

Supplementary Table 3: Suggested list of structured interviews, clinical and laboratory assessments for the investigation of persistent fatigue & symptoms after COVID-19.

Assessment or Investigation	Domain (*COVID-19 specific elements)	Comment	Relevant references
Medical assessment	Thorough medical history and physical examination including functional status, signs of respiratory impairment or heart failure*, pulse oximetry*.	Characterize the fatigue state (e.g., fatigue, weakness, somnolence, dyspnea), identify pre-morbid, concurrent, or <i>de novo</i> contributors to the fatigue state.	<p>Wilson J, Morgan S, Magin PJ, van Driel ML. Fatigue—a rational approach to investigation. <i>Aust Fam Physician</i> 2014; 43: 457–461.</p> <p>Greenhalgh T, Knight M, A’Court C, Buxton M, & Husain L. Management of post-acute covid-19 in primary care. <i>The BMJ</i>. 2020 370.</p> <p>Sandler, C. X., & Lloyd, A. R. Chronic fatigue syndrome: progress and possibilities. <i>Medical Journal of Australia</i>. 2020 212(9), 428–433.</p> <p>National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2020.</p> <p>World Health Organization. Global COVID-19 Clinical Platform Case Report Form (CRF) for Post COVID condition (Post COVID-19 CRF). 2021.</p>
Mental health assessment	Thorough history and current mental state examination.	Characterize the fatigue state (e.g., anxiety, sleep disturbance, motivation loss). Identify pre-morbid, concurrent, or <i>de novo</i> contributors to the fatigue state.	<p>Stadje, R., Dornieden, K., Baum, E. et al. The differential diagnosis of tiredness: a systematic review. <i>BMC Fam Pract</i> 2016 17, 147.</p> <p>Kroenke K, Wood DR, Mangelsdorff AD, Meier NJ, Powell JB. Chronic Fatigue in Primary Care: Prevalence, Patient Characteristics, and Outcome. <i>JAMA</i>. 1988;260(7):929–934.</p> <p>Griffith JP, Zarrouf FA. A systematic review of chronic fatigue syndrome: don’t assume it’s depression. <i>Prim Care Companion J Clin Psychiatry</i> 2008; 10: 120–128.</p> <p>World Health Organization. Clinical management of COVID-19: interim guidance. 2020.†</p> <p>National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2020.</p> <p>World Health Organization. Global COVID-19 Clinical Platform Case Report Form (CRF) for Post COVID condition (Post COVID-19 CRF). 2021.</p>

Blood tests	Full blood count, urea, electrolytes and creatinine levels, liver, and thyroid function tests, C-reactive protein levels or erythrocyte sedimentation rate, and fasting blood glucose, D-dimer,* brain natriuretic peptides,* ferritin*.	Investigations to identify potential causes of chronic fatigue.	<p>Fukuda K, Straus SE, et al. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. <i>Ann Intern Med</i> 1994; 121(12): 953-9.</p> <p>Wilson J, Morgan S, Magin PJ, van Driel ML. Fatigue—a rational approach to investigation. <i>Aust Fam Physician</i> 2014; 43: 457–461.</p> <p>BMJ. BMJ Best Practice Coronavirus disease 2019 (COVID-19). 2020.†</p> <p>National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2020.</p> <p>Shah S, Shah K, Patel SB, et al. Elevated D-dimer levels are associated with increased risk of mortality in COVID-19: a systematic review and meta-analysis. <i>Cardiol Rev</i>. 2020;28(6):295-302. †</p> <p>Aboughdir M, et al. Prognostic value of cardiovascular biomarkers in COVID-19: a review. <i>Viruses</i>. 2020 11;12(5).†</p> <p>World Health Organization. Global COVID-19 Clinical Platform Case Report Form (CRF) for Post COVID condition (Post COVID-19 CRF). 2021.</p>
Imaging and other investigations	Chest x-ray, chest CT*, 12-lead ECG*, echocardiogram*, neuroimaging (MRI)*	Investigations to identify potential causes of ongoing fatigue and/or end organ sequelae of COVID-19.	<p>National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing the long-term effects of COVID-19. 2020.</p> <p>Marshall, J. C., et al. A minimal common outcome measure set for COVID-19 clinical research. <i>Lancet Infect Dis</i> 2020 20: e192–e197.</p> <p>Almqvist J, et al. Neurological manifestations of coronavirus infections - a systematic review. <i>Ann Clin Transl Neurol</i>. 2020;7(10):2057-2071.</p> <p>Castro RA, Frishman WH. Thrombotic complications of COVID-19 infection: a review. <i>Cardiol Rev</i> 2021; 29(1): 43-7.</p> <p>Ojo AS, Balogun SA, Williams OT, Ojo OS. Pulmonary fibrosis in COVID-19 survivors:</p>

