Of several possible ‘psychosocial’ causes of coronary heart disease (CHD), depression probably has the strongest candidature. Since both CHD and cerebrovascular disease (CBVD) share similar pathophysiological roots, it might be expected that if depression caused increased risk of heart attack it would also cause increased risk of stroke. Evidence supporting this latter proposition is both less extensive and less convincing. The public health importance of these issues is considerable, given the contribution of CHD and CBVD to health in general and health inequality in particular and considering the disproportionate experience of depression amongst the disadvantaged.

Much of the current cardiovascular disease primary prevention effort is based on population screening with risk stratification and risk reduction treatment for those exceeding a risk threshold. Risk stratification plays less of a role in secondary prevention where risk reduction treatment is generally assumed to be beneficial. Non-causal risk markers may have a role in stratification but are unlikely to lead to effective risk reduction treatment. These points are worth remembering when considering the relevance of epidemiological evidence to clinical practice.

New evidence of possible practical relevance is provided by the paper by Hermann Nabi and colleagues in the current issue of the IJE. In the Health and Social Support (HeSSup) study, around 24,000 men and women aged 20–54 years were recruited from the Finnish general population in 1998. They completed a questionnaire that included the Beck Depression Inventory along with health and demographic information. Over the next 7 years they were followed up through linkage to hospital and mortality registers. Baseline questionnaire data were also augmented through linkage to prescription records. HeSSup exemplifies the way that routine administrative data can be used to add value to epidemiological studies. Markers of depression (scores of 10 or above on the Beck inventory or prescriptions for antidepressant medication) at recruitment showed typical associations with increased risk of incident fatal and non-fatal CHD events including an apparent dose–response relation with increasing symptom severity. In general, these associations were not apparent in relation to incident CBVD. HeSSup has several strengths; it was large enough to consider both CHD and CBVD outcomes in the same population; it used a standard instrument to measure exposure to depression and backed this up with antidepressant prescription data; outcomes were ascertained from clinical registries and were thus much less likely to be biased in comparison to endpoints based on symptom self-reports. These strengths should be considered alongside weaknesses common to many observational studies. Depression was only measured at baseline and use of anti-depressant prescriptions as an index of depression, though methodologically ingenious, is problematic. Taking treatment as a measure of disease severity in this context is generally questionable as it ignores the possibility that effective treatment may ameliorate the influence of the risk factor; further, irrespective of their effect on depression, anti-depressant drugs may directly influence cardiovascular disease risk.

Alongside these issues of exposure measurement, available covariate information limited the ability to consider questions of confounding and mediation. In addition, the original response rate of HeSSup was relatively low, and older, more socially disadvantaged respondents were under-represented. These factors may have implications for external validity.

As the HeSSup investigators argue, prior evidence for a causal influence of depression on CBVD is inconclusive. If anything, HeSSup makes this evidence more conclusively negative. Longer follow-up in older populations alongside better measurement of exposure to depression may provide a different picture but, until it does, there appears no basis to add depression
to the list of risk factors for CBVD or to change clinical practice. In relation to CHD, the results of HeSSup are confirmatory. A mountain of evidence confirms the status of depression as a risk factor for CHD. The clinical implications, however, remain unclear. Reliable risk markers, causal or non-causal, may have a role in risk stratification though it seems that incorporating new predictive factors in risk prediction tools often adds very little to their clinical usefulness. This may be true of psychosocial risk markers like depression and cardiovascular risk prediction. Similarly, treatment of depression does not appear to be currently indicated as either primary or secondary prevention of CHD. In the case of secondary prevention several large, well-conducted trials confirm that depression can be safely and effectively treated in CHD patients but provide no good evidence that this treatment prevents future CHD events. For primary prevention, there is no relevant experimental evidence and little prospect of obtaining any. Secondary analysis of anti-depressant efficacy trials is unlikely to have sufficient power to be informative. Future trials seem unlikely—treatment of depression is already generally recommended in clinical guidelines for depressed individuals with and without cardiovascular disease. Depression is miserable and erodes quality of life—this is sufficient justification for treatment, irrespective of any effects on cardiovascular disease risk.

Understanding why and how cardiovascular disease happens, including the possible causal role of depression, is still important. HeSSup helps exclude the non-causal explanation of reporting bias. Residual confounding is still possible since in most populations, depression, cardiovascular disease and social disadvantage are inextricably linked. Reverse causation also seems likely. First, occult cardiovascular disease may influence mood in several ways long before diagnosis. Further, adverse cardiovascular risk profiles appear to be increasingly seen as resulting from bad lifestyle choices and it may be hard for ‘high risk’ patients to maintain a cheerful outlook when faced with the prospect of an unhealthy future that will be seen as their own fault. For both these reasons, low mood may precede measurable cardiovascular outcomes by many years. Excluding prevalent, and early incident, cases as in HeSSup, may not overcome this influence.

The question of specificity, however, is interesting. Arguably, all the non-causal explanations discussed above should equally generate an apparent association between depression and both CHD and CBVD. The fact that the association increasingly appears to be specific to CHD could itself be evidence for causality. This raises important questions about mechanism that may yet have implications for the effective prevention and treatment of heart disease and stroke.

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References