the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial. Subjects eligible for this trial had frequent ventricular ectopy (at least 10 PVCs per hour) and were administered multiple screening questionnaires, including the BDI and the SCL-90, as well as measures of hostility, social support, and social participation. The average age of study subjects was 63.8 years and most were married men. About one quarter of the sample had a history of heart failure and about one third had a history of prior MI. There were 34 sudden cardiac deaths after 2 years of follow-up. In the Cox proportional hazards model, biological predictors of sudden cardiac deaths were prior MI (relative risk, 2.86; 95 percent CI, 1.37 to 5.99) and prior congestive heart failure (relative risk, 3.86; 95 percent CI, 1.89 to 7.89). Scores of 10 or higher on the BDI were also associated with a significantly increased risk for sudden cardiac death, SCD (relative risk, 2.45; 95 percent CI, 1.14 to 5.35). When symptoms of fatigue were considered in the multivariate model, the contribution of depression was no longer significant (relative risk, 1.73; 95 percent CI, .076 to 3.98). When cognitive affective symptoms were considered separately, the relationship between mood and SCD was of borderline significance (relative risk, 1.09; 95 percent CI, 0.99 to 1.19). Thus, depressive symptoms were associated with an increased risk of

sudden cardiac death, but this relation was no longer present when symptoms of fatigue were controlled for.

Shiotani et al.[95] evaluated 1,042 consecutive patients for symptoms of depression with the ZDS within 3 months of acute MI. Patients with depression over age 65 had significantly higher cardiac event rates during the first year after MI than did patients over age 65 without depression. There was a trend toward an association of depression and cardiac events in younger patients, but this did not reach statistical significance ($p = 0.11$).

Druss et al.[52] evaluated a group of over 100,000 Medicare patients who sustained an MI, approximately 5 percent of whom had mental illness. Of the group of patients with mental illness, some had an affective disorder (major depression, dysthymia, or bipolar disorder). The group of patients with a mental illness, as well as the subgroup of patients with an affective disorder, had a lower likelihood of receiving cardiac revascularization procedures (percutaneous transluminal coronary angioplasty, PTCA or coronary artery bypass graft surgery, CABG) during the initial MI hospitalization than did the group of patients without mental illness. In a study such as this one, cardiac revascularization procedures may be treated either as an MI treatment or as an outcome variable (i.e., a cardiac event), and therefore this study was included in this question.

Frasure-Smith et al.[106] studied 848 MI survivors and reported cardiac readmissions and procedures during the first year of follow-up. These authors found that depression (BDI score of 10 or higher) during the initial MI hospitalization was associated with a significantly increased number of cardiac readmissions and days of hospitalization. There was no relationship of depression during the initial MI hospitalization and cardiac procedures (cardiac catheterization, angioplasty, or coronary bypass surgery) in the first year post-MI.

Strik et al.[84] studied 315 men who completed measures of emotional distress, including depression, within the first month after the initial MI hospitalization. These authors then measured major adverse cardiac events, defined as cardiac death or recurrent MI, over an average follow-up period of 3.4 years. Although depression alone was a significant predictor of cardiac events (including cardiac death), this relation disappeared when a measure of anxiety was included in the multivariate model.

In a subsequent study with similar methodology, Strik et al.[89] found similar results with a sample of 206 men and women followed for 3 years after their first MI.

As summarized in Evidence Grade Table 2, we concluded that the overall body of evidence on question 3, looking at cardiac events as an outcome, merited a medium quantity of evidence and reasonable quality of evidence despite the presence of some inconsistencies in the evidence (see Appendix F).

Results of Studies on Depression and Quality of Life

Studies that addressed QOL measures reported the relation of depression during the initial MI hospitalization to physical-behavioral function,[6,23,40,65,67,93,111] psychological well-being,[6,63,65,67,109-111] social and work role performance,[6,23,65,93,107,108,111] and personal perception of health[6,23,65] (See Table and Evidence Table 3-4 in Appendix G). Several studies reported on multiple aspects of health-related QOL. Some studies reported the relation of depression at the time of the initial MI hospitalization to QOL measures within the first 12 months post-MI,[63,67,107,108,111] whereas others reported on the relation to QOL at least 12 months post-MI.[6,110]

Two articles reported on the same sample at 4-month follow-up[40] and at 12-month follow-up.[23] Three studies reported on both near- and long- term outcome.[65,93,109]

One study reported that depression as assessed by the HADS during the initial MI hospitalization was prospectively associated with a reduced score on the mental component of the short-form health survey (SF-36 Mental Component Score) but not with the SF-36 Physical Component Score at 5 months post-MI.[67] Another study found that in-hospital depression for females and 1-month post-MI depression for males were prospectively related to the physical domain of QOL at 6 months as assessed by the Quality of Life After MI measure.[111] This study also reported that social aspects of QOL at 6 months were predicted by in-hospital and 1-month depression for women but not for men and that 6-month psychological QOL was not related to depression at either earlier time for either sex.[111] In-hospital depression measured with the BDI was prospectively related to sexual activity and sexual satisfaction of men 3 to 6 months post-MI in a multivariate analysis controlling for demographic (e.g., age, education) and medical (e.g., Killip class, diabetes mellitus) variables.[107] One study among Japanese men documented that in-hospital symptoms of depression after an MI were prospectively related to dichotomously measured return to work in multivariate analysis, but not to time until work resumption or returning to work at a reduced capacity.[108] Thus, during the 1-year rehabilitation period, post-MI depression has been found to be related to physical QOL, social QOL of women, sexual activity and satisfaction among men, return to work of employed men, and health care utilization.

Another study found that QOL 4 months after MI measured with Dartmouth Primary Care Cooperative Information Project (COOP) charts (combining physical, social, role functioning, general health, pain, change in health, social support, and perceived health) was related to in-hospital depression (BDI), having a partner, MI severity and state anxiety, even after controlling for sociodemographic, activity, and illness variables.[40] In a follow-up of this sample,[23] depression, living alone, MI severity (Peel Index score), and state anxiety were found to be independent predictors of 12-month QOL, even when controlling for sociodemographic, activity, and illness variables.

The three repeated-measures studies in this section had remarkable consistency across short-term and long-term follow-ups. Individuals with high in-hospital distress (i.e., above established cutoffs for either HADS-depression or HADS-anxiety scales) scored significantly lower on all eight subscales of the SF-36 (four physical and four psychosocial) at 3-month follow-up.[65] The mean HADS-depression score for the distressed group was significantly higher than for the nondistressed group. Consistent with the 3-month follow-up data, individuals with high in-hospital distress scored significantly lower on all eight subscales of the SF-36 at the 12-month follow-up.[65] DSM-III depressive disorder diagnosed in-hospital with use of the Present State Exam was associated with poorer physical functioning and greater depression severity only at discharge, and with less social connectedness only at the 6-month follow-up, whereas social functioning was significantly worse at the 3-, 6-, 9- and 12-month follow-ups.[93] The third repeated-measures study found that in-hospital depression measured with the BDI was significantly related to psychological distress among male survivors of MI as measured by using the Mental Health Inventory at the 3- to 6-month post-MI follow-up, with controlling for sociodemographic and medical variables.[109] Furthermore, psychological distress at 3 to 6 months moderated the effect of in-hospital depression on psychological distress at the 5-year follow-up among male survivors of MI, also with controlling for sociodemographic and medical variables.[109] Thus, at both early and late follow-up times, in-hospital depression has been shown to be related to physical, psychological, and social health and function.

The 5-year QOL outcomes of patients with acute MI were examined in two studies. In-hospital depression measured with the BDI was significantly related to psychological well-being of women at the 5-year post-MI follow-up, as measured using the Mental Health Inventory and controlling for sociodemographic and medical variables.[110] Similarly, among female survivors of MI, in-hospital depression and self-reported concomitant medical problems were related to psychological distress 5 years later.[110] One 5-year outcome study used cutoffs on the Health Complaint Scale's somatic complaints and disability subscales to define poor QOL. Multivariate analysis found a significant relation between symptoms of depression (ZDS) and poor QOL.[6] Thus, even 5 years after MI, psychological distress and physical health and functioning were related to in-hospital depression independent of other important QOL determinants.

As summarized in Evidence Grade Table 2, we concluded that the overall body of evidence on question 3, looking at quality of life outcomes, merited a medium quantity of evidence and low quality of evidence despite the presence of some inconsistencies in the evidence (see Appendix F).

Results of Studies on Depression and Surrogate Markers of Cardiac Risk

Three studies reported data on surrogate markers of cardiac risk. (See Table Evidence Table 3-1, 3-2, 3-3, and 3-4 in Appendix G.) Carney et al. evaluated HRV in 673 patients with acute MI between October 1997 and January 2000 who were screened for participation in the ENRICHD trial.[112] The depressed subjects were eligible if they had a DSM-IV diagnosis of major or minor depression and a BDI score of 10 or higher within 28 days of admission for acute MI. The control group consisted of patients who were otherwise eligible for ENRICHD but did not meet the depression or social isolation criteria. Major exclusions included atrial fibrillation or flutter, the presence of an implanted electronic cardiac pacemaker, severe medical or severe psychiatric comorbidity, cognitive impairment, or substance abuse. Spectral HRV analysis was performed from ambulatory electrocardiographic monitors for the following bands: ultra low frequency (ULF, 1.15 x 10-5 Hz), very low frequency (VLF, 0.033 to 0.04 Hz) , low frequency (LF, 0.04 to 0.15 Hz), and high frequency (HF, 0.15-0.40 Hz).

All log-transformed indices of HRV were significantly lower in the 307 patients with depression than in the 365 without depression. The depressed patients were significantly younger (mean of 57.1 years versus 60.9 years), more likely to be female (49.5 percent versus 32 percent), more likely to have diabetes mellitus (34.5 percent versus 22.1 percent), and more likely to smoke cigarettes (40.7 percent versus 23.5 percent). After adjustment for the baseline demographic differences, depression remained significantly associated with lower indices of all parameters of HRV except HF power. This study is consistent with greater autonomic dysregulation among post-MI patients with depression as compared with post-MI patients without depression.

Kuijpers et al. studied platelet function after a first MI in 24 patients, 12 of whom met DSM-IV criteria for major depression and 12 of whom did not.[113] There were 10 men and two women in each group; the mean age was 48.0 years in the depressed group and 49.8 years in the group without depression (see Evidence Table 3a-2 in Appendix G). In the depressed group, five patients smoked and one was hypertensive; in the non-depressed group, three smoked and six were hypertensive. At the time of the study all patients in the depressed group were taking aspirin. In the group without depression, 11 were using aspirin and one was using warfarin.

Nondepressed patients were more likely than depressed patients to use ACE inhibitors (nine nondepressed patients versus four depressed patients) and nitrates (four nondepressed patients versus one depressed patient). Platelet factor 4 was significantly higher in patients with depression than in those without depression (mean 17.75 IU/mL versus 9.25 IU/mL, p = 0.02). Depressed patients tended to have higher levels of platelet beta-thromboglobulin (mean rank 15.04 IU/mL vs. 9.96 IU/mL, p = 0.08). Although the sample size of this study was small, the results suggest that despite the use of aspirin, patients with post-MI depression have higher levels of platelet activity.

Lesperance and colleagues reported on the relationship between inflammatory markers and depression in patients with ACS.[91] These authors studied patients 23 to 120 days after discharge from the hospital with a diagnosis of ACS between August 1999 and August 2002 (see Evidence Table 3a-2 in Appendix G). Altogether, 481 patients participated in this study, of whom 35 met DSM-IV criteria for the diagnosis of major depression according to the SCID. Of the 446 patients without depression, 367 (82 percent) had an MI and 74 percent of the depressed patients had an MI. The investigators measured levels of IL-6, soluble intercellular adhesion molecule-1 (sICAM-1), and CRP. Of these inflammatory markers only sICAM-1 was found to differ between depressed and nondepressed patients (mean 5.34 mg/mL versus 5.20 mg/mL). A number of characteristics were associated with higher levels of sICAM-1: older age, female sex, smoking, prior MI or coronary revascularization, metabolic syndrome, body mass index, use of antidepressants or adenosine diphosphate inhibitors, and not taking statins. After adjustment for sex, current smoking, and the presence of metabolic syndrome, depression remained a significant factor associated with higher sICAM-1 levels (p = 0.04). When the current use of antidepressants was included in the model, the effect of major depression was somewhat attenuated (p = 0.06). A significant interaction between depression and the use of statins was found with respect to CRP levels. Among those patients not taking a statin, those with current depression had significantly higher levels of CRP than those without depression. The results of this study demonstrate that patients with depression after ACS have higher levels of some inflammatory mediators that previously have been associated with an increased of coronary disease. However, this particular study, because of its cross-sectional design, could not establish whether these inflammatory markers were increased before the index event.

As summarized in Evidence Grade Table 3, we concluded that the overall body of evidence on question 3, looking at surrogate markers of disease severity as an outcome, merited a low quantity of evidence and high quality of evidence for some surrogate markers and low quality of evidence for others (see Appendix F).

Key Question 4

Question 4. Do post-MI patients with depression who received depression treatment have better outcomes than post-MI depression patients who did not receive such treatment?

Introduction

The preceding sections of this evidence review have focused on the risks associated with having depression after an MI. Most of this evidence is based on observational studies and statistical approaches to determine whether any association between depression and these outcomes is independent of other factors. Studies of treatment for depression can provide

important information on causal inferences for depression and poor outcomes. Treatment studies also address the issue of greatest concern to patients and clinicians: Can treatment reduce any of the increased risks that may be associated with having depression? Question 4 addresses whether post-MI patients with depression have better outcomes with depression treatment than do those without such treatment. An important aspect of this question relates to determining whether it is the resolution of the depression, or the treatment itself, that reduces the risk. For example, if SSRIs improve outcomes, is it because the SSRIs have beneficial platelet effects, or is it because the SSRIs increase the rate of depression resolution? These issues are the motivation for question 4.

Results of Literature Search

Our comprehensive literature search identified 12 articles addressing this question. Eleven studies were randomized clinical trials, and one used a less rigorous method for developing comparison groups. A common reason for eliminating studies was that patients entered into the studies did not all have clinical depression, and the results for the depression subgroup were not presented separately. Such studies do not provide direct evidence regarding question 4. One meta-analysis[116] addressed the question of whether the addition of psychosocial interventions improves the outcome of a standard rehabilitation regimen for patients with CAD. The authors used a broad definition of psychosocial interventions and identified 23 randomized clinical trials. They concluded that the addition of psychosocial treatments to standardized cardiac rehabilitation regimens reduces mortality and morbidity, psychological distress, and some biological risk factors.

Characteristics and Results of Studies

Table and Evidence Table 4.1 , 4.2, 4.3, and 4.4 in Appendix G, highlight characteristics and results of the studies eligible for our question 4. All were based in North America or England, although one study recruited some patients from Australia and Europe.[59] The dates of publication for these studies ranged from 1991 to 2003. There was an excellent balance in the studies with seven addressing psychosocial interventions and five focusing primarily on antidepressant medications. The majority of the subjects had had a recent MI, but some studies included patients with CAD and no MI in the previous 6 months. All of the studies included women and men, but men accounted for about 75 percent of the total participants. Some studies excluded individuals over age 70. Apart from the ENRICHD trial, the ethnic diversity of the study samples was limited.

The largest studies with the highest quality data that most directly address the question are the SADHART or SADHART[59] and the ENRICHD study.[58] SADHART was conducted in 40 outpatient cardiology centers in seven countries. Participants were randomized to 24 weeks of double-blind treatment with either sertraline or placebo. Participants were recruited in the hospital by either chart review or physician referral. Inclusion criteria included being hospitalized for either an MI or unstable angina in the past 30 days. Diagnosis of MI was made according to standard criteria. Unstable angina was defined as having (1) typical ischemic symptoms lasting longer than 10 minutes, (2) being hospitalized, and (3) having changes on an electrocardiogram (ECG) within the previous 12 hours. Alternatively, one could meet criteria for unstable angina by being hospitalized with unstable angina and having known CAD. Depression

was identified with the DIS completed by a trained interviewer and with the self-rated BDI. The DIS was completed within 30 days of the hospitalization. For the DIS the 2-week duration criteria and impairment criteria were eliminated for the diagnosis of major depression because of the complicating cardiac event. Exclusions included (1) uncontrolled hypertension, (2) cardiac surgery anticipated in the next 6 months, (3) MI or cardiac surgery in the previous 3 months, (4) congestive heart failure, (5) bradycardia, and (6) MI or unstable angina of a nonatherosclerotic etiology. Psychiatric exclusions included alcohol or substance abuse, psychotic illness, cognitive impairment, current use of an antidepressant, or initiation of psychotherapy in the past 3 months.

After meeting the initial eligibility criteria for the study, all participants received placebo for 14 days. During this time they completed their cardiovascular tests and a psychiatrist confirmed that their depressive symptoms were present for 2 weeks. Because many of the participants had mild depression, they were stratified by severity of depression, and it was hypothesized that those with more severe depression would have a greater benefit from treatment with sertraline. Participants were started on sertraline 50 mg daily and could be systematically increased to 200 mg daily. The only other psychotropic medications allowed were chloral hydrate and zopiclone. The primary goal for the study was to evaluate the cardiac safety of sertraline. Therefore, the primary outcome was cardiac function, specifically LVEF. Depression outcomes included the BDI and 17-item HAMD (assessed up to 16 weeks) and Clinical Global Severity (assessed up to 24 weeks). Cardiac events were adjudicated by a committee. Revascularization was not considered an endpoint for this study.

Of the 556 individuals who were initially eligible, 369 individuals remained eligible after the 2-week run-in phase and were randomized. Because of the run-in phase, the mean time to start the intervention was 24 days after MI. There were no significant baseline differences between the groups. Most patients were aged between 50 and 70 years and had least two cardiac risk factors. While most had mild to moderate levels of depression, 25 percent met criteria for more severe depression. Most participants completed treatment (mean of 149 days) and achieved a low dose of sertraline at the end (mean of 68 mg daily). Those on sertraline did report more nausea and diarrhea, common side effects of sertraline.

The investigators presented data on 260 participants with baseline and final data (70 percent completion rate). As shown in Table 4.2, there were no differences in cardiac function at follow-up between those on sertraline and those receiving placebo. For important cardiac event outcomes, there was a trend toward lower numbers of events for those on sertraline. For the composite end point of death or cardiovascular events, the relative risk was 0.77 for those on sertraline compared with those on placebo, but the 95 percent confidence interval was moderately wide (0.51 to 1.16).

For depression outcomes, the results generally indicated that the sertraline group had better outcomes. The study groups did not differ on the HAMD ratings but these ratings stopped at 16 weeks. Clinical Global Inventory outcomes were assessed through 24 weeks and did differ between the study groups. For those with a history of recurrent depression, outcomes for those randomized to sertraline were better than for those receiving placebo for both the Clinical Global Severity and HAMD ratings.

About 20 percent of the participants in the study had not experienced a recent MI. Results were not presented separately for those with an MI. No Kaplan-Meier data were presented to determine when the sertraline began to affect cardiac outcomes. It also was not clear how drop outs were handled in the analysis.

A second paper from the SADHART study was also included in our review. This study focused on QOL outcomes.[117] For this analysis more than 90 percent of all randomized patients provided data. Overall, both the sertraline and placebo groups showed improvement in QOL. According to results from the Medical Outcomes Study Short Form 36 (SF-36), the study groups did not differ in Physical Component or Mental Component change scores. However, for the recurrent depression group, there was a significantly positive change on the Mental Component score for those on sertraline compared with those receiving placebo, and there was a trend toward more improvement on the Physical Component score as well. Similar results were found using the Quality of Life Enjoyment and Satisfaction scale (Q-LES-Q).

A second major study addressed the efficacy of treatment for depression in individuals who have depression after an MI—the ENRICHD study.[118] This multicenter trial was designed to measure the effect of a psychosocial and cognitive behavior therapy intervention. A total of 2,481 patients were recruited from eight clinical centers for the study. Eligibility requirements included meeting criteria for either depression (39 percent) or social isolation (26 percent), or both (34 percent). The depression measure was based on the Depression Interview and Structured Hamilton (DISH) instrument. The major modification with this instrument is that patients were eligible if they had depressive symptoms for 1 week, provided they had previously had an episode of major depression. DISH and BDI scores indicated most patients had moderate to minor levels of depression. The participants all had to be enrolled within 28 days of their MI. Initially the participants could not be taking antidepressants, but halfway through the study patients who remained depressed even after taking antidepressants for at least 14 days were included in the study. The criteria used to establish an MI were standard.

Patients were assigned randomly either to the intervention or routine care. Patients in both groups received written materials about cardiac risk factors based on the American Heart Association Active Partnership Program, and those in usual care had physician notification of their depression. The intervention included cognitive behavioral therapy provided first with three individual sessions and then within a group setting. Therapy could last up to 6 months. Intervention patients were referred to study psychiatrists for initiation of pharmacotherapy if they had scores higher than 24 on the HAMD or if they had less than 50 percent reduction in BDI scores after 5 weeks. Pharmacotherapy was usually sertraline and could be continued for up to 12 months.

As shown in Evidence Table 2, study participants had a mean age of 61 years, 44 percent were female, 33 percent were nonwhite, and 47 percent had a high school education or higher. Cardiovascular risk factors were as expected, with 64 percent having a smoking history and 33 percent having diabetes mellitus. Seven percent had a Killip class of III or IV; 83 percent had a cardiac catheterization; and 17 percent had a subsequent CABG surgery. Use of cardiac medications was common.

Between 1996 and 1999, 2,481 patients were randomized. Vital status was ascertained for 93 percent of patients at 6 months and all patients were followed for at least 18 months. Ninety-two percent of those randomized to the intervention received the intervention as assigned. Median time to enrollment was 6 days post-MI, and the intervention started a median of 17 days after MI. Patients attended a median of 14 sessions. At baseline the intervention group was more likely to be on an antidepressant (9.1 percent versus 4.8 percent), and these differences were still apparent at the end of data collection (21 percent versus 14.6 percent).

Depression scores improved for both groups, but the intervention produced significant but modest differences in depression at 6 months as measured by the BDI and HAMD. At 30 months

there were no differences between the intervention and usual care groups in terms of all-cause mortality, cardiovascular mortality, or nonfatal cardiac events. There was a statistically significant interaction between gender, intervention, and risk of death or recurrent nonfatal MI. Men in the intervention group had better outcomes than men in the usual care group, and women in the intervention group had worse outcomes than women in the usual care group.

Although not part of the randomized component of the study, the investigators presented an analysis of whether those on antidepressants had better cardiac outcomes. In both crude analyses and analyses adjusting for baseline variables including age, BDI score, Killip class, ejection fraction, serum creatinine, previous MI and prior diagnosis of congestive heart failure, stroke or transient ischemic attack, pulmonary disease or diabetes, the hazard rate for death or nonfatal MI was 0.63 (95 percent CI, 0.46 to 0.87) for those taking antidepressants compared with those not taking antidepressants. Antidepressant use was modeled as a time-dependent variable.

Overall, this study provided a high-quality counseling intervention that was initiated soon after an MI. It had a modest effect on depression but did not have any effect on cardiac outcomes early or up to 42 months of follow-up. Despite including individuals with only low social support, it did not seem to complicate conclusions related to depression care and outcomes. Any conclusions concerning the effects of antidepressants on cardiac outcomes are less certain. In light of the study protocol, which was to refer those only among the experimental group with high or persistent depression scores to be evaluated for antidepressants, it seems likely that those on antidepressants would have higher depression scores. This non-randomized component of the study could potentially produce selection bias, as antidepressants are related to both the exposure (psychosocial intervention) and the outcomes; thus it makes the experimental group look better than the control group, even if no true association exists. In their analysis the investigators adjusted for baseline BDI scores but not for subsequent BDI scores. It would appear that the analysis presented in the manuscript might underestimate the effect of antidepressants because it did not fully adjust for depression severity. It also would be reassuring to report if the effect of antidepressant therapy was detectable for both those in the usual care group and those in the intervention group. The analysis regarding antidepressants excluded all those who had entered the trial only for low social support. However, it was not clear who the comparison group was in this antidepressant analysis. Also, the study did not adjust for willingness to accept a recommendation to start an antidepressant, which may be a marker for overall adherence to multiple care recommendations.

Other psychosocial intervention studies. With numerous studies demonstrating that depression is a risk for poor outcomes after an MI, several investigations were conducted to determine whether psychosocial interventions might reduce the elevated risk. The minimal risks associated with psychosocial interventions make such interventions attractive for patients who usually require multiple medical interventions for their cardiac care.

Frasure-Smith and colleagues[48] completed a randomized clinical trial involving 1,376 post-MI patients in which they compared a supportive and educational home nursing intervention and usual care. Most of the participants did not have significant problems with anxiety and depression. The mean BDI score was only 8.3 at baseline with 33 percent above the usual cutoff for clinical depression. The intervention was designed to address psychological distress, not specifically depression. The investigators met their target for intervention frequency in 87 to 94 percent of the participants. Contact for most patients receiving the intervention was spread out over 6 to 7 months. Despite meeting their intervention target goals, the investigators found that

mean BDI scores at 1 year had no greater reduction for those in the intervention group than for those in the usual care group. It is unlikely there would be large intervention effects for the subgroup with high levels of depression at baseline if there were no differences in mean change in BDI scores, but data on the subgroup of participants having a score above 10 on the baseline BDI would have been informative. The authors did not provide information on the percentage of patients receiving antidepressant medication or formal psychotherapy. In terms of cardiac death, noncardiac death, nonfatal reinfarctions, or hospital readmission, there were no statistical differences by intervention status. Women in the intervention group tended to do worse than those in the usual care group. For men, there were no significant differences between the intervention and usual care groups. The authors speculated that the intervention nurses did not receive specific training in psychiatric-disorder screening and psychotherapeutic techniques, and this deficiency might account for the lack of effect of the intervention. In addition, the low need for depression treatment at baseline effectively limited power to detect differences in outcome.

Taylor and colleagues[119] tested the effect of a home-based, case-managed, multifactorial risk reduction program with 585 men and women aged 70 years or younger who were hospitalized for an acute MI in one of five San Francisco Bay Area hospitals. The intervention began in the hospital and included screening for psychological distress, monitoring with follow-up phone calls, and referring for mental health treatment when necessary. Patients were assessed at 6 months and 12 months. Of note is the unusual manner in which depressive symptoms were assessed. Depression was assessed with a single question about mood. With depression assessed by a single question, it is nearly impossible to detect any change. During follow-up, depression scores dropped significantly for both groups. There were no differences between the intervention and usual care groups. The intervention was not effective even for those with moderate-to-severe depression scores at baseline.

Johnston et al.[49] randomized by ward and recruited 100 patients from a Scottish hospital within 72 hours of admission for acute MI. Despite randomization at a group level, the study groups were balanced on important baseline characteristics. Randomization was to usual care, inpatient cardiac rehabilitation, or extended rehabilitation. The extended rehabilitation group was followed for up to 6 weeks after discharge and received a mean total of 9.5 sessions with 8.4 hours of contact. Patients and their spouses picked topics and received "nonjudgmental" counseling with a focus on helping patients achieve their objectives. Possible topics included explanation of heart attacks, risk factor modification, or emotional effects after a heart attack. Depression scores, which were measured at baseline, discharge, 2 months, 6 months, and 12 months after discharge with use of the HADS, indicated significantly lower levels of depression for both intervention groups. Unlike most studies the depression scores worsened for the usual care group after leaving the hospital. The authors suggested that their intervention had better results than others because the approach was one-to-one and not group, nurses worked from a treatment manual, and partners were included.

The study by Dracup et al.[47] compared 41 patients who participated in a structured outpatient cardiac rehabilitation program to 100 patients who did not complete cardiac rehabilitation. There was no randomization. All patients were living with a partner. Patient characteristics at baseline were similar for the two groups. Depression was measured with the Multiple Affect Adjective Checklist. Between baseline and 6 months, the cardiac rehabilitation patients had a reduction in their depression score, whereas the group without cardiac rehabilitation had no reduction. These differences were statistically significant, but the statistical adjustment for covariates was not clear.

Brown and colleagues[45] recruited patients from the cardiac rehabilitation centers of five major medical centers. All participants were required to have (1) MI or CABG within the past 4 and 4 to 24 months, (2) prognosis no worse than 3.3 (New York Heart Association Criteria), which indicates a moderately compromised cardiac status, (3) stable cardiac disease and no contraindications to physical activity, (4) onset of depression/anxiety associated with MI/CABG as assessed by the Schedule of Affective Disorders and Schizophrenia, (5) scores greater than 13 on the BDI or above 70 on the SCL-90 - Revised, and (6) spouses, friends, or relatives willing to participate in the treatment intervention. As compared with other study samples, this sample included individuals having higher levels of depression. Participants were randomized to either active treatment or attention control. Active treatment focused on principles of behavior therapy with relaxation training and some cognitive restructuring self-instruction. Treatment, which included 12 weekly sessions, was provided by three different therapists. Clinician ratings were completed by raters blinded to the intervention status of the participants. Both groups improved on depression ratings (self-report and clinician ratings), but at 12 and 15 months the behavior therapy group continued to improve whereas the attention control group began to relapse. No information on cardiovascular outcomes was collected.

The manuscript by Crowe and colleagues[46] describes an observational study with a randomized component in which patients did or did not receive cardiac rehabilitation intervention. It is very difficult to determine the actual study design from the article. Evidence Table 4.4 suggests that both the rehabilitation and usual care group demonstrated major improvement in depression during the follow-up, but there were no differences between the groups.

Other antidepressant intervention studies. Most of the pharmacological studies have used SSRI antidepressant medications. A 1998 study compared nortriptyline (tricyclic antidepressant) with paroxetine (SSRI).[120] As part of this study, 81 individuals younger than 65 years who had ischemic heart disease and moderately severe major depression (16 or higher on the 17-item HAMD) were randomized to either paroxetine or nortriptyline. Each patient completed a 2-week placebo lead-in phase to establish the stability of the depression diagnosis and to complete their cardiovascular tests. About two thirds of the patients had a history of MI, but the MI was not recent. The primary aim of the study was to determine the effect of the two types of antidepressant medication on cardiovascular outcomes. Patients received the study medication in a double-blind fashion for 6 weeks. Both medications were equally effective in reducing depression (60 percent achieved a 50 percent reduction in depressive symptoms). However, more participants withdrew from the nortriptyline than the paroxetine group (10 versus 2). Paroxetine did not have a significant effect on heart rate, blood pressure, conduction intervals, or ventricular arrhythmias. Nortriptyline was associated with an 11 percent increase in heart rate, a significant decline in standing systolic blood pressure, and a decrease in HRV. There was no effect on cardiac conduction. For equally effective treatments, the SSRI had less cardiovascular effects than did the tricyclic antidepressant. This study was funded by Smith-Kline Beecham, the manufacturer of paroxetine.

Another small study looked at the safety and efficacy of fluoxetine in the treatment of patients with major depression after a MI.[50] For this study, depression was confirmed by a clinician-administered HAMD between month 3 and month 12 after an MI, and patients younger than 75 years were eligible. In this double-blind study, 54 patients were randomized to either fluoxetine or placebo for 9 weeks. Despite the small sample size there was nearly a statistically

significant greater reduction in depression for the fluoxetine group than for the placebo group. For the majority of cardiovascular measures there were no differences between those randomized to fluoxetine or placebo. The investigators measured cardiac output using the aortic time velocity integral and found it increased in the placebo group and decreased in the fluoxetine group. The QRS interval was lower in those on fluoxetine than in the placebo group (p=.03). This study was funded by Eli Lilly, manufacturer of fluoxetine.

In 2000 McFarlane and colleagues[121] reported the results of a double-blind, randomized, placebo-controlled study of sertraline in 38 post-MI patients. The total sample was small with 12 randomized to sertraline, 15 to placebo, and 11 non-depressed age-matched controls. Depression was diagnosed with a validated self-report instrument called the Inventory to Diagnose Depression (IDD). The IDD was administered before hospital discharge and again within 2 weeks of the acute infarct. Ejection fractions averaged over 50 percent in each group. Depression scores tended to decrease faster in the sertraline group than the placebo group. Standard deviation of normal R-R interval (SDNN), a measure of HRV, increased by 5 percent in the sertraline group and decreased 9 percent in the placebo group. Lower levels of SDNN have been reported to be a marker for increased cardiac mortality. Differences by study group were not evident in several other markers of HRV. This study was not supported by a pharmaceutical company but by the Heart and Stroke Foundation of Ontario, Canada.

As summarized in Evidence Grade Table 4, we concluded that the overall body of evidence on question 4 merited a medium quantity of evidence and medium to low quality of evidence (see Appendix F).

Quality of Studies

There was a wide variation in the quality of the eligible studies with the larger and more recent studies generally having higher levels of quality. Median quality scores across the various domains of study quality ranged from a low of 50 percent on statistical analysis and measurement of depression to 100 percent on reporting potential conflicts of interest. (See Evidence Table 4.3 in Appendix G)

Key Question 5

Q5. What are the performance characteristics (e.g., sensitivity, specificity, reliability, and predictive value) of instruments that are used to screen for depression (or depressive symptoms) after an acute MI?

Q5a. What are the performance characteristics of instruments that are used to screen for depression (or depressive symptoms) after an acute MI, during hospitalization?

Q5b. What are the performance characteristics of instruments that are used to screen for depression (or depressive symptoms) after an acute MI, within 3 months after hospitalization?

Introduction

Clinicians and investigators need accurate and reliable methods to screen for depression in post-MI patients. The screening assessment methods should have adequate validity, reliability, and diagnostic utility within post-MI populations. Population-specific evaluation of the performance characteristics of assessment tools is particularly important with MI survivors because somatic symptoms of depression are easily mistaken for, and often overlap with, the physical sequelae of MI. Moreover, the timing of the depression assessment may influence its reliability and accuracy given that the hospitalization itself (question 5a) may adversely affect sleep habits, appetite, and other aspects of the usual depression assessment. Adequate validity of an assessment instrument is achieved if the instrument can successfully measure depression and differentiate it from similar, but distinct constructs. Reliability refers to the degree of consistency of a measure. Diagnostic utility refers to the extent to which a measure correctly identifies individuals who meet or do not meet certain diagnostic criteria as determined by a "gold standard," which for depression would typically be a structured interview process. Validity, reliability, and diagnostic utility are multidimensional concepts that gain strength with convergence of evidence. They cannot be established globally for a particular instrument, but rather defined in terms of specific groups or populations and the purpose for which they are used (i.e., screening versus research diagnosis).

As reviewed in the section of the report on questions 1 and 2, numerous measurement instruments have been used to assess depression in post-MI patient populations. Perhaps the two most frequently used instruments are the BDI and the HADS. Evidence was presented in the section of the report on questions 1 and 2 indicating that the BDI tends to produce higher prevalence estimates across studies than the HADS. This finding raises questions about the performance characteristics of these and other measures used with post-MI patients. This section will review evidence related to the validity, reliability, and diagnostic utility of assessment techniques that have been used to evaluate depression in survivors of MI.

Results of Literature Search

After article review, seven articles were eligible for review on question 5. One study was excluded at this point because it did not report specific cutoff criteria used for diagnosing depression. Of the six remaining studies, two also were deemed eligible for question 5a.[119,122] In one of these two studies, the majority of participants (78 percent) were interviewed during hospitalization and the balance post-discharge, but within 28 days of the index MI.[122] Three studies were eligible for question 5b as well as for question 5.[75,90,123] One study reported data relevant to both questions 5a and 5b.[66]

Characteristics of Studies

A summary of key aspects of the six eligible studies is presented in Appendix G Tables 5. Included studies were published between 1988 and 2003. All of the studies were composed entirely of post-MI patients. Two studies reported data on diagnostic utility,[75,90] two on factor/construct validity,[66,119] one on convergent validity,[122] one on discriminant validity,[123] and two on internal consistency reliability.[66,119] Four studies were conducted in Europe,[66,90,119,123] one in Canada,[75] and one in the United States.[122] Only one - which included over 2,000 participants, but provided limited data for this question - was a multicenter study.[122] The other studies included between 52 and 335 participants. The mean age of participants ranged from 51

to 67 years. The ENRICHD study,[122] which was designed to maximize diversity of participants, enrolled 44 percent women and 34 percent non-white participants. The other studies enrolled between 73 and 90 percent men. Only one other study provided data on race; it enrolled only white participants.[90] The ENRICHD study[122] was the only eligible study to report cardiac risk factors, and none of the studies reported MI characteristics such as Killip class or LVEF.

Quality of Studies

As shown in Table 5.2, the number of studies that had a study quality score higher than 50 percent were as follows: five for representativeness of the study population, three for potential bias and confounding, two for description of therapy and management, four for description of assessment protocol, two for test interpretation, two for reporting of outcomes and follow-up, and five for statistical analyses. Only two studies reported information on potential conflicts of interest.

Results of Studies

Table 5.1 presents evidence on performance characteristics of measures of depression with post-MI samples, as reported by the six reviewed articles. The three studies that reported performance data from hospitalized post-MI populations included data on the BDI, the HADS, and the HAMD. The BDI is a 21-item self-report rating scale measuring characteristic attitudes and symptoms of depression. The HAMD is a 17-item observer rated scale to assess the presence and severity of depressive symptoms. The HADS is a 14-item (seven depression items) self-report questionnaire designed to detect symptoms of anxiety and depression in a non-psychiatric hospitalized population.

Internal consistency reliability for the HADS and the HADS Depression subscale (HADS-D) as measured by Cronbach's alpha was found to be 0.82 and 0.72, respectively, in a sample of 194 male and female patients.[119] Another study by the same authors, which included 335 male and female patients, reported internal consistency reliability for the HADS as 0.87, 0.88, and 0.90 at 1 week in-hospital, 6 weeks, and 6 months post-MI and for the HADS-D as 0.76, 0.80, and 0.81 for the same follow-up times.[66] Nunnally has suggested a widely referenced guideline of 0.70 as a lower bound for acceptability of internal consistency reliability. These two studies also reported data from an exploratory factor analysis[119] and confirmatory factor analyses across time[66] that supported the construct validity of the HADS-D as measuring depression distinct from anxiety.

The ENRICHD investigators[122] reported evidence on the convergent validity of the self-report BDI and the HAMD, the items of which were embedded in an SCID. A Pearson correlation coefficient between the BDI and the HAMD was 0.64, close to the low end of the range of similar correlations that have been reported in other clinical settings (0.61 to 0.87).[124] The ENRICHD sample, however, included only individuals with symptoms of depression. This stipulation would be expected to restrict the range of scores on the BDI and HAMD and to lower the correlation coefficient compared to what might be found in a screening sample of both depressed and nondepressed individuals.

Three additional studies reported psychometric data within 3 months after hospitalization for the BDI, the HADS, the HAMD, the Symptom Checklist-90 Depression subscale (SCL-90-Dep), and the ZDS. The SCL-90 is a brief, multidimensional self-report inventory designed to screen

for a wide range of symptoms of psychopathology that includes an index of depression.[125] The ZDS is a 20-item self-rating scale to screen for symptoms of depression.[126]

Two studies assessed the diagnostic utility of measurement instruments as compared with a SCID for DSM diagnosis.[75,90] One of these studies[75] counted any subject with a total BDI score of 1 to 12 as symptomatic, resulting in difficult to interpret concordance data. This study was also limited by its very small sample size. In the other study,[90] data on diagnostic utility (sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were reported on both major depression and combined major and minor depression for the BDI, HADS and HADS-D, HAMD, and SCL-90-Dep as compared with a physician-administered SCID-IV. SCID-IV prevalence for major depression was 11.2 percent and 7.8 percent for minor depression with a combined prevalence of 18.9 percent. Cutoff points were derived by using receiver operating characteristic (ROC) analysis, which attempts to determine optimal sensitivity and specificity. The number of patients included in each comparison ranged from 179 to 206, depending on the measure. For combined major and minor depression, sensitivities ranged from 0.75 for the HADS-D to 0.84 for the BDI. Specificities ranged from 0.72 for the BDI to 0.86 for the HAMD. PPVs ranged from 0.25 for the BDI to 0.41 for the HAMD. NPVs ranged from 0.93 for the SCL-90-Dep to 0.99 for the HAMD. For major depression alone, sensitivities ranged from 0.82 for the BDI to 0.96 for the SCL-90-Dep. Specificities ranged from 0.74 for the SCL-90-Dep to 0.92 for the HAMD. PPVs ranged from 0.32 for the HADS-D to 0.59 for the HAMD. NPVs ranged from 0.96 for the SCL-90-Dep to 0.98 for the HAMD, HADS-D, and BDI. Figures 3 and 4, show sensitivity and specificity data for all measures for major/minor and major depression.

One study[123] reported evidence on the convergent validity of the SCL-90-Dep and the ZDS for 143 patients with a Pearson correlation coefficient ranging from 0.70 to 0.77 across four time periods (1, 3, 6, and 12 months). Evidence related to discriminant validity was also reported for both the SCL-90-Dep and the ZDS as compared with a measure of "vital exhaustion" developed in the Netherlands. That these correlations ranged from 0.75 to 0.83 for the two measures across the four time periods suggests these measures do not discriminate well between depression and post-MI symptoms of fatigue. The construct validity of vital exhaustion, however, is unclear and the measurement instrument used included numerous symptoms of depression. Additionally, in this study patients with a diagnosis of clinical depression, as determined by the HAMD, at baseline were offered antidepressants and withdrawn from the study. The lack of patients with significant symptoms of depression in the study population may have contributed to the lack of differentiation reported between symptoms of depression and vital exhaustion.

As summarized in Evidence Grade Table 5, we concluded that the overall body of evidence on question 5 merited a low quantity of evidence and low quality of evidence (see Appendix F).

Summary of Studies

The measures reviewed here seem to be measuring depression based on adequate sensitivities and specificities across studies as compared with the SCID-IV[90] and evidence from confirmatory and exploratory factor analyses.[66,119] Evidence also exists for convergent validity[122,123] and adequate internal consistency[127] of the measures.

Given the limited number of studies and analyses performed, it is difficult to draw conclusions about performance characteristics at each time period. This is particularly true during the initial MI hospitalization. Overall, however, evidence is relatively scant regarding the

adequacy of the assessment of depression in post-MI populations. None of the measures reviewed here has been normalized explicitly on post-MI populations. In this context, two interrelated concerns predominate. The first relates to construct validity and how well these measures accurately distinguish between symptoms of depression and somatic symptoms related to poor physical health. The study samples covered in this review tended to be small for these purposes. Furthermore, the psychometric methods that were used are relatively weak ones and provide limited information. Existing psychometric methods that are able to establish the equivalence of key measurement characteristics across post-MI and nonhospitalized depressed subjects would be useful in refining assessment practices for depression in MI survivors.

