



Medicines Evidence Commentary

commentary on important new evidence from Medicines Awareness Weekly

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Depression treatment and mortality after myocardial infarction

A multicentre cohort study carried out in the US found that people who had untreated depression who were admitted to hospital with myocardial infarction had a statistically significant greater risk of dying after 1 year than people who did not have depression (adjusted hazard ratio 1.91). People with depression had a similar risk of 1-year all-cause mortality as people who did not have depression provided they received treatment for their depression. However, only 30% of people who were diagnosed with depression subsequently received treatment for it. While this observational study has some limitations, it supports current guidance that identification and appropriate treatment of people who may have depression is valuable and should continue to be carried out in line with the NICE guidelines on [Depression in adults](#) (being [updated](#)) and [Depression in adults with a chronic physical health problem](#), and the NICE quality standard on [depression in adults](#).

Overview and current advice

Depression has been reported to be present in about a quarter of people who have acute coronary syndrome (ACS). Depression after myocardial infarction (MI) has been associated with fatal and nonfatal cardiovascular events, adverse health status outcomes, and costs. However, it has not been known whether recognising depression within an ACS setting, and subsequent treatment would improve prognosis compared with people who have untreated depression ([Smolderen et al. 2017](#)).

Many individuals with common mental health disorders do not seek treatment, and both anxiety and depression often go undiagnosed. The presence of a physical illness can complicate the assessment of depression and some symptoms, such as fatigue, are common to both mental and physical disorders. The NICE quality standard on [depression in adults](#) states that people who may have depression should receive an assessment that identifies the severity of symptoms, the degree of associated functional impairment and the duration of the episode. This includes all people with a chronic physical health problem who may have depression.

The NICE guideline [Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease](#) recommends that people who have depression are treated according to the NICE guidelines on [Depression in adults](#) (being [updated](#)) and [Depression in adults with a chronic physical health problem](#). These guidelines advocate a stepwise approach to treatment. They recommend offering, or referring people for, the least intrusive and most effective intervention first. Therefore, non-drug interventions (such as cognitive behavioural therapy [CBT]) should be the

mainstay of treatment for many people with depression, with drugs generally reserved for more severe illness or when symptoms have failed to respond to non-drug interventions.

If an antidepressant is indicated for an adult with depression, the NICE guideline on [Depression in adults with a chronic physical health problem](#) recommends that it should normally be a selective serotonin reuptake inhibitor (SSRI) in generic form, unless there are interactions with other drugs. Citalopram or sertraline have less propensity for interactions. SSRIs are equally effective as other antidepressants and have a favourable risk–benefit ratio. Where possible, the key goal of an intervention for depression should be complete relief of symptoms (remission) – this is associated with better functioning and a lower likelihood of relapse than lesser degrees of response, as well as potentially better physical health outcomes.

NICE interactive flowcharts on [Myocardial infarction: secondary prevention](#) and [Depression](#) bring together all related NICE guidance and associated products on this topic in a set of interactive topic-based diagrams

New evidence

In order to determine whether treatment of depression improves prognosis in people who have had a MI, a study ([Smolderen et al. 2017](#)) assessed 1-year mortality rates after MI for people with treated and untreated depression, compared with people who did not have depression. Data were taken from an [observational](#), multicentre [cohort study](#), the TRIUMPH study (Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status) that enrolled 4062 people (aged 18 years and over from 24 US hospitals) who had an MI between 11 April 2005, and 31 December 2008. People were included if they had elevated cardiac enzymes (creatinine kinase-MB or troponin-I) within 24 hours of hospital admission and a diagnosis of MI, including long-standing ischaemic symptoms or ST changes on ECG.

The [Patient Health Questionnaire 9-item version](#) (PHQ-9) was used during admission to measure depressive symptoms that participants had been experiencing in the 2 weeks before the MI; a score of 10 or more was considered to predict a diagnosis of major depression. Information on depression recognition and treatment also came from physician notes as well as discharge diagnoses, medications and summaries. In addition, detailed interviews were conducted with participants during admission, further information was taken from charts and participants were followed up by interview at 1, 6 and 12 months after admission. Mortality data came from the Social Security Death Master File (available for 96% of participants). People who had missing evaluations of depressive symptoms were excluded from the study.

