

Attachment 17

Justification of Non-exempted Clinical Evaluation Questionnaires

Summary of Questionnaires to be Administered

1. General Medical History, Gynecologic History (for females), Physical Examination, Review of Medications and Laboratory Examinations

A past medical history, review of medications, physical examination, and screening laboratory tests are necessary to rule out medical causes of illness and to classify a subject as having CFS. The past medical history, review of medications, physical examination, and screening laboratory tests are as approved in the *Survey of CFS Chronic Unwellness in Georgia* (CDC IRB #4121).

Study subjects (and parents of adolescents) will complete the past medical history at home; all female subjects will complete the gynecologic history at home. Upon arrival at the clinic, a nurse or trained laboratory technician will review these questionnaires and clarify ambiguities. In addition, the physician MUST review the medical history during the exam and further clarify any positive medical history by querying the subject and recording additional details in the space reserved 'for office use only' on the form. Study subjects will be asked to bring all current prescription and over the counter medications to clinic, and these will be reviewed and recorded by a nurse.

Each subject will undergo a complete physical examination by the local study physician. The physician will be required to write a summary of his impression from the patient and record his differential diagnosis on the physical exam form. The differential should include whether or not they would consider CFS.

2. Questionnaires Concerning Symptomatology

All of the questionnaires below were approved for use in the completed study of *Survey of CFS and Chronic Unwellness in Georgia* (CDC IRB protocol #4121) or the *First Follow-Up* of that survey. The first three instruments below will be used to classify subjects as either CFS or Unwell. The fourth questionnaire, the Fatigue questionnaire, is administered to the adolescents in clinic in order to get their input (adult subjects are asked these questions by phone). For each questionnaire, we have designated whether it will be administered to adults only, or adults and adolescents.

Symptom Inventory (adults and adolescents). We will use the CDC Symptom Inventory [Wagner *et al.*, 2005] to collect information on occurrence, frequency, and severity of symptoms common in CFS and other fatiguing illnesses. This instrument takes 5 to 10 minutes to complete and is completed at clinic.

Medical Outcomes Study 36-item short-form health survey (SF-36v2) [Ware & Sherborne, 1992] (adults and adolescents): a general

indicator of health status (function and well-being) and includes primarily non-psychiatric health status questions. The SF-36v2 is a well-researched, reliable and valid broad-based, sophisticated instrument with population norms and normative data for a wide variety of medical conditions. The SF-36v2 assesses health-related quality of life in 8 areas: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health; 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions. This instrument takes 10 to 15 minutes to complete.

Multidimensional Fatigue Inventory (MFI) [Smets *et al.*, 1995] (adults and adolescents): a 20-item self-report instrument designed to measure fatigue, covering the dimensions general fatigue, physical fatigue, mental fatigue, reduced motivation and reduced activity. This instrument takes 5 to 10 minutes to complete.

Fatigue (adolescents only). A series of questions that measure the duration of fatigue and how it impacts the lives of adolescents will be administered in clinic. These questions are the same as those asked of adults in the detailed telephone interview. Since parents of adolescents are interviewed by phone about their child, we are providing the child with the opportunity to answer these questions for themselves in clinic. This questionnaire will take 5 minutes to complete.

3. Psychiatric Evaluation

During the clinical evaluation, all subjects will undergo a general psychiatric evaluation administered by experienced licensed psychiatric social workers, clinical psychologists, psychiatric nurse practitioners, or certified research nurses with experience in psychiatric assessments. The objective of the psychiatric evaluation is to identify psychiatric conditions that would exclude diagnosis of CFS, identify psychiatric co-morbidity, and measure psychological characteristics postulated as associated with CFS. All of these instruments were approved by the IRB for clinical evaluation during the *Survey of CFS and Chronic Unwellness in Georgia* (CDC IRB protocol #4121).

Structured Clinical Interview for DSM-IV (SCID) (adults and adolescents). The SCID is a semi-structured interview for collecting a psychiatric history of major Axis I DSM-IV diagnoses. The SCID was approved by the IRB for use in the baseline *Survey of CFS and Chronic Unwellness in Georgia* and the *First Follow-up*. It includes an introductory overview followed by nine modules, seven of which

represent the major axis I diagnostic classes: screening module, mood episodes, psychotic screen, mood disorders, substance use disorders, anxiety disorders, somatoform disorders, eating disorders, and adjustment disorders. Using a decision tree approach, the SCID guides the interviewer in testing diagnostic hypotheses as the interview is conducted. We will use the Research Version of the SCID for this study. The output of the SCID is a record of the presence or absence of each of the disorders being considered, for current episode (past month) and for lifetime occurrence. It requires about 30 to 90 minutes to evaluate the psychiatric status of subjects. Adolescents and parents of adolescents will be told that the parents are entitled to the results of the SCID.