A second concern relates to the intended use of the instruments reviewed and the very low PPVs reported.[90] If these instruments are to be used for general screening that will be followed by a more thorough assessment of those who screen positive, then low PPVs and high NPVs are acceptable, and cutoff points to achieve this objective have been reported.[90] A research setting, however, in which relatively few of those diagnosed with major depression are actually depressed (as compared with diagnosis by SCID-IV) is problematic and reduces the power to detect relationships between depression and outcome variables. Strik and colleagues[90] reported utility statistics for prominent measures of depression that were based on cutoff scores generated by an ROC paradigm intended to maximize combined sensitivity and specificity. This resulted in cutoff points well below those used in normal settings where cutoff points are set pragmatically according to specific clinical or research objectives. A stronger analysis might have included data for commonly used cutoff points. Despite this flaw, the study pointed out a potential problem in research on the relationship between depression and post-MI outcomes. The slightly higher cutoffs normally employed would be expected to lessen but not completely alleviate this problem.

Furthermore, Strik's study provides data relevant to the discrepancy in prevalence rates generated by studies using the BDI as compared with studies using the HADS. For combined major and minor depression, the BDI tends to be highly sensitive relative to the other measures, but with lower specificity. When only major depression is considered, the BDI is the least sensitive measure and is in the middle to lower range of specificities. This suggests that compared with the HADS, SCL-90-Dep, and HAMD, the BDI tends to diagnose patients with less significant depressive symptoms at much higher rates than do the other measures, but it may be less effective in accurately diagnosing major depression. Given the expected distribution of symptoms of depression, the BDI would be expected to identify more patients as having significant symptoms of depression, but it would do a poorer job of consistently identifying those who are most depressed.

In summary, the quality of evidence varies for performance characteristics of instruments that measure symptoms of depression in post-MI populations, both in terms of numbers of patients studied and in terms of types of evidence that have been reported.

Key Question 6

Question 6. Does use of cardiac treatment for patients with acute myocardial infarction differ for those with and those without depression?

Introduction

Patients who are depressed after MI may receive different treatment than patients without depressive symptoms. Several factors could explain this difference in practice. Patients with depression may have a diminished capacity to make important decisions about their health. As a result, depressed patients may be less willing to undergo cardiovascular procedures such as catheterization, percutaneous coronary intervention (PCI), or CABG. Depression may also result in decreased adherence with prescribed medications, refusal to participate in cardiac rehabilitation, and reluctance to make lifestyle changes such as smoking cessation. In addition, physicians and other health care providers may not refer patients with depression for cardiovascular procedures or other therapies like cardiac rehabilitation even when medically appropriate. This practice, in turn, might reflect a bias against depressed patients on the part of health care providers. Alternatively, the depressed patient's perception and communication of cardiovascular symptoms may differ from those of a patient without depression in a manner that makes it less likely for certain treatments to be considered necessary. To evaluate this question we reviewed the English language literature that addressed the relation of depressed mood to use of cardiac treatment after an acute MI.

Results of Literature Search

Our search found nine studies, published between 1982 and 2004, that met criteria for inclusion in this review (see Table 6).

Characteristics of Studies

As shown in Table 9, seven of the nine eligible studies on key question 6 used prospective cohort designs with the other using a retrospective cohort design.[52] Four studies reported whether patients with and without depression differed with regard to prescribed cardiac medications after MI.[79,81,89,128] Three studies evaluated adherence to secondary prevention medications and lifestyle recommendations in depressed and nondepressed patients.[128-130] Two studies evaluated whether patients with post-MI depression received invasive cardiac procedures at a different frequency compared to MI patients without depression. Two studies[131,132] examined factors associated with noncompletion of cardiac exercise rehabilitation.

Quality of Studies

As shown in Table 6.3, the number of eligible studies with scores greater than 50 percent for the following criteria, were as follows: six for representativeness of the study population, one for description of therapy and management, eight for description of the assessment protocol, seven for reporting of outcomes and follow-up, and seven for the statistical analyses. Only three studies provided information about potential conflicts of interest.

Results of Studies

Four studies have evaluated whether depressed and nondepressed post-MI patients are just as likely to be prescribed medications recommended to reduce post-MI risk (see Table 6.4). Ziegelstein et al.[128] in a U.S.-based study found that on hospital discharge depressed post-MI patients were less likely than patients without depression to be prescribed beta-blockers. They

found no difference in discharge prescriptions for aspirin, lipid-lowering therapy and ACE inhibitors between depressed and nondepressed patients. Steeds et al.[79] in a United Kingdom - based study also found that MI patients with depression when compared with those without depression had lower rates of use of beta-blockers (32 percent versus 55 percent, $p = 0.02$) and higher rates of use of calcium channel blockers (37 percent versus 12 percent, $p = 0.02$). Strik et al.[89] monitored 206 Dutch patients with a first MI for up to 3 years. Patients with major or minor depression were prescribed platelet inhibitors at significantly lower rates than those without depression (81 percent versus 95 percent, $p = 0.001$). However, no significant differences were observed between depressed and nondepressed patients in the use of beta-blockers or in the rates of use of PTCA. Lauzon and colleagues[81] studied 550 Canadian post-MI patients and found no difference between depressed and nondepressed patients in prescribed levels of use of aspirin, beta-blockers, lipid-lowering drugs, ACE inhibitors, nitrates, or calcium-channel blockers. They did find that depressed patients had a significantly higher rate of rehospitalization for cardiac complications than nondepressed patients. Overall, these studies were not consistent with each other. The U.S. - and U.K.-based studies both found that depression was associated with decreased use of beta-blockers in post-MI patients, whereas the Dutch and Canadian studies both found that depression was not associated with decreased use of beta-blockers in post-MI patients.

Three studies examined the effect of depression on adherence behaviors after MI (see Table 6-4). In the study performed by Ziegelstein et al.[128] 276 patients were followed for 4 months after an acute MI, and those with major depression and/or dysthymia were less likely to follow dietary, exercise, and stress-reduction recommendations or to take prescribed medications than were patients without depression. Conn et al.[129] assessed multiple self-care behaviors in 94 post-MI patients aged 65 years or older who were deemed capable of self-care. Depression, but not anxiety, was significantly associated with decreased adherence at 1 to 2 years of follow-up for all self-care behaviors assessed: exercise, diet, medications, smoking cessation, and stress management.[128] More recently, Romanelli et al. also studied adherence behaviors in post-MI patients aged 65 years or older.[130] They found that post-MI patients had significantly lower rates of adherence than nondepressed MI patients for use of prescribed medications as well as recommendations for following a low fat diet, increasing exercise, and reducing stress.[52,81] These three studies thus were consistent in showing that depression was associated with decreased adherence to prescribed medications and other risk reduction behaviors in post-MI patients.

Two studies examined the use of invasive procedures after MI (see Table 6-4). Druss et al.[52] reviewed Medicare claims in a national cohort of 113,653 patients coded as having MI and compared the 5,365 coded with a secondary diagnosis of mental disorder to the other 108,288. The patients with the following mental disorders were considered: schizophrenia, affective disorders, substance abuse, and others (excluding dementia and delirium). Those with mental disorders were significantly less likely than those without mental disorders to undergo cardiac catheterization, PTCA, and CABG. This decreased tendency for undergoing invasive cardiovascular procedures among post-MI patients, extended to the subgroup of 315 patients with a mental disorder characterized as an affective disorder, among whom the rates of catheterization, PTCA, and CABG were 33.4 percent, 9.2 percent, and 7.9 percent, respectively. Those rates were significantly lower than the rates observed in the patients without mental illness, which were 43.7 percent, 16.8 percent, and 12.6 percent, respectively. In contrast, Lauzon et al[73] studied 550 post-MI patients in Quebec hospitalized between 1996 and 1998 and found that 23 the rates of undergoing cardiac catheterization, PTCA, and CABG were not lower among those with BDI scores of 10 or higher than among those with BDI scores lower than 10.

Thus, these two studies reported conflicting results about the relation of depression to undergoing invasive procedures in post-MI patients.

One study by Blumenthal et al.[132] evaluated 35 post-MI patients referred for cardiac rehabilitation for factors associated with completion of the prescribed program (see Table 6.2). They found that patients with higher depression scores on the Minnesota Multiphase Personality Inventory (MMPI) were more likely to drop out of the program ($p < 0.03$). However, in multivariate analysis, only ejection fraction, ego strength, and social introversion were associated with continued adherence to the cardiac rehabilitation program. Another study,[133] performed in the United Kingdom examined psychological determinants of attendance in cardiac rehabilitation among 93 patients after an acute MI (see Table 6.2). These investigators found that the best predictors of poor or no attendance were lower perceptions of symptoms and controllability or curability of illness, and less frequent use of problem-focused coping strategies and more frequent use of maladaptive coping strategies. Although depression scores on the HADS were lower among those with poor or no attendance, depression score was not an independent determinant of attendance in cardiac rehabilitation. The higher depression score among attendees suggests that those who are experiencing a greater degree of distress after MI are more likely to attend, but this explanation is not conclusive. Because neither of these studies enrolled a sufficient number of patients with a clinical diagnosis of depression, a definitive conclusion about an independent relationship between depression and completion of recommended cardiac rehabilitation is not possible.

As summarized in Evidence Grade Table 6, we concluded that the overall body of evidence on question 6 merited a low quantity of evidence and medium to low quality of evidence (see Appendix F).

Chapter 4. Discussion

Conclusions and Limitations

Question 1. In patients hospitalized for acute MI what is the prevalence of depression during the initial hospitalization for MI?

Important technical and methodological issues affect the interpretation of studies that address this question. These issues include variations from study to study in (1) the definition of "depression" (modified major depression versus potentially significant symptoms of depression versus definition not specified), (2) the screening instrument or method of diagnosis employed, and (3) the clinical threshold criteria (i.e., cutoffs) used even with the identical screening instrument.

Major depression is reported in about one of every five patients hospitalized for MI. This proportion is fairly consistent among the seven studies that used a SCID to establish this diagnosis.

The reported prevalence of potentially significant symptoms of depression varies more widely (range 10 to 47 percent). This wide range of reported prevalence rates appears to be due almost exclusively to differences in measurement instruments used, and even to differences in threshold criteria applied from study to study when the same instrument was used. Although it is difficult to draw conclusions from small numbers of studies and different assessment methods, the variability in reported prevalence does not appear to be explained by differences in demographic characteristics such as age and sex.

Of note, although the reported prevalence of potentially significant symptoms of depression varies fairly widely from 10 to 47 percent, closer inspection suggests less variability in actual prevalence rates. The study that reported a prevalence rate of 47 percent was the only study that used the revised version of the BDI-II[79] This study was reported in brief format (i.e., as a “Scientific letter”) and without key demographic information. Of the five studies that used a cutoff score of 10 or higher on the BDI,[25, 77, 78, 80, 81] four reported prevalence rates between 32 and 37 percent. The sample size of the study that reported a prevalence rate of 21 percent[80] was relatively small (85 patients).

In general, the reported prevalence of potentially significant symptoms of depression is higher when this diagnosis is based on a BDI score of 10 or higher than when it is based on a HADS score of either 8 or higher or 11 or higher. This difference may be attributed to the BDI’s inclusion of somatic symptoms that may overlap with MI symptoms, whereas the HADS does not include somatic symptoms and is designed for use in hospitalized patients.

Question 1a. What is the prevalence of depression during initial hospitalization for MI in patients with or without a known history of depression as reported by study investigators?

Study investigators reported information about a history of depression in only two studies, and neither provided separate prevalence data for these patients. There is therefore insufficient evidence to address this question.

Question 2. What percentage of patients with post-MI depression continue to have depression (or depressive symptoms) 1 month or longer after initial hospital discharge?

Although 22 studies reported the prevalence of depression in patients 1 month or longer after initial hospital discharge, only three reported the prevalence of depression in patients during the MI hospitalization and then specifically reassessed and reported the prevalence of depression in these same patients at follow-up.

These studies suggest that most patients (60-70 percent) with depression during the initial MI hospitalization continue to have depression (or depressive symptoms) 1 to 4 months later.

Question 3. What is the association of various measures of depression with outcomes in patients with acute MI, independent of known predictors of post-MI outcomes?

Seventeen studies evaluated the relationship between depression, measured shortly after an acute MI, and subsequent mortality. Studies have assessed this relationship as early as 4 months post-MI and as late as 10 years post-MI. Despite the facts that various measures of depression have been used, that different subgroups of depressed patients have been evaluated, and that different post-MI survival times have been assessed, the weight of the evidence is strikingly consistent. Overall, the evidence supports the notion that post-MI depression is associated with a significantly increased risk for subsequent death, whether by cardiac or other causes. Depression appears to be associated with about a 3-fold increased risk of cardiac mortality per se based on at least four studies that addressed cardiac mortality in a total of almost 2,000 patients.[22, 23, 100]

Six studies evaluated the relationship between depression and cardiac events. The study that examined the relation between depression during the initial MI hospitalization and cardiac readmission[106] suggests depression is associated with increased cardiac readmission during the first year, even after controlling for important cardiac variables. That there may be a relation between post-MI depression and cardiac events is indicated by three studies that evaluated this association.[84, 89, 95] Strik et al. found a relation between depression and cardiac events in one study.[84] However, this relation was not significant after anxiety was added to the model. Shiotani et al.[95] evaluated a much larger sample and found a trend toward a multivariate relationship between post-MI depression and cardiac events for patients younger than 65 years and a significant multivariate relationship in those older than 65. None of these three studies presented data on the statistical power to detect differences in cardiac events given the sample sizes. Given the relatively low cardiac event rates, the sample sizes of the studies that did not find a significant independent relation between depression and cardiac events[84, 89] were relatively

small compared with the larger sample size of the studies of Shiotani et al.[95] and Frasure-Smith et al.[106]

During the first year after MI, depression during the initial MI hospitalization has been found to be inversely related to physical QOL, social QOL of women, sexual activity and satisfaction among men, return to work of employed men, and to physical, psychological, and social health and function. Studies show that even as long as 5 years after an MI, in-hospital depression can have a prolonged negative impact on psychological distress and physical health and functioning.

Limitations of the above-mentioned studies included the variety of diagnostic instruments used to assess depression (some of which were not categorical or diagnostic, but continuous in nature); the lack of agreement on what aspects of QOL are of greatest import or how to measure them; limits in the power to draw firm conclusions, based on the small number of subjects included in studies; the degree to which potential confounders were adequately considered; the question of whether it is appropriate to adjust for symptoms of fatigue when analyzing the association between depression and clinical outcomes after an MI; and the absence of data in early post-MI time points (e.g., 30 days).

Question 3a. What is the association of various measures of depression with surrogate markers of cardiac risk in patients with acute MI, independent of known predictors of post-MI outcomes?

Three studies have been performed in post-MI patients to compare HRV, platelet-derived substances, and inflammatory markers in those with and those without depression. All three studies reported differences in at least one surrogate marker between patients with a major depressive syndrome post-MI compared with post-MI groups without depression. All three studies found surrogate markers of increased risk in the patients with post-MI depression. The higher risk profile in all surrogate markers persisted after adjustment for covariates. Thus, a small amount of evidence suggests that post-MI patients with depression have alterations in autonomic function as reflected by decreased HRV, increased platelet activity, and increased levels of soluble adhesion molecule 4. These studies suggest that the risk associated with post-MI depression could be transmitted by multiple biological pathways.

Few studies have evaluated these surrogate markers in post-MI patients with depression and compared them to post–MI patients without depression. All studies have compared only patients with major depressive syndrome to those without major depression. It is unknown whether other forms of depression are also associated with similar changes in these biomarkers.

Question 4. Do post-MI patients with depression have better outcomes with depression treatment than do those without such treatment?

No studies of sufficient power have yet been performed that directly address the question as to whether treatment with antidepressants improves survival in depressed patients after an MI. However, there is evidence that SSRI antidepressants do not have common adverse cardiac effects when administered to early post-MI patients. Increases in rare adverse effects cannot be

excluded. Some evidence suggests that SSRI antidepressants have beneficial effects on surrogate markers of post-MI risk (e.g., HRV, aortic time velocity integral).

There is evidence that both psychosocial intervention and SSRI antidepressants improve depression in post-MI patients. However, the possibility of increases in rare adverse events cannot be excluded. Current clinical trial evidence suggests psychosocial interventions do not improve post-MI cardiac outcomes.

Question 5. What are the performance characteristics (e.g., sensitivity, specificity, and predictive value) of instruments or methods that are used to screen for depression (or depressive symptoms) after MI?

There are insufficient data to allow an adequate assessment of the performance characteristics of instruments or methods used to screen for depression during the initial MI hospitalization.

HAMD has adequate sensitivities and specificities for identifying depression within 3 months after hospitalization for an MI, as compared to a diagnosis of depression based on a SCID. There is also evidence for convergent validity and adequate internal consistency.

None of these measures has been normalized specifically in post-MI populations. It is unclear how well these instruments distinguish symptoms of depression from somatic symptoms related to the MI, to poor physical health, or to the hospitalization itself.

The very low PPVs of these screening instruments (generally in the 25 to 50 percent range) may be acceptable clinically if followed by a more thorough assessment of those who screen positive; however, the low PPVs are particularly problematic if used to detect relationships to outcome variables in the research setting. The study that generated diagnostic utility figures used cutoffs that were slightly lower than those commonly employed in research studies. If the more commonly-used cutoffs had been employed, PPVs would have been slightly higher.

When compared with the HADS, SCL-90-Dep, and HAMD, the BDI tends to diagnose less significant symptoms of depression at higher rates,. It may be less effective in accurately diagnosing major depression.

Important questions remain and further research is needed to improve performance. This research should include more sophisticated analyses of existing measures as well as the potential development of new measurement techniques specifically validated for use with MI survivors.

Question 6. Does the use of cardiac treatment for patients with acute MI differ for those with and those without depression?

Four studies included in this review evaluated whether the use of medications for the secondary prevention of adverse cardiac events post-MI differs between depressed and

nondepressed patients. The findings of these studies were inconsistent. Two studies found that beta-blockers were prescribed less frequently among post-MI patients with depression than among post-MI patients without depression. One study found that aspirin or antiplatelet agents were used less frequently in depressed than nondepressed post-MI patients. Finally, one study found no difference in the use of any recommended medication between depressed and nondepressed post-MI patients. Thus, it remains unclear whether there are significant differences in cardiac medications prescribed to post-MI patients based on the presence or absence of depression.

Three studies evaluated adherence to prescribed medications and secondary prevention measures in post-MI patients and consistently found lower adherence in those with depression than those without depression.

Two good-quality studies, using different methods, came to diverse conclusions about whether the frequency with which cardiac procedures are used varies between post-MI patients with depression and those without depression.

Two small studies examined participation in post-MI cardiac rehabilitation programs and reported discordant results. No conclusion can be reached about the likelihood of patients completing cardiac rehabilitation programs based on the presence or absence of post-MI depression.

Future Research

Question 1. In patients hospitalized for acute MI, what is the prevalence of depression during the initial hospitalization for MI?

Additional studies are needed to define the most clinically relevant measure of "depression" during the initial MI hospitalization. The definition of depression varies considerably from study to study; to determine the most appropriate definition in this setting, clinical relevance should be determined for each definition.

Studies are needed to determine the clinical or demographic factors that are associated with post-MI depression. Given the episodic nature of depression, future studies on this topic should carefully document which patients have had depression diagnosed and/or treated in the past and which patients report significant depressive symptoms in the past that might not have been formally diagnosed or treated.

Question 2. What percentage of patients with post-MI depression continue to have depression (or depressive symptoms) 1 month or longer after initial hospital discharge?

Additional studies are needed that assess depression (or depressive symptoms) in groups of patients during the initial hospitalization and at various times after MI. In particular, the group of patients with depression (or depressive symptoms) during the initial MI hospitalization should be reassessed at certain time points after discharge.

Question 3. What is the association with various measures of depression with outcomes in patients with acute MI, independent of known predictors of post-MI outcomes?

Additional studies are needed to determine the major cause(s) of mortality among depressed post-MI patients and whether these causes differ in distribution from nondepressed post-MI patients. Additional studies also are needed to determine whether patients with depression are at higher risk for malignant arrhythmias than are comparable post-MI patients without depression.

Question 3a. What is the association of various measures of depression with surrogate markers of cardiac risk in patients with acute MI, independent of known predictors of post-MI outcomes?

Additional studies are needed to elucidate the mechanism(s) responsible for increased mortality in patients with post-MI depression. Additionally, studies which establish the time after an MI at which the adverse effects of depression on post-MI outcomes first become evident may yield important indirect insights into potential mechanisms involved.

Studies that evaluate the hemostatic and platelet function of patients with post-MI depression are needed. Studies also should address whether responses to commonly used antiplatelet agents differ between post-MI patients and those without depression.

Question 4. Do post-MI patients with depression have better outcomes with depression treatment than those without such treatment?

Additional studies are needed which evaluate this question. There are actually three questions within this larger question. The first is whether cardiac outcomes are better if depression is successfully treated. The second question is whether cardiac outcomes are better with antidepressant treatment regardless of whether depression improves. The third question is whether cardiac outcomes are better if depression resolves with antidepressant treatment compared to spontaneous resolution. None of these questions has been adequately addressed by the existing literature.

Question 5. What are the performance characteristics of instruments or methods that are used to screen for depression (or depressive symptoms) after MI?

Additional studies are needed to determine the performance characteristics of instruments or methods used to screen for depression (or depressive symptoms) during the initial MI hospitalization. Studies are needed in post-MI patients that examine the ability for depression screening instruments or methods to distinguish symptoms of depression from symptoms attributable to the MI, to poor physical health, or to the hospitalization itself.

Question 6. Does the use of cardiac treatment for patients with acute MI differ for those with and those without depression?

Additional large studies are needed to examine whether the use of diagnostic and therapeutic procedures differs between depressed and non depressed post-MI patients. Studies should also address whether potential differences in procedures are due to differences in providers' recommendations or to differences in patients' acceptance. Further studies also are needed to determine whether the treatment prescribed for post-MI patients differs between those with and those without depression. Future studies should examine the adherence behavior of post-MI patients and evaluate measures that could improve adherence to recommended treatment.

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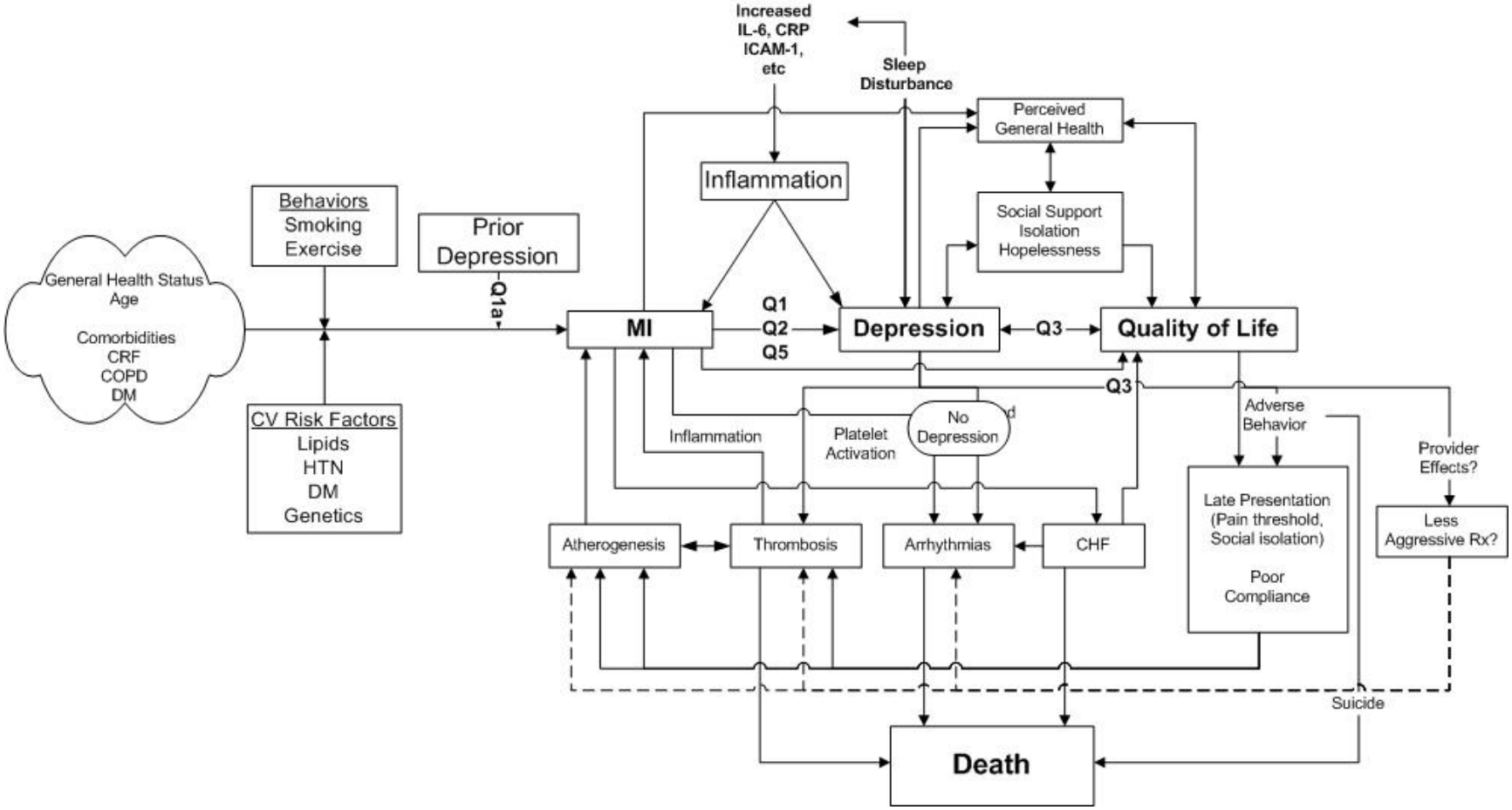
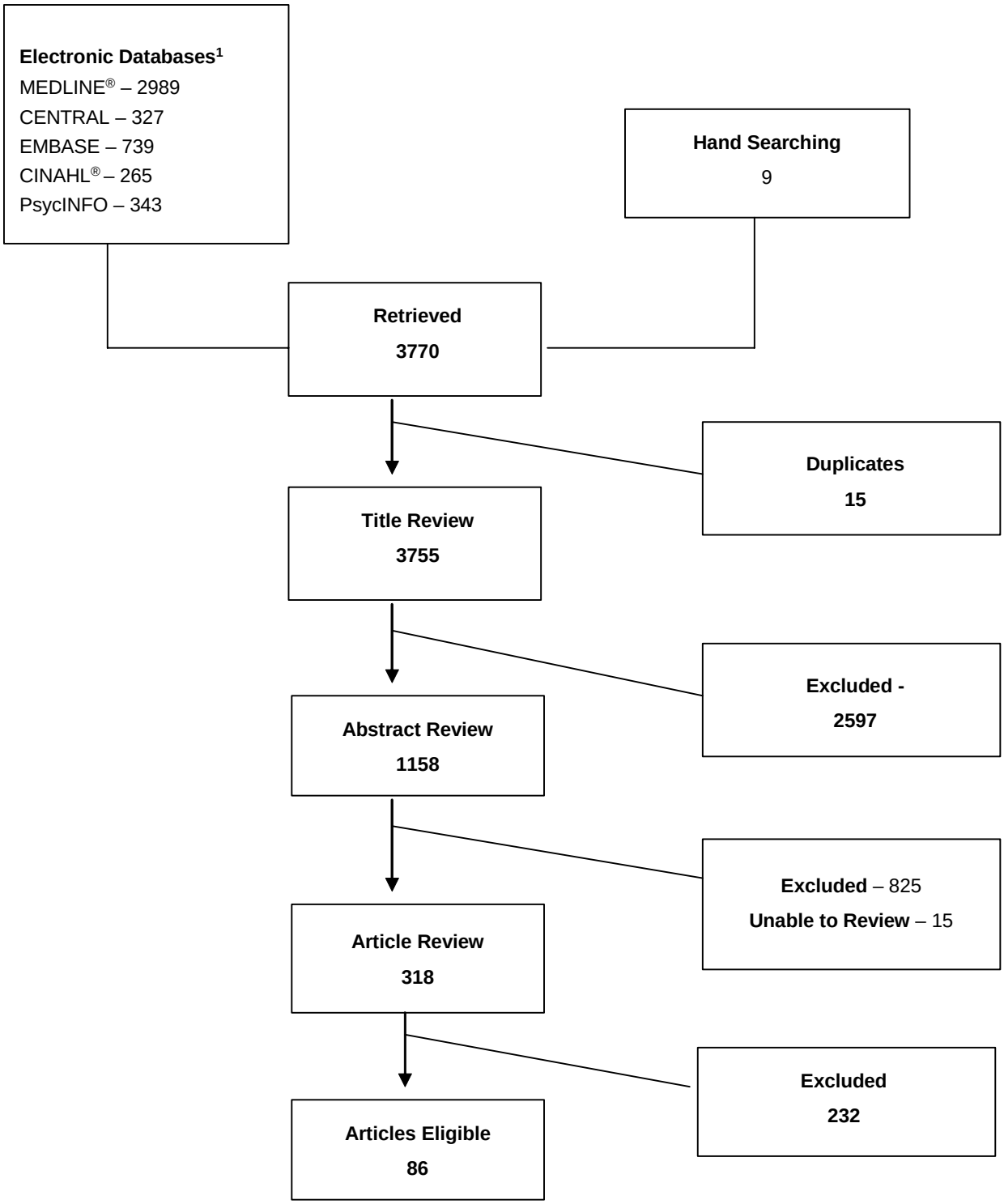
Figure 1. Conceptual Model



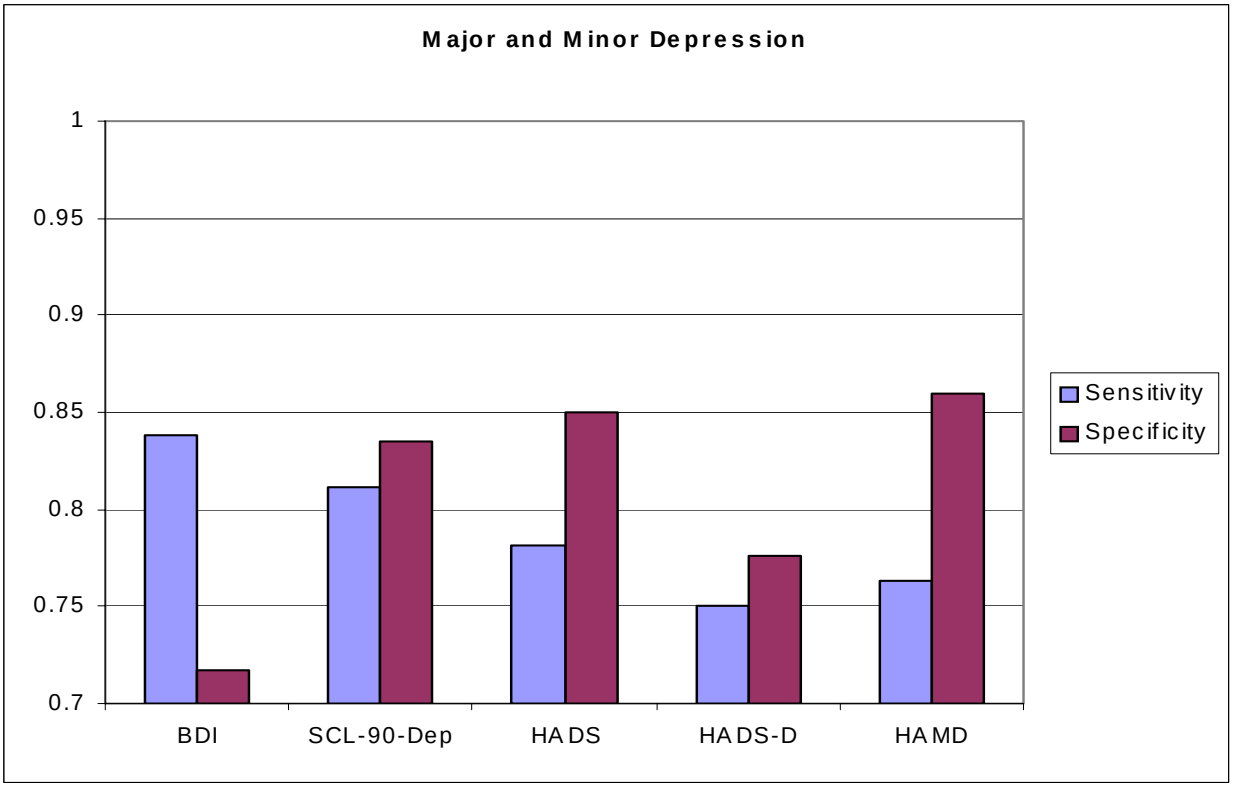
CHF - Congestive heart failure
COPD - Chronic obstructive pulmonary disease
CRF - Cardiac risk factors
CRP - C-reactive protein
DM - Diabetes mellitus
HTN - Hypertension
ICAM-1 - Intercellular adhesion molecule-1
IL-6 - Interleukin-6
MI - Myocardial infarction
Rx - Treatment

Figure 2. Literature Search



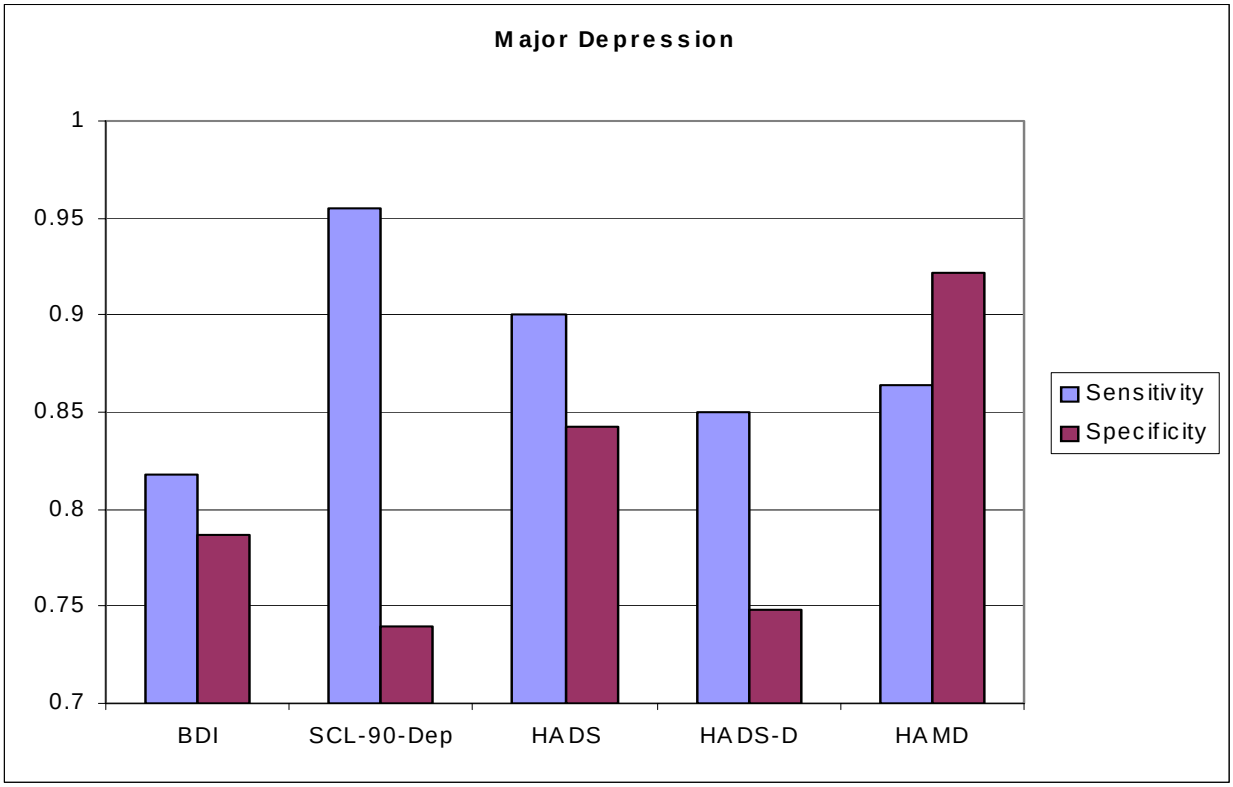
[1] CENTRAL - the Cochrane CENTRAL Register of Controlled Trials; CINAHL® - Cumulative Index of Nursing and Alliance Health Literature.

Figure 3. Sensitivity and Specificity of Instruments used to Screen for Major and Minor Depression Following an Acute Myocardial Infarction



BDI - Beck Depression Inventory
SCL -90 Dep - Symptom Checklist 90 for Depression
HADS - Hospital Anxiety and Depression Scale
HADS-D - Hospital Anxiety and Depression Scale (Depression)
HAMD - Hamilton Rating Scale for Depression

Figure 4. Sensitivity and Specificity of Instruments used to Screen for Major Depression Following an Acute Myocardial Infarction



BDI - Beck Depression Inventory
SCL -90 Dep - Symptom Checklist 90 for Depression
HADS - Hospital Anxiety and Depression Scale
HADS-D - Hospital Anxiety and Depression Scale
HAMD - Hamilton Rating Scale for Depression

Table 1. Summary of Studies on the Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	White (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Method & Time of Assessment of Depression	Prevalence (%)
Taylor, 1986	RCT [d]	USA	173	52	100	NR [e]	NR	NR	NR	NR	HAMD [f]; 3 wk [g] post-MI [h]	13
Bennett, 1988	Pro cohort [i]	Europe	37	62	73	NR	NR	NR	NR	NR	HADS [j]; In hospital [k]	13
Davis, 1988	Pro cohort	Canada	52	51	90	NR	NR	NR	NR	NR	SCID [l], and BDI [m]; In hospital [k]	6, 10
Carney, 1990	Case control	USA	70	53	76	NR	43	16	48	NR	DIS [n]; In hospital	23
Silverstone 1990	Pro cohort	Europe	100	NR	NR	NR	NR	NR	NR	NR	Montgomery-Asberg; In hospital	19
Gilutz, 1991	Pro cohort	Europe; Middle East	Europe: 98; Middle East: 87	NR [o]	NR	NR	NR	NR	Europe: 32; Middle East: 35	NR	Holland Sgroi Anxiety Depression Scale; In hospital, and 10-15 d [p] post-MI	31, 35
Schleifer, 1991	Pro cohort	USA	335	63	64	NR	NR	NR	NR	NR	Nurse Interview; 8-10 d post-MI [k]	30, 17
Forrester, 1992	Cross-sectional	USA	129	59	74	62	NR	NR	NR	NR	PSE [q]; In hospital within 10 d post-MI	19
Legault, 1992	Pro cohort	Canada	52	55	78	NR	NR	NR	NR	NR	BDI; In hospital [k]	18
Kaufmann, 1999	Pro cohort	USA	331	NR [r]	66	NR	50	27	28	38	DIS; In hospital 3-15 d post-MI	27
O'Rourke, 1999	Pro cohort	Europe	70	58	74	NR	NR	NR	NR	NR	HADS; 3 - 5 d post-MI	17
Mayou, 2000	Pro cohort	Europe	344	63	73	NR	NR	34	58	NR	HADS; In hospital, and within 3 d post-MI	18, 8

Table 1. Summary of Studies on the Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	White (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Method & Time of Assessment of Depression	Prevalence (%)
Bush, 2001	Pro cohort	USA	267	65	58	82	43	33	27	59	SCID, and BDI; In hospital within 2-5 d post-MI	17, 20
Brink, 2002	Pro cohort	Europe	114	68	68	NR	35	15	31	NR	HADS; In hospital, and within 1 wk post-MI	11, 8
Lane, 2002	Pro cohort	Europe	288	63	75	93	39	13	43	72	BDI; In hospital within 15 d post-MI [k]	31
Lesperance, 2002	Pro cohort	Canada	896	59	68	NR	35	16	47	NR	BDI; In hospital [k]	32
Luutonen, 2002	Pro cohort	Europe	85	61	77	NR	NR	NR	NR	NR	BDI; In hospital [k]	21
Watkins, 2002	Cross-sectional	USA	204	59	58	65	NR	Non-depressed 31, Depressed 49	Non-depressed 53, Depressed 81	NR	DIS; In hospital 3-9 d post-MI	18
Barefoot, 2003	Pro cohort	USA	196	61	63	67	NR	NR	NR	NR	HAMD, and BDI; within 2 wk post-MI [k]	28, 37
Berkman, 2003	RCT	USA	9279 [s]	63	61	26	60 [t]	33 [t]	64 [t]	57 [t]	SCID; 2-4 wk post-MI	27
Lauzon, 2003	Pro cohort	Canada	550	60	80	96	35	16	40	38	BDI; Within 2 - 3 d of hospitalization [k]	35
Martin, 2003	Pro cohort	Europe	335	67	67	NR	NR	NR	NR	NR	HADS; In hospital, and within 1 wk post-MI [k]	15, 6

Table 1. Summary of Studies on the Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	White (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Method & Time of Assessment of Depression	Prevalence (%)
Rafanelli, 2003	Pro cohort	Europe	61	61	85	NR	NR	NR	NR	NR	SCID; Within 1 mo [u] post-MI	Minor 10, Major 2
Strik, 2003	Pro cohort	Europe	318	52	1	NR	28	9	54	20	SCL-90; 1 mo post-MI	47
Steeds, 2004	Pro cohort	Europe	131	NR	NR	NR	NR	NR	NR	NR	BDI-II; In hospital	47

[a] Hypertension
[b] Diabetes mellitus
[c] Hyperlipidemia
[d] Randomized controlled trial
[e] Not reported
[f] Hamilton Rating Scale for Depression
[g] Week
[h] Myocardial infarction
[i] Prospective cohort study
[j] Hospital Anxiety and Depression Scale
[k] Also assessed at a later point. See Question 2
[l] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders - IV
[m] Beck Depression Inventory
[n] Diagnostic Interview Schedule
[o] In the European population 21% were less than 45 years old, 54% were 46 - 55 years old and 25% were 56 - 60 years old. In the Middle Eastern population 30% were less than 45 years old, 46% were 46 - 55 years old and 24% were 56 - 60 years old
[p] Day
[q] Psychological Stress Evaluator
[r] 45% were less than 65 years old and 56% were greater than 65 years old
[s] Medically eligible and screened for depression
[t] Of those with depression or low social support
[u] Month