For the purpose of analysis, participants were split into 3 groups:

1. no depression (PHQ-9 less than 10; mean reported was 3.1);
2. treated depression (PHQ-9 of 10 or more [mean reported was 14.7] with documentation in their medical records of a diagnosis and treatment [counselling or antidepressants]); and
3. untreated depression (PHQ-9 of 10 or more only; mean reported was 13.7).

Of the 4062 people enrolled in the TRIUMPH study, 3303 (81%) did not have significant depressive symptoms and 759 (19%) were screened positive for potential depression (PHQ-9 scores 10 or over) at the time of their MI. Of the 759 people with depression, 231 (30%) had been treated for depression and 528 (70%) were not treated. Treatment was defined as counselling or prescription for antidepressants, but the nature and intensity of any counselling was not reported and it is unclear what proportions of people received different combinations of these different treatments. Of those with treated depression, 159 (69%) were on antidepressants at discharge after the MI.

When the 3303 participants who did not have depression were compared with the 231 who had treated depression, there was no [statistically significant](#) difference in 1-year mortality rates (6.1% versus 6.7%; adjusted [hazard ratio](#) [HR] 1.12, 95% [confidence interval](#) [CI] 0.63–1.99, $p=0.71$). However, the 528 participants who had untreated depression had a higher 1-year mortality than participants who did not have depression (10.8% versus 6.1%; adjusted HR 1.91, 95% CI 1.39–2.62, $p<0.001$), showing a statistically significant difference.

The authors used [propensity score adjustment](#) to reduce the likelihood of bias arising from various factors, such as additional co-morbidities, that may have affected the outcomes for patients. As a sensitivity analysis, they introduced a variable to examine whether depression treatment, a consequence of depression recognition, was associated with a reduced risk for the association between depression and 1-year mortality. However, they still found no statistically significant difference in 1-year risk of mortality between people with and without treated depression (HR for untreated depression, 1.75, 95% CI, 0.83–3.72, $p=0.14$).

Commentary

Commentary provided by NICE

The authors of this study ([Smolderen et al. 2017](#)) concluded that the results are hypothesis generating and encourage further research to examine the impact of depression recognition and treatment at the time of an MI on subsequent survival. Ideally, this should be done through carefully designed [randomised controlled trials](#) (RCTs). Previous RCTs have failed to show a cardiovascular benefit from treating depression, but they had some limitations, including strict inclusion criteria and inadequate power to assess this properly. An advantage of this study is that the participants reflected people being treated in clinical practice.

A weakness of this [study](#), compared with RCTs, is that it is observational and subject to many [confounding](#) factors. People with depression were generally younger, more likely to be female, less likely to be married or employed, more likely to have relatives with coronary artery disease, a higher heart rate on MI admission, and lower rates of ST-segment–elevation MI. People who had significant symptoms of depression also had higher rates of hypertension, diabetes mellitus, and chronic lung disease, and were likely to be current smokers. People with untreated depression were more often of “minority race” or had lower levels of education, compared with people who had no depression and those with treated depression. Considerable effort was made to control for differences between groups, but it is possible that the authors did not fully account for the imbalances, and also that other confounders existed which were not known and, therefore, not adjusted for.

Further limitations, highlighted by the authors, include that depression symptoms were self-reported, compliance with antidepressants was unknown and type and intensity of any counselling used in treatment was not reported. In addition, this study only looked at all-cause mortality and we do not know what effect treating depression after MI has on specific causes of death, such as death from cardiovascular disease or suicide. The data came from people in the US who had been admitted to hospital with MI; it is not clear whether the same results would be seen in UK patients, where clinical practice and confounding factors might differ.

It is important to note that only 30% of people with depression in this study were treated for their depression. This highlights the need to ensure that people who may be depressed, including those who have had an MI, are properly assessed and treated, in line with the NICE guidelines on [Depression in adults](#) (being [updated](#)) and [Depression in adults with a chronic physical health problem](#), and the NICE quality standard on [depression in adults](#).

Study sponsorship

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References

Smolderen KG, Buchanan DM, Gosch K et al. (2017) [Depression Treatment and 1-Year Mortality After Acute Myocardial Infarction: Insights From the TRIUMPH Registry \(Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status\)](#). *Circulation* 135,1681–1689

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