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Table 2: Closed COFFI cohorts

Cohort name, Country	Major Reference(s)	Participants	Follow-up	CFS Definition(s) Used	Questionnaires/ Data Collected	Samples Collected	Assay Data	Other Investigations
Barts Infectious Mononucleosis (IM) cohort, UK	White 1998 <sup>5</sup>	469 primary care patients approached, 250 recruited, 245 eligible: 108 IM confirmed Epstein-Barr Virus (EBV), 83 non-EBV IM-like, 54 URTI controls	1, 2 & 6 months, patient records to 2.5 years	Empirical fatigue syndrome, Centers for Disease Control (CDC)/ Fukuda, Oxford	20 infectious symptoms, Hospital Anxiety and Depression Scale (HADS), Eysenck Personality Questionnaire (EPQ), days spent in bed, premorbid GP attendance, Research Diagnostic criteria for psychiatric illness), Life Events and Difficulties Schedule, Paced Auditory Serial Addition Test, Present State Exam, Clinical Interview Schedule, Hamilton Depression Rating Scale, Schedule for Affective Disorders and Schizophrenia	Serum, T cells, mouth wash (no longer available)	EBV, Cytomegalovirus (CMV), Human Herpesvirus 6. Hepatitis A and C, toxoplasmosis, adenovirus, influenza A and B, parainfluenza, Respiratory Syncytial Virus, <i>Coxiella burnetti</i> , <i>Mycoplasma pneumoniae</i> , <i>Chlamydia psittaci</i> and anti-streptolysin O antibodies, liver chemistries, B cell regression assay.	Exercise work capacity, cardiovascular response to exercise

Prospective Study of the Natural History of IM Caused by EBV (Seattle, USA)	Buchwald 2000 <sup>6</sup>	Puget Sound area health maintenance organisation primary care facilities, 150 IM patients recruited; 146 at 1 month, 144 at 2 months, 142 at 6 months, 50 at 48 months	1, 2, 6 & 48 months	Not necessarily CFS	Symptom Checklist-90, Short Form (SF)-36, NIH Mental Health Diagnostic Interview Schedule, List of Threatening Experiences, Perceived Social Support Inventory	Serum	Complete blood count with a differential leukocyte count, serum AST, ALT, bilirubin level, and EBV titres.	
Dubbo Infection Outcomes Study (DIOS), Australia	Hickie 2006, <sup>38</sup> Cameron 2006, <sup>22</sup> 2007, <sup>23</sup> 2010, <sup>26</sup> Vollmer-Conna 2007, <sup>24</sup> Kadota 2010 <sup>40</sup>	Laboratory notifications for 855 potential participants from 94 primary care practitioners, 430 contacted, 253 recruited: 68 confirmed EBV, 60 confirmed Ross River Virus, 43 confirmed Q fever, 82 unconfirmed	2 & 6 weeks; 3, 6 & 12 months, and then 6 monthly until recovery (for cases) for at least 5 years	CDC/ Fukuda/ post-infectious fatigue syndrome/ acute sickness response	Structured Clinical Interview for Neurasthenia; Prolonged fatigue state (score $\geq 3$ ) on SOMA somatic symptoms subscale of 34-item Somatic, Psychological Health Report, Physical symptoms Checklist, McGill Pain Questionnaire, Alcohol Use Disorders Identification Test, SF-36, Sleep Assessment	DNA, RNA, plasma, Peripheral blood mono-nuclear cells		Serum and stimulated cytokine levels, transcriptomics, genetic polymorphisms (e.g., cytokines).

					Questionnaire, Brief Disability Questionnaire (BDQ), Health Care Utilization, EPQ, Locus of Control of Behaviour Scale, Illness Behaviour Questionnaire, Illness Impact			
Prospective Study of CFS Following IM (Chicago, USA)	Katz 2009, <sup>7</sup> 2010, <sup>34</sup> 2011, <sup>37</sup> 2013 <sup>35</sup> Broderick 2012 <sup>36</sup>	N=301 adolescents (12-18) with heterophile-positive IM	6, 12 and 24 months following illness	CDC/Fukuda	Autonomic Symptom Checklist, Orthostatic Tolerance Testing, Fatigue Severity Scale, Modifiable Activity Questionnaire, CFS Screening Questionnaire, Occupational Health Assessment, Child Health Questionnaire	Serum, Plasma, Saliva, Urine		Exercise testing, Orthostatic Tolerance Testing, CBC, metabolic, endocrine testing, urinalysis, erythrocyte sedimentation rate, cytokine analysis, salivary cortisol, Natural Killer cell number and function
CEBA (Chronic fatigue following acute EBV infection in Adolescents), Norway	Clinicaltrials.gov	Laboratory identification of IM cases from AHUS University Hospital: 200 adolescents with EBV; 70 healthy controls	6, 9 & 21 months	Canadian, CDC/ Fukuda, Institute of Medicine	Chalder Fatigue Questionnaire score $\geq 4$ (range 0-11), Autonomic Symptom Profile, Peds-QL, Functional	Blood (serum, plasma, peripheral blood mono-nuclear cells),	EBV-DNA by real-time PCR; anti-EBV EBNA IgG and Viral Capsid Antigen IgG and IgM; antibodies against CMV and <i>Borrelia</i>	Accelerometers for monitoring of daily physical activity during seven consecutive days; algometer for assessing

