# Depression, anxiety and their relationship with chronic diseases: a review of the epidemiology, risk and treatment evidence

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## ABSTRACT

**Objective:** To review the evidence for an association between depression and anxiety and the National Health Priority Area conditions — heart disease, stroke, diabetes mellitus, asthma, cancer, arthritis and osteoporosis — and for the effectiveness of treatments for depression and anxiety in these settings.

**Data sources:** Systematic literature search of systematic reviews, meta-analyses and evidence-based clinical practice guidelines published between 1995 and 2007, inclusive.

**Data extraction:** Each review was examined and summarised by two people before compilation.

**Data synthesis:** Depression is more common in all disease groups than in the general population; anxiety is more common in people with heart disease, stroke and cancer than in the general population. Heterogeneity of studies makes determination of risk and the direction of causal relationships difficult to determine, but there is consistent evidence that depression is a risk factor for heart disease, stroke and diabetes mellitus. Antidepressants appear to be effective for treating depression and/or anxiety in patients with heart disease, stroke, cancer and arthritis, although the number of studies in this area is small. A range of psychological and behavioural treatments are also effective in improving mood in patients with cancer and arthritis but, again, the number of studies is small.

**Conclusion:** The evidence for the association of physical illness and depression and anxiety, and their effects on outcome, is very strong. Further research to establish the effectiveness of interventions is required. Despite the limits of current research, policy and practice still lags significantly behind best evidence-based practice. Models of integrated care need to be developed and trialled.


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The co-occurrence of depression and physical illnesses is an important issue. The burden of disease for depression itself is similar to that for heart disease.[1] In any year, nearly 18% of Australians have one of the common mental disorders (depression, anxiety or substance misuse), and 43% of these people have a physical illness.[2] Having a physical illness is one of the strongest risk factors for depression.[3] Moreover, evidence now shows that depression is also a risk factor for physical illness and for early death.[4] Thus, both the depression and the physical illness need to be considered if we are to understand the complexities of this association and the best ways to treat each.

Our aim was to review and outline the evidence in relation to depression and anxiety and the common chronic diseases — those that are the subject of the National Health Priority Areas. These include cardiovascular disease (heart disease and stroke), diabetes mellitus, asthma, cancer, arthritis and osteoporosis. We included anxiety with depression because the two are often coexistent, and not always easily differentiated. We were interested in finding data on the prevalence of depression and anxiety in patients with these diseases, risk factors for depression and anxiety occurring in patients with these diseases, depression and anxiety as possible risk factors for physical illness, and evidence for effective management of comorbid depression and anxiety and physical illness. Because of the broad scope of the study, we limited the review to secondary sources. This review employs the same methods as, and thus extends, an earlier scoping study conducted on behalf of the Australian Government, commissioned by the National Health Priority Action Council in 2004.[5]

## METHODS

Each of the six major disease groups was considered in three sections: epidemiology/prevalence; risk factors; and management. Computer searches of literature databases were conducted in each of these areas. The searches were limited to the best evidence in the form of systematic reviews, meta-analyses and evidence-based clinical practice guidelines (National Health and Medical Research Council [NHMRC] Level 1 evidence).[6]

The same strategy was used to search each health area for thesaurus and freetext search terms for: depression, anxiety and panic; health area (heart disease, stroke, diabetes mellitus, asthma, cancer, arthritis and osteoporosis); and best evidence (randomised controlled trial.pt, meta-analysis.pt, etc). We will provide full search details on request. The following databases were first searched during April and May 2003: Evidence-Based Medicine Reviews, MEDLINE, Pre-MEDLINE, CINAHL, PsycINFO, Australasian Medical Index, PubMed, The Cochrane Library, National Guidelines Clearinghouse, and the Scottish Intercollegiate Guidelines Network. Results were limited to studies in humans and published in English from 1995 onwards. We repeated the search in May 2007 for items published between 2003 and 2007, inclusive. Each review was examined and summarised by two people before compilation.

Systematic reviews were included if they provided documented inclusion/exclusion criteria and a search strategy, and assessed the methods of included primary studies. Reviews that did not report on direct, specific measures of depression or anxiety (including panic) were excluded. To avoid redundancy, where there were recent (2003–2007) reviews we have reported just those; where not, we refer to earlier reviews. Where there was a lack of Level 1 evidence, but there was other significant literature, we have identified it, although it was beyond scope to appraise this evidence.

## RESULTS

A total of 159 reviews were identified (32 on heart disease, 23 on stroke, 19 on diabetes mellitus, 12 on asthma, 36 on cancer, 24 on arthritis and osteoporosis, and 13 general reviews). We will provide a full list on request.

