Principal Investigator	Dr. Stephan Woditschka
Institution	University of North Carolina at Wilmington
Project Summary	This study will be a cross-sectional analysis of de-identified data from the Chronic Fatigue Initiative (CFI) study. Analyses will be restricted to participants who report that a physician or health care provider diagnosed them with ME/CFS. Controls will not be included in the analytic sample. Diagnostic delay (in years) will be calculated as age at physician diagnosis – age at symptom onset. Participants must have non-missing values for both variables to be included in the primary analysis. Data checks will be conducted to identify implausible values (e.g. negative delay). Descriptive statistics will first be used to summarize age at onset, age at diagnosis, and diagnostic delay. The association between age at symptom onset and diagnostic delay will be evaluated using regression modeling, with diagnostic delay as a continuous outcome and age at symptom onset as a continuous predictor. Model assumptions will be assessed, and if delay is substantially skewed, appropriate adjustments will be considered. Secondary analyses may include adjusting for selected demographic and clinical variables in the dataset (sex, comorbidity, etc.) and presenting descriptive comparisons across clinically meaningful age-at-onset groups. All analyses will be conducted using de-identified data in accordance with the NINDS Data Use Certificate and institutional data security requirements.
Project Non-Technical Summary	Myalgic encephalomyelitis/chronic fatigue syndrome is a chronic illness that is often associated with delayed diagnosis. While the length of time between the appearance of symptoms and formal diagnosis has been described in previous research, less is known about whether the age at symptom onset influences how long individuals wait to receive a diagnosis. This study will use existing data from the Chronic Fatigue Initiative study to examine whether individuals who develop ME/CFS symptoms at younger ages experience longer delays before diagnosis by a physician. Diagnostic delay will be measured as the number of years between symptom onset and diagnosis. Understanding whether age at symptom onset is associated with differences in diagnostic timing may help clarify patterns in how ME/CFS is recognized across age groups and contribute to future research on improving timely identification of the illness.
Data Access Granted	CFI
Project Timeline	Approval Date: 4/22/2026 Expected Close-out Date: 4/22/2027

Principal Investigator	Dr. Marcos Lacasa-Cazcarra
Institution	Universidad Internacional de La Rioja (UNIR)
Project Summary	This submission requests data-only access to two mapMECFS studies: CFI, to perform external validation and cross-cohort harmonization of patient-reported outcome measures (PROMs) in ME/CFS. The project focuses on item-level ("raw") questionnaire responses and their official derived scores, with SF-36 as the primary anchor instrument and PSQI as a key target instrument. The work consists exclusively of secondary analysis of de-identified data (no participant contact, no interventions). Biospecimens are not requested in this phase. Primary objectives (CFI data-only) 1. External validation across independent cohorts: Validate whether PROM patterns and relationships observed in our local cohort (UNIR/VHIR) generalize to larger independent cohorts (CFI). 2. SF-36 anchor validation: Assess cross-cohort consistency of SF-36 item-level distributions and derived scores, and quantify comparability between cohorts. 3. PSQI replication and linkage: Using PSQI item-level responses and official scores, evaluate whether sleep-related outcomes replicate and how they relate to SF-36 across cohorts. 4. Scoring reproducibility: Confirm that analyses based on raw item responses reproduce the official derived scores (SF-36, PSQI and other instruments where available), supporting harmonized cross-study analysis. Secondary objectives 5. Secondary interpretation using additional PROM scores: Use available derived scores for additional fatigue, pain, psychological, and symptom instruments to support secondary interpretation and mapping to our local measures (HADS/HAD, FIS-40, COMPASS-31). 6. Exploratory PROM-based subgrouping: Explore whether stable PROM-derived subgroups can be detected consistently across CFI, informing later phases integrating objective measures (e.g., CPET) when available.
Project Non-Technical Summary	We are requesting access to de-identified questionnaire data to confirm that findings from our ME/CFS research replicate in larger independent cohorts. We will focus on two widely used questionnaires—SF-36 (quality of life) and PSQI (sleep)—using both the original responses and the official scores to ensure results are reliable and comparable across studies. This work will help identify consistent patterns in patient-reported outcomes across cohorts and improve reproducibility, without contacting participants and without requesting biospecimens in this phase.
Data Access Granted	CFI and MCAM
Project Timeline	Approval Date: 3/31/2026 Expected Close-out Date: 3/31/2027

Principal Investigator	Professor Joanna Poulton
Institution	The Chancellor, Masters and Scholars of the University of Oxford
Project Summary	The definition of ME/CFS is uncertain.(1) Nevertheless it is important to quantify the disorder, in order to facilitate research. One way to do this is via patient reports. The dePaul Symptom Questionnaire (DSQ) is commonly used to quantify symptoms. Our proposed study will aim to establish the DSQ's psychometric qualities, in order to optimise its use to estimate overall severity. Patient responses to items on the DSQ comprise ordinal scores. It is important to use appropriate mathematical techniques in order to estimate severity from ordinal scores.(2) However, existing psychometric reports did not take this into account.(1,3,4) We will account for the ordinal nature of DSQ ratings using techniques from item response theory (IRT).(5–7) Many questionnaires – including the DSQ – are multidimensional. That is, the questionnaires tap several dimensions of the respondents' experience (e.g. fatigue, pain, sleep disturbance). Multidimensionality threatens the validity of a questionnaire's total score as indicator of overall severity. Nevertheless, researchers commonly sum DSQ scores and use them as indicators of the overall severity of ME/CFS. If the total scores are misleading indicators of overall severity, then this may have major ramifications for all research that uses the DSQ. It remains an open question how best to summarise the scores of multidimensional instruments, in a manner that may be most useful to researchers. One approach to this problem is to use bifactor analysis.(8) This method partitions the variance of the instrument's ratings between the separate dimensions and a latent factor representing overall severity. We will test if a bifactor analysis of the DSQ fits the data better than a single factor, or a multidimensional structure. Ideally, we will be able to develop a bifactor and/or multidimensional IRT model that fits the empirical data from the DSQ. However, while a mathematical model may be valuable in itself, it is important to validate the model using external data. To this end, we will collaborate with Prof Maureen Hanson and her colleagues, to test if the IRT-derived estimates of the severity of ME/CFS fit with physical measures. Prof Hanson and her colleagues have provided evidence that variants of mitochondrial genes may relate to different sub-groups of ME/CFS.(9) We will assess if variants of mitochondrial genes fit better with estimates of severity from IRT-based analyses (e.g. the overall severity and estimates of individual factors from a bifactor model) than with raw DSQ scores. If the proposed research comes to fruition, then we would envisage (1) providing the Chronic Fatigue Initiative with more valid measures of severity than those which are currently available from the DSQ; (2) advancing knowledge concerning the psychometric properties of the DSQ; and (3) potentially, linking individual symptom profiles with variants of mitochondrial genes.

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Project Non-Technical Summary	The definition of Myalgic Encephalomyelitis / Chronic Fatigue Syndrome is uncertain. Nevertheless it is important to quantify the disorder. One approach to this is via patient reports. The dePaul Symptom Questionnaire (DSQ) is a standard instrument to quantify patient reports. Our proposed study will aim to establish the DSQ's psychometric qualities, in order to optimise its use to estimate overall severity.
Data Access Granted	CFI
Project Timeline	Approval Date: 3/22/2023 Expected Close-out Date: 4/22/2024