Table 2. Summary of Studies on the Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	White (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Method & Time of Assessment of Depression	Prevalence
Trelawny, 1987	NR [d]	Europe	32	NR	100	NR	NR	NR	71	NR	Goldberg's CIS [e]; In hospital, 10 d [f] post d/c [g], 2 mo [h] post d/c, 6 mo post d/c	 At 10 d: 20, At 2 mo: 26, At 6 mo: 26
Davis, 1988	Retro cohort [i]	Canada	52	51	90	NR	NR	NR	NR	NR	BDI [j]; 6 - 8 wk [k] post-MI [l]	 At 6 - 8 wk 10
Follick, 1988	RCT [m]	USA	238	55	72	NR	NR	NR	53	NR	SCL-90 [n]; Baseline, 1 mo, 3 mo, 9 mo	 At 9 mo: 10
Schleifer, 1991	Retro cohort	USA	335	64	64	NR	NR	NR	NR	NR	RDC [o] (Nurse Interview); 8-10 d, 3-4 mo	At 3 - 4 mo: Major [p] 14, Minor [q] 19
Legault, 1992	Pro cohort [r]	Canada	52	55	78	NR	NR	NR	NR	NR	BDI; In hospital, 3 mo post-MI, 12 mo post-MI	 At 3 mo: 7, At 12 mo: 9
Garcia, 1994	Cross-sectional	Europe	97	50	100	NR	NR	NR	NR	NR	RDC; In hospital, 1 mo post-MI	Major 11, Minor 27
Travella, 1994	Pro cohort	USA	70 [s]	58	74	NR	NR	NR	NR	NR	HAMD [t], PSE; 3 mo post-MI, 6 mo post-MI, 9 mo post-MI, 12 mo post-MI	At 3 mo: Major 15, Dysthymia 4 ; At 6 mo: Major 21, Dysthymia 3 ; At 9 mo: Major 28, Dysthymia 3; At 12 mo: Major 16, Dysthymia 13

Table 2. Summary of Studies on the Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2) (continued)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	White (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Method & Time of Assessment of Depression	Prevalence
Clarke, 1996	Pro cohort	Canada	52	NR	100	NR	NR	NR	NR	NR	ZDS [u]; 3 mo post-MI	At 3 mo: 24
Lesperance, 1996	Pro cohort	Canada	222	60	78	NR	NR	NR	NR	NR	DIS [v]; 6 mo post-MI, 12 mo post-MI	At 6 mo: 20, At 12 mo: 9
Bennett, 1998	Pro cohort	Europe	37	62	73	NR	NR	NR	NR	NR	HADS [w]; In hospital, 3 mo post-MI	At 3 mo: 3
Lehto, 2000	Retro cohort	Europe	101	62	69	NR	28	15	12	63	DEPS [x]; 20.5 mo (median) post-MI	20.5 mo: 15.8 (median)
Strik, 2001	Pro cohort	Europe	206	60	76	NR	NR	NR	NR	NR	SCID [z], HAMD, SCL-90, BDI, HADS; 1 mo post-MI	At 1 mo Major 11 Minor 8
Lane, 2002	Pro cohort	Europe	288 [q]	63	75	93	NR	NR	NR	NR	BDI; In hospital, 4 mo post-MI, 12 mo post-MI	At 4 mo: 38 At 12 mo: 37
Luutonen, 2002	Pro cohort	Europe	85	61	77	NR	NR	NR	NR	NR	BDI; 6 mos, 18 mos	At 6 mos: 30 At 18 mos 34
Shiotani, 2002	Pro cohort	Asia	1042	64	80	NR	48	32	66	37	ZDS; within 3 mo post-MI	Within first 3 mo: 42

Table 2. Summary of Studies on the Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2) (continued)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	White (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Method & Time of Assessment of Depression	Prevalence
Strik, 2002	Retro cohort	Europe	140	58	76	NR	NR	NR	NR	NR	BDI, HADS, SCL-90 if any one positive assessment with SCID; 3 mo post-MI	Major 11 Minor 2
Aben, 2003	Pro cohort	Europe	200	60	77	NR	NR	NR	NR	NR	BDI, HADS, SCL-90 if any one positive assessment with SCID and HAMD; 1 mo after MI, 3 mo after MI, 6 mo after MI, 9 mo after MI, 12 mo after MI	 At 1 mo: 14 At 3 mo: 19 At 6 mo: 21 At 9 mo: 27 At < 1 yr [aa]: 28
Barefoot, 2003	NR	USA	196	61	63	67	NR	NR	NR	NR	HAMD, BDI; In hospital, 2 wk after first assessment hospitalization	At 2 wks by HAM-D: 17; by BDI: 27
Lauzon, 2003	Pro cohort	Canada	550	60	80	96	35	16	40	38	BDI; In hospital, 1 mo post-MI, 6 mo post-MI, 12 mo post-MI	 At 1 mo: 39 At 6 mo: 39 At 1 yr: 30
Martin, 2003	Cross-sectional	Europe	335	67	67	NR	NR	NR	NR	NR	HADS; 6 wk post-MI, 6 mo post-MI	 At 6 wk: 5 [o] At 6 mo: 5.4 [o] 6 wk: 13 [p] 6 mo: 10 [p]
Strik, 2003	Pro cohort	Europe	318	52	1	NR	28	9	54	20	SCL-90; 1 mo post-MI	At 1 mo: 47
Lesperance, 2004	Pro cohort	Canada	481	60	81	NR	66	NR	15	NR	SCID; Approx. 2 mo post-MI	Approx 2 mo: 7

Table 2. Summary of Studies on the Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2) (continued)

[a] Hypertension
[b] Diabetes mellitus
[c] Hyperlipidemia
[d] Sample of suspected myocardial infarction patients 28 of 32 confirmed
[e] Clinical Interview Schedule
[f] Day
[g] Discharge
[h] Month
[i] Retrospective cohort study
[j] Beck Depression Inventory
[k] Week
[l] Myocardial Infarction
[m] Randomized controlled trial
[n] Symptom Check List 90
[o] Research Diagnostic Criteria
[p] Major depression
[q] Minor depression
[r] Prospective cohort study
[s] With variable numbers at different time points
[t] Hamilton Rating Scale for Depression
[u] Zung Depression Scale
[v] Diagnostic Interview Schedule
[w] Hospital Anxiety and Depression Scale
[x] Depression scale
[z] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders - IV
[aa] Year

Table 3. Summary of Studies on Relation of Depression to Survival after Myocardial Infarction (Question 3)

Study Author, Year	No. Enrolled	Depression Instrument	Outcome Reported			Stat[a]	Dep vs. Non Dep[b]	Multivariate Comparison
			Cardiac Mortality	Total Mortality	Other			
Ahern, 1990	265	BDI [c] profile of mood states	NA [d]	NA	TM [e] or cardiac arrest at baseline	RR [f]	NR [g]	1.38 (CI[h] 0.99 - 1.93)
Ladwig, 1991	560	NR	Low: 0.9; Medium: 2.4; High: 7.5	NA	Sustained VT [i] admission	OR [j]	Mantel-Haenszel p<0.001	2.8 low/med depression, 4.9 low/high depression p=0.07
Frasure-Smith, 1993	222	MIMH DIS [k]	NA	At 6 mos [l]	NA	HR [m]	5.74 (CI 4.61 - 6.87)	4.29 (CI 3.14 - 5.44)
Frasure-Smith, 1999	904	BDI	NA	NA	Arrhythmia; MI recurrence; Revascularization Any hard event	OR	CV [n] death 3.23 (CI 1.65 - 6.33); Arrhythmia 3.11 (CI 1.32 - 7.37); MI recurrence 1.62 (CI 0.93 - 2.8); Revascularization 0.82 (CI 0.53 - 1.26); Any hard events 1.97 (CI 1.25 - 3.13)	3.66 (CI 1.68 - 7.99)
Irvine, 1999	703	BDI	Sudden cardiac death	NA	NA	HR	AMI[o] 0.52 (CI 0.15 - 1.76)	NR
Denollet, 2000	319	ZDS[p]	Cardiac events	NA	QOL[q] poor perceived health at 5 yrs [r], Depressive effect	OR	NR	1.31 (CI 0.53 - 3.24)
Lane, 2000	288	BDI	Dep 9%, NonDep 0.7%	Dep 10.1%, NonDep 8%	Dartmouth chart	OR	NR	NR
Welin, 2000	275	ZDS	17%	24%	Non-fatal recurrent MI; Stroke; Cancer	HR	TM: 2.45 (CI 1.49 - 4.02), CM [s]: 3.54 (CI 1.85 - 6.79)	TM 1.75 (CI 1.02 - 2.99), CM 3.16 (CI 1.38 - 7.25)

Table 3. Summary of Studies on Relation of Depression to Survival after Myocardial Infarction (Question 3) (continued)

Study Author, Year	No. Enrolled	Depression Instrument	Outcome Reported			Stat[a]	Dep vs. Non Dep[b]	Multivariate Comparison
			Cardiac Mortality	Total Mortality	Other			
Bush, 2001	285	SCID [t] BDI	NA	Dep: 13%, NonDep: 3.8%	NA	RR	3.8 p=0.008	3.5 p=0.001
Druss, 2001	88241	NR	NA	NA	NA	HR	Mental 1.19 (CI 1.04 - 1.36), Affective 1.11 (CI 1.03 - 1.18)	NR
Lane, 2001	288	BDI	10%	10%	QOL	OR	CM 1.15 (CI 0.49 - 2.69)	NR
Lane, 2002	288	BDI	Dep: 10%	NA	NA	OR	TM 1.04 (CI 0.5 - 2.16), CM 0.84 (CI 0.37 - 1.90)	NR
Lesperance, 2002	896	BDI	< 5 yrs: 7.2%; 5 - 9 yr: 13.7%; 10-18 yr: 18.5%; > 19 yr: 26.6%	< 5 yr: 10.7%; 5 - 9 yr: 16.2%; 10-18 yr: 23.2%; > 19 yr: 32.9%	NA	HR	BDI 5 - 9: 1.94 (CI 1.16 - 3.25); BDI 10 - 18: 2.8 (CI 1.68 - 4.66); BDI > 19: 1.32 (CI 2.4 - 7.75)	TM BDI 10 - 18: 2.35 (CI 1.53 - 3.61) BDI ≥ 19 (CI 2.16 - 5.92) TM BDI 10 - 18: 3.17 (CI 1.79 - 5.6) BDI ≥ 19: 3.13 (CI 1.56 - 6.27)
Carney, 2003	NR	Depression interview: structured HAMD[u], BDI	NA	Non-fatal AMI	NA	HR	TM 2.4 (CI 1.2 - 4.7) Non-fatal AMI 1.2 (CI 0.7 - 2.0)	TM 2.4 (CI 1.2 - 4.7) Non-fatal AMI 1.2 (CI 0.7 - 2.0)
Frasure-Smith, 2003	NR	NR	At 5 yr	NA	NA	HR	NR	1.44 (CI 91.17-1.78)

[a] Comparison statistic
[b] Depressed versus non-depressed
[c] Beck Depression Inventory
[d] Not applicable
[e] Total mortality
[f] Relative risk

Table 3. Summary of Studies on Relation of Depression to Survival after Myocardial Infarction (Question 3) (continued)

[g] Not reported
[h] Confidence Interval
[i] Ventricular tachycardia
[j] Odds Ratio
[k] National Institute of Mental Health Diagnostic Interview Schedule
[l] Month
[m] Hazard ratio
[n] Cardiovascular
[o] Acute myocardial infarction
[p] Zung Depression Scale
[q] Quality of life
[r] Year
[s] Cardiac Mortality
[t] Structured Clinical Interview for DSM-IV
[u] Hamilton Rating Scale for Depression

Table 4. Summary of Studies on the Relation of Depression to Cardiac Events after Myocardial Infarction (Question 3)

Study Author, Year	No Enrolled	Depression Instrument	Outcome			Stat [a]	Dep vs. Non-Dep [b]	Multivariate Comparison
			Cardiac Events	Cardiac Mortality	Other			
Irvine, 1999	703	Psychological questionnaire	NR [c]	Sudden cardiac death 34, Other cardiac death 16	Vascular death 1, Non-cardiac death 12	RR [d]	NR [e]	Amiodarone group: BDI [f] somatic score 1.10 (CI 0.93,1.29); BDI cognitive-affective score 0.73 (CI 0.52,1.01); Placebo Group: BDI somatic score 1.00 (CI 0.88,1.13); BDI cognitive-affective score 1.09 (CI 0.99,1.89)
Frasure-Smith, 2000	222	Structured baseline interview	Recurrent cardiac events[g]	NA [h]	NA	OR [i]	Any cardiac event: 3.32 (CI 1.69,6.53); ACS [j]: 2.75 (CI 1.32,5.72); Arrhythmic event: 3.65 (CI 0.99,10.47)	Recurrent cardiac events 1.99 (CI 0.92,4.31)
Druss, 2000	NR	ICD-9CM	NA	TM at 1 mo [k]	Likelihood of PTCA [l] or CABG [m] during index hospitalization	OR	TM [n]: Affective disorders 7.3%; No mental disorders 10.8%	TM 0.63 (p=0.2) in patients with affective disorders; Use of PTCA and CABG in patients with affective disorders: PTCA: 0.51 CABG : 0.63

Table 4. Summary of Studies on the Relation of Depression to Cardiac Events after Myocardial Infarction (Question 3) (continued)

Study Author, Year	No Enrolled	Depression Instrument	Outcome			Stat [a]	Dep vs. Non-Dep [b]	Multivariate Comparison
			Cardiac Events	Cardiac Mortality	Other			
Shiotani, 2002	1086	ZDS [o]	Annual cardiac event rate: Dep 31%, Non-dep 24%; Cardiac events: Dep 138, Non-dep 145; MI: Dep 19, Non-dep 15; Arrhythmias: Dep 2, Non-dep 1; RePTCA: Dep 94, Non-dep 110 ; Heart Failure: Dep 7, Non-dep 5; Angina: Dep 6, Non-dep 5	CM [p]: Dep 4 , Non-dep 1	Readmission: Dep: 34, Non-dep: 26	OR	Cardiac events: 1.46 (CI [q] 1.11 - 1.92)	Cardiac events: 1.41 (CI 1.04 - 1.92)
Strik, 2003	318	SCL-90 [r]	Non-fatal MI at 3-4 yrs [s]	Fatal MI at 3 - 4 yrs	Consumption at 3-4yrs [t]	HR [u] OR [v]	Consumption[x]: 1.61 (CI 1.00 - 2.57) [w]	MI:CI 2.32 (CI 1.04 - 5.18) ; Consumption: 1.55 (CI 0.96 - 2.52)

Table 4. Summary of Studies on the Relation of Depression to Cardiac Events after Myocardial Infarction (Question 3) (continued)

Study Author, Year	No Enrolled	Depression Instrument	Outcome			Stat[a]	Dep vs. Non-Dep[b]	Multivariate Comparison
			Cardiac Events	Cardiac Mortality	Other			
Strik, 2004	422	Baseline: SCID; Follow-up: 3 psychiatric self rating scales BDI, SCL-90, HADS [aa]	Major cardiac events 1 mo - 3 yrs [y]; Increased consumption	NR	Consumption 1 mo - 3 yrs	HR[ab] OR[ac]	Cardiac events: 1.1(0.36,3.42); Consumption: 1.66 (CI 0.90 - 3.07)	Cardiac Events: 0.88 (CI 0.26,2.93); Consumption: 1.98 (CI 1.0 - 3.93)

[a] Comparison statistic
[b] Depressed versus non depressed
[c] Not reported
[d] Risk ratio
[e] Depression reported not to be significant predictor of sudden cardiac death in univariate analysis
[f] Beck Depression Inventory
[g] Survived and nonsurvived reinfarctions, admission for unstable angina, arrhythmic deaths, survived cardiac arrests
[h] Not applicable
[i] Odds ratio
[j] Acute coronary syndrome
[k] Month
[l] Percutaneous transluminal coronary angioplasty
[m] Coronary artery bypass graft
[n] Total mortality
[o] Zung Depression Scale
[p] Cardiac mortality
[q] Confidence interval
[r] Symptom Checklist - 90
[s] Years
[t] Cardiac rehospitalization and/or frequent visits
[u] Cardiac events
[v] Health care consumption
[w] Confidence intervals not reported as single variables
[x] Heath care consumption
[y] Death or recurrent myocardial infarction
[z] > 6 visits at cardiac outpatient clinic during follow-up
[aa] Hospital Anxiety and Depression Scale
[ab] Depression as predictor of major cardiac event
[ac] Depression as predictor of health care

Table 5. Summary of Studies on the Relation of Depression to Quality of Life after Myocardial Infarction (Question 3)

Study Author, Year	No. Enrolled	Depression Instrument	Outcome		Stat [b]	Dep vs. Non Dep [c]	Multivariate Comparison
			QOL [a]	Other			
Travella, 1994	129	Present state examination - modified, HAMD [d]	Johns Hopkins functioning inventory, Social functioning exam	NA [e]	Multivariate Rank	NR [f]	Social functioning exam with depression at baseline f=1.85 p=0.17; 3 mos[g] f=7.73 p=0.1; 6 mos f=4.38 p=0.45; 9 mos f=13.45 p=0.001; 12 mos f=7.94 p=09
Drory, 1998	276	BDI [h]	Frequency of sexual activity after MI [i] at 3 - 6 mos, Satisfaction with sexual activity after MI	Depression	Pearson Correlation	Frequency of sexual activity 0.16 (p<0.01); Satisfaction with sexual activity 0.14 (p<0.01)	Frequency of sexual activity: 0.14 (p<0.01); Satisfaction with sexual activity: 0.15 (p<0.01))
Irvine, 1999	703	BDI symptom checklist	Social perception and help, daily living	Sudden cardiac death	Cox [j]	OR [k]	NR
Ladwig, 1999	552	D-S	NA	Perception of angina pectoris	OR	NR	2.98 (CI [l] 1.50 - 5.90)
O'Rourke, 1999	70	HADS [m]	Illness perception questionaire	NA	Regression ANOVA	NR	NR
Soejima, 1999	134	Depression Index	RTW [m]	NA	Logistic regression OR	NR	RTW Extroversion: 3.72 (CI 1.33 - 10.4) Depressive sx[o] in hospital 0.15 (CI 0.02 - 0.87)
Bogg, 2000	220	HADS (II) Global Mood Scale	QOL after MI measure	NA	Regression	NR	Physical QOL male R^2=46, Physical QOL female R^2=27, Baseline anxiety R^2=54

Table 5. Summary of Studies on the Relation of Depression and Quality of Life after Myocardial Infarction (Question 3) (continued)

Study Author, Year	No. Enrolled	Depression Instrument	Outcome		Stat [b]	Dep vs. Non Dep [c]	Multivariate Comparison
			QOL [a]	Other			
Denollet, 2000	322	ZDS [p]	Global Mood Scale, Health complaint scale	NA	Regression OR	NR	Failure to quit smoking 2.3 (CI 1.2 - 4.5); Depressive s/x 3.3 (CI 1.9 - 5.8); Type D personality 2.2 (CI 1.2 - 3.8); EF[q] < 50% 2.0 (CI 1.0 - 3.9); Hyperlipidemia 2.0 (CI 1.1 - 3.4)
Lane, 2000	288	BDI	Dartmouth COOP [r] Charts, BDI	NA	Correlation score	Gender r=0.31, Partner status r=0.24, Living alone r=0.20, Employment status r=0.18, Frequency of exercise r= -0.21, Duration of exercise r= -0.17 BDI r=0.37, State anxiety r=0.28, Treat anxiety r=0.32, Peel Index r=0.27, LOS[s] r=0.15	BDI R^2 0.11 p=0.0001, Partner status 0.05 p=0.002, Peel Index 0.05 p=0.001, State anxiety 0.02
Mayou, 2000	344	HADS	SF-36 Score [t]	NA	HR	At baseline: 51.2 (distressed), 67.5 (non-distressed) p < 0.05; At 3 mos: 38.7 (distressed), 62.3 (non-distressed) p < 0.05; At 12 mos : 47.2 (distressed), 64.0 (non-distressed) p < 0.05	NR

Table 5. Summary of Studies on the Relation of Depression and Quality of Life after Myocardial Infarction (Question 3) (continued)

Study Author, Year	No. Enrolled	Depression Instrument	Outcome		Stat [b]	Dep vs. Non Dep [c]	Multivariate Comparison
			QOL [a]	Other			
Lane, 2001	288	BDI	NR	NA	Regression Correlation	Gender r=0.2, Partner status r=0.22, Living alone r=0.3, Employment status r=0.18, Frequency of exercise r= -0.18, BDI r=0.32, State anxiety r=0.28, Treat anxiety r=0.24, Peel Index r=0.29, Killip class r=0.15, LOS r=0.25	BDI 0.11, Living alone 0.07, Peel Index 0.07, State anxiety 0.03
Brink, 2002	134	HADS	Physical Component SF-36, Mental Component SF-36	NA	Zero order correlation	NR	Physical Component: 0.47**; Mental Component: 0.66**
Drory, 2002	NR	BDI	Perceived health status	NA	Hierarchical regression	NR	Psychological well being
Drory, 2003	NR	BDI	Perceived health status	NA	Regression	NR	NR

[a] Quality of life
[b] Comparison statistic
[c] Depressed versus non-depressed
[d] Hamilton Rating Scale for Depression
[e] Not applicable
[f] Not reported
[g] Month
[h] Beck Depression Inventory
[i] Myocardial infarction
[j] Cox regression
[k] Odds ratio
[l] Hospital Anxiety and Depression Scale
[m] Confidence interval
[n] Return to work
[o] Symptoms
[p] Zung Depression Scale
[q] Ejection fraction
[r] Charts for Primary Care Practices
[s] Length of stay
[t] Medical Outcomes Study Short Form 36 Health Survey

Table 6. Summary of Studies on the Relation of Depression to Biomarkers after Myocardial Infarction (Question 3a)

Study Author, Year	No. Enrolled	Depression Instrument	Outcome Biomarkers	Stat [a]	Depressed vs Non-Depressed	Multivariate Comparison
Carney, 2001	Dep [b] 380 NonDep [c] 424	Screening: ENRICHD [d] modified DSM-IV[e] DISH [f] present depressive episode BDI [g] severity of depression	In univariate analysis all 4 indices of 24 hour HRV[h] were significantly lower in patients with depression. In multivariate analysis all 3 indices except 24 hour HRV were significantly lower in patients with depression.	Linear regression	NR [i]	NR
Kuijpers, 2002	NR	DSM-IV	PF4 [j] was significantly higher in Dep post-MI patients compared to NonDep post-MI patients, p=0.021. There was a trend toward a significantly increased B-TG [k] level with p=0.08, inspite of use of aspirin	Mann-Whitney U	PF4 mean rank 15.75 IU/ml vs. 9.25 IU/ml B-TG mean rank 15.04 IU/ml vs. 9.96 IU/ml	NR
Lesperance, 2004	965	SCID [l]	Dep patients had significantly higher sICAM-1 levels even after adjustment for confounders.These results were only slightly attenuated by adjustment for antidepressant treatment. No significant association between depression and IL6 [n]. Uncertain about the relationship of CRP [o] on depression as patients were on statins.	Linear regression	NR	sICAM 0.095+/-0.044 (with Dep) 0.086+/-0.045 (with antidepressant added to the model)

[a] Comparison statistic
[b] Depressed
[c] Non-depressed
[d] Enhancing Recovery in Coronary Heart Disease Trial
[e] Diagnostic & Statistical Manual of Mental Disorders
[f] Depression Interview and Structured Hamilton
[g] Beck Depression Inventory
[h] Heart rate variability
[i] Not reported
[j] Platelet factor 4
[k] ß-thromboglobulin
[l] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders-IV
[m] Soluble intracellular adhesion molecule 1
[n] Interleukin 6
[o] C-reactive protein

Table 7. Summary of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4)

Study Author, Year	Study Design	Intervention Description	Duration of Intervention; Duration of Follow-Up	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Dracup, 1991	Pro cohort [a]	Group A: Cardiac rehabilitation program; Group B: No participation in a formal program	12 wks [b]; 8 mos [c]	Multiple Affective Adjective Checklist @ 6 mos Group A: 8 , Group B: 13	NA	Multiple Affective Adjective Checklist - Anxiety score Group A: baseline 7, 6 mos 5; Group B: baseline 7, 6 mos 6; Psychosocial Adjustment to Illness Score Group A: baseline 42, 6 mos 36; Group B: baseline 44; 6 mos 42; Marital Adjustment Score Group A: baseline 115, 6 mos 121; Group B: baseline 114; 6 mos 111
Brown, 1993	RCT [d]	Group C: Cognitive behavioral therapy; Group D: Control	12 weekly 1-hour sessions; 3, 9, 15 mos	SCL 90-R [e] Group C: pre 65.1, 3 mos 62.1, 15 mos 56.1; Group D: pre 71.2, 3 mos 62.3, 15 mos 63.3; BDI [f] Group C: pre 12.1, 3 mos 6.9, 15 mos 5.6; Group D: pre 17.3, 3 mos 9.4, 15 mos 10.5; MMPI-168 [g] Group C: pre 74.1, 3 mos 68.1, 15 mos 67.5; Group D: pre 79.2, 3 mos 72.8, 15 mos 77.4	NA	NA

Table 7. Summary of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Intervention Description	Duration of Intervention; Duration of Follow-Up	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Crowe, 1996	RCT	NR	NR; 1 yr [h]	BDI Group E: 3 d 4.1, 3 mos 3.3, 6 mos 2.6, 14 mos 3.2 Group F: 3 d 3.9, 3 mos 3.7; 6 mos 3.3, 14 mos 2.9	NA	NA
Frasure-Smith, 1997	RCT	Group G: Intervention involved combination of emotional support, reassurance, education, practical advice, and referral health resources; Group H: Usual care	1 yr; 12 mos	BDI Group G: baseline 8.1, 12 mos 6.9; Group H: baseline 8.4, 12 mos 7.6	Cardiac mortality Group G: 4.8%; Group H: 3.4%; Myocardial infarction Group G: 4.8%; Group H: 5%; Revascularization Group G: 13.4%; Group H: 14%	Total mortality Group G: 5.5%, Group H: 3.9%
Taylor, 1997	RCT	Group I: Nurse-managed, home-based system for coronary risk factor modification and stress management; Group J: Usual medical care	1 yr; Upto 1 yr	Low levels depressed mood Group I: baseline 1.7, 12 mos 1.3; Group J: baseline 1.8, 12 mos 1.2; Moderate-high levels depressed mood Group I: baseline 6.1, 12 mos 1.4; Group J: baseline 5.7, 12 mos 1.5	Mortality Group I: 4%; Group J: 3%	Low levels anxious mood Group I: baseline 1.9, 12 mos 1.4; Group J: baseline 1.5, 12 mos 1.5; Moderate-high levels anxious mood Group I: baseline 6.1, 12 mos 2.6; Group J: baseline 5.9, 12 mos 2.7; Low levels stress Group I: baseline 2.0, 12 mos 1.7; Group J: baseline 2.0; 12 mos 1.8; Moderate-high levels stress Group I: baseline 6.4, 12 mos 2.8; Group J: baseline 6.7, 12 mos 3.7;

Table 7.Summary of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Intervention Description	Duration of Intervention; Duration of Follow-Up	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Taylor, 1997						Low anger frequency Group I: baseline 2.8, 12 mos 2.2; Group J: baseline 2.6, 12 mos 2.2; Moderate-high anger frequency Group I: baseline 5.6, 12 mos 3.1; Group J: baseline 5.6, 12 mos 3.0
Roose, 1998	RCT	Group K: Paroxetine 10-20 mg/day; Group L: Nortriptyline 25 mg/day	2 wks; 6 wks	NA	Heart rate Group K: baseline 10%, 6 wks 6%; Group L: baseline 11%, 6 wks 7%; Standing pulse rate standing Group K: baseline 11%, 6 wks 11%; Group L: baseline 14%, 6 wks 16%; Supine pulse rate supine Group K: baseline 10%, 6 wks 10%; Group L: baseline 12%, 6 wks 14%; HRV SDNN [i] Group K: baseline 37%, 6 wks 27; Group L: baseline 19%, 6 wks 16%; HRV pNN50 [j] Group K: baseline 10%, 6 wks 4%; Group L: baseline 9%, 6 wks 7%	NA

Table 7.Summary of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Intervention Description	Duration of Intervention; Duration of Follow-Up	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Johnston, 1999	RCT	Group M: Extended program involving additional sessions in the 2 mos after discharge; Group N: Inpatient cardiac rehabilitation program; Group O: Control	6 wks; Up to 1 yr	HADS [k] Group M: baseline 4.1, 12 mos 3; Group N: baseline 4.4, 12 mos 3.6; Group O: baseline 4.6, 12 mos 5.8	NA	HADS Anxiety Score Group M: 1 mo 4.8, 12 mos 3; Group N: 1 mo 5, 12 mos 4.5; Group O: 1 mo 5; 12 mos 6
Strik, 2000	RCT	Group P: Fluoxetine 20 mg/day; Group Q: Placebo	Up to 25 wks; 1, 3, 6, 9 wks then monthly untill 1 yr	HAMD [l] change @ 25 wks Group P: -9.65(7.2), Group Q: -6.9(6.9)	Chest pain Group P: 5; Group Q: 4	GI [m] complaints Group P: 8, Group Q: 6; Agitation Group P: 6, Group Q: 3; Other Group P: 17, Group Q: 12; Rehospitalization Group P: 1, Group Q: 6; Decrease in ATVI [n] Group P: 9, Group Q: 0; QRS [o] interval decrease Group P: 15; QRS interval increase Group Q:9

Table 7.Summary of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Intervention Description	Duration of Intervention; Duration of Follow-Up	Depression Scores	Cumulative Cardiac Events	Other Outcomes
McFarlane, 2001	RCT	Group R: Sertraline 50 mg/day; Group S: Placebo	6 mos; 6 mos	NR	NA	SDNN (SEM) [p] Group R: 1.5 mos 119 (10), 5.5 mos 121 (17); Group S: 1.5 mos 103 (7.9), 5.5 mos 86 (10) ; RMSSD(SEM) [q] Group R: 1.5 mos 28.8 (4,7), 5.5 mos 30 (7.1); Group S: 1.5 mos 26.7 (3), 5.5 mos 23.7 (5.7); LF/HF [r] ratio @ 1.5 mos Group R: 1.34 (0.15), Group S: 1.62 (0.22)
Glassman, 2002	RCT	Group T: Sertraline 50 mg/day daily; Group U: Placebo daily	Group T: 149.5 d; 24 wks; Group U: 153.8 d; 24 wks	CGI - 1 [s] mean score Group T: 2.57, Group U: 2.75; HAMD mean change in score @ 6 mos Group T: -8.4, Group U: -7.6	MI Group T: 5, Group U: 7; Congestive heart failure Group T: 5, Group U:7; Angina Group T: 26, Group U:30	Total mortality Group T: 2, Group U: 5; Composite end-point Group T: 32, Group U:41
Berkman, 2003 ENRICHD	RCT	Group V: Cognitive behavioral therapy, Social problem solving, plus SSRI [t] certain conditions (Sertraline 50 mg/day) Group W: Usual care	180 d; 18 mos	BDI change (baseline- 6 mos) Group V -8.6(9.2), Group W: -5.8(8.9); HAMD change (baseline- 6 mos) Group V -10.1(7.8), Group W: -8.4(7.7)	Cardiac Mortality Group V: 7.8%, Group W: 9.3%; MI Group V: 13.6%, Group W: 13.7%; Revascularization Group V: 17.4%, Group W: 18.5%	Total mortality Group V: 13.6%, Group W: 13.8%; Cardiovascular hospitalization Group V: 35.7%, Group W: 37.6%

Table 7.Summary of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Intervention Description	Duration of Intervention; Duration of Follow-Up	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Swenson, 2003	RCT	Group X: Sertraline 50 mg/day; Group Y: Placebo	24 wks; 18 mos	HAMD score change @ 16 wks Group X: -8.4(0.4), Group Y:-7.6(0.4) BDI score change @ 16 wks Group X:-8.0(0.6), Group Y:-7.3(0.6)	NA	SF-36 [u] Mental Component score change Group X: 17.4, Group Y: 15.2; Physical Component score change Group A: 10.6, Group Y:10.1

[a] Prospective cohort study
[b] Weeks
[c] Months
[d] Randomized controlled trial
[e] Symptom Checklist - 90
[f] Beck Depression Inventory
[g] Minnesota Multiphase Personality Inventory
[h] Year
[i] Heart rate variability - Standard deviation of normal R-R interval
[j] Heart rate variability - the proportion of pairs of adjacent intervals differing by more than 50 ms
[k] Hospital Anxiety and Depression Scale
[l] Hamilton Rating Scale for Depression
[m] Gastrointestinal
[n] Aortic time velocity integral
[o] QRS Interval
[p] Standard deviation of normal R-R interval (Standard error of mean)
[q] Root mean square of successive differences (Standard error of mean)
[r] Low frequency/high frequency
[s] Clinical Global Inventory
[t] Selective serotonin re-uptake inhibitors
[u] Medical Outcomes Study Short form 36 health survey

Table 8. Summary of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	Test	Sensitivity	Specificity	Other
Davis, 1988	Pro cohort [a]	Canada	52	51	90	**#1** SCID [b] nurse & therapist interview			Concordance: 80.8%
						#2 SCID nurse and BDI [c]			Concordance: 13.5%
						#3 Therapist interview and BDI			Concordance: 11.5%
Martin, 2000	Cross-sectional	Europe	194	63.4	73	**#1** HADS [d] all items			Internal consistency: 0.82
						#2 HADS Depression subscale			Internal consistency: 0.72 Exploratory factor analysis reported
Wojciechowski, 2000	Pro cohort	Europe	143	57.8	81	**#1** Zung SDS [e] / SCL-90-Dep [f]			Pearson correlations: 0.70; 0.76; 0.77; 0.75, @ 1, 3, 6, 12 mos [g] post-MI
						#2 Zung SDS / Maastricht Quest (vital exhaustion)			Pearson correlations: 0.79; 0.76; 0.78; 0.81, @ 1, 3, 6, 12 mos post-MI
						#3 SCL-90-Dep / Maastricht Quest (vital exhaustion)			Pearson correlations: 0.75; 0.83; 0.76; 0.76, @ 1, 3, 6, 12 mos post-MI

Table 8. Summary of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5) (continued)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)		Test	Sensitivity	Specificity	Other
Strik, 2001	Cross-sectional	Europe	206	59.9	76	**#1**	SCL - 90	81% major/ minor [h], 96% major [i] only	84% major/minor, 74% major only	PPV [j]: 40% major/minor, 36.8% major only; NPV [k]: 93.3% major/minor, 96.2% major only
						#2	BDI	84% major/minor, 82% major only	72% major/minor, 79% major only	PPV: 25% major/minor, 33% major only; NPV: 98% major/minor, 98% major only
						#3	HADS/ HADS-Depression subscale	HADS: 78% major/minor, 90% major only; HADS-D: 75% major/minor, 85% major only	HADS: 85% major/minor, 84% major only; HADS-D: 78% major/minor, 75% major only	HADS PPV: 45% major/minor, 45% major only; HADS NPV: 99% major/minor, 99% major only; HADS-D PPV: 32% major/minor, 32% major only; HADS-D NPV: 98% major/minor, 98% major only [l]
						#4	17-item HAMD [m]	76% major/minor, 86% major only	86% major/minor, 92% major only	PPV: 41% major/minor; NPV: 99% major/minor, 98% major only

Table 8. Summary of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5) (continued)

Study Author, Year	Study Design	Location	No. of Subjects	Mean Age	Male (%)	Test		Sensitivity	Specificity	Other
Freedland, 2002	Pro cohort	USA	2404	61	56		BDI / HAMD			Pearson correlation: 0.64
Martin, 2003	Pro cohort	Europe	335	67.4	67	**#1**	HADS all items			Internal consistency: 0.87 @ 1 wk, 0.88 @ 6 wks, 0.90 @ 6 mos
						#2	HADS depression subscale			Internal consistency: 0.76 @ 1 wk, 0.8 @ 6 wks, 0.81 6 mos Confirmatory factor analysis reported

[a] Prospective cohort study
[b] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders - IV
[c] Beck Depression Inventory
[d] Hospital Anxiety and Depression Scale
[e] Zung Self-Rating Depression Scale
[f] Symptom Check List 90
[g] Months
[h] Major and minor depression
[i] Major depression
[j] Positive predictive value
[k] Negative predictive value
[l] There appears to be a misprint in original article tables listing positive predictive value and negative predictive value as equal for both major and major/minor depression,which does not reconcile with their statistical data presented.
[m] Hamilton Rating Scale for Depression

Table 9. Summary of Characteristics of Studies on the Relation of Depression to Use of Treatment after Hospitalization for Myocardial Infarction (Question 6)

Study Author, Year	Study Design	Location	Study Group	No. of Subjects	Mean Age	Male (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)
Bennet, 2003	Pro cohort [d]	Europe	NA [e]	37	62	73	NR [f]	NR	NR	NR
Blumenthal, 1982	Pro cohort	USA	NA	35	54	94	NR	NR	NR	NR
Druss, 2000	Retro cohort [g]	USA	Mental disorders	5365	76	52	42	22	23	NR
			No mental disorders	108288	76	46	40	26	15	NR
Ziegelstein, 2000	Pro cohort	USA	BDI [h] ≥10	35	46	46	71	31	31	69
			BDI <10	169	55	59	62	30	27	61
			Major Depression/ Dysthymia	31	42	52	71	36	29	71
			No Major Depression/ Dysthymia	173	54	58	63	31	27	60
Romanelli, 2002	Pro cohort	USA	Depressed	35	75	57	71	49	NR	57
			Not depressed	118	73	55	70	33	NR	60
Bennet, 2003	Pro cohort	Europe	NA	37	62	73	NR	NR	NR	NR
Lauzon, 2003	Pro cohort	Canada	Depressed	191	60	75	34	16	40	35
			Not depressed	359	60	81	36	16	40	39
Whitmarsh, 2003	Pro cohort	Europe	NA	93	64	76	NR	NR	61	NR
Steeds, 2004	Pro cohort	Europe	BDI [f] ≥12	62	NR	NR	NR	NR	NR	NR
			BDI < 12	69	NR	NR	NR	NR	NR	NR
Strik, 2004	Pro cohort	Europe	Depressed	63	NR	67	NR	NR	10	35
			Not depressed	143	NR	80	NR	NR	13	29

[a] Hypertension
[b] Diabetes mellitus
[c] Hyperlipidemia
[d] Prospective cohort study
[e] Not applicable
[f] Not reported
[g] Retrospective cohort study
[h] Beck Depression Inventory

Table 10. Summary of Results of Studies on the Relation of Depression to Use of Treatment after Hospitalization for Myocardial Infarction (Question 6)

Study Author, Year	Study Group	Diagnosis of MI	Method of Assessing of Depression used for Analysis	No. of Subjects	Follow-Up	Cardiac Cath [a] (%)	PTCA [b] (%)	CABG [c] (%)	Aspirin/ Antiplatelet (%)	Beta Blockers (%)
Druss, 2000	Major depression/ affective	ICD-9 [d]	ICD-9	315	16 mos [e]	33 [f]	9	8	NR	NR
	No mental disorders			108288	16 mos	44 [f]	17	13	NR	NR
Ziegelstein, 2000	Major depression/ dysthmia	Pain, EKG [g], CPK-MB [h]	SCID [i] BDI [j] > 10	31	4 mos	NR	NR	NR	NR	72
	Not depressed			173	4 mos	NR	NR	NR	NR	88
Romanelli, 2002	Depressed (BDI ≥10)	Pain, EKG, CPK-MB	SCID	35	4 mos	NR	NR	NR	86	74
	Not depressed			118	4 mos	NR	NR	NR	84	86
Lauzon, 2003	Depressed	NR	BDI-10	191	30 d [k]	57	32	7	NR	NR
	Not depressed	NR		359	30 d	47	25	8	NR	NR
	Depressed	NR	BDI-10	191	1 yr [l]	67	39	19	84	56
	Not depressed	NR		359	1 yr	55	30	16	86	64
Steeds, 2004	Depressed	Pain, EKG, CPK-MB	BDI-12	62	32 mos	NR	NR	NR	NR	32
	Not depressed			69	32 mos	NR	NR	NR	NR	55
Strik, 2004	Depressed/ Minor depression	Pain, EKG, ASAT [m]	SCID	63	1 yr	NR	36	NR	81 [f]	40
	Not depressed			143	1 yr	NR	36	NR	95 [f]	40

[a] Cardiac catheterization
[b] Percutaneous transluminal coronary angioplasty
[c] Coronary artery bypass graft
[d] The International Statistical Classification of Diseases and Related Health Problems
[e] Months
[f] $p < 0.001$
[g] Electrocardiogram
[h] Creatine phosphokinase - muscle brain
[i] Structured Clinical Interview for DSM IV
[j] Beck Depression Inventory
[k] Day
[l] Year
[m] Aspartate aminotransferase

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Strik JJ, Lousberg R, Crijns HJ, et al. Relation of levels of serum lipoproteins to depression after acute myocardial infarction. Am J Cardiol 2002 ; 90(12): 1368-70.

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Swenson JR, O'Connor CM, Barton D, et al. Influence of depression and effect of treatment with sertraline on quality of life after hospitalization for acute coronary syndrome. Am J Cardiol 2003; 92(11): 1271-6.

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Appendix A: Technical Experts and Peer Reviewers

Technical Experts		
Expert Area and Organization	**Name**	**Location**
Partner Organization		
American Academy of Family Physicians (AAFP)	Lee Green MD, MPH	University of Michigan Ann Arbor, MI
Government		
Center for Medicaid and Medicare Services (CMS)	Carlos Cano MD	Woodlawn, MD
Payer		
IPRO	Charles Stimler MD, MPH	Lake Success, NY
University		
Washington University School of Medicine	Robert M. Carney PhD	St. Louis, MO
University of Birmingham	Douglas Carroll PhD	Edgbaston, Birmingham, United Kingdom
Tilburg University	Johan Denollet, PhD	Tilburg, The Netherlands
McGill University	Nancy Frasure-Smith PhD	Montreal, QC Canada
Columbia University	Alexander Glassman MD	New York, NY
Professional Organizations		
American College of Physicians (ACP)	Vincenza Snow MD	Philadelphia, PA

Peer Reviewer		
Expert Area and Organization	**Name**	**Location**
Partner Organization		
American Academy of Family Physicians (AAFP)	Lee Green MD, MPH	University of Michigan Ann Arbor, MI
American Academy of Family Physicians (AAFP)	Belinda Ireland MD, MS	Leawood, KS
Government		
Center for Medicaid and Medicare Services (CMS)	Carlos Cano MD	Woodlawn, MD
Payer		
IPRO	Charles Stimler MD, MPH	Lake Success, NY
University		
Columbia University	Alexander Glassman MD	New York, NY
Professional Organizations		
American College of Physicians (ACP)	Vincenza Snow MD	Philadelphia, PA
American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR)	Douglas R. Southard PhD, MPH, PA-C	Roanoke, VA

Appendix B. Priority Journals for Hand Searching

Priority Journal Titles
American Heart Journal
American Journal of Cardiology
American Journal of Medicine
American Journal of Psychiatry
Annals of Behavioral Medicine
Archives of General Psychiatry
Archives of Internal Medicine
Biological Psychiatry
Circulation
Health Psychology
JAMA
Journal of Behavioral Medicine
Journal of Cardiopulmonary Rehabilitation
Journal of the American College of Cardiology
Psychosomatic Medicine
Psychosomatics

* Tables of Contents reviewed from 1 October 2003 to 30 March 2004.

