



Published in final edited form as:

J Am Coll Cardiol. 2009 September 1; 54(10): 958–959. doi:10.1016/j.jacc.2009.03.081.

Reply to Letter to the Editor: Treatment-Resistant Depression and Sudden Cardiac Death

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Dear Editor

We thank Drs. Carney and Freedland for their perspective. We performed the analyses that they suggested by estimating separate hazard ratios for four categories of women from the Nurses' Health Study, according to presence of severe depressive symptoms (MHI-5 score < 53) and/or reported use of antidepressant medications. In multivariable analyses, the hazard ratios associated with each category are listed below. The risk of sudden cardiac death was significantly elevated among women treated with antidepressants regardless of whether they continue to exhibit severe depressive symptoms. Although the hazard ratio was slightly higher among those who exhibited severe depressive symptoms, confidence intervals overlapped. Also, we did not find evidence for an interaction between MHI-5 score category and antidepressant use in separate multivariable models that used a cross-product term. Therefore, we were unable to find strong evidence in support of Drs. Carney and Freedland's hypothesis in our data; however, we strongly agree that further research into prognosis of depression and treatment-resistant depression, and the underlying mechanisms, is needed.

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Category	Hazard Ratio (95% CI)	P value
MHI-5 score \geq 53, no antidepressant	Referent	
MHI-5 score $<$ 53, no antidepressant	0.76 (0.24-2.43)	0.64
MHI-5 score \geq 53, antidepressant use	3.11 (1.80-5.36)	$<$ 0.001
MHI-5 score $<$ 53, antidepressant use	3.99 (1.69-9.42)	0.002