**1 Epidemiology of depression and anxiety associated with diseases that are National Health Priority Areas**

| Disease | Prevalence | | Effect of time | Age and sex |
|---|---|---|---|---|
| | Depression | Anxiety | | |
| Heart disease | After myocardial infarction or coronary artery disease: 20%;[7] 1.6%–50%;[8] 15%–20%;[9] 20%–28%.[10]<br>Before myocardial infarction: 33%–50%.[11]<br>Heart failure: 25%–30%;[10] 14%–26%.[12] | Panic disorder in patients with coronary artery disease and cardiology outpatients: 10%–50%.[24] | Depression at time of follow-up after myocardial infarction: 60%–70%.[7] | Women with heart disease report more symptoms of anxiety and depression than men.[25] |
| Stroke | Post-stroke: 5%–44%;[13] 6%–34%;[14] 30%–36%.[15] | Increased incidence of generalised anxiety disorder.[14] | Rates of post-stroke depression persist > 6 months.[13,14] | No age or sex associations for post-stroke depression.[15] |
| Diabetes mellitus | Type 2: 8%–52%.[16]<br>Type 1: 12%.[17] | Generalised anxiety disorder in 14% of patients with diabetes; higher in those with type 2.[26] | No systematic reviews found. | Prevalence rates of both depression and anxiety consistently higher in women than men.[26,27] |
| Asthma | No systematic reviews found.<br>Survey data show major depression in 14.4% (compared with 5.7% in patients without asthma).[28] | No systematic reviews found. | No systematic reviews found. | No systematic reviews found. |
| Cancer | At diagnosis: 50%[19] (this is a global measure of distress).<br>Ongoing: 20%–35%.[19]<br>Cancers with poorer prognosis: 20%–50%;[18,19] 7%–50%.[20] | Generally: 15%–23%.[18,19]<br>Colorectal cancer: 15%–23%.[29]<br>With disease progression: up to 69%.[30] | Post-traumatic stress disorder in survivors of childhood cancers: point prevalence, 4.7%–21%;[20] lifetime prevalence, 20.5%–35%.[20] | No systematic reviews found. |
| Arthritis and osteoporosis | Rheumatoid arthritis: 13%–17%;[21,22] up to 80%.[31]<br>High levels of psychological adjustment problems noted in children and adolescents.[32]<br>Osteoporosis: strong and consistent association with depression.[23] | No systematic reviews found.<br>Some single studies found a relationship between arthritis and anxiety.[33,34] | No systematic reviews found. | No systematic reviews found.<br>Younger patients with arthritis more likely to have depression, anxiety and social withdrawal.[35] |

## Epidemiology

The prevalence of depression was markedly and consistently higher in people with heart disease,[7-12] stroke,[13-15] diabetes mellitus,[16,17] cancer,[18-20] rheumatoid arthritis,[21,22] and osteoporosis[23] than in the general population.[2] A summary of the prevalence of comorbid depression, anxiety and panic disorder and other epidemiological factors is shown in Box 1.

The association between heart disease and depression is complex. Rates were similar for myocardial infarction (MI), coronary artery disease, and heart failure,[10,12] although about 33%–50% of people with heart disease have pre-existing depression.[11] Where depression was diagnosed in hospitalised patients with MI, 60%–70% of patients were still depressed at 1–4 months.[7]

Post-stroke depression rates are significantly high (up to 40%), and also persist beyond 6 months.[13-15]

No review was identified for asthma, but data from an Australian survey indicate that, among patients with asthma, the prevalence of depression is more than twice that of populations without asthma.[28]

In patients with cancer, the prevalence of depression has been estimated to be up to four times that in the general population.[18,36] It varies by time from receiving a diagnosis[19] and through stages of disease progression.[30] Prevalence appears to be higher in cancers with poorer prognoses, such as pancreatic, oropharyngeal and breast cancer,[18,19] and colorectal cancer.[29]

Study estimates of the prevalence of major depression in patients with rheumatoid arthritis vary widely, from 13%–17%[21,22] up to 80%,[31] although some of these studies use more general terms, such as "psychiatric comorbidity". Young people with chronic arthritis also have an increased risk of depression, anxiety and social withdrawal.[32] One systematic review found a strong and consistent association between osteoporosis and depression.[23]