Appendix C. Literature Search Strategies

Medline
(myocardial infarction[mh] OR myocardial infarct*[tiab]) AND (depression[mh] OR mental disorder[mh] OR mood disorder[mh] OR depression[tiab] OR depressive symptom*[tiab] OR mood disorder[tiab] OR mental disorder[tiab] OR psychiatric disorder[tiab]) AND eng[la] NOT (animal[mh] NOT human[mh])

Cochrane
(myocardial next infarction) and (depression)

EMBASE
'acute heart infarction'/exp OR 'heart infarct'/exp OR 'heart infarction'/exp OR (myocardial AND ('infarct'/exp OR 'infarction'/exp)) AND ('depression'/exp OR 'mood disorder'/exp OR ((mental OR 'mood'/exp OR psychiatric) AND (disorder))) AND [english]/lim AND [humans]/lim AND [embase]/lim

CINAHL
(((myocardial or myocardiac) and (infarct*)) and ((depression) or (mental disorder) or (mood disorder) or (psychiatric disorder) or (depressive symptom))) and (ZL "ENGLISH")

PsychInfo
((myocardial infarct*) and ((depression) or (mental disorder) or (psychiatric disorder) or (depressive symptom))) and (ZL "ENGLISH")

Appendix D. Abstract Review Form for Primary Literature

Date: **EPC Depression Post-MI Abstract Review Form** **Reviewer: _____**

Data Entry: _____

Record ID:

Title:

Abstract:

Step 1: General Exclusion Criteria

Delete article because (check one):

☐ not in English

☐ does not include human data

☐ no original data

☐ meeting abstract (no full article for review)

☐ other: (specify) _____

☐ **Unclear: get article to decide**

Step 3: Question-Specific Exclusion Criteria

Question 4:

- ○ Not a concurrent comparison study

Questions 5:

- ○ Does not have a validated reference standard

Do not go on if any item above is checked.

Step 2: Article may address following questions (check all that apply):

☐ depression during hospitalization (Q1)
☐ depression during hospitalization w/ & w/out a known history (Q1a)
☐ depression after initial hospitalization (Q2)
☐ depression measures and outcomes (Q3)
☐ depression measures and surrogate markers (Q3a)
☐ outcomes w/ & w/out depression treatment (Q4)
☐ outcomes w/ depression resolution (Q4a)
☐ outcomes w/out depression resolution (Q4b)
☐ screening performance characteristics (Q5)
☐ screening performance characteristics during hospitalization (Q5a)
☐ screening performance characteristics after hospitalization (Q5b)
☐ cardiac treatment differences with depression (Q6)

☐ This article does not apply to any of the questions

☐ Get article for reference regarding:
_____

Appendix E. Abstraction Forms

General Content Review Form

JOHNS HOPKINS EVIDENCE-BASED PRACTICE CENTER

POST MYOCARDIAL INFARCTION DEPRESSION

GENERAL FORM

Article ID: _____ **First Author: _____**

Reviewer 1: _____ **Reviewer 2: _____**

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1. Exclude article from review because (Check one):

does not include human data

no original data

not in English

meeting abstract (no full article for review)

case report or case series (no denominator)

letter

published before 1980

no data reported on when MI occurred relative to when depression assessed

study population is mixed (i.e. cardiac and non-cardiac)

AND

patients with MI not reported separately

patients with MI not reported separately in study (e.g., CAD, MI and unstable angina)

AND

patients with MI represent < 50% of the sample

does not apply to any of the questions

other: (specify) _____

IF ANY OF THE ABOVE IS CHECKED, STOP! DO NOT CONTINUE

Return article and form.

2. Key Questions: (Check all that apply)

Q1. What is the prevalence of depression in patients diagnosed with and hospitalized for acute myocardial infarction (MI)? [*depression assessed during initial hospitalization for MI*]

Q1a. What is the prevalence of depression in patients diagnosed with and hospitalized for acute MI, with and without a history of previous depression as reported by study investigators?

Q2. What percentage of patients with post-MI depression continue to have depression (or depressive symptoms) one or more months after initial hospital discharge? [*depression assessed one or more months after initial hospitalization and not during the initial hospitalization*]

Q3. What is the association of post-MI depression with outcomes independent of other predictors of post-MI outcomes? [*must include at least one of the following outcomes: death, MI, rehospitalization, revascularization, arrhythmias, utilization, quality of life, disability and adherence*]

Q3a.What is the association of post-MI depression with surrogate markers of cardiac risk independent of other predictors of post-MI outcomes? [*must include at least one of the following surrogate markers: heart rate variability, platelet reactivity, C-reactive protein or other markers of inflammation*]

Q4. Do post-MI patients with depression have better outcomes with depression treatment compared to those without depression treatment?

If the study does not involve a concurrent comparison, check this box as not eligible for Q4.

Q4a. Do outcomes differ with or without improvement in depression for post-MI patients with depression that do receive depression treatment?

Q4b. Do outcomes differ with or without improvement in depression for post-MI patients with depression that do not receive depression treatment?

Q5. What are the performance characteristics (e.g., sensitivity, specificity, reliability, and predictive value) of instruments or methods that are used to screen for depression (or depressive symptoms) following an acute MI?

If the study does not use a validated reference standard, check this box as not eligible for Q5.

If the study does not use quantitative methods to assess depression, check this box as not eligible for Q5.

Q5a. During hospitalization?

Q5b. Within 3 months after hospitalization?

Q6. Does the use of cardiac treatment for patients with acute MI differ for those with and without depression?

None of the above. **If this is checked, STOP HERE. Return article and forms**

ASSESSMENT OF STUDY DESIGN AND QUALITY

3. Study design

case control study
nested case control study
cross-sectional study
retrospective cohort study
prospective cohort study
randomized clinical trial
other (specify): _____

CHARACTERISTICS OF STUDY

4. Provide a brief statement of the main aims beginning with "To …"

_____

_____

5. Source of funding (check all that apply):

University
Pharmaceutical company
Government
Private
No funding
Not reported
Other (specify): _____

6. In what geographical area was the study mainly performed (check all that apply)?

North America (USA)
North America (Canada)
South or Central America
Europe
Asia
Africa
Australia

7. Was this a multicenter study?

Yes. Number of centers, if known_____
No
Unclear

8. Data comes from patients diagnosed with MI between which years (mo/yr)

Start: _____/_____ End: _____/_____

Mo. Yr. Mo. Yr.

Not applicable

9. Does this study include patients with acute coronary syndromes other than acute MI?

Yes

No

If yes:

a. How many patients had an acute coronary syndrome?_____

b. What percentage of these patients had an acute MI? _____

c. Was the data for acute MI reported separately?

Yes

No

This item DOES NOT apply to Q1, Q2 & Q5

10. Does this study include patients with mental disorders other than depression?

Yes

No

If yes:

a. How many patients were diagnosed with mental disorders? _____

b. What percentage of these patients had depression or affective disorder? _____

c. Was the data for depression or affective disorder reported separately?

Yes

No

11. Study inclusion and exclusion criteria

NOTE: Record in terms of exclusions if possible

	Not Applicable	Inclusion	Exclusion	Range
Age				_____
Gender				_____
Race				_____
Education				_____
Marital status				_____
Occupation				_____
Cardiac surgery anticipated				_____
Index ACS developed after CABG				_____
Significant bradycardia				_____
MI of non-atherosclerotic etiology				_____
Killip class				_____
Uncontrolled hypertension				_____
Persistent clinically significant abnormalities				_____
Renal dysfunction				_____
Hepatic dysfunction				_____
Other significant nonreactive disease				_____
Women of childbearing potential not using adequate contraception				_____
Alcohol or substance abuse				_____
Psychotic symptoms				_____
History of psychosis, bipolar disorder, organic brain syndrome or dementia				_____
Significant suicide risk				_____
Terminally ill				_____
Serious comorbidities				_____
Cognitive impairment				_____
Non-English speaking				_____
Other:_____				_____
_____				_____
_____				_____
_____				_____
_____				_____

12. Criteria for diagnosis of myocardial infarction: (Check all that apply)

In hospital assessment:

Chest pain

Electrocardiogram

Creatine kinase

Troponin

Other cardiac enzymes

Other (specify): _____

Physician report (e.g., as documented in medical record)

Patient self report

Radionuclide (e.g. thallium) study

Other (specify): _____

Depression measurement:

13. Was a validated questionnaire used to assess depression? (Check at least one)

Beck Depression Inventory (BDI)

Hamilton Rated Scale for Depression (HAM – D)

Zung Self-Assessment Depression Scale

General Health Questionnaire (GHQ)

Center for Epidemiologic Study Depression Scale (CES-D)

Hospital Anxiety and Depression Scale (HADS)

Geriatric Depression Scale

Symptom Check List 90 (SCL-90)

Clinical Global Impression (CGI-1)

Other (specify): _____

No validated questionnaire

14. Was a standardized psychiatric interview used to assess depression? (Check at least one)

Diagnostic Interview Schedule (DIS)

Depression Interview and Structured Hamilton (DISH)

Structured Clinical Interview for DSM-IV (SCID)

Semi-structured Clinical Interview for DSM-IV (SCID)

Other (specify): _____

No standardized psychiatric interview

15. Was a clinical interview by a mental health professional (DSM III, III-R, IV criteria) used to assess depression? (Check at least one)

Yes

No

16. Was another method used to assess depression? (Check at least one)

Review of medical records

Other (specify): _____

Not stated

None

17. Provide a description for each group in reference to acute MI, depression and other key characteristics (e.g. A: Acute MI depression, B: Acute MI without depression)**.**

Group	Description		
	Acute MI	**Depression**	**Other**
A	yes	yes	
	no:_____	no:_____	
B	yes	yes	
	no:_____	no:_____	
C	yes	yes	
	no:_____	no:_____	
D	yes	yes	
	no:_____	no:_____	

Comments:

_____

_____

_____

_____

_____

18. Description of subjects [use % except for total number and age]

	Group A	Group B	Group C	Group D
Total number (N)				
Age (mean +/- SD)				
(Median and range)				
Gender, male %				
Race/ethnicity: Caucasian, %				
Non-Caucasian, %				
African American, %				
Asian American, %				
Hispanic American, %				
Other, _____%				
Marital status, married, %				
Discharged home, %				
Education high school or higher, %				
Employed full/part time, %				
Cardiac risk factors: Hypertension				
Diabetes mellitus				
Smoking				
Hyperlipidemia				
Obesity				
Prior cardiac disease (_____)				
Previous angina				
Previous MI				
Previous heart failure				
Peripheral vascular disease				
Sedentary lifestyle				

Description of subjects [use % except for total number and age]

	Group A	Group B	Group C	Group D
Features of MI:				
Killip Class				
Class I, %				
Class II, %				
Class III, %				
Class IV, %				
Other _____				
Ejection fraction, mean +/- SD				
Other_____				
Maximum creatine kinase mean +/- SD				
Other_____				
Pre-discharge exercise test result in METS, mean				
Received revascularization, %				
History of depression				
Family history of depression				
Received thrombolytics, %				
Other:_____				
_____				
_____				
_____				

Quality Assessment Form

JOHNS HOPKINS EVIDENCE-BASED PRACTICE CENTER

POST MYOCARDIAL INFARCTION DEPRESSION

QUALITY ASSESSMENT FORM

Article ID: _____	**First Author: _____**
Reviewer 1: _____	**Reviewer 2: _____**

REPRESENTATIVENESS OF STUDY POPULATION

1. Did the study describe the setting and population from which the study sample was drawn, and the dates of the study?

a. Adequate (setting AND population described AND start and end date specified)	**2**
b. Fair (setting AND population described but NOT start and end date)	**1**
c. Inadequate (not specified)	**0**

2. Were detailed inclusion/exclusion criteria provided?

a. Adequate (detailed description of specific inclusion and exclusion criteria OR statement that all eligible patients enrolled)	**2**
b. Fair (some description, but would be difficult to replicate based on information provided)	**1**
c. Inadequate (minimal description or not at all)	**0**

3. Was information provided on excluded or non-participating patients?

a. Adequate (all reasons for exclusion AND number excluded OR no exclusion)	**2**
b. Fair (only one of above criteria specified or information not sufficient to allow replication)	**1**
c. Inadequate (none of the above criteria specified)	**0**

4. Does the study describe key patient characteristics at enrollment?

Demographics: age, gender, race/ethnicity, education, marital status, occupation

Medical characteristics: current smoking, Body Mass Index (BMI), diabetes, hypertension, hypercholesterolemia, cerebrovascular disease, peripheral vascular disease, renal insufficiency, cardiac medications, antidepressants

Depression Features: depression measured by validated questionnaire, standardized psychiatric interview, clinical interview by mental health professional, and review of medical records; first episode of depression; recurrent depression; prior episodes of major depression; prior psychotropic treatment

Cardiac Features: cardiac event leading to current hospitalization, left ventricular ejection fraction (LVEF in %), previous MI, previous CABG surgery, previous PTCA, history of congestive heart failure, Killip class, peak CPK

a. Good: 4 of 4 categories described well (i.e., most items in each category described)	**2**
b. Fair: 2 or 3 categories described well	**1**
c. Poor: 0 or 1 categories described	**0**

5. Did the study include a consecutive series of individuals presenting with the relevant symptoms or a randomly selected sample?

a. Consecutive series	**2**
b. Random sample	**2**
c. Other	**1**
d. Unclear	**0**

6. What was recruitment based on?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Predetermined diagnostic criteria	**2**
b. Previous testing with the index test/instrument or the reference standard used in the study	**1**
c. Unclear	**0**
d. Not applicable	**N/A**

BIAS AND CONFOUNDING

7. Was assignment of patients to study group randomized?

[THIS ITEM APPLIES TO Q4 ONLY]

a. Adequate (investigators could not predict assignment)	**2**
b. Partial (date of birth, admission date, hospital record number, or other nonrandom scheme for assignment OR did not state)	**1**
c. Not randomized	**0**
d. Unclear	**0**
e. Not applicable	**N/A**

8. Did the patient groups have any important differences in key patient characteristics?

[THIS ITEM APPLIES TO Q4 ONLY]

Demographics: age, gender, race/ethnicity, education, marital status, occupation, days from index MI to first day of therapy

Medical characteristics: current smoking, Body Mass Index (BMI) kg/m2, diabetes, hypertension, hypercholesterolemia, cerebrovascular disease, peripheral vascular disease, renal insufficiency, cardiac medications, antidepressants

Depression Features: depression measured by instruments such as HAM –D, CGI-1or Beck Depression Inventory; first episode of depression; recurrent depression; prior episodes of major depression; prior psychotropic treatment

Cardiac Features: cardiac event leading to current hospitalization, left ventricular ejection fraction (LVEF in %), previous MI, previous CABG surgery, previous PTCA, history of congestive heart failure, Killip class, peak CPK

a. Groups equivalent in all factors examined	**2**
b. Groups have minor difference in 1 or 2 factors	**1.5**
c. Groups have an important difference in one or more factors OR minor difference in more than two factors	**1**
d. Analysis not done	**0**
e. Not applicable	**N/A**

9. Was the decision to obtain the reference test affected in any way by the results of the study test/instrument, or vice versa?

[THIS ITEM APPLIES TO Q5 ONLY]

[Note: we want to understand the extent to which testing decisions were *independent* of each other. There are two ways for testing not to be independent:

(1) The decision to perform the 2nd test can be dependent on the results of the 1st test

(2) The decision to include a patient in the study can be based on a referral for testing]

a. Decision to test was NOT affected by either (1) above OR (2) above	**2**
b. Decision to test was affected by either (1) above OR (2) above	**0**
c. Unclear	**0**
d. Not applicable	**N/A**

10. Was there blinding of study test interpretation, reference test interpretation, and clinical data?

[THIS ITEM APPLIES TO Q5 ONLY]

[Note: This question concerns *blinding*: not independence of interpretations]

a. Excellent (ALL 3 blinded, including both test interpretations with each other)	**2**
b. Good (test interpretations blinded to each other but not to clinical data)	**1**
c. Fair (test interpretations blinded to clinical data but not to each other)	**0.5**
d. Poor (no blinding OR not stated)	**0**
e. Not applicable	**N/A**

11. Was interpretation of the study test performed by *two* or more independent observers?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (multiple observers AND independent)	**2**
b. Fair (multiple observers but NOT independent)	**1**
c. Inadequate (Neither OR not stated)	**0**
d. Not applicable (e.g., if using self rating or test doesn't require interpretation)	**N/A**

12. Was interpretation of the reference test performed by *two* or more independent observers?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (multiple observers AND independent)	**2**
b. Fair (multiple observers but NOT independent)	**1**
c. Inadequate (Neither OR not stated)	**0**
d. Not applicable (e.g., if using self rating or test doesn't require interpretation)	**N/A**

13. Were the reference standard and the index test measured before any interventions were started with knowledge of test results?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Yes	**2**
b. No	**0**
c. Unclear	**0**
d. Not applicable	**N/A**

14. If the study was a controlled clinical trial, was there blinding of clinicians, patients, and outcome assessors?

[THIS ITEM APPLIES TO Q4 ONLY]

a. Excellent (All three blinded, including all treatment arms)	**2**
b. Good (Only 2 of the 3 blinded, or some but not all of the arms)	**1.5**
c. Fair (Only 1 of the 3 blinded)	**1**
d. Poor (No blinding or not stated)	**0**
e. Not applicable	**N/A**

DESCRIPTION OF THERAPY/MANAGEMENT

15. How well did the study describe details of the cardiac therapy regimen given for the MI? (e.g., types of procedures, types of medications, dose intensity, duration of therapy)

a. Adequate – detailed enough that it could be replicated	**2**
b. Fair – one or two key features not described	**1**
c. Inadequate – not described	**0**
d. Not applicable	**N/A**

16. Did the study describe details of the psychiatric treatment given for post-MI depression?

a. Adequate (treatment fully described)	**2**
b. Fair (some description, but information not sufficient to allow replication)	**1**
c. Inadequate (not described)	**0**
d. Not applicable	**N/A**

17. How was the description of *other* medical or psychiatric treatments given study subjects while they were in the study? (e.g., other medications or procedures, psychiatric medications other than study drug, psychiatric therapy other than therapy being studied)

a. Adequate (other treatment fully described)	**2**
b. Fair (some description, but information not sufficient to allow replication)	**1**
c. Inadequate (not described)	**0**
d. Not applicable	**N/A**

18. How did the study describe details of the flow of participants through each stage? For each group the number of participants randomly assigned, receiving intended treatment, completing the study protocol and analyzed for the primary outcome.

[THIS ITEM APPLIES TO Q4 ONLY]

a. Adequate	**2**
b. Fair (one of the above NOT described)	**1**
c. Inadequate (more than one of above NOT described)	**0**

19. How was the assessment of adherence to the therapy of interest?

[THIS ITEM APPLIES TO Q4 ONLY]

a. Adequate (strong methods AND results of assessment reported in detail)	**2**
b. Fair (weak methods such as self-report OR results of assessment not reported in detail but NOT both)	**1**
c. Inadequate (neither reported)	**0**
d. Not appliacable	**N/A**

DESCRIPTION OF THE ASSESSMENT PROTOCOLS

20. Was data collection planned before the index test/instrument and reference standard were performed (prospective study)**?**

[THIS ITEM APPLIES TO Q5 ONLY]

a. Yes	**2**
b. No	**1**
c. Unclear	**0**

21. Did the study describe details of the methods used for the initial diagnosis of depression?

[THIS ITEM *DOES NOT* APPLY TO Q5]

a. Adequate (used a validated questionnaire or standardized interview process OR enough description to replicate)	**2**
b. Fair (not a validated questionnaire or standardized interview process OR enough description to replicate)	**1**
c. Inadequate (no description)	**0**

22. Was the interpretation criteria for a positive diagnosis of depression described?

[THIS ITEM *DOES NOT* APPLY TO Q5]

a. Adequate (enough description to replicate)	**2**
b. Fair (some description, but not enough to replicate)	**1**
c. Inadequate (no description)	**0**

23 Did the study describe details of the reference standard used to assess the study test/instrument protocol?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (enough description to replicate)	**2**
b. Fair (some description, but not enough to replicate)	**1**
c. Inadequate (no description)	**0**
d. Not applicable	**N/A**

24. Did the study report the time interval between performance of the index test/instrument and the reference standard?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Yes AND it was within 1 day	**2**
b. Yes AND it was more than 1 day but less than 1 week	**1**
c. Yes AND it was 1 week or more	**0**
d. Unclear	**0**
e. Not applicable	**N/A**

TEST/INSTRUMENT INTERPRETATION

25. Were the interpretation criteria of a positive depression test/instrument described for the study test?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (enough description to replicate)	**2**
b. Fair (some description, but not enough to replicate)	**1**
c. Inadequate (no description)	**0**
d. Not applicable	**N/A**

26. Did all individuals receiving the study test/instrument also receive the reference test?

[THIS ITEM APPLIES TO Q5 ONLY]

a. All (all received BOTH tests)	**2**
b. Some (some received both tests)	**1**
c. None (no one received both tests)	**0**
d. Unclear	**0**
e. Not applicable	**N/A**

27. Were the interpretation criteria of a positive depression test/instrument described for the reference test?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (enough description to replicate)	**2**
b. Fair (some description, but not enough to replicate)	**1**
c. Inadequate (no description)	**0**
d. Not applicable	**N/A**

28. Was a summary index of test performance (e.g., sensitivity/specificity, area under ROC curve) **reported for the study test AND an indicator of variability** (standard error, confidence interval)**?**

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (both reported)	**2**
b. Fair (test performance but no index of variability)	**1**
c. Inadequate (no information given)	**0**
d. Not applicable	**N/A**

29. Were methods for calculating test reproducibility described?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (enough description to replicate)	**2**
b. Fair (some description, but not enough to replicate)	**1**
c. Inadequate (no description)	**0**
d. Not applicable	**N/A**

30. Did the authors describe how indeterminate results, missing responses and outliers of the index test/instrument and the reference test were handled?

[THIS ITEM APPLIES TO Q5 ONLY]

a. Adequate (enough description to replicate)	**2**
b. Fair (some description, but not enough to replicate)	**1**
c. Inadequate (no description)	**0**
d. Not applicable	**N/A**

OUTCOMES AND FOLLOW-UP

31. Did the study report the numbers or reasons for withdrawals from the study protocol or patients otherwise lost to follow-up?

a. Adequate (both numbers AND reasons reported, OR no withdrawals)	**2**
b. Fair (only numbers OR reasons reported)	**1**
c. Inadequate (neither given)	**0**
d. Not applicable (no longitudinal follow-up was performed)	**N/A**

32. What was the percentage of patients that withdrew from the study protocol or were lost to follow-up?

[THIS ITEM APPLIES TO Q2, Q3, Q4 AND Q6 ONLY]

a. None	**2**
b. < 10%	**1.5**
c. 10 - 20%	**1**
d. > 20%	**0**
e. Not stated	**0**
f. Not applicable (no follow-up)	**N/A**

33. How did the investigators determine whether the patients received cardiac treatment?

[THIS ITEM APPLIES TO Q6 ONLY]

a. Adequate (clear definitions of type of treatment AND exact techniques to assess whether treatments received)	**2**
b. Fair (some description, but information not sufficient to allow replication)	**1**
c. Inadequate (no information provided)	**0**
d. Not applicable	**N/A**

34. How were cardiac heart disease outcome measures defined? (e.g., left ventricular ejection fraction (%), heart rate variability, blood pressure, standard ECG, runs of ventricular premature contractions, occurrence of cardiovascular events – myocardial infarction, stroke, severe angina, congestive heart failure, death)

[THIS ITEM APPLIES TO Q3 & Q4 ONLY]

a. Adequate (clear definitions of each outcome AND exact techniques to assess the outcome)	**2**
b. Fair (some description, but information not sufficient to allow replication)	**1**
c. Inadequate (no information provided)	**0**
d. Not applicable (cardiac outcomes not measured OR no intervention)	**N/A**

35. How were depression outcome measures defined? (e.g., instruments such as Hamilton Rated Scale for Depression (HAM –D) and Beck Depression Inventory (BDI) scores, validated questionnaires, standardized psychiatric interview, clinical interview by mental health professional (DSM III or IV))

[THIS ITEM APPLIES TO Q3 & Q4 ONLY]

a. Adequate (clear definitions of each outcome measure AND exact techniques to assess the outcome)	**2**
b. Fair (some description, but information not sufficient to allow replication)	**1**
c. Inadequate (no information provided)	**0**
d. Not applicable (no intervention)	**NA**

36. Were the same tools for diagnosing depression and the mode of administration used for baseline and follow up?

a. Adequate (tool AND method of administration are same)	**2**
b. Fair (same tool but different mode of administration)	**1**
c. Inadequate (different tool)	**0**
d. Not applicable (e.g., no follow-up assessment of depression)	**N/A**

37. Did the study assess and report adverse effects experienced by patients?

[THIS ITEM APPLIES TO Q4 ONLY]

a. Adequate (cardiovascular adverse events AND at least one non-cardiovascular adverse effect assessed and reported)	**2**
b. Fair (only cardiovascular events mentioned OR non-cardiovascular adverse effects mentioned, but NOT fully assessed and reported)	**1**
c. Inadequate (cardiovascular adverse events NOT mentioned)	**0**
d. Not applicable (no intervention)	**N/A**

38. What was the planned length of follow-up since initiation of treatment?

[THIS ITEM APPLIES TO Q3, Q4 AND Q6 ONLY]

a. >= 1 year	**2**
b. 6 - 11 months	**1.5**
c. 3 - 5 months	**1**
d. < 3 months	**0**
e. Not stated	**0**
f. Not applicable (no follow-up)	**N/A**

STATISTICAL ANALYSIS

39. Was the statistical test of all analyses clearly identified?

a. Adequate (identified for all analyses)	**2**
b. Fair (identified for some of the analyses)	**1**
c. Inadequate (not identified)	**0**
d. Not applicable (no statistical tests needed)	**N/A**

40. Was loss to follow-up handled appropriately in the analysis?

[THIS ITEM APPLIES TO Q2, Q3, Q4 &Q6 ONLY]

a. No loss to follow-up	**2**
b. By intention to treat (or by original group assignment)	**2**
c. Sensitivity analysis	**1**
d. None of the above	**0**
e. Not applicable (no follow-up)	**N/A**

41. For primary endpoints of the evaluation, does the study report the magnitude of difference between groups OR magnitude of the association between outcomes and patient characteristics AND an index of variability – including pre-post testing (e.g., test statistic, p value, standard error, confidence interval) **?**

[THIS ITEM APPLIES TO Q3, Q4 & Q6]

a. Adequate (BOTH reported with index of variability using standard error or confidence intervals)	**2**
b. Fair (BOTH reported with index of variability using only test statistic or p value)	**1**
c. Inadequate (one OR both not reported)	**0**
d. No comparisons (descriptive analysis only)	**0**
e. Qualitative analysis only	**N/A**
f. Not applicable (e.g., no comparison group)	**N/A**

42. Was adequate adjustment made for confounding in the analysis from which the main findings were drawn?

a. Adequate (adjusted for all potential confounding factors that differed between groups)	**2**
b. Fair (adjusted for some but not all potential confounding factors)	**1**
c. Inadequate (did not adjust for confounding factors or unclear whether potential confounding factors differed between groups)	**0**
d. Not applicable (e.g., groups did not differ in important patient characteristics)	**N/A**

43. Was the prevalence of depression reported using a 95% confidence interval?

[THIS ITEM APPLIES TO Q1 & Q2 ONLY]

a. Yes	**2**
b. No	**0**
c. Not applicable	**N/A**

CONFLICTS OF INTEREST

44. Did the study report identify the sources of funding and the type and degree of involvement of the funding agency?

a. Adequate (source AND type or degree of involvement OR no funding)	**2**
b. Fair (source only)	**1**
c. Inadequate (neither)	**0**

Question 1 and 2 Form

JOHNS HOPKINS EVIDENCE-BASED PRACTICE CENTER

POST MYOCARDIAL INFARCTION DEPRESSION

QUESTION 1 & 2 FORM

Article ID: _____	**First Author: _____**
Reviewer 1: _____	**Reviewer 2: _____**

CHARACTERISTICS OF STUDY

1. Criteria used for diagnosis of depression:

For baseline assessment (during hospitalization for MI)

standard

modified (e.g., duration or impairment)

not applicable

For follow-up/ assessment (after hospitalization for MI)

standard

modified (e.g., duration or impairment)

not applicable

2. Timing of the depression measurement (check all that apply):

during hospitalization, NOS

within first two days

3 - 13 days after MI

2 - 4 weeks after MI

1 - 5 months after MI

6 - 11 months after MI

1 - 2 years after MI

> 2 years after MI

other: specify _____

unclear

3. Minimum duration of symptoms to meet criteria:

At baseline

<2 weeks

=2 weeks

>2 weeks

not specified

At follow-up

<2 weeks

=2 weeks

>2 weeks

not specified

not applicable (no follow-up)

4. Symptoms of depression in relation to MI hospitalization:

symptoms appeared after hospitalization

symptoms appeared before hospitalization

both populations included

not specified

not applicable

5. Depression treatment given between initial hospitalization and the next period of assessment.

depression treatment given

If yes, assignment of treatment:

random

non-random

not stated

depression treatment not given

no information available

not applicable

6. Severity of depression (Check all that apply):

depression reported as continuous variable

depression reported as categorical variable

depression reported as dichotomous variable

not specified

severity not measured

RESULTS OF STUDY

7. What number and percentage of patients had depression during hospitalization?

Depression	n	%	95% CI
primary instrument_____> _____			
major depression			
minor depression			
major/minor depression			
other affective disorders			
other: _____			
other: _____			

Not applicable

8. What number and percentage of patients had depression at the first follow-up visit after the cardiac event?

Depression	n	%	95% CI
primary instrument_____> _____			
major depression			
minor depression			
major/minor depression			
other affective disorders			
other: _____			
other: _____			

Not applicable

9. When was the first follow-up visit? _____weeks or _____months

Not applicable

10. What number and percentage of patients had depression at the last follow-up visit after the cardiac event?

Depression	n	%	95% CI
primary instrument_____> _____			
major depression			
minor depression			
major/minor depression			
other affective disorders			
other: _____			
other: _____			

Not applicable

11. When was the last follow-up visit? _____weeks or _____months or _____years

Not applicable

12. Other comments about the study not already reported:

_____

_____

_____

_____

_____

_____

_____

_____

_____

Question 3 Form

JOHNS HOPKINS EVIDENCE-BASED PRACTICE CENTER
POST MYOCARDIAL INFARCTION DEPRESSION

QUESTION 3 FORM

Article ID: _____ **First Author: _____**

Reviewer 1: _____ **Reviewer 2: _____**

RESULTS OF STUDY

Outcome events
NOTE: Report number AND/OR % population. ***Include DENOMINATOR IF different from total***

Outcome	Depression n (%)	No Depression n (%)
1. Total no. in group at enrollment (N)		
2. Total no. in group available for analysis at last follow-up		
3. Mean/median follow-up mean median		

Comments:

_____

_____

_____

Outcome	Depression n (%)	No Depression n (%)	P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
				Univariate	Multivariate
4. Total Mortality at					
a. 1 month					
b. 2 months					
c. 3 months					
d. 6 months					
e. 12 months					
f. last follow-up _____ record mean/median follow-up					
5. Cardiac Mortality at					
a. 1 month					
b. 2 months					
c. 3 months					
d. 6 months					
e. 12 months					
f. last follow-up _____ record mean/median follow-up					
6. Myocardial Infarction(recurrent)					
a. 1 month					
b. 2 months					
c. 3 months					
d. 6 months					
e. 12 months					
f. last follow-up _____ record mean/median follow-up					

Outcome	Depression n (%)	No Depression n (%)	P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
				Univariate	Multivariate
7. Arrhythmias					
a. 1 month					
b. 2 months					
c. 3 months					
d. 6 months					
e. 12 months					
f. last follow-up _____ record mean/median follow-up					
8. Revascularization procedure					
a. 1 month					
b. 2 months					
c. 3 months					
d. 6 months					
e. 12 months					
f. last follow-up _____ record mean/median follow-up					

Outcome	Depression			No Depression			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
	Mean	SD	CI	Mean	SD	CI		Univariate	Multivariate
9. Utilization of healthcare services (specify) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
10. Cost of care (specify how defined) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
11. Quality of life (specify instrument) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Outcome	Depression			No Depression			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
	Mean	**SD**	**CI**	**Mean**	**SD**	**CI**		Univariate	Multivariate
12. **Depression Score** (specify instrument) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
13. **Patients with depression** (specify how defined) _____	**n (%)**			**n (%)**					
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Outcome	Depression n (%)			No Depression n (%)			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
								Univariate	Multivariate
14. **Disability** (specify how measured) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
15. **Heart rate variability** (specify how measured) _____	**Mean**	**SD**	**CI**	**Mean**	**SD**	**CI**			
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Outcome	Depression n (%)			No Depression n (%)			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
								Univariate	Multivariate
16. **Heart rate variability** (specify how measured) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
17. **Heart rate variability** (specify how measured) _____	**Mean**	**SD**	**CI**	**Mean**	**SD**	**CI**			
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Outcome	Depression n (%)			No Depression n (%)			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
								Univariate	Multivariate
18. **Heart rate variability** (specify how measured) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
19. **Platelet reactivity** (specify how defined) _____	**Mean**	**SD**	**CI**	**Mean**	**SD**	**CI**			
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Outcome	Depression			No Depression			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
	Mean	SD	CI	Mean	SD	CI		Univariate	Multivariate
20. **Platelet reactivity** (specify how defined) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
21. **C-reactive protein**									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Outcome	Depression			No Depression			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
	Mean	**SD**	**CI**	**Mean**	**SD**	**CI**		Univariate	Multivariate
22. **Other markers of inflammation** (specify) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
23. **Other markers of inflammation** (specify) _____	**n (%)**			**n (%)**					
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Outcome	Depression			No Depression			P-value	Comparison Statistic (+ 95% Confidence Interval) Relative Risk Odds Ratio Hazard Ratio	
	Mean	**SD**	**CI**	**Mean**	**SD**	**CI**		Univariate	Multivariate
24. **Other outcomes** (specify) _____									
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									
25. **Other outcomes** (specify) _____	**n (%)**			**n (%)**					
a. 1 month									
b. 2 months									
c. 3 months									
d. 6 months									
e. 12 months									
f. last follow-up _____ record mean/median follow-up									

Comments:

_____

_____

26. Which one of the following outcomes was the dependent variable in the main multivariate analyses?

None

Total mortality

Cardiac mortality

Myocardial Infarction (recurrent)

Arrhythmias

Revascularization procedure

Utilization (of health care facility)

Cost of care

Quality of life

Depression

Disability and adherence

Heart rate variability

Platelet reactivity

C-reactive protein

Other markers of inflammation (specify): _____

Other outcomes (specify): _____

27. What were the independent variables in the main multivariate analysis?
(Check one box in each row)

Factor	p <= 0.05	p > 0.05	Not Considered
Age			
Gender			
Race/Ethnicity			
Hypertension			
Diabetes Mellitus			
Serum Cholesterol			
Smoking			
Previous MI			
Left ventricular ejection fraction (LVEF)			
Killip Class			
History of depression			
Social Support			
Other cardiac factor: (specify) _____			
Other cardiac factor: (specify) _____			
Other depression measure: (specify) _____			
Other depression measure: (specify) _____			
Other: (specify) _____			
Other: (specify) _____			

28. Which one of the following outcomes was the dependent variable in the other multivariate analysis?

None

Total mortality

Cardiac mortality

Myocardial Infarction (recurrent)

Arrhythmias

Revascularization procedure

Utilization (of health care facility)

Cost of care

Quality of life

Depression

Disability and adherence

Heart rate variability

Platelet reactivity

C-reactive protein

Other markers of inflammation (specify): _____

Other outcomes (specify): _____

29. What were the independent variables in the other multivariate analysis? (Check one box in each row)

Factor	p <= 0.05	p > 0.05	Not Considered
Age			
Gender			
Race/Ethnicity			
Hypertension			
Diabetes Mellitus			
Serum Cholesterol			
Smoking			
Previous MI			
Left ventricular ejection fraction (LVEF)			
Killip Class			
History of depression			
Social Support			
Other cardiac factor: (specify) _____			
Other cardiac factor: (specify) _____			
Other depression measure: (specify) _____			
Other depression measure: (specify) _____			
Other: (specify) _____			
Other: (specify) _____			

Question 4 Form

JOHNS HOPKINS EVIDENCE-BASED PRACTICE CENTER
POST MYOCARDIAL INFARCTION DEPRESSION

QUESTION 4 FORM

Article ID: _____	**First Author:** _____
Reviewer 1: _____	**Reviewer 2:** _____

CHARACTERISTICS OF STUDY

1. For each group, provide a brief description of the intervention (less than 10 words)

Group A: _____

_____

Group B: _____

_____

Group C: _____

_____

Group D: _____

_____

2. Treatment

	Group A	Group B	Group C	Group D
Antidepressant drug				
Starting dose (mg or units/kg)				
Frequency of administration (e.g., QD, BID)				
Duration of intervention in days				
Cognitive behavioral therapy				
Interpersonal therapy				
Psychosocial therapy				
Cardiac rehabilitation				
Others_____				

3. Protocol adherence achieved

NOTE: Report mean of value OR median if only median reported

		Group A	**Group B**	**Group C**	**Group D**
Days from MI to starting antidepressant	mean median				
Target no. of psychotherapy sessions					
No. of psychotherapy sessions achieved	mean median				
No. of weeks on study drug	mean median				
Daily dose achieved in mg per day	mean median				

4. Outcome events

NOTE: Report number AND/OR % of population. ***Include DENOMINATOR IF different from total***

Outcome	**Group A** **n / %**	**Group B** **n / %**	**Group C** **n / %**	**Group D** **n / %**	**P-value**	**Comparison statistic** Risk Ratio Odds Ratio Hazard Ratio	**What groups are compared?** (If other than A vs. B)
Total no. in group at enrollment (N)							
Total no. in group available for analysis at last follow-up							
Mean/median follow-up mean median							
Total mortality at							
1 month, n (%)							
2 months, n (%)							
3 months, n (%)							
6 months, n (%)							
12 months, n (%)							
last follow-up at _____ months, n (%) (if >12 months)							
Cardiac mortality at							
1 month, n (%)							
2 months, n (%)							
3 months, n (%)							
6 months, n (%)							
12 months, n (%)							
last follow-up at _____ months, n (%) (if >12 months)							

Outcome	**Group A** **n / %**	**Group B** **n / %**	**Group C** **n / %**	**Group D** **n / %**	**P-value**	**Comparison statistic** Risk Ratio Odds Ratio Hazard Ratio	**What groups are compared?** (If other than A vs. B)
Myocardial infarction at							
1 month, n (%)							
2 months, n (%)							
3 months, n (%)							
6 months, n (%)							
12 months, n (%)							
last follow-up at _____ months, n (%) (if >12 months)							
Revascularization procedures at							
1 month, n (%)							
2 months, n (%)							
3 months, n (%)							
6 months, n (%)							
12 months, n (%)							
last follow-up at _____ months, n (%) (if >12 months)							

Outcome	Group A n / %			Group B n / %			Group C n / %			Group D n / %			P Value	Comparison statistic Risk Ratio Odds Ratio Hazard Ratio	What groups are compared? (if other than A vs. B)
	Mean	SD+	CI++	Mean	SD+	CI++	Mean	SD+	CI++	Mean	SD+	CI++			
Quality of life: Instrument_____ _____ Score at															
1 month, n (%)															
2 months, n (%)															
3 months, n (%)															
6 months, n (%)															
12 months, n (%)															
last follow-up at _____ months, n (%) (if >12 months)															
Cost of care: definition_____ mean costs at															
1 month, n (%)															
2 months, n (%)															
3 months, n (%)															
6 months, n (%)															
12 months, n (%)															
last follow-up at _____ months, n (%) (if >12 months)															

+ CI - Confidence Interval
++ SD – Standard Deviation

Outcome	Group A n / %			Group B n / %			Group C n / %			Group D n / %			P Value	Comparison statistic Risk Ratio Odds Ratio Hazard Ratio	What groups are compared? (if other than A vs. B)
	Mean	SD+	CI++	Mean	SD+	CI++	Mean	SD+	CI++	Mean	SD+	CI++			
Depression: Instrument_____ _____ Score at															
1 month, n (%)															
2 months, n (%)															
3 months, n (%)															
6 months, n (%)															
12 months, n (%)															
last follow-up at _____ months, n (%) (if >12 months)															
Other outcome: (specify) _____ at															
_____month(s), n (%)															
_____months, n (%)															
Other outcome: (specify) _____ at															
_____month(s), n (%)															
_____months, n (%)															

+ CI - Confidence Interval
++ SD – Standard Deviation

Comments:_____

_____

_____

5. Subgroup analyses

Subgroup characteristics	Main outcome(s) reported	Results in subgroups	P–value

6. Summary of main conclusions:

_____

_____

_____

_____

_____

_____

Question 5 Form

JOHNS HOPKINS EVIDENCE-BASED PRACTICE CENTER
POST MYOCARDIAL INFARCTION DEPRESSION

QUESTION 5 FORM

Article ID: _____	First Author: _____
Reviewer 1: _____	Reviewer 2: _____

1. Results of test utility (specify study test _____)

		Statistic	Confidence Interval (P)
Sensitivity			
Specificity			
Reproducibility	Intra-rater		
	Inter-rater		
Percent agreement/correlation with validated questionnaire			
Percent agreement/correlation with psychiatric interview			
Percent agreement/correlation with mental health professional			
Other :_____			
Other :_____			

2. Results of test utility (specify study test _____)

		Statistic	Confidence Interval (P)
Sensitivity			
Specificity			
Reproducibility	Intra-rater		
	Inter-rater		
Percent agreement/correlation with validated questionnaire			
Percent agreement/correlation with psychiatric interview			
Percent agreement/correlation with mental health professional			
Other :_____			
Other :_____			

3. Results of test utility (specify study test _____)

		Statistic	Confidence Interval (P)
Sensitivity			
Specificity			
Reproducibility	Intra-rater		
	Inter-rater		
Percent agreement/correlation with validated questionnaire			
Percent agreement/correlation with psychiatric interview			
Percent agreement/correlation with mental health professional			
Other :_____			
Other :_____			

4. Other comments:

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

_____

Question 6 Form

JOHNS HOPKINS EVIDENCE-BASED PRACTICE CENTER

POST MYOCARDIAL INFARCTION DEPRESSION

QUESTION 6

Article ID: _____ **First Author: _____**

Reviewer 1: _____ **Reviewer 2: _____**

RESULTS OF STUDY

1. What number and percentage of subjects received the following procedures?

Cardiac Procedure	**Group A n (%)**	**Group B n (%)**	**Group C n (%)**	**Group D n (%)**	**Comparison statistic** (+ 95% CI) Risk Ratio Odds Ratio Hazard Ratio	**P value**	**What groups are compared?** (if other than A vs. B)
Catheterization							
Revascularization (CABG or percutaneous intervention)							
Percutaneous intervention (angioplasty, stenting)							
CABG							
Thrombolytic therapy							
Other:_____							

Not applicable (N/A)

2. What number and percentage of subjects received and/or were recommended the following lifestyle interventions?

Lifestyle Interventions	**Group A n (%)**	**Group B n (%)**	**Group C n (%)**	**Group D n (%)**	**Comparison statistic** (+ 95% CI) Risk Ratio Odds Ratio Hazard Ratio	**P value**	**What groups are compared?** (if other than A vs. B)
Smoking cessation							
Physical exercise							
Weight management							
Dietary lipid management							
Other:_____							

Not applicable (N/A)

3. What number and percentage of subjects received and/or were recommended the following medications?

Medications	**Group A n (%)**	**Group B n (%)**	**Group C n (%)**	**Group D n (%)**	**Comparison statistic** (+ 95% CI) Risk Ratio Odds Ratio Hazard Ratio	**P value**	**What groups are compared?** (if other than A vs. B)
ACE inhibitors							
Beta-blockers							
Statins							
Aspirin							
Other antiplatelet therapy							
Anticoagulants							
Other:_____							

Not applicable (N/A)

4. What number and percentage of subjects received a referral for a cardiac rehabilitation program, and what number and percentage of subjects participated in a cardiac rehabilitation program?

