Response to Major Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis and Early Cardiovascular Disease: AHA Guidelines

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I read with interest the guidelines of cardiac Risk in MDD and Bipolar affective disorder patients[1]. They are very detailed but there are some areas like Cardiac Imaging aspects, Molecular biology like MicroRNAs etc which have been overlooked.

There is not a single mention of Cardiac MR, Cardiac CT or other imaging modalities in the guidelines or future directions. I would therefore like to stress the importance of cardiac imaging modalities in future studies and guidelines of mood disorders and psychiatric diseases.

1. Goldstein B, Carnethon M, Matthews K, McIntyre R, Miller G, Raghuveer G, Stoney C, Wasiak H, McCrindle B. Major Depressive Disorder and Bipolar Disorder Predispose Youth to Accelerated Atherosclerosis and Early Cardiovascular Disease. *Circulation*. 2015;:CIR.0000000000000229.

Reply to Dr. Aitzaz Bin Sultan

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We thank Dr. Bin Sultan for his letter highlighting the importance of future studies focusing on molecular biology and cardiovascular imaging among youth with mood disorders. While the main focus of the Scientific Statement "Major depressive disorder and bipolar disorder predispose youth to accelerated atherosclerosis and early cardiovascular disease" was clinical, we strongly concur with Dr. Bin Sultan. Employing cutting edge molecular biology and cardiovascular imaging methods are important for gaining a better understanding of the pathophysiology underlying the link between mood disorders and cardiovascular disease. Indeed, we and other writing group members are currently undertaking such studies, and we are aware of other groups doing so as well.

With regard to molecular biology, our statement highlighted inflammation and oxidative stress, although we acknowledged that other processes and markers may also be implicated. Our Statement highlighted that the strength of the association of mood disorders with atherosclerosis and cardiovascular disease biomarkers exceeds what can be explained by lifestyle, medications, and/or traditional cardiovascular risk factors. This suggests the importance of examining the association of molecular biological processes and markers relevant to atherosclerosis with non-invasive subclinical atherosclerosis surrogates. Whereas non-invasive vascular imaging studies among youth with conditions such as obesity and diabetes have incorporated molecular biological biomarkers, this approach to parsing cardiovascular risk has received limited attention among youth with mood disorders. In a recent preliminary study of adolescents with bipolar

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disorder, we reported a strong positive association between levels of lipid hydroperoxides and greater mean and maximum carotid intima media thickness (as determined by ultrasound).[1] Larger, controlled, prospective studies are warranted.

With regard to cardiovascular imaging, it is important to highlight an excellent prior Scientific Statement by Urbina and colleagues, titled "Noninvasive assessment of subclinical atherosclerosis in children and adolescents".[2] Many studies that examine subclinical atherosclerosis measures among youth employ methods, such as ultrasound (carotid intima media thickness, flow-mediated dilation) and applanation tonometry (pulse wave velocity), with challenges regarding precision and reliability. There is a dearth of studies using magnetic resonance imaging (MRI) atherosclerosis surrogates among youth. One potential advantage of MRI is that it could reduce variability and enable smaller study samples.[3] The latter consideration is especially important when undertaking research constrained to both an age-range sub-group (youth) and a diagnostic sub-group (major depressive disorder, bipolar disorder) of the population. Another potential advantage of MRI is that it allows for studies that concurrently examine vascular phenotypes in multiple locations in the same scanning session, including cerebral blood flow and cerebrovascular reactivity, carotid plaque anatomy, pulse wave velocity, and cardiac myocardial perfusion among others.

Ultimately, molecular biology and vascular imaging approaches will help clarify whether mood disorders among youth are in part vascular conditions with biologically linked disturbances in both cerebral and peripheral vascular beds.

References:

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2.   Urbina EM, Williams RV, Alpert BS, Collins RT, Daniels SR, Hayman L, Jacobson M, Mahoney L, Mietus-Snyder M, Rocchini A, Steinberger J and McCrindle B. Noninvasive Assessment of Subclinical Atherosclerosis in Children and Adolescents: Recommendations for Standard Assessment for Clinical Research: A Scientific Statement From the American Heart Association. *Hypertension*. 2009;54:919-950.

3.   Duivenvoorden R, de Groot E, Elsen BM, Laméris JS, van der Geest RJ, Stroes ES, Kastelein JJP and Nederveen AJ. In Vivo Quantification of Carotid Artery Wall Dimensions: 3.0-Tesla MRI Versus B-Mode Ultrasound Imaging. *Circulation: Cardiovascular Imaging*. 2009;2:235-242.