Few systematic reviews were found that examined the prevalence of anxiety disorders. A high prevalence of panic disorder is found in patients with cardiac disorders (10%–50%).[24] Evidence-based clinical practice guidelines report anxiety to be high in patients with cancer,[19,29] with estimates ranging up to 69% as disease progressed.[30] A systematic review of post-traumatic stress disorder in survivors of childhood cancer reported a point prevalence of 4.7%–21% and a lifetime prevalence of 20.5%–35%.[20]

Women with heart disease tend to report more symptoms of depression and anxiety than men,[25] although some authors have suggested that this may be due to reporting bias. Among patients with diabetes, the prevalence of both

**2 Risk factors among depression and anxiety and diseases that are National Health Priority Areas**

| Disease | Depression | Anxiety |
|---|---|---|
| Heart disease | Most reviews conclude depression is a risk factor for heart disease.[9,11,49-52] However, because of heterogeneity, some suggest methodological problems leave the matter unresolved.[8,48] | Inconsistent findings.[9,10,52,53] |
| Stroke | Depression is a risk factor for stroke.[54]<br>Risk factors for post-stroke depression: past history of depression, other psychiatric disturbance, dysphasia;[41] functional impairment, living alone, social isolation;[41] physical disability, stroke severity, cognitive impairment, lack of social support or isolation;[42] inconsistent evidence about lesion location.[55,56] | No systematic reviews found. |
| Diabetes mellitus | Depression is a risk factor for type 2 diabetes.[18,46]<br>Risk factors for depression in diabetes mellitus: type 2 diabetes mellitus, particularly for women and socioeconomically disadvantaged people.[18]<br>Clinical outcomes: depression is associated with poor adherence to treatment recommendations and poorer outcomes.[10,18,43,57] | Clinical outcomes: anxiety is a risk factor for poor glycaemic control, although effect sizes are small.[58] |
| Asthma | Risk factors for depression in asthma: significant association between depression or depressive symptoms and severity of asthma.[10]<br>Clinical outcomes: psychological dysfunction is a risk factor for frequent exacerbation.[59]<br>Insufficient evidence of association with depression and risk of fatal or near-fatal asthma.[60] | No systematic reviews found. |
| Cancer | No evidence for depression or psychosocial factors as a cause of cancer.[61]<br>Inconsistent evidence about depression and anxiety and risk of relapse.[62]<br>Risk factors for depression in cancer: younger age, increasing illness, advanced stage of illness, disease recurrence, unrelieved symptoms, pain, medications with depressive side effects, body image changes, previous mental health or substance misuse problems;[37] chemotherapy, adjuvant therapy or radiation therapy; progressive disease in palliative care;[36] secondary lymphoedema.[63]<br>In melanoma: interferon treatment can cause depression and anxiety.[18]<br>In lung cancer: being female, living alone, helpless/hopeless coping style, fatigue, physical symptom burden and physician-rated performance status are risk factors for depression.[29]<br>Clinical outcomes: untreated depression can lead to decreased compliance with medical care, prolonged hospital stays, increased morbidity and possibly increased mortality.[44] | Risk factors for anxiety in cancer diagnosis and treatment: uncontrolled pain, some drug treatments, some investigative procedures such as computed tomography and magnetic resonance imaging, and exacerbation of pre-existing anxiety;[19] secondary lymphoedema.[63]<br>Anxiety in prostate cancer is higher with "watchful waiting" than after prostatectomy.[64] |
| Arthritis and osteoporosis | Some evidence for depression as a risk factor for osteoporosis.[18,47,65]<br>Risk factors for depression in arthritis: lower education levels and workplace support;[38] lower social support or social networks;[66] greater limitation of workplace activity.[38]<br>Risk factors for depression in rheumatoid arthritis: pain.[38-40] | No systematic reviews found. |

depression and anxiety in women is significantly higher than in men.[26,27]

Patients with rheumatoid arthritis who experience depression tend to be younger than those who do not.[35]

The wide variation in overall prevalence rates of depression and anxiety has been attributed to methodological issues, and differences in rating tools and diagnostic criteria.

## Risk

Risk factors for depression in National Health Priority Area diseases include at least some or all of the following: worsening condition,[37] unrelieved pain,[37-40] dysphasia,[41] functional impairment,[41] social isolation,[41,42] past history of psychological disturbance,[41] and diagnostic and treatment regimens.[18,36]

Comorbid depression is a risk factor for increased disease severity[10] because of non-compliance with treatment and greater complications,[18,43] and is associated with longer hospital stays, increased morbidity[44] and increased mortality.[13]

Depression may be a risk factor for developing heart disease,[7,9,24,25] stroke,[45] diabetes mellitus[18,46] and osteoporosis.[47] However, some reviewers noted significant heterogeneity between, and lack of power within, the reviewed studies, and therefore concluded that depression is not yet firmly established as an independent risk factor, at least for heart disease.[8,48] A summary of risk factors among depression and anxiety and National Health Priority Area diseases is shown in Box 2.