	Group A n (%)	**Group B n (%)**	**Group C n (%)**	**Group D n (%)**	**Comparison statistic** (+ 95% CI) Risk Ratio Odds Ratio Hazard Ratio	**P value**	**What groups are compared?**
Type of Program: _____ _____							
Referral							
Participation							

Not applicable (N/A)

5. Among studies that evaluated depression as a potential barrier to cardiac treatment, what were the other factors influencing cardiac treatment for patients with acute MI?

	Statistically Significant	**Not Statistically Significant**	**Reported as Qualitatively Important**	**Reported as Qualitatively Not Important**	**Not Assessed**
Lack of referral	☐	☐	☐	☐	☐
Medical illness	☐	☐	☐	☐	☐
Other psychiatric illness	☐	☐	☐	☐	☐
Don't need treatment / exercise alone	☐	☐	☐	☐	☐
Too busy	☐	☐	☐	☐	☐
Transportation	☐	☐	☐	☐	☐
Cost of treatment	☐	☐	☐	☐	☐
Low socioeconomic status	☐	☐	☐	☐	☐
Unemployment	☐	☐	☐	☐	☐
Lack of insurance / inadequate insurance	☐	☐	☐	☐	☐
Lack of availability of tertiary medical centers	☐	☐	☐	☐	☐
Communication barrier	☐	☐	☐	☐	☐
Lack of effective aftercare	☐	☐	☐	☐	☐
Other:_____	☐	☐	☐	☐	☐
Other:_____	☐	☐	☐	☐	☐
Other:_____	☐	☐	☐	☐	☐

Not applicable (N/A)

6. Was depression found to be a significant barrier to cardiac treatment ($p < 0.05$)?

Yes

No

Not applicable (N/A)

7. Subgroup Analyses

Subgroup Characteristics	Main Outcome(s) Reported	Results in Subgroups	p-value

Comments not captured by previous questions:

_____

_____

_____

_____

_____

Appendix F. Grading the Strength of Evidence

Evidence Grade Table 1. Grading of the Quality of Evidence on the Prevalence of Depression After Myocardial Infarction (Questions 1 and 2)

	During Initial Hospitalization	One or More Months after Hospitalization
Quantity of Evidence: Number of studies	23	23
Total number of patients studied	14,017	5,216
Quality and Consistency of Evidence: Were study designs appropriate for determining prevalence? (yes = high quality; no = low quality)	No	No
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	0
Did the studies have important inconsistency? (-1)	-1	-1
Was there some (-1) or major (-2) uncertainty about the directness or extent to which the people, measures and outcomes are similar to those of interest?	0	-1
Were data imprecise or sparse? (-1)	0	0
Did the studies have high probability of reporting bias? (-1)	0	0
Did the studies show strong evidence of association between depression and myocardial infarction? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	Not Applicable	Not Applicable
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	Not Applicable	Not Applicable
What was median (and range) of estimated prevalence?	~26% Range 2- 47%	~21%* Range 2.7- 47%
Overall quality grade (high, medium, low, very low)	Medium	Medium

*NOTE – Numbers based on data at 1-3 months (N=17)
Evidence grading scheme as described in: Grade Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490-7.

Evidence Grade Table 2. Grading of the Quality of Evidence on the Independent Association of Measures of Depression with Clinical Outcomes in Patients with Acute Myocardial Infarction (Question 3)

	Survival	Cardiac Events	Quality of Life
Quantity of Evidence: Number of studies	14	6	14
Total number of patients studied	92958	116,697	3, 381
Quality and Consistency of Evidence: Were study designs appropriate for determining the association between depression and outcomes? (yes = high quality; no = low quality)	Yes	Yes	Yes
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	0	-1
Did the studies have important inconsistency? (-1)	-1	0	0
Was there some (-1) or major (-2) uncertainty about the directness or extent to which the people, measures and outcomes are similar to those of interest?	0	-1	-1
Were data imprecise or sparse? (-1)	0	0	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0
Did the studies show strong evidence of association between depression and outcomes? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	+1	0	0
Did the studies have evidence of a dose-response gradient? (+1)	+1	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0

Evidence Grade Table 2. Grading of the Quality of Evidence on the Independent Association of Measures of Depression with Clinical Outcomes in Patients with Acute Myocardial Infarction (Question 3) (Continued)

	Survival	Cardiac Events	Quality of Life
What was median (and range) of estimated association?	Not Applicable	Not Applicable	Not Applicable
Overall quality grade (high, medium, low, very low)	High	Medium	Very low
Importance of outcome (critical, important, or not important)	Critical	Important	Important

Evidence grading scheme as described in: Grade Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490-7.

Evidence Grade Table 3. Grading of the Quality of Evidence on the Independent Association of Measures of Depression with Surrogate Measures of Disease Severity in Patients with Acute Myocardial Infarction (Question 3a)

	Heart Rate Variability	Beta-Thromboglobulin	Platelet Factor 4	Soluble Intercellular Adhesion Molecule-1	Interleukin-6	C - Reactive Protein
Quantity of Evidence: Number of studies	1	1	1	1	1	1
Total number of patients studied	804	24	24	481	481	481
Quality and Consistency of Evidence: Were study designs appropriate for determining the association between depression and the surrogate measures? (yes = high quality; no = low quality)	Yes	Yes	Yes	Yes	Yes	Yes
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	-1	-1	-1	-1	-1
Did the studies have important inconsistency? (-1)	0	0	0	0	0	0
Was there some (-1) or major (-2) uncertainty about the directness or extent to which the people, measures and outcomes are similar to those of interest?	0	0	0	0	0	0
Were data imprecise or sparse? (-1)	0	-1	-1	0	0	0
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	0	0

Evidence Grade Table 3. Grading of the Quality of Evidence on the Independent Association of Measures of Depression with Surrogate Measures of Disease Severity in Patients with Acute Myocardial Infarction (Question 3a) (Continued)

	Heart Rate Variability	Beta-Thromboglobulin	Platelet Factor 4	Soluble Intercellular Adhesion Molecule-1	Interleukin-6	C - Reactive Protein
Did the studies show strong evidence of association between depression and the surrogate measures? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	0	0	0	0	0	0
Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0	0	0
What was median (and range) of estimated association?	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable	Not Applicable
Overall quality grade (high, medium, low, very low)	High	Low	Low	High	High	High
Importance of outcome (critical, important, or not important)	Important	Important	Important	Important	Important	Important

Evidence Grade Table 3. Grading of the Quality of Evidence on the Independent Association of Measures of Depression with Surrogate Measures of Disease Severity in Patients with Acute Myocardial Infarction (Question 3a) (Continued)

Evidence grading scheme as described in: Grade Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490-7.

Evidence Grade Table 4. Grading of the Quality of Evidence on the Efficacy of Depression Treatment for Myocardial Infarction Patients with Depression (Question 4)

	Medications	**Psychosocial Interventions**
Quantity of Evidence: Number of studies	5	7
Total number of patients studied	Active group: 490 Control group: 408	Active group: 2356 Control group: 2361
Quality and Consistency of Evidence: Were study designs randomized trials (high quality), non-randomized controlled trials (medium quality), or observational studies (low quality)?	5 randomized controlled trials	6 randomized controlled trials, 1 prospective cohort
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	-1
Did the studies have important inconsistency? (-1)	No	No
Was there some (-1) or major (-2) uncertainty about the directness or extent to which the people, interventions and outcomes are similar to those of interest?	No	No
Were data imprecise or sparse? (-1)	-1	-1
Did the studies have high probability of reporting bias? (-1)	No	No
Did the studies show strong evidence of association between treatment and outcomes? (“strong” if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); “very strong” if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	No	No
Did the studies have evidence of a dose-response gradient? (+1)	No	No
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	No	No

Evidence Grade Table 4. Grading of the Quality of Evidence on the Efficacy of Depression Treatment for Myocardial Infarction Patients with Depression (Question 4) (Continued)

	Medications	**Psychosocial Interventions**
What was median (and range) of estimated treatment effect?	Depression: unable to assess due to the different methods of assessing depression used, the different follow-up times and the different antidepressants evaluated. Total mortality: unable to assess, as only one study reported results for total mortality (Relative Risk for death was 0.39 with 95% confidence intervals between 0.08 and 1.39 comparing sertraline to placebo).	Depression: difficult to assess due to the different methods of assessing depression used and the different follow-up times. Total Mortality (range) (follow-up from 12-18 months) Intervention group:4-13.6% Control group: 3-13.8%
Overall quality grade (high, medium, low, very low)	Medium	Low
Importance of outcome (critical, important, or not important)	Important	Important

Evidence grading scheme as described in: Grade Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490-7.

Evidence Grade Table 5. Grading of the Quality of Evidence on the Performance Characteristics of Methods Used to Screen for Depression After Myocardial Infarction (Question 5)

	BDI	HADS	SCL-90 Dep.	Zung	HAM-D
Quantity of Evidence: Number of studies	3	3	2	1	2
Total number of patients studied	2,739	735	349	143	2,687
Quality and Consistency of Evidence: Were study designs appropriate for determining the performance characteristics of the screening methods? (yes = high quality; no = low quality)	Yes	Yes	Yes	No	Yes
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	-1	0	-1	-2	-1
Did the studies have important inconsistency? (-1)	0	0	0	0	0
Was there some (-1) or major (-2) uncertainty about the directness or extent to which the people, measures and outcomes are similar to those of interest?	0	0	0	0	0
Were data imprecise or sparse? (-1)	-1	0	-1	-1	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the estimated validity and reliability? (+1)	+1	0	0	0	+1

Evidence Grade Table 5. Grading of the Quality of Evidence on the Performance Characteristics of Methods Used to Screen for Depression After Myocardial Infarction (Question 5) (Continued)

	BDI	HADS	SCL-90 Dep.	Zung	HAM-D
What was median (and range) of estimated sensitivity, specificity and reliability?	Sensitivity: MDD* .82 (1 study) Specificity: MDD .79 (1 study) Reliability: No data	Sensitivity: MDD .90 (1 study) Specificity: MDD .84 (1 study) Reliability: .88 (.82, .90)	Sensitivity: MDD .96 (1 study) Specificity: MDD .74 (1 study) Reliability: No Data	Sensitivity: No data Specificity: No data Reliability: No data	Sensitivity: MDD .86 (1 study) Specificity: MDD .92 (1 study) Reliability: No Data
Overall quality grade (high, medium, low, very low)	Low	Medium	Low	Very Low	Low

* Major depressive disorder

Evidence grading scheme as described in: Grade Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490-7.

Evidence Grade Table 6. Grading of the Quality of Evidence on Whether Use of Recommended Treatment for Patients with Acute Myocardial Infarction Differs For Those With and Without Depression (Question 6)

	Cardiac Procedures	Lifestyle Interventions	Medications	Cardiac Rehabilitation
Quantity of Evidence: Number of studies	3	1	4	2
Total number of patients studied	109359	108	1244	128
Quality and Consistency of Evidence: Were study designs appropriate for determining the association between depression and use of treatment? (yes = high quality; no = low quality)	Yes	Yes	Yes	Yes
Did the studies have serious (-1) or very serious (-2) limitations in quality? (Enter 0 if none)	0	0	0	0
Did the studies have important inconsistency? (-1)	-1	0	-1	0
Was there some (-1) or major (-2) uncertainty about the directness or extent to which the people, measures and outcomes are similar to those of interest?	-1	-1	-1	-1
Were data imprecise or sparse? (-1)	0	-1	0	-1
Did the studies have high probability of reporting bias? (-1)	0	0	0	0
Did the studies show strong evidence of association between depression and use of treatment? ("strong" if significant relative risk or odds ratio > 2 based on consistent evidence from 2 or more studies with no plausible confounders (+1); "very strong" if significant relative risk or odds ratio > 5 based on direct evidence with no major threats to validity (+2))	0	0	0	0

Evidence Grade Table 6. Grading of the Quality of Evidence on Whether Use of Recommended Treatment for Patients with Acute Myocardial Infarction Differs For Those With and Without Depression (Question 6) (Continued)

	Cardiac Procedures	Lifestyle Interventions	Medications	Cardiac Rehabilitation
Did the studies have evidence of a dose-response gradient? (+1)	0	0	0	0
Did the studies have unmeasured plausible confounders that most likely reduced the magnitude of the observed association? (+1)	0	0	0	0
What was median (and range) of estimated association?	Not Applicable	Not Applicable	Not Applicable	Not Applicable
Overall quality grade (high, medium, low, very low)	Low	Very low	Low	Low

Evidence grading scheme as described in: Grade Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004; 328: 1490-7.

Evidence Table 1.1. Characteristics of Studies on Prevalence of Depression During Hospitalization For Acute Myocardial Infarction (Question 1)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Taylor, 1986	RCT [a]	Only MI [b] patients	A[c] > 70; F[d]; medically unable to undergo treadmill exercise testing 3 wk[e] post-MI	Multicenter, 2	USA	NR [f]	To document the psychosocial status of uncomplicated MI patients eligible for a 3 week treadmill exercise test, to determine the impact of home exercise training on psychosocial status compared to a group training program or no exercise training, and to determine the relationship among psychosocial factors and medical outcome in these patients.
Bennett, 1988	Pro cohort [g]	Only MI patients	A > 75; anticipating cardiac surgery; previous MI; presence of other major physical conditions	Single center	Europe	NR	To investigate the magnitude of changes in coronary risk behavior and mood 3 months following first MI.
Davis, 1988	Pro cohort	Only MI patients	A > 65; psychiatric Rx [h]	Single center	Canada	NR	To identify optimal methods of detecting depression in medically ill subjects.
Carney, 1990	Case control	Only MI patients	A ≥ 70; serious co-morbid conditions; unable to complete interview and psychological testing; previous MI; h/o[i] angioplasty/CABG[j] surgery; CHF[k]; valvular heart disease; "severe" DM[l]; chronic medical illness; severe mental impairment	Single center	USA	NR	To determine whether a major degressive disorder in hospital predicts insomnia two weeks prior to MI.
Silverstone, 1990	Pro cohort	Only MI patients	NR	NR	Europe	NR	To investigate the time course of depressive symptoms following severe medical illness and to assess the importance of somatic symptoms in particular.

Evidence Table 1.1. Characteristics of Studies on Prevalence of Depression During Hospitalization For Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Gilutz, 1991	Pro cohort	Only MI patients	A < 34 or > 70; previous MI; DM; HTN [m]; any other chronic disease	Multicenter, 2	Europe; Middle East	Europe: 1979 - 1980; Middle East: 1983 - 1986	To evaluate causal attribution patterns and whether these can predict patient rehabilitation outcome.
Schleifer, 1991	Pro cohort	Only MI patients	Terminal noncardiac conditions; cognitively impaired; too ill to participate; non-English speaking; undergoing CABG; died prior to day 8 post-MI	Multicenter, 2	USA	Aug 1983 - May 1985	To evaluate the contribution of cardioactive medication on depression at follow-up controlling for baseline depression.
Forrester, 1992	Cross-sectional	Only MI patients	A ≥ 80; too ill to be interviewed; delirium/dementia; h/o coarse brain injury; scheduled for CABG; angioplasty; residence outside of metro Baltimore	Multicenter, 3	USA	NR	1. To find prevalence of depression among post-MI patients. 2. To investigate predisposing factors (eg cardiac history, acute medical factors, cognitive + social factors) of depression.
Legault, 1992	Pro cohort	Only MI patients	A < 18 or > 70; language/literacy problems; medical status precluding psychiatric assessment; previous admission to CCU [n]	Single center	Canada	Dec 1986 - Jan 1988	To assess prevalence of psychiatric morbidity during hospitalization and follow up. To evaluate associations between psychiatric morbidity with cardiac diagnosis and morbidity.
Kaufmann, 1999	Pro cohort	Only MI patients	Another medical condition likely to influence 1-yr [o] survival; insufficient English; cognitive problems interfering with interview; clinically unable to complete interview	Single center	USA	Jan 1995 - Dec 1995	To examine the independent impact of major depression and hostility on mortality rate a 6 and 12 months after discharge from hospital in patients with a myocardial infarction.

Evidence Table 1.1. Characteristics of Studies on Prevalence of Depression During Hospitalization For Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
O'Rourke, 1999	Pro cohort	Only MI patients	A ≥ 76; non-English speaking; recurrent MI; emergency angioplasty; emergency cardiac bypass	Multicenter, 2	Europe	NR	To examine predictive power of psychosocial variables (self-efficacy beliefs, locus of control, illness perception, social support, anxiety, depression) on health service utilization 6 months following MI.
Mayou, 2000	Pro cohort	Only MI patients	A ≥ 80; no other criteria specified; event occurred within 28 d [p] of preceding event	Multicenter	Europe	Nov 1994 - Nov 1995	To investigate the significance of emotional distress immediately after a myocardial infarction as a predictor of physical, psychological, and social outcome and resource use.
Brink, 2002	Pro cohort	Only MI patients	Serious co-morbid conditions; dementia; non-Swedish; recurrent MI	Single center	Europe	Oct 1998 - Sep 1999	To explore health related quality of life in first time myocardial infarction patients, five months after the heart attack.
Lane, 2002	Pro cohort	Only MI patients	MI resulted from CABG/angioplasty; co-morbidity likely to cause death within 12 mos; non-English speaking; cognitively impaired; medically unable to complete assessment within 15 d post-MI	Multicenter, 2	Europe	Jun 1997 - Aug 1998	To examine the relationship between symptoms of depression following MI & 3 year survival status.
Lesperance, 2002	Pro cohort	Only MI patients	Other life-threatening conditions; non-French/non-English speaking; cognitively impaired/physically unstable to complete interview; lived too far from hospital for f/u [q]	Multicenter	Canada	Jan 1991 - Nov 1994	To evaluate a dose relationship between depression symptoms and long term cardiac mortality, confirm that any impact of depression symptoms remain significant after control for measures of cardiac disease severity, compare the impact of depression measurement during hospitalization and a 1 year and evaluate the prognostic importance of changes in depressive symptoms over the first post MI year.

Evidence Table 1.1. Characteristics of Studies on Prevalence of Depression During Hospitalization For Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Luutonen, 2002	Pro cohort	Only MI patients	A > 75	Multicenter, 2	Europe	Mar 1998 - Aug 1998	To investigate the prevalence of depressive symptoms and the self reported psychiatric treatment after MI.
Watkins, 2002	Cross-sectional	Only MI patients	Not in sinus rhythm; cross spectral analysis of SBP[r] power and RR [s] interval; showed no patients of coherence of 0.5 or greater; unable to complete interview due to severe physical disability or altered mental status	Single center	USA	NR	To evaluate whether depression is associated with impaired baro reflex sensitivity in patients with AMI [t].
Barefoot, 2003	Pro cohort	Only MI patients	Index ACS [u] developed after CABG/PTCA [v]; cognitively impaired; likely to die in 1 yr; limited physical capacity; participation in conflicting research protocol	Multicenter, 8	USA	Jun 1996 - Aug 1996	To assess the relations between social support and depression in post MI patients at the time of hospitalization and 2 weeks afterwards.
Berkman, 2003	RCT	Only MI patients	Index ACS after surgery; h/o of active substance abuse; h/o psychosis; h/o suicide risk; severe dementia; non cardiac condition likely to be fatal within 1y; too ill/ refused to participate; participating in other research protocol; inaccessible for intervention/f/u; receiving psychotherapy; before Apr 1998 patients on antidepressant after Apr 1998 patients on antidepressant but who remained depressed were included	Multicenter, 8	USA,	Oct 1996 - Oct 1999	To determine whether mortality and recurrent infarction are reduced by treatment of depression and LPSS [w] with cognitive behavior therapy supplemented with an SSRI [x] when indicated in patients enrolled with 28 days after MI.
Lauzon, 2003	Pro cohort	Only MI patients	Non-English/non-French speaking; physically incapable of responding to a questionaire; unable to give informed consent	Multicenter, 10	Canada	Dec 1996 - Nov 1998	To measure the prevalence and prognostic impact of depressive symptoms after acute myocardial infarction.

Evidence Table 1.1. Characteristics of Studies on Prevalence of Depression During Hospitalization For Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Martin, 2003	Pro cohort	Only MI patients	Medically unsuitable for cardiac rehab [y]; died before/shortly after starting rehab program; refused cardiac rehab	Multicenter, 3	Europe	NR	To determine the factor structure of the HADS [z] in a clinical population following MI and to establish change-sensitivity characteristics and psychometric reliability of the HADS in this patient group.
Rafanelli, 2003	Pro cohort	Only MI patients	Not referred to cardiac rehab program	Single center	Europe	NR	To study the prevalence of psychological distress in the setting of cardiac rehabilitation.
Steeds, 2004	Pro cohort	Only MI patients	A > 75; incapable of providing informed written consent; other ACS except MI	Single center	Europe	1999 - 2000	To determine the prevalence of an elevated BDI [aa] and to determine the relation between BDI score and prognosis in UK [ab] population following MI.

[a] Randomized controlled trial
[b] Myocardial infarction
[c] Age
[d] Female
[e] Week
[f] Not reported
[g] Prospective cohort study
[h] Treatment
[i] History of
[j] Coronary artery bypass graft
[k] Congestive heart failure
[l] Diabetes mellitus
[m] Hypertension
[n] Coronary care unit
[o] Year
[p] Day
[q] Follow-up

Evidence Table 1.1. Characteristics of Studies on Prevalence of Depression During Hospitalization For Acute Myocardial Infarction (Question 1) (continued)

[r] Systolic blood pressure
[s] Respiratory rate
[t] Acute myocardial infarction
[u] Acute coronary syndrome
[v] Percutaneous transluminal coronary angioplasty
[w] Low perceived social support
[x] Selective serotonin reuptake inhibitor
[y] Rehabilitation
[z] Hospital Anxiety and Depression Scale
[aa] Beck Depression Inventory
[ab] United Kingdom

Evidence Table 1.2. Characteristics of Patients in the Studies on Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction
Taylor, 1986	173	52	100	NR	86	NR [d]	NR	NR	NR	NR	NR
Bennett, 1998	37	62	73	NR	NR	NR	NR	NR	NR	NR	NR
Davis, 1988	52	51	90	NR	48	NR	NR	NR	NR	NR	NR
Carney, 1990	70	53	76	NR	NR	43	16	48	NR	NR	NR
Silverstone, 1990	100	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gilutz; 1991	Europe: 98; Middle East: 87	NR [e]	NR	NR	Europe: 85; Middle East: 96	NR	NR	Europe: 32; Middle East: 35	NR	NR	NR
Schleifer, 1991	335	63	64	NR	NR	NR	NR	NR	NR	NR	42
Forrester, 1992	129	59	74	62	55	NR	NR	NR	NR	NR	40
Legault, 1992	52	55	78	NR	NR	NR	NR	NR	NR	NR	NR
Kaufmann, 1999	331	NR [f]	66	NR	70	49	27	28	38	Class I: 44; Class II: 48; Class III: 8; Class IV: 1	45
O'Rourke, 1999	70	58	74	NR	73	NR	NR	NR	NR	NR	NR

Evidence Table 1.2. Characteristics of Patients in the Studies on Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction
Mayou, 2000	344	63	73	NR	NR	NR	34	58	NR	NR	46
Brink, 2002	114	68	68	NR	72	35	15	31	NR	NR	NR
Lane, 2002	288	63	75	93	70	39	13	43	72	Class II - IV: 51	NR
Lesperance, 2002	896	59	68	NR	72	35	16	47	NR	Class II - IV: 31	EF [g] 35%: 19%
Luutonen, 2002	85	61	77	NR	NR	NR	NR	NR	NR	NR	NR
Watkins, 2002	204	59	58	65	NR	NR	NonDep [h] 31, Dep [i] 49	NonDep 53, Dep 81	NR	NR	NonDep 46, Dep 48
Barefoot, 2003	196	61	63	67	NR	NR	NR	NR	NR	NR	NR
Berkman, 2003,	9279 [j]	63	62	26	52	60	33	64	57	Class III - IV: 7	NR
Lauzon, 2003	550	60	80	96	70	35	16	40	38	Class II - IV: 18	NR
Martin, 2003	335	67	67	NR	NR	NR	NR	NR	NR	NR	NR
Rafanelli, 2003	61	61	85	NR	NR	NR	NR	NR	NR	NR	NR
Steeds, 2004	131	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

[a] Hypertension
[b] Diabetes
[c] Hyperlipidemia

Evidence Table 1.2. Characteristics of Patients in the Studies on Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1) (continued)

[d] Not reported
[e] In the European population 21% were less than 45 years old, 54% were 46 - 55 years old and 25% were 56 - 60 years old. In the Middle Eastern population 30% were less than 45 years old, 46% were 46 - 55 years old and 24% were 56 - 60 years old
[f] 45% were less than 65 years old and 56% were greater than 65 years old
[g] Ejection Fraction
[h] Non depressed
[i] Depressed
[j] Medically eligible and screened for depression

Evidence Table 1.3. Assessment of Study Quality in Studies on the Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1)

Study Author, Year	Representativeness	Description Therapy & Management	Description Assessment Protocol	Outcomes & Follow-Up	Statistical Analyses	Conflicts
Taylor, 1986	50%	0%	100%	100%	50%	50%
Bennett, 1988	10%	0%	100%	50%	0%	0%
Davis, 1988	30%	0%	100%	67%	42%	0%
Carney, 1990	45%	0%	88%	N/A	33%	75%
Silverstone, 1990	10%	0%	100%	75%	33%	0%
Gilutz, 1991	45%	0%	75%	N/A	0%	0%
Schleifer, 1991	80%	0%	100%	67%	29%	50%
Forrester, 1992	70%	0%	88%	N/A	33%	50%
Legault, 1992	80%	0%	100%	50%	75%	75%
Kaufmann, 1999	90%	0%	100%	75%	38%	0%
O'Rourke, 1999	50%	0%	100%	50%	19%	0%
Mayou, 2000	65%	0%	100%	67%	19%	75%
Brink, 2002	65%	0%	100%	63%	50%	50%
Lane, 2002	50%	N/A	100%	0%	50%	0%
Lesperance, 2002	85%	0%	100%	79%	50%	100%
Luutonen, 2002	80%	N/A	N/A	83%	50%	0%
Watkins, 2002	30%	0%	50%	N/A	42%	75%

Evidence Table 1.3. Assessment of Study Quality in Studies on the Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1) (continued)

Study Author, Year	Representativeness	Description Therapy & Management	Description Assessment Protocol	Outcomes & Follow-Up	Statistical Analyses	Conflicts
Barefoot, 2003	45%	0%	100%	50%	25%	100%
Berkman, 2003	90%	0%	100%	92%	94%	100%
Lauzon, 2003	65%	0%	100%	71%	25%	50%
Martin, 2003	60%	0%	100%	50%	33%	0%
Rafanelli, 2003	50%	0%	100%	0%	50%	50%
Steeds, 2004	30%	0%	100%	50%	50%	0%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 6 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), and whether the same tools for diagnosing depression were used for baseline and follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether adjustment was made for confounding (2 points), and whether confidence intervals were reported (2 patients).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency

Evidence Table 1.4. Results of Prevalence of Depression During Hospitalization for Acute Myocardial Infarction (Question 1)

Study Author, Year	Diagnosis of MI [a]	Diagnosis of Depression	Depression Assessment Method [b]	Criteria	Prevalence (%)	Depression Severity Measure [c]	Comments
Taylor, 1986	NR [d]	Modified baseline assessment	HAMD [e]	HAMD ≥ 10	3 wk [f] post-MI 13	Dichotomous variable	NA [g]
Bennett, 1988	NR	Standard baseline assessment	HADS [h]	HADS ≥ 11	In hospital [i] 13	Dichotomous variable	NA
Davis, 1988	NR	Standard baseline assessment	BDI [j]	BDI ≥ 13	In hospital 10	Dichotomous variable	NA
Carney, 1990	Chest pain compatible with ischemia, ECG [k], Creatine kinase (MB [l] fraction)	Modified baseline assessment	DIS [m]	DSM-III [n] criteria for Major Depressive Episode	In hospital 23	Dichotomous variable	DIS was administered by two trained lay interviewers. Two senior clinicans independently reviewed interview results using DSM-III-R criteria with 100% agreement between both clinicians.
Silverstone, 1990	NR	Standard baseline assessment	Montgomery-Asberg	M-A [o] ≥ 21	In hospital 19	Dichotomous variable	Study included for acute medical illnesses. Data during hospitalization reported separately for MI.
Gilutz, 1991	NR	Standard baseline assessment	Holland Sgroi Anxiety Depression Scale	Mild, Moderate/ Severe Depression	In hospital 31, 10-15 d [p] post-MI 35	Categorical variable	Specific cutoffs not provided for depression and no data on depression measure reported.
Schleifer, 1991	Compatible history, cardiac enzyme elevation, Q waves, or 24 hrs [q] ST-T wave abnormalities	Modified baseline assessment	Nurse Interview	RDC [r] criteria for major, minor depression	8-10 d [i] Maj dep 17; Min dep 30	Categorical variable	Major depression was assessed as (lowered mood AND 4 symptoms) ≥1 week. Minor depression was assessed as (lowered mood AND 2 symptoms) ≥1 week.No mention of DSM criteria.

Evidence Table 1.4. Results of Prevalence of Depression During Hospitalization for Acute Myocardial Imfarction (Question 1) (continued)

Study Author, Year	Diagnosis of MI [a]	Diagnosis of Depression	Depression Assessment Method [b]	Criteria	Prevalence (%)	Depression Severity Measure [c]	Comments
Forrester, 1992	Creatine kinase	Modified baseline assessment:	PSE [s]	DSM - III criterion for Major Depression	In hospital: within 10 d post-MI 19	Dichotomous variable	NA
Legault, 1992	"Conventional clinical criteria" confirmed by ECG and elevation of MB-Ck [t]	Standard baseline assessment	BDI	BDI ≥ 16	In hospital [f] 18	Dichotomous variable	Authors reported demographics for MI unstable angina, and non cardiac chest pain. Data reported seperately for MI.
Kaufmann, 1999	In hospital assessment: chest pain, ECG, Ck	Standard baseline assessment	DIS	DIS score ≥ 5	In hospital: 3-15 d post-MI 27	Dichotomous variable	NA
O'Rourke, 1999	WHO [d] criteria	Standard baseline assessment	HADS	HADS ≥ 8	3 - 5 d post-MI 17	Dichotomous variable	NA
Mayou, 2000	In hospital assessment: ECG, other cardiac enzymes	Standard baseline assessment	HADS	HADS ≥ 8, HADS ≥ 11	In hospital 18, within 3 d post-MI 8	Categorical variable	NA
Brink, 2002	NR	Standard baseline assessment	HADS	HADS ≥ 8, HADS ≥ 11	In hospital 11, within 1 wk post-MI 8	Categorical variable	NA
Lane, 2002	In hospital assessment: chest pain, ECG, Ck	Standardbaseline assessment	BDI	BDI ≥ 10	In hospital: within 15 d post-MI [i] 31	Dichotomous variable	NA
Lesperance, 2002	Symptom enzyme and ECG criteria	Standard baseline assessment	BDI	BDI ≥ 10	In hospital [f] 32	Dichotomous variable	NA
Luutonen, 2002	In hospital assessment: chest pain, ECG, Ck	Standard baseline assessment	BDI	BDI ≥ 10	In hospital [f] 21	Dichotomous variable	NA

Evidence Table 1.4. Results of Prevalence of Depression During Hospitalization for Acute Myocardial Imfarction (Question 1) (continued)

Study Author, Year	Diagnosis of MI [a]	Diagnosis of Depression	Depression Assessment Method [b]	Criteria	Prevalence (%)	Depression Severity Measure [c]	Comments
Watkins, 2002	In hospital assessment: cardiac enzymes, ECG	Modified baseline assessment,	DIS	DSM - IV criteria for Major Depression	In hospital: 3 - 9 d post-MI 18	Dichotomous variable	NA
Barefoot, 2003	Characteristic enzymes, MI compatible symptoms	Standard baseline assessment	HAMD, BDI	"Signs of Depression", BDI ≥ 10	Within 2 wk post-MI [i] 28, 37	Categorical, dichotomous variable	NA
Berkman, 2003	Characteristic enzymes, MI compatible symptoms	Modified baseline assessment	Structured Interview for DSM-IV	DSM - IV criteria for Major Depression	2-4 wk post-MI 27	Dichotomous variable	The study is an RCT [v] with treatment given for 6 or more months - CBT [w] ± sertraline.
Lauzon, 2003	In hospital assessment: ECG	Standard baseline assessment	BDI	BDI ≥ 10	Within 2 - 3 d of hospitalization [i] 35	Dichotomous variable	NA
Martin, 2003	In hospital assessment: ECG, Troponin, ST wave elevation, patient history	Standard baseline assessment	HADS	HADS ≥ 8, HADS ≥ 11	In hospital 15, within 1 wk post-MI [i] 6	Categorical variable	NA
Rafanelli, 2003	In hospital assessment: chest pain, shortness of breath, ECG, Ck	Modified baseline assessment	SCID [x]	DSM-IV criterion for Major, Minor Depression	Within 1 mo [y] post-MI 2, 10	Dichotomous variable	NA
Steeds, 2004	NR	Standard baseline assessment	BDI-II	BDI-II ≥ 12	In hospital 47	Dichotomous variable	NA

[a] Myocardial infarction
[b] Method of assessing of depression used for analysis
[c] How severity of depression was measured
[d] Not reported
[e] Hamilton Rating Scale for Depression
[f] Week
[g] Not applicable
[h] Hospital Anxiety and Depression Scale

Evidence Table 1.4. Results of Prevalence of Depression During Hospitalization for Acute Myocardial Imfarction (Question 1) (continued)

[i] Also assessed at later point. See Table 2
[j] Beck Depression Inventory
[k] Electrocardiogram
[l] Muscle brain
[m] Diagnostic Interview Schedule
[n] Diagnostic & Statistical Manual of Mental Disorders
[o] Montgomery-Asberg
[p] Day
[q] Hours
[r] Research Diagnostic Criteria
[s] Psychological Stress Evaluator
[t] Creatine kinase
[u] World Health Organization
[v] Randomized controlled trial
[w] Cognitive behavioral therapy
[x] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders - IV
[y] Month

Evidence Table 2.1. Characteristics of Studies on Prevalence of Depression After Hospitalization For Acute Myocardial Infarction (Question 2)

Study Author, Year	Study Design	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Trelawny, 1987	Sample of suspected MI [a] patients 28 of 32 confirmed	A [b] > 65; F [c]; unmarried	NR [d]	Europe	NR	To describe responses of patients following admission for possible MI and study relationships of 4 aspects of outcome- work, exercise, leisure, and sexual activity.
Davis, 1988	Retro cohort [e]	A > 65; receiving psychiatric Rx [f]	NR	Canada	NR	To identify optimal methods of detecting depression in medically ill subjects.
Follick, 1988	RCT [g] of transtelephonic system	A > 70	Multicenter, 2	USA	NR	To examine the effects of an outpatient risk-management system on psychological, work and social functional status among post-MI patients.
Schleifer, 1991	Retro cohort	Terminal noncardiac illness; undergoing CABG [h]; died prior to day 8 post-MI; discharged; transferred to another facility; too ill to participate in interview; cognitively impaired; non-English speaking	Multicenter, 2	USA	Aug 1983 - May 1985	To evaluate the contribution of cardio active medications to depression in patients recovering from an MI.
Legault, 1992	Pro cohort	A < 18 or > 70; literacy problems; medical status precluding psychiatric assessment	Single center	Canada	Dec 1986 - Jan 1988	To assess prevalence of psychiatric morbidity during hospitalization and follow up. To evaluate association between psychiatric morbidity with cardiac diagnosis and morbidity.
Garcia, 1994	Cross-sectional	A > 65; F; illiteracy; concomitant diseases; previous MI	Single center	Europe	NR	To determine influence of coping strategies, personality variables and emotional states in early phase of MI and later psychopathology displayed by patients.

Evidence Table 2.1. Characteristics of Studies on Prevalence of Depression After Hospitalization For Acute Myocardial Infarction (Question 2) (continued)

Study Author, Year	Study Design	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Travella, 1994	Pro cohort	Anticipating cardiac surgery; serious comorbidity; cognitively impaired; treated depression; brain injury	Multicenter, 3	USA	NR	To examine the course and clinical correlates of depression during the first year after MI.
Clarke, 1996	Pro cohort	A > 70; F; CABG pending; previous MI; unmarried/not living in stable relationship	Multicenter, 4	Canada	NR	To test the hypothesis that over-protectiveness of patients after MI by the spouse has a negative effect on recovery.
Lesperance, 1996	Pro cohort	MI after surgery; non-English/non-French speaking; comorbidity likely to influence survival; not medically stable	Single center	Canada	Aug 1991 - July 1992	To study how common major depression is prior to MI; are there medical and psychological correlates to history of major depression and does this influence a patient's medical and psychological evolution during the year after MI.
Bennett, 1998	Pro cohort	A > 75; anticipating cardiac surgery; non-atherosclerotic MI; previous MI; other physical conditions	Single center	Europe	NR	To investigate the magnitude of changes in coronary risk behavior and mood 3 months following first MI.
Lehto, 2000	Retro cohort	A > 70; DEPS[†] score not available; outside catchment area	Single center	Europe	NR	To study the prevalence of depression at least 6 months after various coronary heart disease events and the associations between depression and clinical variables.
Strik, 2001	Pro cohort	Recurrent MI; unable to fill out questionnaires	NR	Europe	May 1997 - Sep 1999	To assess sensitivity and specificity of 3 self-report questionnaires and one observer rating scale as screening instruments for depression following first MI.

Evidence Table 2.1. Characteristics of Studies on Prevalence of Depression After Hospitalization For Acute Myocardial Infarction (Question 2) (continued)

Study Author, Year	Study Design	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Lane, 2002	Pro cohort	Serious comorbidity; cognitively impaired; non-English speaking; MI from CABG/angiography; medically unstable within 15 d [j] post-MI; other conditions that would lead to death within 12 mo[k]	Multicenter, 2	Europe	Jan 1997 - Aug 1998	To assess prevalence of depression and anxiety in post-MI patients during hospitalization and follow-up and to assess association of post-MI depression and anxiety with mortality and quality of life at 12 month follow-up.
Luutonen, 2002	Pro cohort	NR	NR	Europe	Mar 1998 - Aug 1998	To investigate the prevalence of depressive symptoms and self-reported psychiatric treatment after MI.
Shiotani, 2002	Pro cohort	Died in hospital; unable to verbally communicate; major psychiatric disease; refused registry	Multicenter, 25	Asia	Apr 1998 - Apr 2000	To investigate the impact of the depressive symptoms on prognosis of elderly patients with acute MI.
Strik, 2002	Retro cohort	Data not available for serum lipid at 1 mo; AMI [l] diagnosis not explicit	NR	Europe	May 1997 - Sep 1999	To study relation of levels of serum lipoproteins to depression after acute MI.
Aben, 2003	Pro cohort	Psychotic symptoms; cognitive impairment; depressive episode week before MI; major psychiatric disorder; intracerebral disease	Single center	Europe	NR	To compare the cumulative 1 year incidence of depression after stroke and after MI taking into consideration differences in age, sex, and the level of handicap.
Barefoot, 2003	NR	Index ACS[m] after surgery/PTCA[n]; cognitively impaired; h/o post-procedure MI; likely to die in 1 yr[o]; limited physical capacity; participating in conflicting research protocol	Multicenter, 8	USA,	Jun 1996 - Aug 1996	To assess the relations between social support and depression in post MI patients at the time of hospitalization and 2 weeks afterwards.

Evidence Table 2.1. Characteristics of Studies on Prevalence of Depression After Hospitalization For Acute Myocardial Infarction (Question 2) (continued)

Study Author, Year	Study Design	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Lauzon, 2003	Pro cohort	Transfer from other hospital; incapable of responding to questionnaire; unable to give consent	NR	Canada	Dec 1996 - Nov 1998	To measure the prevalence and prognostic impact of depressive symptoms after acute MI.
Martin, 2003	Cross-sectional	Medically unsuitable for cardiac rehab; died before/shortly after starting program	Multicenter, 3	Europe	NR	To determine the factor structure of the HADS [p] in a population following MI and to establish change-sensitivity characteristics and psychometric reliability of the HADS in this patient group.
Strik, 2003	Pro cohort	F; h/o [q] psychosis; cognitively impaired; non-Dutch speaking; comorbid life-threatening condition; h/o MI	Single center	Europe,	May 1994 - Sep 1999	To examine whether depression is a better predictor of incomplete recovery after MI than anxiety, and to examine the effect of emotional distress not only on major cardiac events but also on re-hospitalization and health care consumption.
Lesperance, 2004	Pro cohort	Life expectancy < 2 yr due to medical illness; cognitively impaired; non-English/non-French speaking; ACS due to medical illness	Multicenter, 2	Canada	Aug 1999 - Aug 2001	To determine whether or not depression is associated with higher levels of inflammatory markers in patients recovering from ACS.