	<p>Cognitive performance: Cambridge Neuropsychological Test Automated Battery (CANTAB)</p> <p>Cognitive Function Index (CFI)</p>	<p>CANTAB (proprietary): Includes tests of memory, attention, and executive function and is administered via a touch-sensitive computer screen. The CANTAB allows a decomposition of complex tasks commonly used in clinical assessment into their cognitive components. Tests include versions of the Wisconsin Card-Sorting Test, the Tower of London, and the Delayed Matching-to-Sample Test. Is non-verbal and largely language and culture independent.</p> <p>CFI: Measurement of cognitive performance. Assessment includes the California Verbal Learning Test, the Rey-Osterrieth Complex Figure Test, the computerized NES continuous performance test, the Trail Making Test A and B, the grooved pegboard test, and the WAIS-III Vocabulary and Digit Span subtests. Eight factors were identified including: verbal learning and memory, visual learning and memory, focused attention, simple information processing, sustained attention, general verbal ability, complex information processing, and fine motor speed.</p>	<p>predictive factors and risk reduction strategies. <i>Pulm Med</i> 2020; 6175964.</p> <p>Shafi AMA, Shaikh SA, Shirke MM, Iddawela S, Harky A. Cardiac manifestations in COVID-19 patients-A systematic review. <i>J Card Surg</i> 2020; 35(8): 1988-2008.</p> <p>World Health Organization. Global COVID-19 Clinical Platform Case Report Form (CRF) for Post COVID condition (Post COVID-19 CRF). 2021.</p> <p>Sahakian BJ, Owen AM. Computerized assessment in neuropsychiatry using CANTAB: discussion paper. <i>J R Soc Med</i> 1992;85:399– 402.</p> <p>Brimacombe M, Lange G, et al. Cognitive Function Index for Patients with Chronic Fatigue Syndrome. <i>J Of Chronic Fatigue Syndrome</i> 2004; 12(4): 3-23.</p>
Interviews	Domain	Comment	Relevant reference
Semi-structured Clinical Interview for Neurasthenia (SCIN)	Fatigue and related symptoms	Publicly available semi-structured clinical interview that assesses various aspects of fatigue (e.g., “fatigue” (including physical and mental fatigability), “pain symptoms”, “neurocognitive difficulties”, “sleep problems” and “mood disturbance”). Captures patterns of occurrence of symptoms & degree to which each symptom causes functional impairment.	Bennett, B et al. Characterization of Fatigue States in Medicine and Psychiatry by Structured Interview. <i>Psychosomatic Medicine</i>. 76(5), 379–388.
Composite International Diagnostic Instrument (CIDI)	Mood disturbance	CIDI: A computerized structured interview for assessment of mental disorders. Measures prevalence, severity, determines burden of mental health disorders. Supported by the World Health Organization (WHO), the CIDI has been widely used in large epidemiologic studies and therefore allows for national comparisons of psychiatric prevalence rate. Can be administered by trained lay interviewers.	Andrews G, Peters L. The psychometric properties of the Composite International Diagnostic Interview. <i>Soc Psychiatry Psychiatr Epidemiol</i> 1998;33:80–8. Robins LN, et al. The Composite International Diagnostic Interview. An epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. <i>Arch Gen Psychiatry</i>. 1988 Dec;45(12):1069-77.
Structured Clinical Interview for		SCID: A semi-structured interview guide for major mental health disorders. Must be administered by trained interviewers.	Spitzer RL, Williams JB, Gibbon M, First MB. The Structured Clinical Interview for DSM-III-R (SCID).

DSM-IV Axis I (SCID)			I. History, rationale, and description. Arch Gen Psychiatry 1992;49:624-9.
Diagnostic Interview Schedule (DIS)		DIS: A structured diagnostic interview designed to assess specific symptoms, chronology, duration and associated impairments. Can be administered by trained lay interviewers.	Diagnostic Interview Schedule. Arch Gen Psychiatry 1982; 39(12): 1442-5.
Structured Diagnostic Interview for Sleep patterns and disorders (DISP)	Sleep	Publicly available structured interview that screens for a range of sleep disorders (delayed sleep phase, hypersomnia, insomnia, narcolepsy with cataplexy, period limb movement disorder, restless legs syndrome, rapid eye movement sleep behavior disorder, sleep apnea) and clinical impact (symptom course, impairment, severity and treatment). Can be administered by trained lay interviewers.	Merikangas KR, et al. The structured diagnostic interview for sleep patterns and disorders: rationale and initial evaluation. Sleep Med. 2014;15(5):530-5.

* COVID-19 specific elements

† This reference is regarding the management of acute COVID-19. The relevance for persistent COVID-19 symptoms is uncertain.