# A1. PROJECT TITLE

The Association of Autonomic Dysfunction with the Relationship between Depression and Coronary Disease

## A2. PROJECT NARRATIVE

The mechanisms underlying the increased cardiovascular mortality seen in comorbid depression and coronary artery disease are not well understood. Dysfunction of the autonomic nervous system is seen in both diseases and serves as a common mechanistic pathway for further evaluation. The goal of this study is to evaluate the relationship of heart rate variability, a biomarker of autonomic function, with depression and coronary artery disease in a well-characterized cohort of patients to elucidate potential targets for intervention.

## A3. PROJECT ABSTRACT

Comorbid depression and coronary artery disease (CAD) lead to a three-fold increase in cardiovascular mortality, but the mechanisms behind this pathology remain poorly understood. This is major public health issue as depression remains a leading cause of disability globally and CAD is the leading cause of death. Up to 1 of every 5 patients with CAD have comorbid depression, yet interventions from increased screening for depression and treatment through traditional methods have not shown any impact on overall outcomes. A potential mechanistic pathway for depression and CAD is dysfunction of the autonomic nervous system (ANS). Vagal nerve stimulation, for example, improves refractory depression and reduces chest pain from ischemic heart disease, suggesting that strong shared biological relationships exist. Heart rate variability (HRV) serves as an electrocardiographic biomarker of autonomic function, by measuring the sympathetic and parasympathetic outflow to the sinoatrial node of the heart. Low HRV represents autonomic dysfunction. We have shown that that a novel HRV measure, *Dyx*, shows promise as a predictor of abnormal myocardial perfusion, and in preliminary analysis shows a relationship with depression. We seek to explore the potential of HRV to serve as a means of investigating dysfunction of both central processes such as depression and peripheral cardiovascular reflexes as they relate to obstructive CAD. We hypothesize that low HRV will be associated with both depression and coronary artery disease in a dose-response manner, and that this relationship will be modified by age and sex. In the pilot study on this cohort, preliminary data that these associations exist. To fully characterize this association between depression, CAD, and ANS dysfunction, we will examine the changes in HRV in a cohort of 200 participants with both depression and CAD, either disease, or neither. Aim 1 will compare the depressive symptom burden with ANS dysfunction as measured by Dyx amongst other HRV measures. Aim 2 will compare the presence of obstructive CAD with ANS dysfunction as measured by Dyx. The interaction of age, sex, and time of day of HRV measurement with the findings will be considered. The proposed analyses will provide plausible evidence that the ANS dysfunction links both depression and CAD, with the long-term goal of identifying interventions that target ANS dysfunction to reduce mortality.