					Disability Inventory, Brief Pain Inventory, Life Event Checklist , HADS, Child-Adolescent Perfectionism Scale, Toronto Alexithymia Scale-20 item, Brief Illness Perception Questionnaire, Karolinska Sleep Questionnaire, The Penn State Worry Questionnaire, Wechsler Intelligence Scale for Children, Delis-Kaplan Executive Function System, Hopkins Verbal Learning Test-Revised, Wechsler Abbreviated Scale of intelligence	urine (morning spot), hair	<i>burgdorferi</i> ; cytokines; plasma catechol-amines; candidate gene single nucleotide polymorphisms; number and cytotoxic function of natural killer cells; cortisol from urine and hair	pain threshold; cardiovascular assessment; cognitive assessment.
Auckland IM & Campylobacter gastroenteritis cohorts, NZ	Spence 2007, <sup>21</sup> Moss-Morris and Spence 2006; <sup>12</sup> Moss-	Laboratory identification of 2547 CG cases, ~1500 questionnaires	3 and 6 months	British (Sharpe), CDC/ Fukuda	HADS, Illness Perceptions Questionnaire - Revised, Perceived Stress	None	None	

	Morris <i>et al</i> 2011 <sup>20</sup>	sent, 758 returned, 620 recruited: CG (n=592); after 3 months N = 581, after 6 months N = 547			Scale, Behavioural Responses to Illness Questionnaire, The negative subscale of the Positive & Negative Perfectionism Scale			
Dutch Q fever (and LRTI & Legionnaires' disease) studies: - <b>Cohort 2010-11</b>  - <b>Legionnaires' disease</b>	<b>Cohort 2010-11:</b> Van Loenhout, J of Inf 2015 <sup>31</sup>  <b>Legionnaires' disease:</b> Van Loenhout, J of Inf 2014 <sup>30</sup>	<b>Cohort 2010-11:</b> Eligible: 376 Participated: 336 Drop-outs: 58.  <b>Legionnaires' disease:</b> Eligible: 243 Included: 190	<b>Cohort 2010-11:</b> 3, 6, 9, 12, 18, and 24 months  <b>Legionnaires' disease:</b> 12 months after onset illness	No CFS diagnosis used.  (Laboratory confirmed Q fever; applies for all Q fever patients in the cohorts)	<b>Cohort 2010-11:</b> Short Form 36 (SF-36) and Nijmegen Clinical Screening Instrument (NCSI)  <b>Legionnaires' disease:</b> SF-36 and NCSI questionnaire			
Qure Study, NL	Keijmel 2017 <sup>42</sup>	180 Q fever patients randomised to 6 months' cognitive behavioural therapy(CBT), 60 doxycycline or 60 placebo; follow-up to 12 months post-treatment intention to treat analysis, N = 154,	12 months	Q fever Fatigue Syndrome – diagnostic criteria similar to CDC/Fukuda but requiring laboratory-proven acute Q	Sickness Impact Profile  Symptom Checklist 90, Self Observation List, Checklist Individual Strength	No study-specific samples collected. Routinely-collected sera may have been stored from time	<i>C burnetti</i> serology, liver enzymes, doxycycline levels	Actometer

		52 doxycycline, 52 placebo, 50 CBT.		fever in the context of an acute illness with fever		of initial diagnosis.		
Bergen Giardiasis cohort, Norway	Wensaas 2012, <sup>14</sup> Morch 2013, <sup>17</sup> Hanevik 2014 <sup>18</sup>	Laboratory notified giardiasis (2004 outbreak, N=1252); age/gender-matched controls: n=817 at 3 years, 748 at 6 years, 590 at 10 years At 5 years, 53 of 253 assessed for CFS	3, 5, 6 and 10 years	CDC/ Fukuda	Chalder Fatigue Questionnaire score $\geq 4$ (range 0-11); Rome III diagnostic questionnaire for irritable bowel syndrome and functional dyspepsia.	Stool, Serum and PBMC in subgroup of patients	<i>Giardia lamblia</i> cysts detected by direct microscopy or by a faecal antigen test (ImmunoCard STAT! Cryptosporidium/ <i>Giardia</i> rapid assay; Meridian Bioscience, Inc)	Sleepiness (3, & 6 years), Asthma and allergy (3, & 6 years), Overactive bladder (6 years), Fibromyalgia (10 years)

