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Depression post-myocardial infarction

Van Melle *et al* (2007) reported that cardiac prognosis post-myocardial infarction was not improved by antidepressant treatment (MIND–IT trial). The SADHART and ENRICHD trials reported similar findings and Carney & Freedland (2007), in their commentary in the same issue, suggest these negative findings are a result of insufficient statistical power in the trials. These results are disappointing but perhaps they might have been anticipated.

There is strong evidence that individuals with depression show increased morbidity and mortality from coronary heart disease (Rugulies, 2002) but the mechanisms involved remain unclear. Individuals with a history of recurrent depression, who are otherwise healthy, show increased inflammation, platelet activation, endothelial dysfunction, and reduced heart rate variability and baroreceptor sensitivity. However, with the exception of platelet function, which improves with selective serotonin reuptake inhibitors, these anomalies are not corrected by antidepressant treatment. Furthermore, endothelial function and baroreceptor sensitivity, which can lead respectively to progression of the atherosclerotic process and to sudden cardiac death, do not improve when depressive symptoms are in remission (Broadley *et al*, 2006). Thus there is no evidence that treatment of depressive symptoms post-myocardial infarction corrects these underlying pathological processes and, if it does not, cardiac outcomes disclosed by clinical trials are unlikely to show improvement irrespective of their statistical power. By analogy, although hyperglycaemia characterises diabetes, tight glucose control alone has only a modest impact on cardiovascular events. Similarly, depressive illness is characterised by acute episodes of depression, but other systemic abnormalities are present and persist between acute depressive episodes. Accordingly, it may be unreasonable to believe that treatments assessed by their influence on the affective state alone will reduce cardiovascular events.

Although it is important to alleviate the suffering associated with developing depression post-myocardial infarction and improve prognosis by addressing the secondary effects of depression (e.g. reduced adherence to treatment and poor health behaviours), treatment needs to be aimed at earlier stages of the disorder. Atherosclerosis begins in childhood and becomes manifest much later in life, with myocardial infarction as a very late presentation. Similarly, depression is a lifelong disorder with onset in early adulthood. It should be noted that currently depression is not even included in cardiovascular risk tables and that individuals with depression might benefit from introduction of statins, or other preventative measures.

We agree with Carney & Freedland (2007) that treatments for depression might alter the risk of cardiac events via pathways that are unrelated to their effects on depression. However, if the focus of research were shifted to the study of earlier stages of coronary heart disease in people with depression, this could be clarified by monitoring earlier indices of heart disease in relation to treatment of depression. It is also recognised that mechanisms for associations between depression and onset of heart disease may differ from those between depression and progression of coronary heart disease post-myocardial infarction. These pathways need to be better understood and present evidence suggests that survival times following myocardial infarction could be improved by developing treatments for depression that also target the underlying cardiovascular abnormalities and by augmenting these by preventative programmes for coronary heart disease in individuals with mood disorders.

Coronary heart disease and depression are two major public health problems and it is of concern that reports of treatments for depression failing to enhance survival post-myocardial infarction may result in less interest in studying the links between them.

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Van Melle *et al* (2007) present findings from their randomised controlled trial examining the effects of antidepressant treatment for depression following myocardial infarction. I would like to comment on the design of the study. Patients were allocated to two arms: antidepressant treatment and care as usual. Patients in the care-as-usual arm were not told about their research diagnosis of depression. The authors quote Zelen (1979), thus implying that they are following the research design he proposed. However, Zelen's method seems best suited to trials where there is a 'gold standard' control treatment available and the trial is attempting to evaluate a new experimental treatment (Zelen, 1979). In this design, the ethical concerns are mainly about randomising before consent is sought. It must be pointed out that after randomisation, consent is sought from patients in the experimental arm. If they decline, they are moved to the 'gold standard' arm (Torgerson, 2001). I am not sure whether the trial of van Melle *et al* fits into this category.

Furthermore, there are ethical issues about not informing patients about their diagnosis of depression. I am disappointed that the paper did not discuss these in further detail. Their information pack stated