Personality Diagnostic Questionnaire (PDQ-4) (adults only). The Personality Diagnostic Questionnaire-4th Edition (PDQ-4) is a 100 item, self-administered, true/false questionnaire that yields personality diagnoses consistent with the DSM-IV diagnostic criteria for the axis II disorders. It takes approximately 20 to 30 minutes to complete. It is widely used in clinical practice and in research projects throughout the US and has been translated in several different languages.

Because the SCID and the PDQ-4 provide only categorical diagnoses, we will administer additional standard rating scales to quantify core symptoms of interest. The following instruments will be given at the clinic during the time slot allotted for questionnaires.

Self-Rating Depression Scale (SDS) (adolescents and adult). This self-report scale was designed to quantify the severity of current major depression in 20 items. Most guidelines suggested that index scores of less than 50 are within the normal range, while scores of 50 to 59 indicate minimal or mild depression, 60 to 69 indicate moderate depression and scores above 70 indicate severe depression. It requires about five minutes to complete and 10 to 15 minutes to evaluate the psychiatric status of subjects.

Spielberger State-Trait Anxiety Inventory (STAI) (adults only). The self-report instrument was designed to assess levels of state anxiety and trait anxiety, through 40 items scored by a Likert-scale. State anxiety can be defined as a transient momentary emotional status that results from situational stress. Trait anxiety represents a predisposition to react with anxiety in stressful situations. The STAI requires approximately 10 to 15 minutes to complete.

Davidson Trauma Scale (DTS) (adults and adolescents if indicated by SCID results). The DTS was designed as a self-report scale measuring frequency and severity of PTSD symptoms in three clusters: intrusion, avoidance, and hyperarousal. For the 17 frequency and severity items,

the Cronbach's alpha was 0.99, for the frequency items alone it was 0.97 and for the severity items 0.98. The scale showed good convergent and discriminant validity. Davidson proposed a threshold of 40 for a total symptom score to predict the onset of a PTSD. The Davidson PTSD Scale requires approximately 5 to 10 minutes to complete.

4. Assessment of Early and Adult Life Experiences

The assessment of the stress history will focus on early and lifetime trauma experiences and their relationship to chronic fatigue. Because of the increasing evidence for a role of stress during development as a risk factor for CFS, and because of the evidence that symptoms of CFS are often exacerbated by acute life stress, we will include a detailed assessment of stress history in the present study. The following instruments will be given at the clinic during the time slot allotted for questionnaires.

Childhood Trauma Questionnaire (CTQ-SF) (adults only). This short-form of the Childhood Trauma Questionnaire was designed to assess retrospectively perceived childhood abuse and neglect. The 28-item self-report instrument consists of five clinical scales: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. The short form takes about 10 to 20 minutes to complete.

Traumatic Life Events Questionnaire (TLEQ) (adults only). This self-report instrument assesses exposure to 21 types of potentially traumatic events that proceed gradually from stressors that are not highly personal (e.g., natural disasters, motor vehicle accidents) to events that are personally sensitive to many people (e.g., intimate partner abuse, sexual abuse). Registry candidates are asked to indicate the frequency of occurrence of each trauma and whether they experienced intense fear, helplessness or horror relating to the DSM-IV PTSD A2 criterion. The TLEQ requires approximately 10 to 15 minutes to complete.

Life Experiences Survey (LES) (adults only). This self-report instrument was developed to evaluate major life events in the past year. The first section of the questionnaire lists 47 experiences and allows the respondent to add three additional life events and was designed for use in the general population. The format of the LES asks subjects to rate separately the desirability and impact of events that they have experienced in the last 12 months divided into two semesters. The questionnaire provides a positive change score by summing the impact ratings of events designated as positive by the subject and a negative change score summing the negative ratings. By adding these two values, a total change score can be obtained, representing the total amount of change. The LES requires approximately 10 to 15 minutes to complete.

5. Assessment of Stress and Coping

Complex psychological traits such as attribution styles, coping strategies and personality traits cannot be reliably assessed by telephone interview. We will therefore assess these traits in individuals that are invited to clinic. The following published

instruments have demonstrated reliability and validity and will be administered at clinic.

Perceived Stress Scale (PSS) (adults and adolescents) measures the degree to which situations in life experienced during the previous month are perceived as stressful. The PSS has 10 items that assess how predictable, uncontrollable, and overloading participants considered their lives. The PSS requires approximately 5 minutes to complete. Adults will complete this questionnaire as part of the telephone interview. Adolescents will be administered this questionnaire in clinic, as part of the Adolescent Health Questionnaire.

Illness Management Questionnaire (IMQ) (adults and adolescents with fatigue only). The illness management questionnaire (IMQ) was designed to assess coping in CFS by the use of 45 items. The IMQ was not used in the *Survey of Chronic Fatigue Syndrome and Chronic Unwellness in Georgia* (CDC IRB protocol #4121) but has been approved for the *First Follow-Up* of that study. The IMQ yields four factors: maintaining activity, accommodating to the illness, focusing on symptoms and information seeking. Scales based upon these factors together predicted 26%, 27%, and 22% of the variance in functional impairment, anxiety, and depression, respectively (Ray *et al.*, 1993). It is suggested that the IMQ may be employed to relate ways of coping to outcomes in CFS. This instrument requires approximately 10 to 15 minutes to complete.

