

NCT number not provided yet

Dr. Sherwin Toribio has guided the repeated-measures design, with the purpose of assessing change overtime for the four study groups. He will also help us control for potential confounders (nitrate level, biological sex, medication) to improve statistical strength where appropriate. For our primary outcome (i.e., 6MWT), power analysis, based on effect size of 0.80 indicates that experiments must be performed on a minimum of 12 patients per group for an alpha of 0.05 and power of 80% based on previously established means [34]. To achieve 90% power the patient n would be increased to 16 per group and is used for this proposal, which includes accounting for dropout. For our secondary outcome experimental power analysis, an alpha of 0.05 and power of 80%, indicates the minimum number of patients allowed 1) Gardiner n = 13; 2) shear-stress n = 14; 3) flow-mediated vasodilation n = 12; 4) near-infrared spectroscopy n = 15; 5) arterial stiffness n = 8; and 6) gastrocnemius muscle oxidative capacity n = 14. Therefore, we have chosen 16 participants per group to provide sufficient power to resolve differences for our measurements and to provide a margin for dropouts ~17% in supervised exercise studies [55]. Analysis of variance will be used to detect differences between two or more groups. Repeated measures ANOVA will be used for primary and secondary outcomes when multiple measurements (e.g., 6MWT, Gardiner, shear-rate, blood pressure,  $\text{NO}_3^-/\text{NO}_2^-$ , microvascular assessments) are performed. The groups will be block randomized (n = 5 per block) into a randomly selected group. If significant main effects are detected, the Newman-Keuls method will be performed for post hoc analysis.