## Management

Treatment modalities are considered under pharmacological interventions and psychological, behavioural and educational interventions (see Box 3).

No systematic reviews of pharmacological therapies for treatment of depression were identified for asthma or arthritis and osteoporosis.

There is a consistent body of evidence for the effectiveness of selective serotonin reuptake inhibitors (SSRIs) for treating depression in patients with cancer.[18,86,87]

In heart disease, SSRIs were safe and had modest efficacy in patients with MI or unstable angina with recurrent or severe depression,[67] but did not significantly reduce cardiac adverse events.[50]

In stroke, there was evidence of effectiveness of antidepressants for treating depression;[69,70] however, for prevention of depression, there was inconsistent evidence for the efficacy of antidepressants.[72,73]

In diabetes mellitus, antidepressants (nortriptyline) ameliorated depression but decreased glycaemic control,[75] whereas monoamine oxidase inhibitors increased hypoglycaemia and increased food cravings.[76]

**3 Management of depression and anxiety: pharmacological and psychological, behavioural and educational interventions**

| Disease | Pharmacotherapy | Psychological, behavioural and educational interventions |
|---|---|---|
| Heart disease | Sertraline: 20% fewer adverse cardiac events compared with placebo (randomised controlled trial, non-significant finding);[50] modest efficacy in patients with myocardial infarction with depression or unstable angina with recurrent or severe depression.[67]<br>Fluoxetine: effective for patients with mild depression.[67]<br>Insufficient research to demonstrate cardioprotective benefits of selective serotonin reuptake inhibitors.[50,67] | Randomised controlled trial found modest effect of cognitive behaviour therapy (CBT) on depression and social isolation.[50]<br>Some evidence of effectiveness for relaxation therapies and exercise-based rehabilitation in patients with ischaemic heart disease or mild to moderate heart failure.[45,68]<br>No significant effect on progression of heart disease.[50] |
| Stroke | Small but significant benefit of pharmacotherapy (selective serotonin reuptake inhibitors, tricyclic antidepressants and psychostimulants) in treating post-stroke depression and reducing depressive symptoms.[69,70]<br>Duration of treatment correlated with improvement in depressive symptoms.[71]<br>Prophylactic effect inconsistent: some evidence for post-stroke depression rates being lower in patients treated with antidepressants;[72] no clear benefit of pharmacotherapy in more recent review.[73] | Small but significant effect of psychotherapy on improving mood and preventing depression.[72]<br>Psychological therapy not effective in treating established post-stroke depression.[74] |
| Diabetes mellitus | Antidepressants: ameliorated depression but decreased glycaemic control;[75] increased hypoglycaemia and food cravings.[76] | Self-management training and CBT reduce depression, anxiety and distress.[77]<br>CBT effective in adults in reducing blood glucose levels,[77] although not all studies show this.[78]<br>In children and adolescents, psychological interventions, including CBT, improve: emotional and behavioural problems;[79] disease management;[80] individual and family functioning;[81] and glycaemic control.[78] |
| Asthma | No systematic reviews found. | Psychological interventions have positive effect on emotional and behavioural problems, and disease management in children,[79,82] but not adults.[83]<br>Education and relaxation improve function and wellbeing in adults.[84]<br>Progressive relaxation, CBT, biofeedback[82,84] and family therapy[85] are effective in children. |
| Cancer | Consistent evidence of effectiveness for pharmacological treatment of depression in cancer patients.[18,86,87]<br>No systematic reviews were identified that evaluated the effectiveness of pharmacological agents for anxiety. | CBT, behaviour therapy, counselling, psychotherapy, education/information, relaxation and social support alleviate depression and anxiety.[19,36,88]<br>Psychosocial and psychoeducational interventions are effective for depression.[86,88]<br>School reintegration, health education, home visitation, social work intervention and skills development have no effect on depression; they produce a small reduction in anxiety in children and adolescents.[89]<br>Limited consistent evidence of effectiveness for alternative and complementary therapies. Some low-level evidence for: St John's wort for mild depression;[90] hypnotherapy for reducing anxiety and patient-reported pain in children;[91,92] guided imagery;[93] massage and/or aromatherapy for reducing anxiety.[94]<br>Provision of information[88,95] or summaries or recordings of consultations[89,96] are not effective by themselves in reducing anxiety or depression. |
| Arthritis and osteoporosis | No systematic reviews found.<br>A single study found that antidepressants were effective in reducing depression in patients with rheumatoid arthritis.[97] | Effective in reducing depression in patients with rheumatoid arthritis and osteoarthritis: CBT;[98] biofeedback, education and relaxation;[99] exercise.[100]<br>Effective in reducing anxiety: biofeedback, education and relaxation;[101] exercise.[100]<br>Not effective: educational interventions.[102] |

