Medical Xpress

Symptoms of depression causally linked to risk of coronary heart disease in UK

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A report that will be published tomorrow provides strong evidence that the symptoms of depressive disorder are causally associated with the risk of coronary heart disease, and as such should be considered a potentially modifiable risk factor for the occurrence of CHD.

The findings, from the Whitehall II study of more than 10,000 civil servants in the UK, are published in the *European Journal of Preventive Cardiology*.

Findings from former studies on the association of depression with cardiovascular diseases are described by the investigators as "heterogeneous", with associations ranging from nil to strong. Among their explanations for the inconclusive results are bias because of "reverse causation" (by which vascular disease is the origin of the depression, not the consequence), and variability in the accuracy of "depressive symptoms" in previous studies.

They thus write: "With repeated exposure measurements over a long period of adult life, causal inference would be strengthened if (a) reverse causation was excluded as an explanation for the link between depressive disorder and vascular events, and (b) a dose–response effect was evident." Both tests were applied in this study.

The Whitehall II study began in 1985-88 when the health of 10,308 civil servants working in 20 London-based departments was assessed by clinical examination and the 30-item General Health Questionnaire.

Subsequent assessments were made every two-to-three years, with "exposure" to depression measured on six occasions over the 20-year study period. All participants were followed for major CHD events and stroke.

Results over the five-year observation cycles showed a cumulative effect of depressive symptoms on the risk of CHD consistent with an increasing dose-response. Thus, there was no added risk of CHD among those who showed evidence of depressive symptoms during one or two of the questionnaire assessments, but a 100% increase in risk in those who reported symptoms at three or four of the assessments.

However, the association of depressive symptoms with stroke was only apparent with short follow-up, suggesting that this association was an effect of reverse causation. "In other words," said investigator Dr Eric Brunner from the Department of Epidemiology and Public Health, University College London, UK, "depressive symptoms may be a sign of imminent stroke, but are not causally related." In addition, there was no evidence over the full study period of any dose-response effect with stroke. Both these findings, said Dr Brunner, suggest that in the case of stroke the depressive symptoms are a consequence of vascular disease, not its cause.

Thus, say the authors: "This finding provides evidence supporting a causal relationship between depression and CHD, in contrast to the findings in relation to stroke."

Dr Brunner adds: "European prevention guidelines refer to depression as a coronary risk factor, and in our study repeated episodes of depressive symptoms accounted for 10% of all CHD events in the study population. However, this figure relies on the strong assumption of a direct causal mechanism. Whether or not the association is causal, supporting individuals to recover from chronic or repeated episodes of depression

has merit, particularly if the individual is then better able to reduce any vascular risk, for example by quitting smoking."

In considering an explanation for the different effect of depression on stroke and CHD risk, Dr Brunner proposed a possible effect of blood pressure. "Depressive symptoms have been linked with low blood pressure," he said, "and this linkage will tend to confound the association between depression and stroke." Blood pressure is particularly important for stroke risk, but is only one of several risk factors for CHD.

More information: Brunner EJ, Shipley MJ, Britton AR, et al. Depressive disorder, coronary heart disease, and stroke: dose–response and reverse causation effects in the Whitehall II cohort study. *Eur J Prevent Cardiol* 2014; DOI: 10.1177/2047487314520785

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