[a] Myocardial infarction
[b] Age
[c] Female
[d] Not reported
[e] Retrospective cohort study
[f] Treatment
[g] Randomized controlled trial
[h] Coronary artery bypass graft
[i] Depression
[j] Day
[k] Month

Evidence Table 2.1. Characteristics of Studies on Prevalence of Depression After Hospitalization For Acute Myocardial Infarction (Question 2) (continued)

[l] Acute myocardial infarction
[m] Acute coronary syndrome
[n] Percutaneous transluminal coronary angioplasty
[o] Year
[p] Hospital Anxiety and Depression Scale
[q] History of

Evidence Table 2.2. Characteristics of Patients in the Studies on Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction (%)
Trelawny, 1987	32	NR [d]	100	NR	100	NR	NR	71	NR	NR	NR
Follick, 1988	238	55	72	NR	NR	NR	NR	53	NR	NR	NR
Davis, 1988	52	51	90	NR	48	NR	NR	NR	NR	NR	NR
Schleifer, 1991	335	64	64	NR	NR	NR	NR	NR	NR	NR	42
Legault, 1992	52 [e]	55	78	NR	NR	NR	NR	NR	NR	NR	NR
Garcia, 1994	97 [f]	50	100	NR	69	NR	NR	NR	NR	NR	NR
Travella, 1994	70 [g]	58	74	NR	NR	NR	NR	NR	NR	NR	NR
Lesperance, 1996	222	60	78	NR	NR	NR	NR	NR	NR	Class I - IV: depressed: 20, non depressed: 19	44
Clarke, 1996	52	NR	100	NR	NR	NR	NR	NR	NR	NR	NR
Lehto, 2000	101	62	69	NR	NR	28	15	12	63	NR	NR
Luutonen, 2002	85	61	77	NR	NR	NR	NR	NR	NR	NR	NR
Shiotani, 2002	1042	64	80	NR	NR	48	32	66	37	Class II-IV: 12.5	NR
Strik, 2002	140	58	76	NR	NR	NR	NR	NR	NR	NR	53
Aben, 2003	200	60	77	NR	NR	NR	NR	NR	NR	NR	NR
Martin, 2003	335	67	67	NR	NR	NR	NR	NR	NR	NR	NR

Evidence Table 2.2. Characteristics of Patients in the Studies on Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2) (continued)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction (%)
Barefoot, 2003	196	61	63	67	NR	NR	NR	NR	NR	NR	NR
Strik, 2003	318	52	1	NR	NR	28	NR	54	20	NR	NR
Strik, 2004	206	59	76	NR	NR	NR	NR	13	30	NR	NR
Lane, 2002	288 [h]	63	75	93	NR	NR	NR	NR	NR	NR	NR
Bennett, 1998	37	62	73	NR	NR	NR	NR	NR	NR	NR	NR
Strik 2001	206	60	76	NR	NR	NR	NR	NR	NR	NR	NR
Luutonen, 2002	85	61	77	NR	NR	NR	NR	NR	NR	NR	NR
Lauzon, 2003	550	60	80	96	70	35	16	40	38	Class II - IV: 18	NR
Lesperance, 2004	481	60	81	NR	NR	66	NR	15	NR	NR	NR

[a] Hypertension
[b] Diabetes
[c] Hyperlipidemia
[d] Not reported
[e] Patients with myocardial infarction of 92 total
[f] 67 were assessed at 1 month
[g] With variable numbers at different time points
[h] 199 available at 4 months; 188 at 12 month

Evidence Table 2.3. Assessment of Study Quality in Studies on Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2)

Study Author, Year	Representativeness	Description Therapy & Management	Description Assessment Protocol	Outcomes & Follow-Up	Statistical Analyses	Conflict
Trelawny, 1987	15%	8%	38%	0%	44%	50%
Davis, 1988	35%	0%	100%	0%	42%	0%
Follick, 1988	25%	50%	50%	0%	17%	50%
Schleifer, 1991	90%	17%	100%	17%	0%	50%
Legault, 1992	90%	25%	100%	0%	75%	75%
Garcia, 1994	55%	0%	100%	0%	0%	0%
Travella, 1994	70%	38%	88%	17%	33%	50%
Clarke, 1996	50%	0%	100%	0%	0%	0%
Lesperance, 1996	60%	17%	88%	8%	25%	0%
Bennett, 1998	10%	0%	100%	8%	0%	0%
Lehto, 2000	45%	0%	88%	N/A	0%	0%
Strik, 2001	80%	0%	100%	N/A	50%	0%
Lane, 2002	90%	0%	100%	0%	50%	0%
Shiotani, 2002	80%	N/A	N/A	0%	50%	50%
Strik, 2002	75%	8%	100%	0%	50%	0%
Barefoot, 2003	50%	0%	100%	0%	25%	100%

Evidence Table 2.3. Assessment of Study Quality in Studies on Prevalence of Depression After Hospitalization for Acute Myocardial Infarction (Question 2) (continued)

Study Author, Year	Representativeness	Description Therapy & Management	Description Assessment Protocol	Outcomes & Follow-Up	Statistical Analyses	Conflict
Aben, 2003	80%	0%	100%	0%	33%	0%
Lauzon, 2003	65%	33%	100%	8%	13%	50%
Martin, 2003	65%	8%	100%	8%	33%	0%
Strik, 2003	65%	25%	100%	0%	50%	0%
Lesperance, 2004	90%	33%	100%	0%	19%	50%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 6 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), and whether the same tools for diagnosing depression were used for baseline and follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether adjustment was made for confounding (2 points), and whether confidence intervals were reported (2 patients).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 2.4. Results of Studies on Prevalence of Depression After Hospitalization for Myocardial Infarction (Question 2)

Study	Diagnosis of MI	Depression Assessment Method [a]	Criteria	Depression Severity Measure [b]	Prevalence (%)	Commments
Trelawny, 1987	Confirmed by cardiologist	Goldberg's clinical interview schedule	Depression not specified	NR [c]	10 d [d] 20; 2 mos [e] 26; 6 mos 26	Group consisted of married men admitted to an ER [f] with suspected MI [g] ≤ 65 years.
Davis, 1988	MI patients admitted to CCU [h]	BDI [i]	≥ 13	Categorical variable	6-8 wks [j] 10	Prevalence of depression measured by 3 methods 17 BDI rating 27 SCID [k] rating
Follick, 1988	In-hospital assessment, chest pain, ECG [l], creatine kinase	SCL-90 [m]	No standard definition of depression	Dichotomous variable	Baseline 16; 9 mos 10	NA [n]
Schleifer, 1991	In-hospital assessment, chest pain, creatine kinase, ECG	RDC [o] (Nurse Interview)	Major/Minor depression	Categorical variable	8-10 d: Major [p] 17, Minor [q] 30; 3-4 mos: Major 14, Minor= 19	Major depression assessed as (lowered mood and 4 symptoms) ≥ 1 week. Minor depression assessed as (lowered mood and 2 symptoms) ≥ 1 week.
Legault, 1992	In-hospital assessment, ECG, creatine kinase.	BDI	≥ 16	Dichotomous variable	3 mos 7; 12 mos 9	Authors reported demographics for MI, unstable angina, and non cardiac chest pain. Only the data on MI patient captured. Follow up at 3 months and 12 months, with initial.
Garcia, 1994	In-hospital assessment	RDC	Major/Minor depression	Continous variable, Categorical variable	1 mo: Major 11, Minor 27	All patients with first MI assessed for depression - no control. Data reported at hospitalization for MI (diagnosis standard not provided) included only means & CIs [r] for personality type A, and mood measures(including BDI).

Evidence Table 2.4. Results of Studies on Prevalence of Depression After Hospitalization for Myocardial Infarction (Question 2) (continued)

Study	Diagnosis of MI	Depression Assessment Method [a]	Criteria	Depression Severity Measure [b]	Prevalence (%)	Commments
Travella, 1994	ECG, CPK [s]	HAMD [t] PSE [u]	Major/Minor dysthymia	Categorical variable	In hospital: MDD [v] 26, Dys [w] 3; 3 mos: MDD 15, Dys 4; 6 mos: MDD 21, Dys 3; 9 mos: MDD 28, Dys 3; 12 mos MDD 16, Dys 13	NA
Clarke, 1996	In-hospital assessment	ZDS [x]	NR	Dichotomous variable	3 mos 24	NA
Lesperance, 1996	In-hospital assessment, chest pain, creatine kinase, new Q waves	DIS [y]	Depression	NR	6 mos 21; 12 mos 9	NA
Bennett, 1998	In-hospital assessment	HADS [z]	≥ 11	Dichotomous variable	3 mos 3	NA
Lehto, 2000	Interviews and clinical examinations at least 6 months after the cardiac events, physician report	DEPS [aa]	≥ 9	Continuous variable, Dichotomous variable	At least 6 mos post-MI [d] 16	NA
Strik, 2001	In-hospital assessment, ECG, AST, clinical picture	SCID, HAMD, SCL-90, BDI, HADS	Major/Minor depression	Dichotomous variable	1 mo Major 11, Minor 8	NA

Evidence Table 2.4. Results of Studies on Prevalence of Depression After Hospitalization for Myocardial Infarction (Question 2) (continued)

Study	Diagnosis of MI	Depression Assessment Method [a]	Criteria	Depression Severity Measure [b]	Prevalence (%)	Commments
Lane, 2002	In-hospital assessment, chest pain, ECG, creatine kinase	BDI	≥ 10	Continuous variable, Dichotomous variable	4 mos 38; 12 mos 37	NA
Luutonen, 2002	In-hospital assessment, chest pain, ECG, creatine kinase	BDI	≥ 10	Continuous variable, Categorical variable	6 mos 30; 18 mos 34	NA
Shiotani, 2002	In-hospital assessment, chest pain, ECG, creatine kinase,	ZDS	≥ 40%	Dichotomous variable	Within first 3 mos 42	Depression not assessed during hospitalization. SDS [ab] mailed within 3 months.
Strik, 2002	In-hospital assessment, chest pain, ECG, AST	BDI, HADS, SCL-90 if any one positive assessment with SCID	Major or minor depression	Dichotomous variable	3 mos: Major 11, Minor 2	NA
Aben, 2003	In-hospital assessment, chest pain, ECG, AST [ac]	BDI, HADS, SCL-90 if any one positive assessment with SCID and HAMD	Depression	Dichotomous variable	1 mo 14	The study reports incident cases of depression at 1, 3, 6, 9, and 12 months. Cumulative incidence of depression in table 2.
Barefoot, 2003	In-hospital assessment, ECG, cardiac enzyme	NR	HAMD d/x [ad], BDI ≥10	Continuous variable, categorical variable	2 wks: HAMD 17, BDI 27	NA
Lauzon, 2003	In-hospital assessment, ECG	BDI	≥ 10	Dichotomous variable	1 mo 39; 6 mos 39; 1 yr 30	NA

Evidence Table 2.4. Results of Studies on Prevalence of Depression After Hospitalization for Myocardial Infarction (Question 2) (continued)

Study	Diagnosis of MI	Depression Assessment Method [a]	Criteria	Depression Severity Measure [b]	Prevalence (%)	Commments
Martin, 2003	In-hospital assessment, ECG, troponin, patient history	HADS	≥ 11 (probable depression) ≥ 8 (possible depression)	Continuous variable, Dichotomous variable	1 wk: ≥ 8: 15, ≥ 11: 6; 6 wk: ≥ 8: 13, ≥ 11: 5; 6 mos: ≥ 8: 10, ≥ 11: 5	NA
Lesperance, 2004	In-hospital assessment, chest pain, ECG,creatine kinase	SCID	Major depression	Dichotomous variable	Approx 2 mos: 7	NA

[a] Method of assessing of depression used for analysis
[b] How severity of depression was measured
[c] Not reported
[d] Day
[e] Month
[f] Emergency room
[g] Myocardial infarction
[h] Coronary care unit
[i] Beck Depression Inventory
[j] Weeks
[k] Structural Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders IV
[l] Electrocardiogram
[m] Symptoms Checklist 90
[n] Not applicable
[o] Research Diagnostic Criteria
[p] Major depression
[q] Minor depression
[r] Confidence intervals
[s] Creatine phosphokinase
[t] Hamilton Rating Scale for Depression
[u] Present State Examination
[v] Major Depressive Disorder

Evidence Table 2.4. Results of Studies on Prevalence of Depression After Hospitalization for Myocardial Infarction (Question 2) (continued)

[w] Dysthymia
[x] Zung Depression Scale
[y] Diagnostic Interview Schedule
[z] Hospital Anxiety and Depression Scale
[aa] Depression Scale
[ab] Self-Rating Depression Scale
[ac] Aspartate amino transferase
[ad] Diagnosis

Evidence Table 3.1A. Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Ahern, 1990	Pro cohort [a]	Only MI [b] patients	Age > 70, index ACS [c] after symtoms, non-atherosclerotic MI, pulmonary hypertension, symptomatic urinary tract infection, chronic active hepatitis, nonischemic MI, women of child bearing age, < 10 PVCs/hr [d], non English speaking	Multicenter, 10	USA, Canada	NR [e]	To test the predictive association between biobehavioral factors and mortality or cardiac arrest.
Ladwig, 1991	Pro cohort	Only MI patients	Age > 66, female	Multicenter	Europe	Jan 1983 - Dec 1985	To assess incidence of hyperactive behaviour and persistence and depression in the post-acute phase after MI.
Frasure-Smith, 1993	Pro cohort	Only MI patients	Cognitively impaired, medical condition likely to impact 6 mos survival, non English or non French speaking, too unstable to complete interview	Single center	Canada	Jul 1991 - Jun 1992	To determine if the diagnoses of major depression in patients hospitalized following MI would have an independent impact on cardiac mortality over the first 6 months after discharge.
Frasure-Smith, 1999	Pro cohort	Only MI patients	Life threatening conditions, cognitively impaired, non French, lived too far to return to follow up, administrative reasons, physician refusal, participation in other research early discharge	Multicenter, 10	Canada	Jul 1991 - 1994	To assess gender differences in the impact of depression on 1 year cardiac mortality in patients hospitalized for an acute MI.
Irvine, 1999	RCT [g]	Only MI patients	Age > 65,more than 1 MI, non Gottenberg residents	Multicenter	Canada	Jun 1996 - Nov 1995	To examine the impact of depressive symptoms and social support on a 2-year sudden cardiac death risk, controlling for fatigue symptoms.
Denollet, 2000	Pro cohort	Patients with ACS	Serious co-morbidity	Single center	Europe	Jan 1989 - Dec 1992	To test the hypothesis that both cardiac disorder and emotional distress confer an increased risk of cardiac events and impaired QOL [h] despite appropriate cardiac treatment.

Evidence Table 3.1A. Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Lane, 2000	Pro cohort	Only MI patients	Index ACS after symptoms:, another condition likely to lead to death within 12 mos, non English speaking, medically unstable, MI, CABG [i], PCI [j]	Multicenter	Europe	Jan 1997 - Aug 1988	To determine the impact of depression and anxiety on mortality and quality of life in patients hospitalized for an acute MI.
Welin, 2000	Pro cohort	Only MI patients	NR	Multicenter	Europe	Oct 1985 - Oct 1987	To test whether the 10 year prognosis after MI is related to psychological stress, lack of social support, anxiety, and/or depressive tendency.
Bush, 2001	Pro cohort	Only MI patients	Serious co-morbidity likely to die in 6 mos of medical condition, not admitted to the cardiology service, died or transferred, other facility within 48 hrs of hospitalization	Single center	USA	Jul 1995 - Dec 1996	To determine whether minimal symptoms of depression that are less than those considered clinically significant are associated with increased mortality risk after MI.
Druss, 2001	Pro cohort	Only MI patients	Age < 65, terminally ill, cognitively impaired, died during current admission, DNR [k] order, dementia	Multicenter	USA	Feb 1994 - Jul 1995	To investigate whether difference in quality of medical care might explain a portion of the excess mortality associated with mental disorders in the year after MI.
Lane, 2001	Pro cohort	Only MI patients	Index ACS after surgery, serious co-morbidities, cognitively impaired, non English, medically unstable	Multicenter	Europe	Jan 1997 - Aug 1998	To determine the impact of symptoms of depression and anxiety on mortality and quality of life in patients hospitalized for AMI[l].
Lane, 2002	Pro cohort	Only MI patients	NR	Multicenter	Europe	Jun 1997 - Aug 1998	To examine the relationship between symptoms of depression following MI & 3 year survival status.

Evidence Table 3.1A. Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Lesperance, 2002	Pro cohort	Only MI patients	NR	Multicenter	Canada	Jan 1991 - Nov 1994	To evaluate a close relationship between depression symptoms and long-term cardiac mortality, confirm that any impact of depression symptoms remain significant after control for measures of cardiac disease severity, compare the impact of depression measurement during hospitalization and a year later and evaluate the prognostic importance of changes in depressive symptoms over the first post-MI year.
Carney, 2003	Pro cohort	Only MI patients	H/o [m] psychosis, cognitively impaired, life threatening medical illness, to ill to participate, TCA [n] or MAOI [o] or other anti-depressant that may affect heart rate variability, refused logistically, unable to participate	Multicenter	USA	Oct 1997 - Jan 2000	To determine if depression was associated with an increased risk of mortality and nonfatal recurrent MI in a subsample of the ENRICHD [p] trials depressed patients compared with a group of nondepressed patients recruited for an ancillary study.
Frasure-Smith, 2003	Pro cohort	Only MI patients	Index ACS after surgry, cognitively impaired:, non English or non French, life threatening illness, physical inability to complete hospital interview, living to far to return to hospital for f/u [q], physician refusal, participation in other research	Multicenter	Canada	Jan 1991 - Sep 1994	To examine the relative importance of depression, anxiety,anger, and social support in predicting 5-years cardiac related mortality following an MI and assess the role of any common underlying dimensions.

[a] Prospective cohort study
[b] Myocardial infarction
[c] Acute coronary syndrome
[d] Premature ventricular contractions per hour
[f] Not reported
[g] Randomized controlled trial
[h] Quality of life

Evidence Table 3.1A. Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3) (continued)

[i] Coronary artery bypass graft
[j] Percutaneous coronary intervention
[k] Do not resuscitate
[l] Acute myocardial infarction
[m] History of
[n] Tetracyclic antidepressant
[o] Monoamine oxidase inhibitor
[p] Enhancing Recovery in Coronary Heart Disease
[q] Follow-up

Evidence Table 3.1B. Characteristics of Studies on the Relation of Depression to Cardiac Events in Patients After Myocardial Infarction (Question 3)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Irvine, 1999	RCT [a]	Only MI [b] patients	non English or non French speaking, not well enough to complete questionaire	Multicenter	Canada	NR [c]	To examine the impact of depressive symptoms and social support on a 2-year sudden cardiac death risk, controlling for fatigue symptoms.
Druss, 2000	Retro cohort[d]	Only MI patients	Age < 65 yrs [e], terminally ill, transfer from another hospital, do not resuscitale order, not fee for service	Multicenter	USA	Feb 1994 - Jul 1994	To assess whether having a comorbid mental disorder is associated with a lower likelihood of cardiac catheterization and/or vascularization after AMI [f].
Frasure-Smith, 2000	Retro cohort	Only MI patients	Non-English or non-French speaking, life threating condition, cognitively impaired, physically unstable, live far from hospital, administrative reason	Multicenter	Canada	M-HART [g]: 1991 - 1995 EPPI [h]: NR	To examine the relationship between post-MI depression and physician costs, including both out patient care and hospital readmissions.
Shiotani, 2002	Pro cohort [i]	Only MI patients	Died in hospital, unable to verbally communicate, major psychological disease, refused registry	Multicenter	Asia	Apr 1998 - Apr 2000	To investigate the impact of the depressive symptoms on prognosis of the elderly patients with AMI.
Strik, 2003	Pro cohort	First MI	H/o [j] psychosis, cognitively impaired, non Dutch speaking	Single center	Europe	May 1994 - Sep 1999	1) To examine whether depression is a better predictor of incomplete recovery after MI than anxiety. 2) To examine the effect of emotional distress not only on major cardiac events but also on re-hospitalization and increased health care consumption.
Strik, 2004	Pro cohort	First MI	H/o psychosis,cognitively impaired, cant express themselves, non Dutch speaking, lived more than 50 kms [k], co-morbid life threatening illness	Single center	Europe	NR	1)To evaluate whether cumulative 1 year incidence of major and minor depression in a consecutive cohort is as high following MI in first MI patients. 2)To evaluate whether in the above patient population major and minor depressive symptoms, predicted cardiac mortality and morbidity upto 3 years post MI.

[a] Randomized controlled trial
[b] Myocardial infarction
[c] Not reported
[d] Retrospective cohort study

Evidence Table 3.1B. Characteristics of Studies on the Relation of Depression to Cardiac Events in Patients After Myocardial Infarction (Question 3) (continued)

[e] Years
[f] Acute myocardial infarction
[g] Montreal Heart Attack Readjustment Trial
[h] Emotions and Prognosis Post-Infarct Study
[i] Prospective cohort study
[j] History of
[k] Kilometers

Evidence Table 3.1C. Characteristics of Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruit-ment Period	Study Objective
Travella, 1994	Pro cohort [a]	Only MI[b] patients	Attempted cardiac surgery,serious co-morbidities,cognitively impaired, h/o [c] depression	Multicenter	USA	NR [d]	To examine the course of clinical correlates of depression going the first year after MI.
Drory, 1998	Pro cohort	Only MI patients	Females, previous AMI [e], not sexually active prior to MI	Multicenter	Asia	NR	To examine important diverse sociodemographic, medical and psychological variables as potential predicton of sexual activity, satisfaction in male patients following a first AMI.
O'Rourke, 1999	Pro cohort	included patients with ACS [f] other than MI. Data for MI not reported separately	Age>76, non-English, recurrent MI, emergency angioplasty, emergency cardiac by pass	Multicenter	Europe	NR	To examine predictive power of psychosocial variables (self-efficacy beliefs, locus of control, illness perception, social support, anxiety, depression) on health service utilization 6 months following MI.
Soejima, 1999	Pro cohort	Only MI patients	NR	Multicenter	Asia	Apr 1992 - Jan 1996	To investigate psychosocial and clinical factors related to work resumption, delay in returning to work and level of work activity after acute myocardial infarction in Japanese male patients.
Bogg, 2000	Pro cohort	Only MI patients	CVA [g]	Single Center	Europe,	NR	To assess the influences of gender on quality of life among post MI patients with depression.
Denollet, 2000	Pro cohort	322 patients with ACS, 50.31% patients with MI No data for MI reported separately	Serious co-morbidities	Single center	Europe,	Jan 1989 - Dec 1992	To test the hypothesis that both cardiac disorder and emotional distress confer an increased risk of cardiac events and impaired QOL [h] despite appropriate cardiac treatment.

Evidence Table 3.1C. Characteristics of Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruit-ment Period	Study Objective
Lane, 2000	Pro cohort	Only MI patients	Index ACS after surgery, serious co-morbidities, another medical condition likely to lead to death within the next 12 months, non-English, medically unstable, too unstable to complete the baseline assessment within 15 days of their infarction	Multicenter	Europe,	Jan 1997 - Aug 1998	To determine the impact of depression and anxiety on mortality quality of life in patients hospitalized for an acute myocardial infarction.
Mayou, 2000	Pro cohort	Only MI patients	Age > 80 years	Multicenter	Europe	Nov 1994- Nov 1995	To investigate the significance of emotional distress imediately after a myocardial infarction as a predictor of physical, psychological, and social outcome and resource use.
Lane, 2001	Pro cohort	Only MI patients	Index ACS after surgery, serious co-morbidities, cognitively impaired, non-English, medically unstable	Multicenter	Europe,	Jan 1997- Aug 1998	To determine the impact of symptoms of depression and anxiety on mortality and quality of life in patients hospitalized for AMI
Brink, 2002	Pro cohort	Only MI patients	Serious co-morbidities, dementia, non- Swedish	Single Center	Europe,	Oct 1998 - Sep 1999	To explore health related quality of life in first time myocardial infarction patients, five months after the heart attack.
Drory, 2002	Pro cohort	Only MI patients	Previous MI	Multicenter	Asia,	NR	To evaluate differential and independent impact of socio-demographic medical and psychologic variables assessed at hospital discharge on patients short and long term mental health.

Evidence Table 3.1C. Characteristics of Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruit-ment Period	Study Objective
Drory, 2003	Pro cohort	Only MI patients	Men, previous MI	Multicenter	Asia,	NR	To compare the long term psychologic well being and psychologic distress, after a first acute myocardial infarction of women with those of men and those of a normative community sample of women and to examine the relation of socio-demographic, medical and psychologic variables to the long-term psychologic well-being and psychologic distress of women.

[a] Prospective cohort study
[b] Myocardial infarction
[c] History of
[d] Not reported
[e] Acute myocardial infarction
[f] Acute coronary syndrome
[g] Cardiovascular angioplasty
[h] Quality of life

Evidence Table 3.2A. Patient Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married [a] (%)	Education [b] (%)	Employed [c] (%)	HTN [d] (%)	DM [e] (%)	Smoking (%)	Lipid [f] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction	H/o [g] Dep (%)
Ahern, 1990	265	NR [h]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Ladwig, 1991	560	NR	100	NR	NR	NR	NR	Group A: 109, Group B: 36, Group C: 33	NR	Group A: 222, Group B: 79, Group C: 45	NR	NR	EF [i] < 35%: 22	NR
Frasure-Smith, 1993	222	NR	78	NR	NR	> 8 yrs [j]: 69	NR	30	12	40	NR	21	43, EF: 95% CI[k](42.1% to 45.7%)	NR
Frasure-Smith, 1999	Female: 283, Male: 613	Female: 63, Male: 58	68	NR	Female: 51, Male: 18	< 7yrs: Female: 38 Male: 23	NR	Female: 52, Male: 28 (n=612)	Female: 23, Male: 13	Female: 45, Male: 49	NR	Class I: Female: 57, Male: 75 Class II: Female: 15, Male: 11; Class III: Female: 25, Male: 12; Class IV: Female: 3, Male: 2	Female:71, Male: 47; EF < 35%, Female: 18, Male: 20; Mean: Female: 50, Male: 47	NR
Irvine, 1999	634	64	83	NR	74	14	NR	NR	15	NR	NR	NR	NR	NR

Evidence Table 3.2A. Patient Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married [a] (%)	Education [b] (%)	Employed [c] (%)	HTN [d] (%)	DM [e] (%)	Smoking (%)	Lipid [f] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction	H/o [g] Dep (%)
Denollet, 2000	Event Free: 270, CV[l] Event: 22, Total Events: 49	Event Free: 38, CV Event: 59, Total Events: 53	Event Free: 92, CV Event: 95, Total Events: 94	NR	NR	NR	NR	Event Free: 32, CV Event: 27, Total Events: 29	NR	Total Events: 20	Event Free: 36 , CV Event: 36 , Total Events: 37	NR	Event Free: 16, CV Event: 36, Total Events: 33	Event Free: 32, CV Event: 55 , Total Events: 51
Lane, 2000	BDI [m] > 10: 89, BDI < 10: 199	BDI > 10: 63, BDI < 10: 63	BDI > 10: 62, BDI < 10: 80	BDI > 10: 91, BDI < 10: 94	BDI > 10: 67, BDI < 10: 71	BDI > 10: 10, BDI < 10: 10	BDI > 10: 24, BDI < 10: 36	BDI > 10: 42, BDI < 10: 37	BDI > 10: 19, BDI < 10: 10	BDI > 10: 44, BDI < 10: 43	BDI > 10: 74, BDI < 10: 79	Class II - IV: BDI > 10: 58, BDI < 10: 49	NR	NR
Welin, 2000	275	NR	84	NR	NR	NR	NR	21	9	19	NR	NR	NR	NR
Bush, 2001	271	64.8	58	86	79	NR	NR	66	35	29	62%	Class II - IV: 41	EF > 35%: 71, EF < 35%: 29	18
Druss, 2001	Mental [n]: 4664, No Mental : 83577	Mental: 76, No Mental : 76	Mental : 53 No Mental : 47	NR	NR	Mental: 6, No Mental: 0	NR	Mental : 42, No Mental : 40	Mental : 22, No Mental : 26	Mental : 22, No Mental : 15	NR	NR	EF: >55%, Mental: 14, No Mental : 15	NR

Evidence Table 3.2A. Patient Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married [a] (%)	Education [b] (%)	Employed [c] (%)	HTN [d] (%)	DM [e] (%)	Smoking (%)	Lipid [f] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction	H/o [g] Dep (%)
Lane, 2001	Group A: 89, Group B: 199	Group A: 63, Group B: 63	Group A: 62, Group B: 80	Group A: 91, Group B: 94	Group A: 91, Group B: 94	Group A: 10, Group B: 10	Group A: 24, Group B: 36	Group A: 42, Group B: 37	Group A: 19, Group B: 10	Group A: 44, Group B: 43	Group A: 74, Group B: 79	Class II - IV: Group A: 58, Group B: 49	NR	NR
Lane, 2002	Dep [o]: 89, NonDep [p]: 199	Dep: 63, NonDep: 63	75	93	Dep: 71, NonDep: 67	Dep: 10, NonDep: 10	Dep: 24, NonDep: 36	Dep: 42, NonDep: 37	Dep: 19, NonDep: 10	Dep: 44, NonDep: 43	NR	Class II - IV: Dep: 55, NonDep: 49	NR	NR
Lesperance, 2002	870	59	68	NR	36	NR	NR	35	16	47	NR	Class I - IV: 31	19 (n=889)	NR
Carney, 2003	Group A: 358, Group B: 408	Group A: 57, Group B: 61	Group A: 53, Group B: 62	Group A: 28, Group B: 21	NR	NR	NR	NR	Group A: 33, Group B: 22	NR	NR	Class III: Group A: 6, Group B: 4	EF < 40 %, Group A: 24, Group B: 22	NR
Frasure-Smith, 2003	887	59	69	NR	NR	NR	NR	NR	NR	62	NR	NR	NR	NR

[a] Married or partnered
[b] High School or higher education
[c] Employed full-time or part-time
[d] Hypertension
[e] Diabetes
[f] Hyperlipidemia
[g] History of
[h] Not reported
[i] Ejection fraction

Evidence Table 3.2A. Patient Characteristics of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3) (continued)

[j] Years
[k] Confidence interval
[l] Cardiovascular
[m] Beck Depression Inventory
[n] Mental disorder/no mental disorder
[o] Depressed
[p] Non-depressed

Evidence Table 3.2B. Patient Characteristics of Studies on the Relation of Depression to Cardiac Events in Patients After Myocardial Infarction (Question 3)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Mean Ejection Fraction	History of Depression (%)
Irvine, 1999	634	64	83	NR [d]	15	NR	NR	NR	NR
Druss, 2000	Mental [e]: 5365 No Mental [f]: 108288	Mental: 50 No Mental: 49	Mental: 52 No Mental: 46	Mental: 42 No Mental: 40	Mental: 22 No Mental: 26	Mental:22 No Mental: 151	NR	EF [g] ≥ 55% Mental: 14 No Mental: 14	NR
Frasure-Smith, 2000	848	NR	69	34	16	48	NR	EF ≤ 35%: 17	NR
Shiotani, 2002	Dep [h]: 438 NonDep [i]: 604	Dep: 63 NonDep: 64	Dep: 81 NonDep: 80	Dep: 49 NonDep: 46	Dep: 36 NonDep: 29	Dep: 70 NonDep: 62	Dep: 35 NonDep: 39	NR	NR
Strik, 2003	318	58	100	28	9	54	20	EF ≤ 50%: 45	NR
Strik, 2004	Dep: 63 NonDep: 143	NR	Dep: 84 NonDep: 74	NR	NR	Dep: 10 NonDep: 13	Dep: 35 NonDep: 29	EF < 50% Dep: 77, NonDep: 31; EF > 50% Dep: 56, NonDep: 69	Dep: 32 NonDep: 13

[a] Hypertension
[b] Diabetes
[c] Hyperlipidemia
[d] Not reported
[e] Any mental disorder
[f] No mental disorder
[g] Ejection fraction
[h] Depressed
[i] Non-depressed

Evidence Table 3.2C. Patient Characteristics of Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3)

Study Author, Year	No. of Sub-jects	Mean Age	Male (%)	Non-White (%)	Married (%)	Education[a] (%)	Employed[b] (%)	HTN[c] (%)	DM[d] (%)	Smoking (%)	Lipid[e] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction	History of Depression (%)
Travella, 1994	Dep[f]: 18, NonDep[g]: 52	Dep: 63, NonDep: 57	Dep: 54, NonDep: 82	Dep: 44, NonDep: 36	NR	Dep: 12, NonDep: 12	NR	NR	NR	NR	NR	NR	NR	Dep: 28, NonDep: 10
Drory, 1998	276	51	100	33 rest of group from Europe/ American/ Israel	99	13	NR	NR	9	NR	NR	Class I: 83, Class II: 16, Class III: 1, Class IV: 1	NR	NR
O'Rourke 1999	EHM[h]: 45, No EHM[i]: 25	EHM: 58, No EHM: 60	EHM: 73, No EHM: 76	NR	EHM: 73, No EHM: 72	NR	EHM: 31, No EHM: 44	NR	NR	NR	NR	NR	NR	NR
Soejima, 1999	134	54	100	NR	NR	NR	100	34	22.5 (14.8, 30.3)	74.8	31.5 (22.9,40.2)	Class I: 847(78.0-91.4), Class II:15.3 (8.6-22.6)	56	NR
Bogg, 2000	220	NR	77	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Denollet, 2000	Free[j]: 270, Cardiac[k]: 22, Total[l]: 49	Free: 38, Cardiac: 59, Total: 53	Free: 92, Cardiac: 95, Total: 94	NR	NR	NR	NR	Free: 32 (85), Cardiac: 27 (6), Total: 29 (14)	NR	Free: 17 (45), Cardiac: 18 (4), Total: 20 (10)	Free: 36 (103), Cardiac: 36 (8), Total: 37 (18)	NR	Free: 16 (43), Cardiac: 36 (8), Total: 33 (16)	Free: 32 (85), Cardiac: 55 (12), Total: 51 (25)

Evidence Table 3.2C. Patient Characteristics of Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	No. of Sub-jects	Mean Age	Male (%)	Non-White (%)	Married (%)	Education[a] (%)	Employed[b] (%)	HTN[c] (%)	DM[d] (%)	Smoking (%)	Lipid[e] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction	History of Depression (%)
Lane, 2000	Dep: 89, NonDep: 199	Dep: 63, NonDep: 63	Dep: 62, NonDep: 80	Dep: 9, NonDep: 7	NR	Dep: 10, NonDep: 10	Dep: 24, NonDep: 36	Dep: 42, NonDep: 37	Dep: 19, NonDep: 9	Dep: 44, NonDep: 43	Dep: 35, NonDep: 39	Class I: Dep: 41, NonDep: 51, Class II: Dep: 56, NonDep: 49	NR	NR
Mayou, 2000	Total: 344, Distress[m]: 51, NonDistress[n]: 293	Total: 63, Distress: 58, NonDistress: 64	Total: 73 Distress: 69, NonDistress: 74	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Lane, 2001	Dep: 89, LowDep[o]: 199	Dep: 63, LowDep: 63	Dep: 62, LowDep: 80	Dep: 9, LowDep: 7	NR	Dep: 10, LowDep:	Dep: 24, LowDep: 36	NR	NR	NR	NR	NR	NR	NR
Brink, 2002	Women: 37, Men: 77	Women: 72, Men: 65	68	NR	Women: 60, Men: 78	Women: 78, Men: 71	NR	Women: 51, Men: 28	Women: 16, Men: 15	Women: 24, Men: 34	NR	NR	NR	NR

Evidence Table 3.2C. Patient Characteristics of Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3) (continued)

Study Author, Year	No. of Sub-jects	Mean Age	Male (%)	Non-White (%)	Married (%)	Education[a] (%)	Employed[b] (%)	HTN[c] (%)	DM[d] (%)	Smoking (%)	Lipid[e] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction	History of Depression (%)
Drory, 2002	209	52	100	NR	NR	12	NR	NR	NR	NR	NR	Class I: 81 Class II: 17 Class III: 1 Class IV: 1	NR	NR
Drory, 2003	62	56	0	20	NR	12	NR	NR	NR	NR	NR	Class II - IV: 16	NR	NR

[a] High School or higher
[b] Employed full-time or part-time
[c] Hypertension
[d] Diabetes
[e] Hyperlipidemia
[f] Depressed
[g] Not depressed
[h] Received Edinburgh Heart Manual
[i] Did not received Edinburgh Heart Manual
[j] Event free
[k] Fatal and non fatal cardiac events at 5 years
[l] Cardiac events and revascularization at 5 years
[m] Distressed cases at baseline
[n] Not distressed cases at baseline
[o] Low levels of depression as indicated by Beck Depression Inventory score less than 10

Evidence Table 3.3A. Assessment of Study Quality in Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3)

Study Author, Year	Representativeness	Description of Therapy & Management	Description of Assessment Protocol	Outcomes and Follow-Up	Statistical Analyses	Conflicts
Ahern, 1990	75%	25%	100%	69%	63%	50%
Ladwig, 1991	30%	0%	38%	69%	38%	100%
Frasure-Smith, 1993	75%	17%	100%	88%	63%	50%
Frasure-Smith, 1999	100%	0%	100%	30%	63%	50%
Irvine, 1999	70%	58%	100%	63%	63%	50%
Denollet, 2000	60%	8%	100%	85%	81%	0%
Lane, 2000	95%	8%	100%	88%	88%	0%
Welin, 2000	70%	0%	100%	80%	63%	50%
Bush, 2001	75%	0%	100%	78%	56%	0%
Druss, 2001	90%	0%	100%	94%	75%	100%
Lane, 2001	95%	25%	100%	42%	69%	0%
Lane, 2002	50%	N/A	100%	60%	75%	0%
Lesperance, 2002	95%	42%	100%	90%	75%	100%
Carney, 2003	85%	42%	100%	60%	81%	50%
Frasure-Smith, 2003	70%	0%	100%	88%	88%	50%

Evidence Table 3.3A. Assessment of Study Quality of Studies on the Relation of Depression to Survival in Patients After Myocardial Infarction (Question 3) (continued)

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 12 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), whether the cardiac outcome measures were defined (2 points), whether the depression outcome measures were defined (2 points), whether the same tools for diagnosing depression were used for baseline and follow-up (2 points) and the planned length of follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether the magnitude of the difference for primary endpoints or magnitude of association between outcomes and index variability is reported (2 points) and whether adjustment was made for confounding (2 points).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 3.3B. Assessment of Study Quality in Studies on the Relation of Depression to Cardiac Events in Patients After Myocardial Infarction (Question 3)

Study Author, Year	Representativeness	Description of Therapy & Management	Description of Assessment Protocol	Outcomes and Follow-Up	Statistical Analyses	Conflicts
Irvine, 1999	70%	58%	100%	63%	63%	63%
Druss, 2000	85%	8%	50%	50%	100%	75%
Shiotani, 2002	80%	17%	100%	92%	75%	83%
Strik, 2003	65%	25%	100%	56%	106%	81%
Strik, 2004	75%	8%	100%	83%	75%	79%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 12 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), whether the cardiac outcome measures were defined (2 points), whether the depression outcome measures were defined (2 points), whether the same tools for diagnosing depression were used for baseline and follow-up (2 points) and the planned length of follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether the magnitude of the difference for primary endpoints or magnitude of association between outcomes and index variability is reported (2 points) and whether adjustment was made for confounding (2 points).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 3.3C. Assessment of Study Quality in Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3)

Study Author, Year	Representativeness	Description of Therapy & Management	Description of Assessment Protocol	Outcomes and Follow-Up	Statistical Analyses	Conflicts
Travella, 1994	70%	38%	88%	80%	50%	65%
Drory, 1998	60%	0%	100%	58%	50%	54%
Irvine, 1999	70%	58%	100%	63%	63%	63%
Ladwig, 1999	30%	0%	38%	69%	38%	53%
O'Rourke, 1999	60%	0%	100%	63%	19%	41%
Soejima, 1999	75%	0%	63%	63%	69%	66%
Bogg, 2000	35%	0%	50%	97%	50%	73%
Denollet, 2000	60%	8%	100%	85%	81%	83%
Lane 2000	95%	8%	100%	88%	88%	88%
Mayou, 2000	75%	17%	100%	58%	50%	54%
Lane, 2001	75%	0%	100%	63%	63%	63%
Brink, 2002	75%	0%	100%	78%	56%	67%
Drory, 2002	45%	0%	100%	58%	44%	51%
Drory, 2003	20%	0%	50%	40%	50%	45%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population

Evidence Table 3.3C. Assessment of Study Quality in Studies on the Relation of Depression to Quality of Life in Patients After Myocardial Infarction (Question 3) (continued)

(2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 12 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), whether the cardiac outcome measures were defined (2 points), whether the depression outcome measures were defined (2 points), whether the same tools for diagnosing depression were used for baseline and follow-up (2 points) and the planned length of follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether the magnitude of the difference for primary endpoints or magnitude of association between outcomes and index variability is reported (2 points) and whether adjustment was made for confounding (2 points).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 3.4A. Assessment of Depression in Studies on the Relation of Depression to Survival in Patients after Myocardial Infarction (Question 3)

Study Author, Year	No Screened	No Enrolled	Depression Instrument	Time of Baseline Assessment	Mean Follow -up	Total Number at Enrollment		Total at Follow-Up
						Depressed	Non-Depressed	
Ahern, 1990	502	265	BDI [a] profile of mood states	6 - 60 d [b]	1 yr [c]	NR [d]	NR	NR
Ladwig, 1991	779	560	NR	3 wks [e] post MI	6 mos [f]	"Extreme depression": 80	480	NR
Frasure-Smith, 1993	332	222	MIMH DIS [g]	5 - 15 d	6 mos	35	187	NR
Frasure-Smith, 1999	2512	904	BDI	After transfer from CCU [h] to ward	1 yr	290	606	896
Irvine, 1999	969	703	BDI	20 - 59 d	2 yrs	NR	NR	634
Denollet, 2000	322	319	ZDS [i]	Within 2 mos post-MI	5 yrs	Event free: 32%; CV [j] Events: 50%; Total Events: 57%	Event free: 68%; CV Events: 45%; Total Events: 49%	NR
Lane, 2000	437	288	BDI	Within 15 d post-MI	4 mos	89	199	263
Welin, 2000	333	275	ZDS	3 - 6 d post-MI	10 yr	ZDS > 40: 37%	ZDS < 40: 63%	NR
Bush, 2001	696	285	SCID [k] BDI	2.5 d post-MI	4 mos	73	194	271
Druss, 2001	NR	88241	NR	NR	NR	NR	NR	NR
Lane, 2001	437	288	BDI	Within 15 d post-MI	12 mos	89	199	257
Lane, 2002	437	288	BDI	Within 15 d post-MI	3 yrs	89	199	250
Lesperance, 2002	NR	896	BDI	Transfer from CCU to ward	5 yrs	290	606	715
Carney, 2003	NR	NR	Depression interview: structured HAMD [l] and BDI	Within 28 d post-MI	Upto 30 mos	358	408	NR

