

Table 1: Sources of Questions and References in Cases and Controls

Assessment	Method	Time of Administration
Cognitive Function	Digital Symbol Substitution Test ³³	Baseline and repeated after 2 weeks via web-based survey
Depression	Patient Health Questionnaire – 9 (PHQ-9) ³⁴ 9 items with score range from 0-27 Scores of 5, 10, 15, and 20 represent cut-points for mild, moderate, moderately severe and severe depression,	Baseline and repeated after 42weeks via web-based survey
Anxiety	GAD-7 ³⁵ is a concise scale with only 7 items aimed at screening for anxiety disorders using a 4 point Likert scale ranging from not at all to nearly every day. Its validity and reliability have been tested in both clinical and general population settings. Total scores range between 0 and 21 where higher scores are indicative of higher severity. Scores below 5 are indicative of minimal anxiety, scores between 5 and 9 indicate mild anxiety, scores between 10 and 14 indicate moderate anxiety and scores between 15 and 21 indicate severe anxiety.	Baseline and repeated after 2 weeks via web-based survey
ECG*	12-Lead ECG: Standard 12 lead ECG with interpretation completed by our cardiologist co-investigators *Continuous 7-day ECG: In a subset of participants to detect arrhythmias, heart rate variability	Taken at baseline visit Fitted at Baseline
Blood pressure	Resting Supine and Sitting using Omron BP Machine	Baseline
Spirometry	Portable spirometer to assess FeV1, measured with a portable spirometer (MicroGP; MicroMedical, Chatham, IL, USA), without spirographs, with use of a standardised protocol. ⁴³	Baseline
Hand Grip Strength	Grip Strength measured using a Jamar dynamometer ³⁸	Baseline
Symptoms	Checklist Used in ACT trial ⁴⁷	Baseline
Serum samples	hs-C Reactive Protein (CRP) – Beckman Coulter Unicel DxC 600 - High Sensitivity C-Reactive Protein cat# 378020 Troponin – Roche Cobas 8000 Troponin T hs cat# 05092744190, D-Dimer – Roche Cobas 6000 Tina-quant D-Dimer Gen 2 cat# 04912551190 NT-ProBNP – Roche Cobas 8000 ProBNP II cat# 04842464190	Baseline
Interheart Risk Score	Non-Lab based Risk Score (ref) is predictive of incident CVD and death ³⁷	Baseline
Post COVID Function Scale		Baseline
Substance Use	Self reported amount, type, frequency of alcohol, cigarettes, marijuana, other drugs	Baseline
EQ-5D	Consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. ³⁶ Mean from Canada survey = 81.3 (14.6) in men and women aged 45-56 years ⁴⁴	Baseline
Social Determinants of Health ⁴⁰	- Self-reported Ancestry - Annual Household income, employment status, marital status, - Educational attainment, social supports, neighbour trust - Multigenerational households, healthcare benefits - Sick pay - Trust in healthcare system - Vaccine Status	Baseline
Six Minute Walk Test	Participants walk a measured circuit for six minutes and the final distance is recorded. ³⁹	Baseline

*In a subset of cases (with severe symptoms of tachycardia or palpitations) and matched controls a 7 day pocket ECG monitor will be used

Table 2: Sample Size Considerations (with 330 cases to 660 controls), 2-sided α of 0.05

Primary measure	Controls	Putative effect Size Difference	Power	Source
Cognitive Function: DSST	73.9 (16)	3.5	90%	Anand et al. 2020 ⁴¹
Secondary measures	Controls	Cases	Power	Source
Grip Strength	30.6 (11.1) kg	5 kg decrease	>99%	Leong et al. 2015 ³⁸
Spirometry: GLI FEV ₁ /FVC	Z score 0 (1.0)	±0.5	>99%	Quanjer et al. 2012 ⁴⁵
6 minute walk test	593 (57) m -men 638 (44) m -women	54 m decrease	>99%	Wise et al. 2005 ³⁹
Depression: PHQ-9	2.79 (2.74-2.85)	5 point increase	>99%	Nwachukwu et al. 2020 ⁴⁶
Anxiety: GAD-7	4.33 (3.23)	5 point increase	>99%	Nwachukwu et al. 2020 ⁴⁶
Quality of Life: EQ-5D VAS	81.3 (14.6)	10 point decrease	>99%	Xie et al. 2016 ⁴⁴

References:

33. Jaeger J. Digit Symbol Substitution Test: The Case for Sensitivity Over Specificity in Neuropsychological Testing. *Journal of Clinical Psychopharmacology*. 2018;38(5):513-519.
34. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. *Journal of General Internal Medicine*. 2001;16(9):606-613.
35. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. *Archives of Internal Medicine*. 2006;166(10):1092-1097.
36. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727-1736.
37. McGorrian C, Yusuf S, Islam S, et al. Estimating modifiable coronary heart disease risk in multiple regions of the world: the INTERHEART Modifiable Risk Score. *European Heart Journal*. 2010;32(5):581-589.
38. Leong DP, Teo KK, Rangarajan S, et al. Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. *Lancet*. 2015;386(9990):266-273.
39. Wise RA, Brown CD. Minimal clinically important differences in the six-minute walk test and the incremental shuttle walking test. *Copd*. 2005;2(1):125-129.
40. Anand SS, Razak F, Davis A, et al. Social disadvantage and cardiovascular disease: development of an index and analysis of age, sex, and ethnicity effects. *International Journal of Epidemiology*. 2006;35(5):1239-1245.
41. Anand SS, Friedrich MG, Desai D, et al. Reduced Cognitive Assessment Scores Among Individuals With Magnetic Resonance Imaging Detected Vascular Brain Injury. *Stroke*. 2020;51(4):1158-1165.
42. Gulko E, Oleksk ML, Gomes W, et al. MRI Brain Findings in 126 Patients with COVID-19: Initial Observations from a Descriptive Literature Review. *American Journal of Neuroradiology*. 2020;41(12):2199-2203.
43. Duong M, Islam S, Rangarajan S, et al. Mortality and cardiovascular and respiratory morbidity in individuals with impaired FEV(1) (PURE): an international, community-based cohort study. *The Lancet Global health*. 2019;7(5):e613-e623.
44. Xie F, Pullenayegum E, Gaebel K, et al. A Time Trade-off-derived Value Set of the EQ-5D-5L for Canada. *Med Care*. 2016;54(1):98-105.
45. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *The European respiratory journal*. 2012;40(6):1324-1343.
46. Nwachukwu I, Nkire N, Shalaby R, et al. COVID-19 Pandemic: Age-Related Differences in Measures of Stress, Anxiety and Depression in Canada. *International Journal of Environmental Research and Public Health*. 2020;17(17):6366.
47. <https://www2.phri.ca/ACT-COVID-19/>