Cognitive behaviour therapy (CBT) was a modestly effective treatment for depression and anxiety in patients with heart disease,[50] adult patients with diabetes,[77] children with asthma,[82] and people with a range of cancers.[37,88] CBT has also been shown to be effective in reducing depression in patients with rheumatoid arthritis and osteoarthritis.[98] There was some evidence of effectiveness for other interventions, such as relaxation therapies in patients with mild to moderate heart failure[45,68] and cancer,[19] and possibly for patients with rheumatoid arthritis when combined with education and biofeedback.[99,101] Exercise and exercise-based rehabilitation was effective in people with ischaemic heart disease,[45,68] and patients with rheumatoid arthritis and depression and anxiety.[100] A summary of the range of interventions is shown in Box 3.

## DISCUSSION

This review of Level 1 evidence of the association between depression and anxiety and physical illness provides an overview of the current research and knowledge in the area. We have not examined the details of individual studies, but have reported the conclusions of the original reviewers. Our review shows that there is a strong association between physical illness and depression and anxiety in all the National Health Priority Area disease groups — that is, that having a physical illness is a risk factor for depression and/or anxiety. Depression, in particular, is also associated with worse functional outcomes for people with physical diseases. Furthermore, the evidence is growing, and supports considering depression as an important risk factor for disease and disease-specific outcomes in heart disease, stroke and diabetes. The actual nature of the association is more uncertain. There are developed biological theories linking depression and heart disease, stroke and diabetes, although research in the area is hampered by the heterogeneity of the clinical conditions. This would be a worthwhile field for future research. Large prospective studies will be required to establish the links with greater certainty.

There is preliminary evidence for modest effectiveness of antidepressant medications in treating depression, and this has been shown for, in particular, heart disease, stroke, cancer and arthritis. Psychological therapies also appear to be effective in reducing depression and anxiety in patients with heart disease, cancer and asthma. Behavioural treatments (eg, psycho-education, relaxation) have been shown to be effective in reducing depression and anxiety in patients with cancer and arthritis. Although these and other treatments may be expected to lead to improvements in mood, functioning and wellbeing, in general, the number of studies that have been completed in each disease group is small, and much more research is needed to provide certainty.

In light of the weight of evidence for increased morbidity and mortality associated with depression and anxiety in these physical illnesses, it becomes apparent that the research task of finding effective solutions is lagging a long way behind. The problem of depression in patients who are physically ill needs to be tackled for these reasons, as well as simply to relieve the suffering that depression brings. Potentially useful targets for research include examining the effectiveness and safety of antidepressant medications, and the effectiveness of psychological and behavioural interventions in the physically ill. The "management" of depression and anxiety is complicated, as is the "management" of chronic illness. Because of the interaction of these two components, solutions will need to be integrated. It is therefore timely to develop and test the clinical and cost-effectiveness of integrated disease management systems for depression in physically ill patients.

There are models to guide this, although systems of chronic disease management have been slow to be taken up by the health system, and evidence for their usefulness is still limited.[103] Furthermore, although effective models for incorporating care for depression in chronic disease management do exist,[104] they are very few in number. At present, health care is linear — we treat the physical disease first, and then refer the patient for mental health care, or vice versa.[105] This is not effective, efficient or cost-effective. Models of integrated care need to be implemented and evaluated. Based on the principles of chronic disease management and the findings of this review, an integrated disease management system could include screening and monitoring, good disease information and self-management advice, as well as a range of cognitive and behavioural strategies applied in a stepped or tiered model.

Our review has drawn together the evidence around the question of depression and anxiety occurring with the common chronic diseases that are the subject of the National Health Priority Areas. The results highlight a substantial body of evidence supporting the interactive effect of depression and anxiety and these physical illnesses. Policy and practice is lagging behind the known evidence. Our review of research shows that there are promising interventions and systems which ought to be developed and tested. Attention needs to be given to matters of research, policy and practice to achieve the necessary improvements in patient outcomes.

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## COMPETING INTERESTS

None identified.

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