Evidence Table 3.4A. Assessment of Depression in Studies on the Relation of Depression to Survival in Patients after Myocardial Infarction (Question 3) (continued)

Study Author, Year	No Screened	No Enrolled	Depression Instrument	Time of Baseline Assessment	Mean Follow -up	Total Number at Enrollment		Total at Follow-Up
						Depressed	Non-Depressed	
Frasure-Smith, 2003	NR	NR	NR	NR	12 mos	NR	NR	NR

[a] Beck Depression Inventory
[b] Day
[c] Year
[d] Not reported
[e] Weeks
[f] Months
[g] National Institute of Mental Health Diagnostic Interview Schedule
[h] Coronary care unit
[i] Zung Depression Scale
[j] Cardiovascular
[k] Structured Clinical Interview for DSM-IV
[l] Hamilton Rating Scale for Depression

Evidence Table 3.4B. Assessment of Depression in Studies on the Relation of Depression to Cardiac Events in Patients after Myocardial Infarction (Question 3)

Study Author, Year	No. Screened	No. Enrolled	Depression Instrument	Time of Baseline Assessment	Mean Follow-Up	Total Number at Enrollment		No. at Follow-Up	Total Number at Follow-Up	
						Depressed	Non Depressed		Depressed	Non Depressed
Irvine, 1999	969	703	Psychological questionnaire	After 2 wks [a] during post randomization	2 yrs [b]	634	NR [c]	NR	NR	NR
Frasure-Smith, 2000	337	222	Structured baseline interview	1 wk following admission	1 yr	260	588	NR	NR	NR
Druss, 2000	All patient discharged from acute care hospital with diagnosis of AMI [d]	NR	ICD-9CM [e]	During index admission	30 d [f]	NR	NR	NR	NR	NR
Shiotani, 2002	1828	1086	Zung [g]	Zung mailed within 3 mos [h] after the onset of AMI.	12 mos	438	604	1042	NR	NR
Strik, 2003	407	318	SCL-90 [i]	1 mo post-MI [j]	3-4 yrs post-MI	NR	NR	NR	NR	NR
Strik, 2004	NR	422	Baseline: SCID [k] Follow-up: 3 psychiatric self rating scales BDI[l], SCL-90,HADS [m]	1 mo post-MI	NR	63	143	NR	59	131

[a] Weeks
[b] Years
[c] Not reported
[d] Acute myocardial infarction
[e] The International Statistical Classification of Diseases and Related Health Problems
[f] Day

Evidence Table 3.4B. Assessment of Depression in Studies on the Relation of Depression to Cardiac Events in Patients after Myocardial Infarction (Question 3) (continued)

[g] Montreal Heart Attack Readjustment Trial
[h] Zung Self-Rating Depression Scale
[i] Months
[j] Symptom Checklist - 90
[k] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders IV
[l] Beck Depression Inventory
[m] Hamilton Anxiety and Depression Scale

Evidence Table 3.4C. Depression Assessment of Studies on the Relation of Depression to Quality of Life in Patients after Myocardial Infraction (Question 3)

Study Author, Year	No. Screened	No. Enrolled	Depression Instrument	Time of Baseline Assessment	Mean Follow-Up	Total Number at Enrollment		No. at Follow-Up
						Depressed	NonDepressed	
Travella, 1994	NR [a]	129	Present state examination - modified, HAM-D [b]	During hospitalization	12 months	18	52	70
Drory, 1998	NR	276	BDI [c]	7 days	3 - 6 months	NR	NR	276
Irvine, 1999	969	703	BDI symptom checklist	2 weeks	2 years	NR	NR	634
Ladwig, 1999	NR	552	Depressivitats-Skaln	17-21 days	6 months	74	466	376
O'Rourke, 1999	85	70	HADS [d]	3-5 days	6 months	12	58	55
Soejima, 1999	136	134	Depression Index	"soon after MI [e]"	NR	NR	NR	NR
Bogg, 2000	231	220	HADS (II) Global mood scale	3-4days	6 months	NR	NR	NR
Denollet, 2000	NR	322	Zung [e]	Within 2 months	5 years	NR	NR	299
Lane 2000	437	288	BDI	Within 15 days	4 months	89	199	263
Mayou, 2000	546	344	HADS	3 days	3 months, 12 months	51	293	224
Lane, 2001	437	288	BDI	Within 15 days	12 months	89	199	263

Evidence Table 3.4C. Depression Assessment of Studies on the Relation of Depression to Quality of Life in Patients after Myocardial Infraction (Question 3) (continued)

Study Author, Year	No. Screened	No. Enrolled	Depression Instrument	Time of Baseline Assessment	Mean Follow-Up	Total Number at Enrollment		No. at Follow-Up
						Depressed	NonDepressed	
Brink, 2002	144	134	HADS	Within 1week	5 months	NR	NR	114
Drory, 2002	NR	NR	BDI	1 week	3 months, 6 months & 5 years	NR	NR	209
Drory, 2003	NR	NR	BDI	1 week	5 years	NR	NR	62

[a] Not reported
[b] Hamilton Rating Scale for Depression
[c] Beck Depression Inventory
[d] Hospital Anxiety and Depression Scale
[e] Zung Self-Rating Depression Scale

Evidence Table 3.5A. Results of Studies on the Relation of Depression to Survival in Patients after Myocardial Infarction (Question 3)

Study Author, Year	Outcome Reported			Stat [a]	Depressed vs.[b] Non Depressed	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	Cardiac Mortality	Total Mortality	Other				
Ahern, 1990	NA [c]	NA	TM [d] or cardiac arrest at baseline	RR [e]	NR [f]	1.38 (CI [g] 0.99 - 1.93) p < 0.05	Previous MI [h], LVEF [h], 3-9 PVCs/min [i] at baseline ECG [h], Use of digitalis [h], Use of B-blocker [h], MI [j] transmural
Ladwig, 1991	Low: 0.9; Medium: 2.4; High: 7.5	NA	Sustained VT [k] admission	OR [l]	Mantel-Haenszel p<0.001	2.8 low/med depression, 4.9 low/high depression p=0.07	
Frasure-Smith, 1993		At 6 mos [m]	NA	HR [n]	5.74 (CI 4.61 - 6.87) p = 0.0006	4.29 (CI 3.14 - 5.44) p = 0.013	Previous MI [h], Killip Class
Frasure-Smith, 1999	NA	NA	Arrhythmia; MI recurrence; Revascularization; Any hard event	OR	CV death: 3.23 (CI 1.65 - 6.33); Arrhythmia 3.11 (CI 1.32 - 7.37); MI recurrence: 1.62 (CI 0.93 - 2.8); Any hard events: 1.97 (CI 1.25 - 3.13); Revascularization: 0.82 (CI 0.53 - 1.26)	3.66 (CI 1.68 - 7.99)**	Age, Smoking daily, LVEF [o] ≤ 35% men [h], LVEF < 35% women, BDI[p] > 10 [h], Killip >2, non Q wave MI [h]
Irvine, 1999	Sudden cardiac death	NA	NA	HR	AMI [q]: 0.52 (CI 0.15 - 1.76)	NR	Prev MI [h], CHF [r h], dyspnea/fatigue [h], social participation, social network contacts [h], BDI somatic [h], BDI affective [h]

Evidence Table 3.5A. Results of Studies on the Relation of Depression to Survival in Patients after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome Reported			Stat [a]	Depressed vs.[b] Non Depressed	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	Cardiac Mortality	Total Mortality	Other				
Denollet, 2000	Cardiac events	NA	QOL [s]: Poor perceived health at 5 yrs [t], Depressive effect	OR	NR	1.31 (CI 0.53 - 3.24) p=0.56	Hyperlipidemia [h], failure to quit smoking [h], LVEF ≤ 50%[h], Type D personality [h]
Lane, 2000	Dep [u]: 9%, NonDep [v]: 1%	Dep: 10.1%, NonDep: 8%	Dart Dartmouth chart	OR	NR	NR	Peel Index score [h], length of hospital stay [h], Killip class [h]
Welin, 2000	17%	24%	Non fatal recurrent MI; Stroke; Cancer	HR	TM: 2.45 (CI 1.49 - 4.02) ***, CM [w]: 3.54 (CI 1.85 - 6.79)***	TM 1.75 (CI 1.02 - 2.99)*, CM 3.16 (CI 1.38 - 7.25)***	Gender [h], Social support [h], LV failure [h], Ventricular dysrhythmia [h], Post-MI depression [h]
Bush, 2001	NA	Dep: 13%, NonDep: 4%	NA	RR	3.8 p=0.008	3.5 p=0.001	Age [h], EF [x] 35% [h], DM†, Killip class, Depression [h], CAD [y]
Druss, 2001	NA	NA	NA	HR	Mental: 1.19 (CI 1.04 - 1.36), Affective 1.11 (CI 1.03 - 1.18)	NR	Smoking cessation, ASA [z], ACE [aa], Lytics
Lane, 2001	10%	10%	QOL	OR	CM 1.15 (CI 0.49 - 2.69)	NR	Age [h], Peel index [h], Killip class [h],

Evidence Table 3.5A. Results of Studies on the Relation of Depression to Survival in Patients after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome Reported			Stat [a]	Depressed vs.[b] Non Depressed	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	Cardiac Mortality	Total Mortality	Other				
Lane, 2002	Dep: 10%	NA	NA	OR	TM: 1.04 (CI 0.5 - 2.16), CM: 0.84 (CI 0.37 - 1.90)	NR	Age [h], Killip class [h], Peel [h], Urban [h], Education [h], Beta-blocker [h]
Lesperance, 2002	< 5 yr: 7%; 5 - 9 yr: 14%; 10-18 yr: 19%; > 19 yr: 27%	44***; < 5 yr: 11%; 5 - 9 yr: 16%; 10-18 yr: 23%; > 19 yr: 33%	NA	HR	BDI 5 - 9: 1.94 (CI 1.16 - 3.25) p=0.01; BDI 10 - 18: 2.8 (CI 1.68 - 4.66) p<0.001; BDI > 19: 1.32 (CI 2.4 - 7.75) p<0.001	TM: BDI 10 - 18: 2.35 (CI 1.53 - 3.61)*** BDI ≥ 19 (CI 2.16 - 5.92)*** TM: BDI 10 - 18: 3.17 (CI 1.79 - 5.6)*** BDI ≥ 19: 3.13 (CI 1.56 - 6.27)***	Age [h], gender, HT h/o Rx [ab], smoking, previous MI [h], LVEF [h], Killip Class > 1, thrombolysis [h], Q wave MI, education < 8y, unmarried, revascularization [h], B blockers, Diabetes, BDI > 10
Carney, 2003	NA	NA	Non Fatal AMI	HR	NR	TM 2.4 (CI 1.2 - 4.7)** Non-Fatal AMI 1.2 (CI 0.7 - 2.0)*	Age [h], DM [h], Smoking (ever smoker)[h], LVEF < 50%[h], LVEF< 40%[h], Coronary bypass after index MI [h]

Evidence Table 3.5A. Results of Studies on the Relation of Depression to Survival in Patients after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome Reported			Stat [a]	Depressed vs.[b] Non Depressed	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	Cardiac Mortality	Total Mortality	Other				
Frasure-Smith, 2003	At 5 yr	NA	NA	HR	NR	1.44 (CI 91.17-1.78)***	Age [h], Female, Smoking, Previous MI [h], LVEF ≤ 35%[h], Killip Class > I, Social support, Thrombolysis at index admission [h], Q wave MI, Negative affectivity[h], Overt anger, Education < 8y, Revascularization of index admission [h], B-blocker at discharge [h], BDI - cognitive [h], BDI - somatic [h], Diabetic medicine at discharge [h]

[a] Comparison statistic
[b] Versus
[c] Not applicable
[d] Total mortality
[e] Risk ratio
[f] Not reported
[g] Confidence interval
[h] Significant at $p<0.05$
[i] Premature ventricular contractions per minute
[j] Myocardial infarction

Evidence Table 3.5A. Results of Studies on the Relation of Depression to Survival in Patients after Myocardial Infarction (Question 3) (continued)

[k] Ventricular tachycardia
[l] Odds ratio
[m] Months
[n] Hazard ratio
[o] Left ventricular ejection fraction
[p] Beck Depression Inventory
[q] Acute myocardial infarction
[r] Congestive heart failure
[s] Quality of life
[t] Years
[u] Depressed
[v] Non Depressed
[w] Cardiac mortality
[x] Ejection fraction
[y] Coronary artery disease
[z] Acetylsalicyclic Acid
[aa] Acute coronary event
[ab] History of hypertension treatment

Evidence Table 3.5B. Results of Studies on the Relation of Depression to Cardiac Events after Myocardial Infarction (Question 3)

Study Author, Year	Outcome			Stats [a]	Univariate Comparison	Multivariate Comparison	Independent Predictor Variables Adjusted for in the Multivariate Analyses
	Cardiac Events	Cardiac Mortality	Other				
Irvine, 1999	NR [b]	Sudden cardiac death 34 Other cardiac death 16	Vascular death 1, non-cardiac death 12	RR [c]	Depression not reported to be significant predictor of SCD [d] in univariate analysis	Amiodarone Group: BDI [e] somatic score 1.10(0.93,1.29) BDI cognitive-affective score 0.73 (0.52,1.01) Placebo Group: BDI somatic score 1.00(0.88,1.13) BDI cognitive-affective score 1.09(0.99,1.89)	Prev MI [f], prev CHF [g], dyspnea/fatigue, social participation, social network contacts
Frasure-Smith, 2000	Recurrent cardiac events (survived and nonsurvived reinfarctions), admission for unstable angina, arrhythmic deaths, survived cardiac arrests.	NA [h]	NA	OR [i]	Any cardiac event: 3.32 (1.69,6.53) Acute coronary syndrome 2.75 (1.32,5.72) Arrhythmic event: 3.65 (0.99,10.47)	Recurrent cardiac events 1.99(0.92,4.31)	Prev MI, Prescription of ACE-I [j] at discharge, previous depression, anxiety.
Druss, 2000	NA	Total mortality at 1 month	Likelihood of PTCA [k] or CABG [l] during index hospitalization	OR	Total Mortality 7.3% in patients with affective disorders compared to 10.8% in patients with no mental disorders.	Total Mortality 0.63 (p=0.2) in patients with affective disorders RR for use of PTCA and CABG in patients with affective disorders: PTCA: 0.51 CABG : 0.63	Age, gender, race/ethnicity, HT [m], DM[n], smoker, prev MI, LVEF [o], angina, pulse, discharged home, PTCA past yr, CABG past yr, SBP [p], CCF, anterior infarction, thrombolysis Rx [q], shock

Evidence Table 3.5B. Results of Studies on the Relation of Depression to Cardiac Events after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome			Stats [a]	Univariate Comparison	Multivariate Comparison	Independent Predictor Variables Adjusted for in the Multivariate Analyses
	Cardiac Events	Cardiac Mortality	Other				
Shiotani, 2002	Annual cardiac event rate 31.2% in Dep [r] patient and 23.9% in NonDep [s] patient. Cardiac events: Dep 138, NonDep 145; MI: Dep 19, NonDep 15; Arrhythmias: Dep 2, NonDep 1; RePTCA: Dep 94 ,NonDep 110 ; Heart Failure: Dep 7, NonDep 5; Angina: Dep 6, NonDep 5	Cardiac Mortality: Dep 4 NonDep 1	Readmission Dep: 34 NonDep: 26	OR	Cardiac Events: 1.46 (CI [t] 1.11 - 1.92)	Cardiac Events: 1.41(CI 1.04 - 1.92)	Age, gender, HT, DM, smoking, Killip Class ≥ 2, peak creatinine kinase, depressive symptoms
Strik, 2003	Non Fatal MI at 3-4 yrs [u]	Fatal MI at 3 - 4 yrs	Healthcare consumption at 3-4 yrs [v]	HR- cardiac events OR- Health care consumption	CI- Not reported as single variables. Healthcare Consumption: 1.61 (CI 1.00 - 2.57)	MI:CI 2.32 (1.04 - 5.18) ; Healthcare Consumption: 1.55 (CI 0.96 - 2.52)	Age> 58 yrs, LVEF≤50%, use of antidepressants

Evidence Table 3.5B Results of Studies on the Relation of Depression to Cardiac Events after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome			Stats [a]	Univariate Comparison	Multivariate Comparison	Independent Predictor Variables Adjusted for in the Multivariate Analyses
	Cardiac Events	Cardiac Mortality	Other				
Strik, 2004	Major cardiac events 1 mo - 3 yrs (included death/recurrent MI; increased health care consumption, > 6 visits at the cardiac outpatient clinic during follow up)	NA	Healthcare consumption 1m - 3 yrs	Depression as predictor of major cardiac event-HR; depression as predictor of health care consumption- OR	Cardiac events: 1.1(0.36,3.42) Healthcare Consumption1.66 (CI 0.90 - 3.07)	Cardiac Events: 0.88(0.26,2.93) Healthcare Consumption 1.98 (CI 1.0 - 3.93)	Age > 58 yrs, gender, smoking(current), LVEF < 50%, PTCA, thrombolysis

[a] Comparison statistic
[b] Not reported
[c] Risk ratio
[d] Sudden cardiac death
[e] Beck Depression Inventory
[f] Myocardial infarction
[g] Congestive heart failure
[h] Not applicable
[i] Odds ratio
[j] Angiotensin I converting enzyme
[k] Percutaneous coronary angioplasty
[l] Coronary artery bypass graft
[m] Hypertension
[n] Diabetes
[o] Left ventricular ejection fraction
[p] Systolic blood pressure
[q] Treatment
[r] Depressed
[s] Non-depressed
[t] Confidence interval
[u] Years
[v] Cardiac rehospitalization and/or frequent visits

Evidence Table 3.5C. Results of Studies on the Relation of Depression to Quality of Life in Patients after Myocardial Infarction (Question 3)

Study Author, Year	Outcome		Comparison Statistic	Univariate Comparison	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	QOL [a]	Other				
Travella, 1994	Johns Hopkins functioning inventory, Social functioning exam	NA [b]	Multivariate Rank	NR [c]	Social functioning exam with depression after baseline: f=1.85 (p=0.167); 3mos [d]: f=7.73 (p=0.1), 6mos f=4.38 (p=0.45) , 9mos: f=13.45 (p=0.001), 12mos f=7.94 (p=009)	NR
Drory, 1998	Frequency of sexual activity after MI at 3 - 6mos, Satisfaction with sexual activity after MI [e]	Depression	Pearson Correlation	Frequency of sexual activity -0.16 (p<0.01); Satisfaction with sexual activity -0.14 (p<0.01);	Frequency of sexual activity: -0.14(p<0.01); Satisfaction with sexual activity: -0.15(p<0.01))	Age, Race/ethnicity, Diabetes, Previous heart disease, Other medical conditions, Depression by BDI, Perceived health prior to MI, Frequency prior to AMI [f], Education,
Irvine, 1999	Social perception and help, daily living	Sudden cardiac death	Cox	OR [g]	NR	Prev MI, Prev CHF [h], Dyspnea/Fatigue, Social participation, Social network contacts
Ladwig, 1999	NA	Perception of angina pectoris	OR	NR	2.98 (CI [i] 1.50 - 5.90)	Age > 50years, SBP [j] > 160 mmHG [k], Pre-infarction angina, Recurrent infarction, SES [l], Stroke, Non-fatal cardiac events, Re-infarction, Cardiac surgery, Hospitalization for severe angina, Episode of unconsciousness

Evidence Table 3.5C. Results of Studies on the Relation of Depression to Quality of Life in Patients after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome		Comparison Statistic	Univariate Comparison	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	QOL [a]	Other				
O'Rourke, 1999	Illness perception questionnaire	NA	Regression ANOVA	NR	NR	Anxiety, Control, Consequences
Soejima, 1999	RTW [m]	NA	Logistic regression OR	OR	RTW Extroversion 3.72 (CI 1.33 - 10.4) Despressive Sx [n] in hospital 0.15 (CI 0.02 - 0.87)	Age, Gender (male), Extraversion, Depressive Sx in Hospital , Education, Occupation
Bogg, 2000	QOL after MI	NA	Regression	NR	Physical QOL male R^2=46, Physical QOL female R^2=27, Baseline anxiety R^2=54	NR
Denollet, 2000	Global mood scale, Health complaint scale	NA	Regression or OR	NR	Failure to quit smoking 2.3 (1.2 - 4.5); Depressive sx 3.3 (1.9 - 5.8); Type D personality 2.2 (1.2 - 3.8); EF [o] < 50% 2.0 (1.0 - 3.9); Hyperlipidemia 2.0 (1.1 - 3.4)	NR
Lane 2000	Dartmouth COOP [p] Charts, BDI [q]	NA	Correlation score	Gender R=0.31, Partner status R=0.24, Living alone R=0.20, Employment status R=0.18, Frequency of exercise R= -0.21, Duration of exercise R= -0.17 BDI R=0.37, State anxiety R=0.28, Treat anxiety R=0.32, Peel Index R =0.27, LOS [r] R=0.15	BDI R^2= 0.11 (p=0.0001), Partner status 0.05 (p=0.002), Peel Index 0.05 (p=0.001), State anxiety 0.02	BDI, Peel Index, Partner status, State anxiety

Evidence Table 3.5C. Results of studies on the Relation of Depression to Quality of Life in Patients after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome		Comparison Statistic	Univariate Comparison	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	QOL [a]	Other				
Mayou, 2000	SF-36 Score [s]	NA	HR [t]	Total mortality: NR; At baseline: 51.2(distressed), At baseline: 67.5(non distressed) p<0.05; At 3 mos: 38.7(distressed), At 3m: 62.3(non distressed) p<0.05; At 12 mos: 47.2(distressed), At 12 mos: 64.0(non distressed) p<0.05	Total mortality: NR	NR
Lane, 2001	NR	NA	Regression Correlation	Gender R=0.2, Partner status R=0.22, Living alone R=0.3, Employment status R=0.18, Frequency of exercise R= -0.18, BDI R=0.32, State anxiety R=0.28, Treat anxiety R=0.24, Peel Index R=0.29, Killip class R=0.15, LOS R=0.25	BDI 0.11, Living alone 0.07, Peel Index 0.07, State anxiety 0.03	BDI, Peel Index, Partner status, State anxiety
Brink, 2002	Physical Component SF-36, Mental Component SF-36	NA	Zero order Correlation	NR	Physical Component:-0.47; Mental Component: -0.66	HADS [u]-anxiety, Coping, Health complaints
Drory, 2002	Perceived health status	NA	Hierarchical Regression	NR	Psychological well being	Sense of coherence, Depression, Education, Social support

Evidence Table 3.5C. Results of studies on the Relation of Depression to Quality of Life in Patients after Myocardial Infarction (Question 3) (continued)

Study Author, Year	Outcome		Comparison Statistic	Univariate Comparison	Multivariate Comparison	Independent Variables Adjusted for in Multivariate Analyses
	QOL [a]	Other				
Drory, 2003	Perceived health status	NA	Regression	NR	NR	Health status, Concomitant health problems, Perceived health status

[a] Quality of life
[b] Not applicable
[c] Not reported
[d] Months
[e] Myocardial infarction
[f] Acute myocardial infarction
[g] Odds ratio
[h] Congestive heart failure
[i] Confidence interval
[j] Systolic blood pressure
[k] Millimeters of mercury
[l] Socio-economic status
[m] Return to work
[n] Symptoms
[o] Ejection fraction
[p] Dartmouth Primary Care Cooperative Information Project charts
[q] Beck Depression Inventory
[r] Length of stay
[s] Medical Outcomes Study 36-item short form questionnaire
[t] Hazard ratio
[u] Hospital Anxiety and Depression Scale

Evidence Table 3a.1. Characteristics of Studies on the Relation of Depression to Biomarkers in Patients After Myocardial Infarction (Question 3a)

Study Author, Year	Study Design	Target Population	Exclusion Criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Carney, 2001	Pro cohort [a]	Only MI [b] patients	Active suicidal ideation, h/o [c] of alcoholism/substance, cognitively impaired, life threatening medical illness, severe psychiatric disorder, physically unable to complete the interview, lived too far away, atrial fibrillation or flutter, implanted pacemaker	Multicenter,4	USA	Oct 1997 - Jan 2000	To determine if depression is associated with reduced heart rate variability in patients with a recent MI.
Kuijpers, 2002	Pro cohort	Only MI patients	Previous MI	NR [d]	Europe	NR	To investigate whether platelet function is increased in depressed patients with first MI using PF 4 [e] and B-TG [f] as markers compared with a group of non-depressed post-MI patients matched for age, sex, and size of MI.
Lesperance, 2004	Pro cohort	481 patients with ACS [g] 81.7% with MI Data for MI not reported seperately.	Terminally ill < 2 years, cognitively impaired, non French speaking, ACS secondary to medical illness, too far from intervention site, using antibiotics	Multicenter,2	Canada	Aug 1999 - Aug 2001	To determine whether or not depression is associated with higher levels of inflammatory markers in patients recovering from acute coronary syndromes.

[a] Prospective cohort study
[b] Myocardial infarction
[c] History of
[d] Not reported
[e] Platelet factor 4
[f] Beta-thromboglobulin
[g] Acute coronary syndrome

Evidence Table 3a.2. Patient Characteristics of Studies on the Relation of Depression to Biomarkers in Patients After Myocardial Infarction (Question 3a)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	Married (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Killip Class (I-IV) (%)	Mean Ejection Fraction	H/o [d] Depression (%)
Carney, 2001	Dep: 307, NonDep: 366	Dep: 57, NonDep: 4	Dep: 50, NonDep: 68	Dep: 57, NonDep: 77	Dep: 22, NonDep: 20	Dep: 35, NonDep: 22	Dep: 41, NonDep: 23	NR [e]	NR	Dep: 46, NonDep: 47	NR
Kuijpers, 2002	Dep: 12, NonDep: 12	Dep: 48, NonDep: 50	Dep: 95, NonDep: 95	NR	Dep: 8, NonDep: 50	NR	Dep: 42, NonDep: 25	NR	NR	NR	NR
Lesperance, 2004	NonDep: 446, Dep: 35	NonDep: 60, Dep: 57	NonDep: 82, Dep: 66	NR	NonDep: 66, Dep: 66	NonDep: 32, Dep: 43	NonDep: 14, Dep: 43	NonDep: 48, Dep: 74	NR	EF[f] < 45%, NonDep: 28%[g] Dep: 31%	NonDep: 15, Dep: 40

[a] Hypertension
[b] Diabetes
[c] Hyperlipidemia
[d] History of
[e] Depressed
[f] Non-depressed
[g] Not reported
[h] Ejection fraction
[i] N=434

Evidence Table 3a.3. Assessment of Study Quality in Studies on the Relation of Depression to Biomarkers in Patients After Myocardial Infarction (Question 3a)

Study Author, Year	Representativeness	Description of Therapy & Management	Description of Assessment Protocol	Outcomes and Follow-Up	Statistical Analyses	Conflicts
Carney, 2001	80%	17%	100%	58%	75%	79%
Kuijpers, 2002	40%	50%	100%	50%	75%	75%
Lesperance, 2004	90%	33%	100%	50%	0%	75%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 12 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), whether the cardiac outcome measures were defined (2 points), whether the depression outcome measures were defined (2 points), whether the same tools for diagnosing depression were used for baseline and follow-up (2 points) and the planned length of follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether the magnitude of the difference for primary endpoints or magnitude of association between outcomes and index variability is reported (2 points) and whether adjustment was made for confounding (2 points).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 3a.4. Depression Characteristics of Studies on the Relation of Depression to Biomarkers in Patients after Myocardial Infarction (Question 3a)

Study Author, Year	No. Screened	No. Enrolled	Depression Instrument	Time of Baseline Assessment	Mean Follow-Up	Total Number at Enrollment		Total Number at Last Follow-Up		No at Follow-Up
						Dep [a]	NonDep [b]	Dep	NonDep	
Carney, 2001	NR [c]	Dep 380 NonDep 424	Screening: ENRICHD [d] modified DSM-IV [e] DISH [f]: present depressive episode BDI [g]: severity of depression	Recent acute MI [h] (≤28 d[i])	NA [j]	307	366	NA	NA	NA
Kuijpers, 2002	NR	NR	DSM-IV	3-6 mos [k] after first MI	NA	12	12	NR	NR	NA
Lesperance, 2004	2716	965	SCID [l]	2 mos after hospital discharge	NA	35	446	NR	NR	NA

[a] Depressed
[b] Non-depressed
[c] Not reported
[d] Enhancing Recovery in Coronary Heart Disease
[e] Diagnostic & Statistical Manual of Mental Disorders
[f] Depression Interview and Structured Hamilton
[g] Beck Depression Inventory
[h] Myocardial infarction
[i] Day
[j] Not applicable
[k] Months
[l] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders-IV

Evidence Table 3a.5. Results of Studies on the Relation of Depression to Biomarkers in Patients after Myocardial Infarction (Question 3a)

Study Author, Year	Outcome: Biomarkers	Comparison Statistic	Depressed vs [a] Non-Depressed	Multivariate Comparison	Independent Predictor Variables Adjusted for in the Multivariate Analyses	Comments
Carney, 2001	In univariate analysis all 4 indicies of 24 hour HRV [b] were significantly lower in patients with depression. In multi-variate analysis all 3 indices except 24 hour HRV were significantly lower in patients with depression.	Linear regression	NR [c]	NR	Age, Gender, Diabetes smoking status.	Patients assessed for depression after excluding patients with score ≥10 on Orientation Memory concentration test. The ENRICHD [d] modified DSM-IV[e] criteria allowed to be eligible if depressive symptoms present for atleast 7 days provided if patient had atleast one prior depressive episode.
Kuijpers, 2002	PF4 [f] was significantly higher in depressed post MI patients compared to non-depressed post MI patients, p=0.021. There was a trend toward a significantly increased B-TG [g] level with p=0.08, inspite of use of aspirin	Mann-Whitney U	PF4 mean rank 15.75 IU/ml vs 9.25 IU/ml B-TG mean rank 15.04 IU/ml vs 9.96 IU/ml	NR	Age, Gender, Size of MI	No patients with diabetes, renal or hepatic failure. Small sample size Depressed patients did not use any anti-depressant medication. All patients were treated with anti hypertensive medications.
Lesperance, 2004	Depressed patients had significantly higher sICAM-1 [h] levels even after adjustment for confounders. These results were only slightly attenuated by adjustment of antidepressant treatment. No significant association between depression and IL6 [i]. Uncertain about the relationship of CRP [j] on depression as patients were on statins.	Linear regression	NR	sICAM 0.095+/-0.044 (with depression) 0.086+/-0.045 (with antidepressant added to the model)	Gender [k], Smoking [k], Metabolic syndrome [k]	Results derived from single blood sample with no inferences about the time course of inflammatory markers in relationship to cardiac event Higher non response rate.

Evidence Table 3a.5. Results of Studies on the Relation of Depression to Biomarkers in Patients after Myocardial Infarction (Question 3a) (continued)

[a] Versus
[b] Heart rate variability
[c] Not reported
[d] Enhancing Recovery in Coronary Heart Disease Trial
[e] Diagnostic & Statistical Manual of Mental Disorders
[f] Platelet factor 4
[g] Beta thromboglobulin
[h] Serum levels of soluble anti-intercellular adhesion molecule-1
[i] Interleukin 6
[j] C-reactive protein
[k] Significant at $p < 0.05$

Evidence Table 4.1. Characteristics of Studies of Treatment of Post-Myocardial Infarction Depression (Question 4)

Study Author, Year	Study Design	Target Population	Exclusion criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Dracup, 1991	Pro cohort [a]	141 patients with CABG [b] 69% with MI [c] No separate data for MI patients provided	A [d] < 25 or ≥ 80; h/o [e] psychosis; bipolar disorder; non-English speaking; MI/CABG > 12 mos	Multicenter, 6	USA	May 1985 - Apr 1989	To compare the psychosocial adaptation of patients who participated in a multidimensional cardiac rehabilitation program with that of patients who did not.
Brown, 1993	RCT [g]	81 patients with ACS[h] included 62.5% with MI No separate data for MI patients provided	A < 43 or > 75; unstable medical condition; severe depression status before cardiac event; suicidal ideation; changes in county residence; unwilling/unable to include partner	Multicenter, 5	USA	May 1994 - Dec 1997	To evaluate effectiveness of behavior therapy for treating distress in patients diagnosed with depression and/or anxiety after an MI or CABG.
Crowe, 1996	RCT	Only MI patients	A > 73; non-English speaking; unable to complete questionnaire; unable to exercise with cycle ergometer/treadmill at low levels/limited by musculoskeletal; neurological/other medical conditions	Multicenter, 6	Canada	Mar 1985 - Apr 1988	To assess patients for symptoms of anxiety and depression while they were hospitalized for acute MI and to describe the occurrence of symptoms of anxiety and depression in a selected group of patients during the first year after the acute MI.
Frasure-Smith, 1997	RCT	Only MI patients	Life-threatening conditions; cognitively impaired; residence from study hospital > 20 miles; deafness; refusal by patient physician; participation in other trials; no telephone; non-English/non-French speaking	Multicenter, 10	Canada	Jan 1991 - Sep 1994	To find out whether a program of monthly screening for psychological distress combined with supportive and educational home nursing interventions for distressed patients would reduce 1-year cardiac mortality for men and women.

Evidence Table 4.1. Characteristics of Studies of Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Target Population	Exclusion criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Taylor, 1997	RCT	Only MI patients	A > 70; serious comorbid conditions; non-English speaking; substance abuse/other psychological problems	Multicenter, 5	USA	1988 - 1991	To assess effects of a nurse-case managed, mutlifactorial risk reduction program on psychological distress among post-MI patients.
Roose, 1998	RCT	81 patients with ACS included 62.5% with MI No separate data for MI patient provided	MI within 3 mos; QTc [i] > 460 ms; taking class I antiarrhythmic; taking warfarin; unstable angina/cressendo	Multicenter, 4	USA	Not specified	To compare the efficacy, cardiovascular effects and safety of an SSRI [j](paroxetine) with a tricyclic antidepressant (nortriptyline hydrochloride) in depressed patients with ischemic heart disease.
Johnston, 1999	RCT	Only MI patients	A > 70; non-English speaking; unable to give informed consent	Single center	Europe	Jan 1992 - Feb 1983	To see after a first MI, whether patients who receive an inpatient cardiac rehabilitation demonstrate equal or greater benefit than those receiving normal care or an extended program.
Strik, 2000	RCT	Only MI patients	A < 18 or > 75; hepatic dysfunction; other significant non-reactive disease; psychosis; bipolar disorder; organic brain syndrome; dementia; serious comorbidity; pregnant or lactating; use of psychotropic drugs; right ventricular filling pressure > 30 mmHg; ATVI [k]< 20 cm; hypersensitivity to fluoxetine	Multicenter, 2	Europe	May 1994 - Dec 1997	To investigate the efficacy and safety of the anti-depressant fluoxetine in patients with depression after their first MI.
McFarlane, 2001	RCT	Only MI patients	CHF [l]; life threatening illness; inability to complete questionnaire; already on antidepressants; 24 hour pre-discharge holter monitoring with AF [m]/ventricular ectopic beat > 100/hour	Single center	Canada	Sep 1996 - Mar 1999	To determine whether sertraline, an SSRI, facilitates rate of recovery of cardiac autonomic function after an acute MI in patients with depression

Evidence Table 4.1. Characteristics of Studies of Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Target Population	Exclusion criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Glassman, 2002	RCT	369 patients with ACS 79.67%,with MI No separate data for MI provided	Anticipating cardiac surgery within 6m; index ACS < 3 mos after surgery; resting HR [n] < 40/min; Killip Class > III; uncontrolled HTN [o]; persistent clinically significant abnormalities; renal dysfunction; hepatic dysfunction; other significant noncardiac illness; anemia; cocaine use; alcohol or substance abuse; women of childbearing potential not using adequate contraception; psychosis; bipolar disorder; organic brain syndrome; dementia; significant suicide risk; terminally ill; MMSE [p] < 23; concomitant Rx [q] with class I anti-arrhythmic	Multicenter, 40	USA Canada Europe Australia	Apr 1997 - Apr 2001	To evaluate safety and efficacy of sertraline treatment of MDD [r] in patients hospitalized for MI or unstable angina and free of other life threatening illness.
Berkman, 2003	RCT	Only MI patients	Noncardiac conditions fatal within 1y; too ill to participate; participating in another protocol; major psychiatric comorbidity; imminent risk for suicide; physician disallowed participation; receiving psychotherapy for depression; MI following PCI [s] or CABG	Multicenter, 8	USA	Oct 1996 - Oct 1999	To determine whether mortality and recurrent infarction are reduced by treatments of depression and LPSS [t] with cognitive behavior therapy, supplemented with SSRI when indicated, in patients enrolled within 28 days after MI.

Evidence Table 4.1. Characteristics of Studies of Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Study Design	Target Population	Exclusion criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Swenson, 2003	RCT	Included cases of MI and unstable angina. Patients of unstable angina not recruited till 1998 No separate data for MI provided	Anticipating cardiac surgery; index ACS < 3 mos after surgery; non-atherosclerotic MI; Killip Class > III; uncontrolled HTN; persistent clinically significant abnormalities; renal dysfunction; hepatic dysfunction; other significant cardiac disease; women of childbearing A not using adequate contraception; alcohol or substance abuse; psychosis; bipolar disorder; organic brain syndrome; dementia; resting HR < 40/min; Rx with class I antiarrhythmic; reserpine; guanethidine; clonidine; methyldopa; anticonvulsants; neuroleptics; antidepressant; regular benzodiazepine; initiation of psychotherapy in 3m prior to study entry	Multicenter, 7 countries 40 outpatient cardiology centers and psychiatry clinics	USA, Canada, Europe, Australia	Apr 1997 - Apr 2001	To examine the effect of sertraline treatment on quality of life and functioning in patients diagnosed with major depression who had been recently hospitalized for acute MI or unstable angina.

[a] Prospective cohort study
[b] Coronary artery bypass graft
[c] Myocardial infarction
[d] Age
[e] History of
[f] Months
[g] Randomized controlled trial
[h] Acute coronary syndrome
[i] QT Interval corrected for heart rate
[j] Selective serotonin reuptake inhibitor
[k] Aortic time velocity integral
[l] Congestive heart failure
[m] Atrial fibrillation
[n] Heart rate
[o] Hypertension

Evidence Table 4.1. Characteristics of Studies of Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

[p] Mini Mental State Evaluation
[q] Treatment
[r] Major depressive disorder
[s] Percutaneous Coronary Intervention
[t] Low perceived social support

Evidence Table 4.2. Characteristics of Patients in Studies of Treatment of Post-Myocardial Infarction Depression (Question 4)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	Married [a] (%)	Education [b] (%)	Employed [c] (%)	HTN [d] (%)	DM [e] (%)	Smoking (%)	Lipid [f] (%)	Killip Class (%)	Mean Ejection Fraction (%)	H/o [g] Dep (%)
Dracup, 1991	41[h]; 100[i]	63[h]; 63[i]	93[h]; 88[i]	NR	95[h]; 97[i]	34[h]; 15[i]	39[h]; 46[i]	NR	NR	NR	NR	NR	NR	NR
Brown, 1993	20[i]; 20[j]	63i; 58[j]	55i; 90[j]	100i; 100[j]	90[i]; 85[j]	100[i]; 100[j]	NR	NR	NR	NR	NR	NR	NR	NR
Crowe, 1996	99[j]; 102[i]	55	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Frasure-Smith, 1997	692[k]; 684[l]	59[k]; 59[l]	66k; 65[l]	NR	NR	NR	NR	Reported HTN Rx[m]: 37[k]; 34[l]	NR	49[k]; 50[l]	NR	Class I: 63[k], 66l; Class II: 16[k]; 14[l]; Class III - IV: 21[k]; 20[l]	49[k], 49[l] EF[n] ≤ 35%: 16[k]; 16[l]	NR
Taylor, 1997	199[s]; 179[l]	57[s]; 57[l]	80[s]; 75[l]	76[s]; 80[l]	78[s]; 82[l]	NR	Full time: 74[s]; 69[l]	NR	NR	41[s]; 39[l]	NR	NR	NR	NR
Roose, 1998	41[r]; 40[t]	58[r]; 58[t]	88[r]; 78[t]	NR	NR	NR	NR	NR	NR	NR	NR	NR	58[r]; 60[t]	73[r]; 67[t]
Johnston, 1999	29k; 38[l]; 33[l]	57[k]; 54[l]; 57[l]	67[k]; 71[l]; 59[l]	NR	NR	100[k]; 100[l]; 100[l]	NR	NR	NR	48[k]; 74[l]; 61[l]	NR	NR	NR	NR
Strik, 2000	27[v]; 27[p]	54[v]; 59[p]	77[v]; 62[p]	NR	NR	NR	NR	NR	NR	NR	NR	NR	51[v]; 51[u]	NR
McFarlane, 2001	12[r]; 15[t]	56[r]; 56[t]	67[r]; 53[t]	NR	NR	NR	NR	50[r]; 38[t]	30[r]; 23[t]	58[r]; 67[t]	NR	NR	53[r]; 58[t]	NR
Glassman, 2002	186[w]; 183[u]	57[w]; 58[u]	63[w]; 64[u]	74[w]; 79[u]	NR	NR	NR	61[w]; 69[u]	31[w]; 30[u]	27[w]; 28[u]	70[w]; 67[u]	Class II-IV: 7.1[w]; 7.1[u]	54[w]; 52[u]	52[w]; 50[u]
Berkman, 2003	1238[s]; 1243[l]	61[s]; 61[l]	57[s]; 56[l]	67[s]; 66[l]	53[s]; 51[l]	48[s]; 46[l]	NR	60[s]; 61[l]	32[s]; 33[l]	64[s]; 65[l]	58[s]; 56[l]	Class III - IV 7[s]; 7[l]	NR	NR
Swenson, 2003	184[r]; 183[u]	57[r]; 58[u]	63[r]; 64[u]	74[r]; 79[u]	55[r]; 72[u]	73[r]; 69[u]	38[r]; 38[u]	61[r]; 69[u]	30[r]; 31[u]	78[r]; 74[u]	69[r]; 67[u]	Class II - IV 7.0[r]; 7.1[u]	54[r]; 52[u]	NR

[a] Married or living with a partner
[b] Education high school or higher

Evidence Table 4.2. Characteristics of Patients in Studies of Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

[c] Employment full-time or part-time
[d] Hypertension
[e] Diabetes mellitus
[f] Hyperlipidemia
[g] History of
[h] Cardiac rehabilitation
[i] Usual care
[j] Rehabilitation
[k] Psychosocial intervention
[l] Behavioral intervention
[m] Treatment
[n] Ejection fraction
[o] Usual care, no supportive therapy
[p] Extended cardiac counseling
[q] Inpatient cardiac counseling
[r] Intervention
[s] Paroxetine
[t] Nortriptyline
[u] Placebo
[v] Fluoxetine
[w] Sertraline

Evidence Table 4.3. Assessment of Study Quality in Studies of Treatment of Post-Myocardial Infarction Depression (Question 4)

Article ID	Representativeness	Bias and Conflict	Description Therapy and Management	Description Protocol	Outcomes and Follow-Up	Statistical Analyses	Conflicts
Dracup, 1991	35%	33%	34%	34%	34%	34%	34%
Crowe, 1996	80%	38%	59%	48%	53%	51%	52%
Frasure-Smith, 1997	85%	88%	86%	87%	87%	87%	87%
Roose, 1998	70%	58%	64%	61%	63%	62%	62%
Johnston, 1999	60%	88%	74%	81%	77%	79%	78%
McFarlane, 2001	75%	88%	81%	84%	83%	84%	83%
Berkman, 2003	100%	63%	81%	72%	77%	74%	75%
Swenson, 2003	90%	100%	95%	98%	96%	97%	97%
Brown, 1993	70%	75%	73%	74%	73%	73%	73%
Taylor, 1997	70%	50%	60%	55%	58%	56%	57%
Strik, 2000	85%	83%	84%	84%	84%	84%	84%
Glassman, 2002	95%	88%	91%	89%	90%	90%	90%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Bias and Confounding: Percentage score was based on a total maximum score of 6 points. This included assessment of whether patients were randomly assigned to study groups (2 points), wether patient groups had important differences in patient characteristics (2 points), and whether there was blinding of test interpretation (2 patients)

Description of Therapy: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), whether there was adequate description of other treatments given (2

Evidence Table 4.3. Assessment of Study Quality in Studies of Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

points), whether description of the flow of participants was adequate (2 points), and whether assessment of adherence to therapy was given.

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 12 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), whether cardiac outcome measures were defined (2 points), whether depression outcome measures were defined (2 points), whether the same tools for diagnosing depression were used for baseline and follow-up (2 points), whether the length of follow-up was planned (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether adjustment was made for confounding (2 points), and whether confidence intervals were reported (2 patients).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 4.4. Results of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4)

Study Author, Year	Random [a]	Meds SSRI [b]	Psycho-therapy	Cardiac Rehabilitation	Duration of Interven-tion	Duration of FU [c]	Drop-Out Rate	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Dracup, 1991	NA [d]	NA	NA	A: Cardiac Rehabilitation Program B: No participation to a formal program	12 wks [e]	6 mos [f]	NR [g]	Multiple Affective Adjective Checklist @ 6mos A: 8 , B: 13	NA	Multiple Affective Adjective Checklist Anxiety A: baseline 7, 6 mos 5; B: baseline 7, 6 mos 6; Psychosocial adjustment to Illness A: baseline 42, 6 mos 36; B: baseline 44; 6 mos 42; Marital Adjustment A: baseline 115, 6 mos 121; B: baseline 114; 6 mos 111
Brown, 1993	4 to 24 mos	NA	C: Cognitive Behavioral Therapy; D: Control	NA	C: 12 wkly 1-hr sessions; D: 12 wkly 1-hr sessions	C: 3, 9, 15mos; D: 3, 9, 15 mos	NR	SCL 90-R C: pre 65.1, 3 mos 62.1, 15 mos 56.1; D: pre 71.2, 3 mos 62.3, 15 mos 63.3; BDI C: pre 12.1, 3 mos 6.9, 15 mos 5.6; D: pre 17.3, 3 mos 9.4, 15 mos 10.5; MMPI-168 C: pre 74.1, 3 mos 68.1, 15 mos 67.5; D: pre 79.2, 3 mos 72.8, 15 mos 77.4	NA	NA

Evidence Table 4.4. Results of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Random [a]	Meds SSRI [b]	Psycho-therapy	Cardiac Rehabilitation	Duration of Interven-tion	Duration of FU [c]	Drop-Out Rate	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Crowe, 1996	6 wks	NA	NA	NA	NR	1 yr [k]	18%	BDI E: 3 d 4.1, 3 mos 3.3, 6 mos 2.6, 14 mos 3.2; F: 3 d 3.9, 3 mos 3.7; 6 mos 3.3, 14 mos 2.9;	NA	NA
Frasure-Smith, 1997	NR	NA	NA	G: Intervention that involved a combination of emotional support, reassurance, education, practical advice & health resources. H: usual care	1 yr	12 mos	6.5%	BDI G: baseline 8.1, 12 mos 6.9; H: baseline 8.4, 12 mos 7.6	Cardiac Mortality G: 4.8%; H: 3.4%; MI [l] G: 4.8%; H: 5%; Revascularization G: 13.4%; H: 14%	Total Mortality G: 5.5%, H: 3.9%

Evidence Table 4.4. Results of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Random [a]	Meds SSRI [b]	Psycho-therapy	Cardiac Rehabilitation	Duration of Interven-tion	Duration of FU [c]	Drop-Out Rate	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Taylor, 1997	Day 3 or as soon as their medical condition stabilized	NA	NA	I: Nurse-managed, home-based system for coronary risk factor modification and stress management. J: Usual medical care	1 yr	Upto 1 yr	I: 29%; J: 37%	Low levels depressed mood I: baseline 1.7, 12 mos 1.3; J: baseline 1.8, 12 mos 1.2; Moderate-high levels depressed mood I: baseline 6.1, 12 mos 1.4; J: baseline 5.7, 12 mos 1.5	Mortality I: 4%; J: 3%	Low levels anxious mood I: baseline 1.9, 12 mos 1.4; J: baseline 1.5, 12 mos 1.5; Moderate-high levels anxious mood I: baseline 6.1, 12 mos 2.6; J: baseline 5.9, 12 mos 2.7; Low levels stress I: baseline 2.0, 12 mos 1.7; J: baseline 2.0; 12 mos 1.8; Moderate-high levels stress I: baseline 6.4, 12 mos 2.8; J: baseline 6.7, 12 mos 3.7; Low anger frequency I: baseline 2.8, 12 mos 2.2; J: baseline 2.6, 12 mos 2.2; Moderate-high anger frequency I: baseline 5.6, 12 mos 3.1; J: baseline 5.6, 12 mos 3.0

Evidence Table 4.4. Results of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Random [a]	Meds SSRI [b]	Psycho-therapy	Cardiac Rehabilitation	Duration of Interven-tion	Duration of FU [c]	Drop-Out Rate	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Roose, 1998	NS	K: Paroxe-tine 10-20mg/ day, L: Nortrip-tyline 25mg/ day	NA	NA	2 wks	6 wks	NR	Heart rate K: baseline 10%, 6 wks 6%; L: baseline 11%, 6 wks 7%; Standing pulse rate standing K: baseline 11%, 6 wks 11%; L: baseline 14%, 6 wks 16%; Supine pulse rate supine K: baseline 10%, 6 wks 10%; L: baseline 12%, 6 wks 14%; HRV SDNN K: baseline 37%, 6 wks 27; L: baseline 19%, 6 wks 16%; HRV pNN50 K: baseline 10%, 6 wks 4%; L: baseline 9%, 6 wks 7%	NA	NA

Evidence Table 4.4. Results of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Random [a]	Meds SSRI [b]	Psycho-therapy	Cardiac Rehabilitation	Duration of Interven-tion	Duration of FU [c]	Drop-Out Rate	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Johnston, 1999	Within 72 hrs	NA	NA	M: Extended program involving additional sessions in the 2m after discharge. N: Inpatient cardiac rehabilitation program O: Control	6 wks	Up to 1 yr	NR	HADS M: baseline 4.1, 12 mos 3; N: baseline 4.4, 12 mos 3.6; O: baseline 4.6, 12 mos 5.8	NA	HADS Anxiety M: 1 mo 4.8, 12 mos 3; N: 1 mo 5, 12 mos 4.5; O: 1 mo 5; 12 mos 6
Strik, 2000	3 - 12 mos	A: Fluoxe-tine 20mg/ day; B: Placebo	NA	NA	Maximum 25 wks	Up to 1 yr	A: 33%; B: 19%	HAMD change @ 25 wks Group P: -9.65(7.2), Group Q: -6.9(6.9)	NA	Chest Pain A: 5; B: 4 GI Complaints A: 8; B: 6; Agitation A: 6; B: 3; Other A: 17; B: 12; Rehospitalization A: 1; B: 6 Decrease in ATVI A: 8; B: 0; QRS interval decrease A: 15; QRS interval increase B:9

Evidence Table 4.4. Results of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Random [a]	Meds SSRI [b]	Psycho-therapy	Cardiac Rehabilitation	Duration of Interven-tion	Duration of FU [c]	Drop-Out Rate	Depression Scores	Cumulative Cardiac Events	Other Outcomes
McFarlane, 2001	At discharge from MI	Sertra-line 50mg daily, Placebo daily	NA	NA	6 mos	6 mos	29%	NR	NA	SDNN(SEM) at 1.5 mos A:119 (10), B:103 (7.9), SDNN(SEM) at 5.5 mos A: 121 (17), B: 86 (10) RMSSD(SEM) at 1.5 mos A: 28.8 (4,7), B: 26.7 (3); RMSSD(SEM) at 5.5 mos A: 30 (7.1), B: 23.7 (5.7); LF/HF ratio at 1.5 mos A: 1.34 (0.15), B: 1.62 (0.22)
Glassman, 2002	33.7 (9.9) days	A: Sertra-line 50mg/d daily; B: Placebo daily	N/A	N/A	149.5 for sertraline and 153.8 days for placebo group	24 wks	A: 18%; B: 12%	CGI - 1 mean score A: 2.57, B: 2.75; HAM-D mean change in score at 6 mos A: -8.4, B: -7.6	MI A: 5, B: 7; Congestive heart failure A:5, B:7 Angina A:26, B:30	Total Mortality A: 2; B: 5; Composite End-point A: 32, B:41

Evidence Table 4.4. Results of Studies on Treatment of Post-Myocardial Infarction Depression (Question 4) (continued)

Study Author, Year	Random [a]	Meds SSRI [b]	Psycho-therapy	Cardiac Rehabilitation	Duration of Interven-tion	Duration of FU [c]	Drop-Out Rate	Depression Scores	Cumulative Cardiac Events	Other Outcomes
Berkman, 2003	Within 28 days	Sertra-line 50mg/d	A: Usual care B: Cognitive behavioral therapy, Social problem solving, plus SSRI certain conditions	NA	180 days	A: 18 mos; B: 18 mos	NR	BDI change (baseline- at 6 mos) A: -5.8(8.9), B -8.6(9.2) HRSD change (baseline- at 6 mos) A: -8.4(7.7) B -10.1(7.8)	Cardiac Mortality A: 115 (9.3%); B: 96 (7.8%); MI (recurrent non-fatal) A: 170 (13.7%); B: 168 (13.6%), Revascularization A: 230 (18.5%); B: 216 (17.4%)	Total Mortality A: 172 (13.8%); B: 168 (13.6%); Cardiovascular hospitalization A: 467 (37.6%); B: 442 (35.7%)
Swenson, 2003	A: 34 B: 34	A: Sertra-line 50mg/daily; B: Place-bo daily	NA	NA	24 wks	A: 18 mos; B: 18 mos	NR	HAMD score change at 16 wks A: -8.4(0.4) B:-7.6(0.4) BDI score change at 16 wks A:-8.0(0.6) B:-7.3(0.6)	NR	SF-36 Mental component change score A:17.4 B:15.2 Physical component change score A:10.6 B:10.1

[a] Time to randomization after myocardial infarction
[b] Medications selective serotonin reuptake inhibitor
[c] Follow-up
[d] Not applicable
[e] Weeks
[f] Months
[g] Not reported
[h] Symptom Checklist 90
[i] Beck Depression Inventory
[j] Minnesota Multiphase Personality Inventory
[k] Year
[l] Myocardial infarction

Evidence Table 5.1. Characteristics of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5)

Study Author, Year	Study Design	Exclusion Criteria	Study Site	Recruitment Period	Study Objective	Number of Subjects	Mean Age	Males (%)
Davis, 1988	Pro cohort [a], single center	Age > 65; psychiatric treatment	Canada	NR [b]	To identify optimal methods of detecting depression in medically ill subjects.	52	51	90
Martin, 2000	Cross-sectional, single center	Non-English speaking	Europe	NR	To determine the utility of HADS [c] in acute MI [d] patients by examination of the instrument's underlying factor structure.	194	63.4	73
Wojciechowski, 2000	Pro cohort, single center	Age < 18 or > 75; previous MI	Europe	May 1994 - Jan 1996	To investigate whether or not depression and vital exhaustion are separate entities.	143	57.8	81
Strik, 2001	Cross-sectional, single center	Recurrent MI	Europe	May 1997 - Sep 1999	To assess sensitivity and specificity of 3 self-report questionnaires and one observer rating scale as screening instruments for major and minor depression following first MI.	206	59.9	76
Freedland, 2002	Pro cohort	AMI [e] post CABG [f]/invasive procedure; significant other medica/major psychiatric comorbidity; psychiatric medications/ psychotherapy	USA	Oct 1996 - Oct 1999	To evaluate the effects of a psychosocial intervention on cardiovascular morbidity and mortality in post-MI patients exhibiting depression and/or social isolation.	2404	61	56
Martin, 2003	Pro cohort, multi-center	NR	Europe	NR	To determine the factor structure of the HADS in a clinical population following MI and to determine change-sensitivity characteristics and psychometric reliability of the HADS in this patient group.	335	67.4	67

[a] Prospective cohort

Evidence Table 5.1. Characteristics of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5) (continued)

[b] Not reported
[c] Hospital Anxiety and Depression Scale
[d] Myocardial infarction
[e] Acute myocardial infarction
[f] Coronary artery bypass graft

Table 5.2. Assessment of Study Quality in Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5)

Study Author, Year	Representativeness	Bias and Confounding	Assessment of Therapy and Management	Description of Assessment Protocol	Test/ Interpretation	Outcomes and Follow-Up	Statistical Analyses	Conflicts of Interest
Davis, 1988	46%	50%	0%	58%	33%	50%	25%	0%
Wojciechowski, 2000	75%	67%	42%	58%	71%	100%	100%	0%
Martin, 2003	71%	0%	8%	100%	33%	75%	100%	0%
Martin, 2000	75%	40%	0%	17%	42%	0%	100%	50%
Strik, 2001	83%	40%	0%	67%	50%	N/A	100%	0%
Freedland, 2002	100%	60%	0%	50%	17%	100%	50%	100%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Bias and Confounding: Percentage score was based on a total maximum score of 10 points. This included assessment of whether the decision to obtain the reference test was affected by results of the study instrument (2 points), whether there was blinding of test interpretation (2 patients), whether interpretation of the study test was performed by two or more independent observers (2 patients), whether interpretation of the reference test was performed by two or more independent observers (2 points), and whether the reference standard and study test were measured before interventions were started with knowledge of test results (2 points).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Test Interpretation: Percentage score was based on a total maximum score of 12 points. This included assessment of the description of interpretation criteria of the study test for depression (2 points) and of the reference test (2 points), whether individuals receiving the study test also received the reference test (2 points), whether a summary index of test performance and index of variability was reported for the study test (2 points), whether methods for calculating test reproducibility were described (2 patients), and whether authors described how indeterminate results were handled (2 patients).

Table 5.2. Assessment of Study Quality in Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5) (continued)

Outcomes and Follow-up: Percentage score was based on a total maximum score of 6 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), and whether the same tools for diagnosing depression were used for baseline and follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether adjustment was made for confounding (2 points), and whether confidence intervals were reported (2 patients).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 5.3. Results of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5)

Study	Test		Sensitivity	Specificity	Other
Davis, 1988	**#1**	SCID [a] nurse & therapist interview	NR [b]	NR	Concordance: 80.8%
	#2	SCID nurse and BDI [c]	NR	NR	Concordance: 13.5%
	#3	Therapist interview and BDI	NR	NR	Concordance: 11.5%
Martin, 2000		HADS [d] all items / including HADS Depression subscale	NR	NR	Internal consistency 0.82 for HADS, 0.72 for HADS-D; Exploratory factor analysis reported
Wojciechowski, 2000	**#1**	Zung [e] / SCL-90-Dep [f]	NR	NR	Pearson correlations:0.70; 0.76; 0.77; 0.75, at 1, 3, 6, 12 months after MI [g]
	#2	Zung SDS / Maastricht Quest (vital exhaustion)	NR	NR	Pearson correlations: 0.79; 0.76; 0.78; 0.81, at 1, 3, 6, 12 months after MI
	#3	SCL-90-Dep / Maastricht Quest (vital exhaustion)	NR	NR	Pearson correlations: 0.75; 0.83; 0.76; 0.76, at 1, 3, 6, 12 months after MI

Evidence Table 5.3. Results of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5) (continued)

Study	Test		Sensitivity	Specificity	Other
Strik, 2001	**#1**	SCL-90	81.1% (for major and minor depression), 95.5% (for major depression only)	83.5% (for major and minor depression), 74% (for major depression only)	PPV [h]: 40% (for major and minor depression), 36.8% (for major depression only); NPV [i]: 93.3% (for major and minor depression), 96.2% (for major depression only)
	#2	BDI	83.8% (for major and minor depression), 81.8% (for major depression only)	71.7% (for major and minor depression), 78.7% (for major depression only)	PPV: 25.3% (for major and minor depression), 33.3% (for major depression only); NPV: 98.3% (for major and minor depression), 97.9% (for major depression only)
Strik, 2001	**#3**	HADS/ HADS-Depression subscale	HADS 78.1% (for major and minor depression), 90% (for major depression only); HADS-D [j] 75% (for major and minor depression), 85% (for major depression only)	HADS 85% (for major and minor depression), 84.3% (for major depression only); HADS-D 77.6% (for major and minor depression), 74.8% (for major depression only)	HADS PPV: 45.2% (for major and minor depression), 45.2% (for major depression only); HADS NPV: 99.3% (for major and minor depression), 99.3% (for major depression only); HADS-D PPV: 32.1% (for major and minor depression), 32.1% (for major depression only); HADS-D NPV: 98.4% (for major and minor depression), 98.4% (for major depression only) Note: There appears to be a misprint in original article tables listing PPV and NPV as equal for both major and major/minor depression, which does not reconcile with other statistical data presented.
	#4	17-item HAM-D [k]	76.3% (for major and minor depression), 86.4% (for major depression only)	86.0% (for major and minor depression), 92.2% (for major depression only)	PPV: 40.7% (for major and minor depression), NPV: 99.3% (for major and minor depression), 98.2% (for major depression only)

Evidence Table 5.3. Results of Studies on Methods of Screening for Depression in Myocardial Infarction Patients (Question 5) (continued)

Study	Test		Sensitivity	Specificity	Other
Freedland, 2002		BDI / HAM-D	NR	NR	Pearson correlation = 0.64
Martin, 2003		HADS all items / including HADS Depression subscale	NR	NR	Internal consistency: 0.87 for HADS, 0.76 for HADS-D at 1 week; 0.88 for HADS, 0.80 for HADS-D at 6 weeks; 0.90 for HADS, 0.81 for HADS-D at 6 months; Confirmatory factor analysis reported

[a] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders IV
[b] Not reported
[c] Beck Depression Inventory
[d] Hospital Anxiety and Depression Scale
[e] Zung Self Rating Depression Scale
[f] Symptom Check List 90
[g] Myocardial infarction
[h] Positive predictive value
[i] Negative predictive value
[j] Hospital Anxiety and Depression Scale - depression subscale
[k] Hamilton Rating Scale for Depression

Evidence Table 6.1. Characteristics of Studies on Relation of Depression to Use of Treatment in Patients after Hospitalization for Myocardial Infarction (Question 6)

Study	Study Design	Target Population	Exclusion criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Blumenthal, 1982	Pro cohort [a]	Only MI [b] patients (recent MI)	NR [c]	Single center	USA	NR	To determine whether baseline physiological and psychological factors determine drop-out from cardiac rehabilitation program.
Conn, 1991	Retro cohort [d]	Only MI patients (MI in preceding 1-2 years)	Multiple MI; planned/received cardiac surgery; received daily assistance from paid health care worker; institutionalized; unable to participate in interview	Single center	USA	NR	To examine relationship between anxiety, depression, self-care and QOL [e] among older adult MI survivors.
Druss, 2000	Retro cohort	Only MI patients (Medicare claims for MI)	Age < 65; transferred to/from other facility; terminal illness; DNR [f] order	Mutlicenter	USA	Feb 1994 - Jul 1995	To assess whether having a comorbid mental disorder is associated with a lower likelihood of cardiac catheterization and/or revascularization after acute MI.
Ziegelstein, 2000	Pro cohort	Only MI patients (acute MI)	Unable to interview due to being cognitive impairment/medically unstable; transferred to other facility; died < 48 hours post-MI	Single center	USA	NR	To determine whether depression affects adherence to recommendations intended to reduce the risk of cardiac events after an MI.
Romanelli, 2002	Pro cohort	Only MI patients (acute MI)	Age < 65; major cognitive problems; unable to interview due to medical instability within first 5days post-MI; comorbid non-cardiac illness likely to cause death within the next 6months; transferred to another facility; died within first 48 hours post-MI	Single center	USA	NR	To determine the significance of post-MI depression in individuals aged 65 and older.

Evidence Table 6.1. Characteristics of Studies on Relation of Depression to Use of Treatment in Patients after Hospitalization for Myocardial Infarction (Question 6) (continued)

Study	Study Design	Target Population	Exclusion criteria	Number of Study Sites	Study Site	Recruitment Period	Study Objective
Bennet, 2003	Pro cohort	First acute MI	Age > 75; prior MI; need for cardiac surgery	Single center	Europe	NR	To determine if affective and social-cognitive variables predict risk behavior for CHD [g] after MI.
Lauzon, 2003	Pro cohort	Only MI patients (acute MI)	Non-English/non-French speaking; transferred from another hospital; physically incapable of responding to a questionnaire; unable to give informed consent	Mutlicenter, 10	Canada	Dec 1996 - Nov 1998	To measure the prevalence and prognostic impact of depressive symptoms after acute myocardial infarction.
Whitmarsh, 2003	Pro cohort	Only MI patients (acute MI able to participate in cardiac rehabilitation)	NR	Single center	Europe	Oct 1999 - May 2000	To identify psychological determinants of non-attendance at cardiac rehabilitation.
Steeds, 2004	Pro cohort	Only MI patients (acute MI)	Age > 75; incapable of giving written; informed consent	Single center	Europe	1999 - 2000	To determine the prevalence of an elevated BDI [h] and to determine the relation between BDI score and prognosis in a UK population following MI.
Strik, 2004	Pro cohort	Only MI patients (first MI)	Major psychiatric disorders other than affective disorder; cognitive dysfunction; non-Dutch speaking; lived more than 50km away from study center; comorbid life-threatening illness	Single center	Europe	NR	To evaluate prospectively cumulative 1 year incidence of major and minor depression in consecutive cohort of patients following first MI. Secondly to evaluate whether Major and minor depression, and depressive symptoms, predicted cardiac mortality and morbidity up to 3 years post MI.

[a] Prospective cohort

Evidence Table 6.1. Characteristics of Studies on Relation of Depression to Use of Treatment in Patients after Hospitalization for Myocardial Infarction (Question 6) (continued)

[b] Myocardial infarction
[c] Not reported
[d] Retrospective cohort study
[e] Quality of life
[f] Do not resuscitate
[g] Coronary heart disease
[h] Beck Depression Inventory

Evidence Table 6.2. Results of Studies of Relation of Depression to use of Treatment in Patients after Hospitalization for Myocardial Infarction (Question 6)

Study Author, Year	No. of Subjects	Mean Age	Male (%)	White (%)	HTN [a] (%)	DM [b] (%)	Smoking (%)	Lipid [c] (%)	Killip Class [d] (%)	Mean Ejection Fraction	History of Depression (%)
Blumenthal, 1982	35	54	NR[e]	NR	NR	NR	NR	NR	NR	NR	NR
Conn, 1991	94	74	50	NR	NR	NR	NR	NR	NR	NR	NR
Druss, 2000	5365[f]; 08288[g]	76	52[f]; 46[g]	92[f]; 91[g]	42[f]; 41[g]	22[f]; 26[g]	23[f]; 15[g]	NR	NR	EF > 55%: 14[f], 14[g]; EF 40 - 54%: 29[f], 29[g]; EF < 40%: 52[h], 52[g]	NR
Ziegelstein; 2000	35[i]; 169[j]; 31[k]; 173[l]	46[i]; 55[j]; 42[k]; 54[l]	46[i]; 59[j]; 52[k]; 58[l]	NR	71[i]; 62[j]; 71[k]; 63[l]	31[i]; 30[j]; 36[k]; 31[l]	31[i]; 27[j]; 29[k]; 27[l]	69[i]; 61[j]; 71[k]; 60[l]	Class II: 31[i], 37[j], 32[k], 35[l]; Class III: 32[i], 37[j], 32[k], 35[l]; Class IV: 31[i], 37[j], 32[k], 35[l]	37[i]; 23[j]; 23[k]; 25[l]	45[i]; 11[j]; 33[k]; 12[l]
Romanelli; 2002	35[h]; 118[m]	75[h]; 74[m]	57[h]; 55[m]	97[h]; 90[m]	71[h]; 70[m]	49[h]; 33[m]	NR	57[h]; 60[m]	Class > I: 54[h]; 49[m]	EF ≤ 35%: 50[h] ; 33[m]	NR
Bennet; 2003	37	62	73	NR	NR	NR	NR	NR	NR	NR	NR
Lauzon; 2003	191[h]; 359[m]	60[h]; 60[m]	75[h]; 81[m]	94[h]; 97[m]	34[h]; 36[m]	16[h]; 16[m]	40[h]; 40[m]	35[h]; 39[m]	Class I: 81[h]; 83[m]	NR	NR
Whitmarsh; 2003	93	64	76	100	NR	NR	61	NR	NR	NR	NR
Steeds; 2004	62[n]; 69[o]	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Strik; 2004	63[h]; 143[m]	59	67[h]; 80[m]	NR	NR	NR	10[h]; 13[m]	35[h]; 29[m]	NR	EF ≥ 50%: 56[h]; 70[m]	32[h]; 13[m]

[a] Hypertension
[b] Diabetes
[c] Hyperlipedemia
[d] Killip Class I - IV
[e] Not reported
[f] Mental disorders

Evidence Table 6.2. Results of Studies of Relation of Depression to use of Treatment in Patients after Hospitalization for Myocardial Infarction (Question 6) (continued)

[g] No mental disorders
[h] Depressed
[i] BDI >10
[j] BDI <10
[k] Major depression/dysthymia
[l] No major depression/dysthmia
[m] Not depressed
[n] BDI 12
[o] BDI < 12

Evidence Table 6.3. Assessment of Study Quality in Studies of Depression to Use of Treatment in Patients after Hospitalization for Myocardial Infarction (Question 6)

Author, Year	Representativeness of Study Population	Description of Therapy and Management	Description of Assessment Protocol	Outcomes and Follow-Up	Statistical Analyses	Bias and Confounding	Conflicts of Interest
Conn, 1991	90%	17%	100%	71%	0%	0%	100%
Druss, 2000	15%	0%	50%	25%	25%	0%	0%
Ziegelstein, 2000	85%	9%	50%	50%	84%	100%	50%
Strik, 2004	75%	58%	50%	50%	67%	0%	0%
Steeds, 2004	40%	0%	100%	50%	50%	0%	0%
Blumenthal, 1982	25%	0%	25%	100%	75%	25%	150%
Whitmarsh, 2003	60%	0%	88%	17%	50%	25%	0%
Romanelli, 2002	75%	25%	50%	50%	50%	0%	0%
Lauzon, 2003	65%	33%	100%	100%	33%	0%	100%

Representativeness: Percentage score was based on a total maximum score of 10 points. This included assessment of how well the study described the study setting and population (2 points), inclusion/exclusion criteria (2 points), non-participating patients (2 points), patient characteristics at enrollment (2 patients), and whether the study used a consecutive series or randomly selected sample (2 patients).

Bias and Confounding: Percentage score was based on a total maximum score of 10 points. This included assessment of whether the decision to obtain the reference test was affected by results of the study instrument (2 points), whether there was blinding of test interpretation (2 patients), whether interpretation of the study test was performed by two or more independent observers (2 patients), whether interpretation of the reference test was performed by two or more independent observers (2 points), and whether the reference standard and study test were measured before interventions were started with knowledge of test results (2 points).

Description of Therapy: Percentage score was based on a total maximum score of 6 points. This included assessment of how well the study described details of the cardiac therapy given (2 points), whether the study described details of the psychiatric treatment given (2 points), and whether there was adequate description of other treatments given (2 points).

Description of Assessment: Percentage score was based on a total maximum score of 4 points. This included assessment of the description of methods used for initial diagnosis of depression (2 points), and the description of the interpretation criteria for a diagnosis of depression (2 points).

Evidence Table 6.3. Assessment of Study Quality in Studies of Depression to Use of Treatment in Patients after Hospitalization for Myocardial Infarction (Question 6) (continued)

Test Interpretation: Percentage score was based on a total maximum score of 12 points. This included assessment of the description of interpretation criteria of the study test for depression (2 points) and of the reference test (2 points), whether individuals receiving the study test also received the reference test (2 points), whether a summary index of test performance and index of variability was reported for the study test (2 points), whether methods for calculating test reproducibility were described (2 patients), and whether authors described how indeterminate results were handled (2 patients).

Outcomes and Follow-up: Percentage score was based on a total maximum score of 6 points. This included assessment of whether the study reported numbers or reasons for withdrawals or those lost to follow-up (2 points), the percentage of patients withdrawn or lost to follow-up (2 points), and whether the same tools for diagnosing depression were used for baseline and follow-up (2 points).

Statistical Analyses: Percentage score was based on a total maximum score of 8 points. This included assessment of whether statistical tests were clearly identified (2 points), whether loss to follow-up was handled appropriately (2 points), whether adjustment was made for confounding (2 points), and whether confidence intervals were reported (2 patients).

Conflict of Interest: Percentage score was based on a total maximum score of 2 points. This involved determination of whether the study identified the sources of funding and involvement of the funding agency.

Evidence Table 6.4. Results of Studies on the Relation of Depression to Use of Treatment after Hospitalization for Myocardial Infarction (Question 6)

Study Author, Year	Study Group	Diagnosis of MI	Method of Assessing Depression Used for Analysis	No. of Subjects	Follow-Up	Cardiac Cath [a] (%)	PTCA [b] (%)	CABG [c] (%)	Aspirin/ Antiplatelet (%)	Beta Blockers (%)
Druss, 2000	Major depression/ affective	ICD-9 [d]	ICD-9	315	16 mos [e]	33 [f]	9	8	NR	NR
	No mental disorders			108288	16 mos	44 [f]	17	13	NR	NR
Ziegelstein, 2000	Major depression/ dysthmia	Pain, EKG [g], CPK-MB [h]	SCID [i] BDI [j] > 10	31	4 mos	NR	NR	NR	NR	72
	Not depressed			173	4 mos	NR	NR	NR	NR	88
Romanelli, 2002	Depressed (BDI ≥10)	Pain, EKG, CPK-MB	SCID	35	4 mos	NR	NR	NR	86	74
	Not depressed			118	4 mos	NR	NR	NR	84	86
Lauzon, 2003	Depressed	NR	BDI-10	191	30 d [k]	57	32	7	NR	NR
	Not depressed	NR		359	30 d	47	25	8	NR	NR
	Depressed	NR	BDI-10	191	1 yr [l]	67	39	19	84	56
	Not depressed	NR		359	1 yr	55	30	16	86	64
Steeds, 2004	Depressed	Pain, EKG, CPK-MB	BDI-12	62	32 mos	NR	NR	NR	NR	32
	Not depressed			69	32 mos	NR	NR	NR	NR	55
Strik, 2004	Depressed/ Minor depression	Pain, EKG, ASAT [m]	SCID	63	1 yr	NR	36	NR	81 [f]	40
	Not depressed			143	1 yr	NR	36	NR	95 [f]	40

[a] Cardiac catheterization
[b] Percutaneous transluminal coronary angioplasty
[c] Coronary artery bypass graft
[d] The International Statistical Classification of Diseases and Related Health Problems
[e] Months
[f] $p < 0.001$
[g] Electrocardiogram
[h] Creatine phosphokinase - muscle brain

Evidence Table 6.4. Results of Studies on the Relation of Depression to Use of Treatment after Hospitalization for Myocardial Infarction (Question 6) (continued)

[i] Structured Clinical Interview for Diagnostic & Statistical Manual of Mental Disorders IV
[j] Beck Depression Inventory
[k] Day
[l] Year
[m] Aspartate aminotransferase

Excluded Studies

Ades PA, Savage PD, Tischler MD, et al. Determinants of disability in older coronary patients. Am Heart J 2002; 143(1): 151-6.
No data on when MI occurred relative to when depression assessed

Ades PA, Waldmann ML, McCann WJ, et al. Predictors of cardiac rehabilitation participation in older coronary patients. Arch Intern Med 1992; 152(5): 1033-5.
Patients with MI not reported separately and MI patients represent less 50% of sample

Ahto M, Isoaho R, Puolijoki H, et al. Coronary heart disease and depression in the elderly--a population-based study. Fam Pract 1997; 14(6): 436-45.
No data on when MI occurred relative to when depression assessed

Al-Ruzzeh S, Mazrani W, Wray J, et al. The Clinical Outcome and Quality of Life Following Minimally Invasive Direct Coronary Artery Bypass Surgery. J Card Surg 2004; 19(1): 12-16.
Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

Baer PE Cleveland SE Montero AC. Improving post-myocardial infarction recovery status by stress management training during hospitalization. J Card Rehab 1985; 5(4): 191-197.
Does not apply

Baker RA, Andrew MJ, Schrader G, et al. Preoperative depression and mortality in coronary artery bypass surgery: preliminary findings. Anz J Surg 2001; 71(3): 139-42.
No data on when MI occurred relative to when depression assessed

Beck CA, Joseph L, Belisle P, et al. Predictors of quality of life 6 months and 1 year after acute myocardial infarction. Am Heart J 2001; 142(2): 271-9.
Does not apply

Bennett P, Brooke S. Intrusive memories, post-traumatic stress disorder and myocardial infarction. Br J Clin Psychol 1999; 38 (Pt 4): 411-6.
Does not apply

Bennett P, Lowe R, Mayfield T, et al. Coping, mood and behaviour following myocardial infarction: results of a pilot study. Cor Health Care 1999; 3(4): 192-8.
Does not apply

Bennett P, Mayfield T, Norman P, et al. Affective and social-cognitive predictors of behavioural change following first myocardial infarction. Br J Health Psychol 1999; 4(3): 247-256.
Does not apply

Bennett P, Owen RL, Koutsakis S, et al. Personality, social context and cognitive predictors of post-traumatic stress disorder in myocardial infarction patients. Psychol Health 2002; Vol 17(4): 489-500.
Does not apply

Berkman L, Jaffe A, Carney R, et al. Enhancing recovery in coronary heart disease (ENRICHD) study intervention: Rationale and design. Psychosom Med 2001; 63(5): 747-755.
No original data

Berkman LF, Leo-Summers L, and Horwitz RI. Emotional support and survival after myocardial infarction. A prospective, population-based study of the elderly. Ann Intern Med 1992; 117(12): 1003-9.
Does not apply

Bhatia MS, Tiwari A, Balkrishna, et al. Type A behaviour, life events & myocardial infarction. Indian J Med Res 1990; 92: 95-100.
Does not apply

Bianchi G, Fergusson D, and Walshe J. Psychiatric antecedents of myocardial infarction. Med J Aust 1978; 1(6): 297-301.
Published before 1980

Billing E, Lindell B, Sederholm M, et al. Denial, anxiety, and depression following myocardial infarction. Psychosom 1980; 21(8): 639-41, 644-5.
Does not apply

Black JL, Allison TG, Williams DE, et al. Effect of intervention for psychological distress on rehospitalization rates in cardiac rehabilitation patients. Psychosom 1998; 39(2): 134-43.
Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

Boone T. Patient reactions to the exercise staff, program and prescription following myocardial infarction. Am Corr Ther J 1986; Vol 40(3): 62-67.
Does not apply

Bremer Schulte M, Pluym B, and Van Schendel G. Reintegration with Duos: A self-care program following myocardial infarction. Patient Educ Counsel 1986; Vol 8(3): 233-244.
Does not apply

Brezinka V, Dusseldorp E, and Maes S. Gender differences in psychosocial profile at entry into cardiac rehabilitation. J Cardiopulm Rehabil 1998; 18(6): 445-9.
Patients with MI not reported separately and MI patients represent less 50% of sample

Brown JH. Depression after myocardial infarction. Can Med Assoc J 1976; 114(3): 187.
Published before 1980

Brown MA, Munford A. Rehabilitation of post MI depression and psychological invalidism: a pilot study. Int J Psych Med 1983-1984; 13(4): 291-8.
Case report or case series

Brown N, Melville M, Gray D, et al. Quality of life four years after acute myocardial infarction: short form 36 scores compared with a normal population. Heart 1999; 81(4): 352-8.
Does not apply

Bruhn JG, Chandler B, and Wolf S. A psychological study of survivors and nonsurvivors of myocardial infarction. Psychosom Med 1969; 31(1): 8-19.
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Does not apply

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Does not apply

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No original data

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Does not apply

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Does not apply

Carney RM, Freedland KE, Eisen SA, et al. Major depression and medication adherence in elderly patients with coronary artery disease. Health Psychol 1995; 14(1): 88-90.
Patients with MI not reported separately and MI patients represent less 50% of sample

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Letter

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Patients with MI not reported separately and MI patients represent less 50% of sample

Carney RM, Freedland KE, Stein PK, et al. Effects of depression on QT interval variability after myocardial infarction. Psychosom Med 2003; Vol 65(2): 177-180.
Does not apply

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

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Does not apply

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Does not apply

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Unable to review

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Does not apply

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Does not apply

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Does not apply

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Does not apply

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Does not apply

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Does not apply

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Does not apply

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Does not apply

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Duplicate citation

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No usable data

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Does not apply

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

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Does not apply

Denollet J, Sys SU, and Brutsaert DL. Personality and mortality after myocardial infarction. Psychosom Med 1995; 57(6): 582-91.
Does not apply

Denollet J, Sys SU, Stroobant N, et al. Personality as independent predictor of long-term mortality in patients with coronary heart disease. Lancet 1996; 347(8999): 417-21.
Does not apply

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disorders and quality of care among postacute myocardial infarction outpatients. J Nerv Ment Dis 2002; 190(1): 51-3.
Does not apply

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Does not apply

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Does not apply

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Does not apply

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

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Does not apply

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No original data

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Does not apply

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Does not apply

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Does not apply

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Does not apply

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Does not apply

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No data on when MI occurred relative to when depression assessed

Friedmann E, Thomas SA. Pet ownership, social support, and one-year survival after acute myocardial infarction in the Cardiac Arrhythmia Suppression Trial (CAST). 1998; 187-201.
No data on when MI occurred relative to when depression assessed

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Published before 1980

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Does not apply

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Patients with MI not reported separately and MI

patients represent less 50% of sample

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No original data

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Does not apply

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Case report or case series

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Letter

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

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Does not apply

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Does not apply

Havik OE, Maeland JG. Changes in smoking behavior after a myocardial infarction. Health Psychol 1988; 7(5): 403-20.
Does not apply

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Study population mixed and MI patients not reported separately

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Patients with MI not reported separately and MI patients represent less 50% of sample

Hlatky MA, Haney T, Barefoot JC, et al. Medical, psychological and social correlates of work disability among men with coronary artery disease. Am J Cardiol 1986; 58(10): 911-5.
Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

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Does not apply

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

Ickovics JR, Viscoli CM, and Horwitz RI. Functional recovery after myocardial infarction in men: the independent effects of social class. Ann Intern Med 1997; 127(7): 518-25.
Does not apply

Johnston M, Pollard B, and Hennessey P. Construct validation of the hospital anxiety and depression scale with clinical populations. J Psychosom Res 2000; 48(6): 579-84.
Reports depression as a continuous variable

Jones DA, West RR. Psychological rehabilitation after myocardial infarction: multicentre randomised controlled trial. BMJ 1996; 313(7071): 1517-21.
Does not apply

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Julkunen J, Saarinen T. Psychosocial predictors of recovery after a myocardial infarction: Development of a comprehensive assessment method. Ir J Psychol 1994; Vol 15(1): 67-83.
Does not apply

Kavanagh T, Shephard RJ, and Tuck JA. Depression after myocardial infarction. Can Med Assoc J 1975; 113(1): 23-7.
Published before 1980

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Patients with MI not reported separately and MI patients represent less 50% of sample

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Does not apply

Kishi Y, Robinson RG, and Kosier JT. Suicidal ideation among patients with acute life-threatening physical illness: patients with stroke, traumatic brain injury, myocardial infarction, and spinal cord injury. Psychosom 2001; 42(5): 382-90.
Study population mixed and MI patients not reported separately

Kishida H, Saito T, Fukuma N, et al. Combination of ambulatory electrocardiographic monitoring and psychological testing in coronary artery disease patients. Jpn J Med 1990; 29(4): 384-90.
Does not apply

Koenig HG, Meador KG, Cohen HJ, et al. Depression in elderly hospitalized patients with medical illness. Arch Intern Med 1988; 148(9): 1929-36.
Study population mixed and MI patients not reported separately

Kohn LM, Sleet DA, Carson JC, et al. Life changes and urinary norepinephrine in myocardial infarction. J Human Stress 1983; 9(2): 38-45.
Does not apply

Kozmar D, Catipovic-Veselica K, Galic A, et al. Depression in acute coronary syndrome. Psychol Rep 2003; 93(3 Pt 2): 1105-8.
Reports depression as a continuous variable

Kugler J, Dimsdale JE, Hartley LH, et al. Hospital supervised vs home exercise in cardiac rehabilitation: effects on aerobic fitness, anxiety, and depression. Arch Phys Med Rehabil 1990; 71(5): 322-5.
Depression status at baseline not available

Kuijpers PMJC, Hamulyak K, Strik JJMH, et al. Beta-thromboglobulin and platelet factor 4 levels in post-myocardial infarction patients with major depression. Psych Res 2002; Vol 109(2): 207-210.
Duplicate citation

Kurosawa H, Shimizu Y, Nishimatsu Y, et al. The relationship between mental disorders and physical severities in patients with acute myocardial infarction. Jpn Circ J 1983; 47(6): 723-8.
No validated depression measure used

Ladwig KH, Lehmacher W, Roth R, et al. Factors which provoke post-infarction depression: results from the post-infarction late potential study (PILP). J Psychosom Res 1992; 36(8): 723-9.
Does not apply

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