Social Support Questionnaire (SSQ) (adults and adolescents). The SSQ is designed to measure the number of social support sources available to individuals, as well as their satisfaction with available support by 27 items. The SSQ was not used in the *Survey of CFS and Chronic Unwellness in Georgia* (CDC IRB protocol #4121) but was approved for use in the *First Follow-Up* of that study. Participants are asked (a) to list all of the people they can count on for support in different domains (e.g., Who do you know whom you can trust with information that could get you in trouble?) and their relationship with the individual, and (b) to rate on a 6-point scale how satisfied they are with each person's support. Average satisfaction with spousal support can be calculated by summing the satisfaction scores for spouse support and dividing by the number of times the spouse is mentioned as a source of support. The SSQ requires approximately 10 to 15 minutes to complete.

The Ironson-Woods Spirituality/Religiousness Index (adults and adolescents). The Ironson-Woods SR Index consists of 25 items grouped under 7 categories: (1) Comfort, strength, peace, (2) Feeling a connection, less alone, (3) Existential/afterlife, (4) View of God, (5) Somatic/illness recovery, (6) Religious behavior, (7) View of others, compassion for others. The items were developed from interviews with

60 medically ill patients, 20 with cancer, 20 with HIV and 20 with cardiac illness, who identified themselves as spiritual, religious or both (by Woods and Ironson in a separate study). The key purpose to development of this scale was to include items that were both pertinent to traditional religion and relevant for those who described themselves as spiritual only or as both religious and spiritual.

The Ironson-Woods SR Index has been documented to have very good test-retest reliability (0.88) and the overall Cronbach alpha was .94 (with category alpha's ranging from .85 to .94). It was also tested against 3 other instruments that measured spirituality/religiousness and correlated highly (Hoge and Duke Religiosity Scales and the Use of Religion to Cope subscale from the COPE instrument ($r = .66, .60, .70$, respectively). This instrument should take no more than 5 minutes to complete.

Illness Perception Questionnaire - Revised Version (IPQ-R) (adolescents and adults). The IPQ-R is a recently developed and widely used quantitative measure of illness representations containing 70 items. The revised version stemmed from a need to deal with minor psychometric problems with two subscales, and to include additional subscales, assessing cyclical timeline perceptions, illness coherence, and emotional representations. Reliability analyses provided good evidence for both the internal reliability of the subscales and the short (3 week) and long term (6 month) retest reliability. The IPQ-R also demonstrated sound discriminant, known group and predictive validity. This instrument takes 10 to 20 minutes to complete. For adolescents, this questionnaire will be bundled with 2 other questionnaires: Perceived Stress and Sense of Community, to be administered at clinic.

Sense of Community. (adults and adolescents). Sense of Community (SOC) is a construct to measure a sense of membership to a group. SOC is related to a greater sense of well-being and self-efficacy. There are 4 dimensions of the SOC: (1) membership in the community; (2) influence of members over the community, and community influence over its members; (3) shared community values, needs, perceived reward for community participation; (4) shared emotion, that is, member engagement in quality interactions and having a shared feeling of value for the community. There are 12 items in this questionnaire and it takes about 5 minutes to complete. The Cronbach's alpha for this instrument = .54; higher scores represent higher perceived SOC. Adolescents will be administered this questionnaire in clinic, as part of a 3-part questionnaire bundle that also includes Health Perceptions and Perceived Stress. Adults will complete this questionnaire at home as part of the Health Services Utilization questionnaire. Adolescents will be administered this questionnaire in clinic, as part of the Adolescent Health Questionnaire.

Ways of Coping Questionnaire (WCQ); (adults and adolescents). The WCQ was approved by the IRB for use in the *Baseline Survey*. This instrument is a 66-item questionnaire containing a wide range of thoughts and acts that people use to deal with the internal and/or external demands of specific stressful encounters. There are four different factor solutions from three different authors. The WCQ requires approximately 15 to 25 minutes to complete and will be completed on tablet PCs using CASI.

6. Assessment of Economic Impact (adults only)

Economic Impact will be assessed by collecting data from clinic participants using a questionnaire developed by the CFS research group at CDC and Abt Associates. The Economic Impact Questionnaire was approved by the IRB for use in the *Survey of CFS and Chronic Unwellness in Georgia* (CDC IRB protocol #4121) and *First Follow-up Study*. This instrument will be included in the appointment packet of materials to be completed at home and brought to the clinic appointment. It collects information regarding health insurance, money spent on medical care, earnings, employment status, and other items to assess direct and indirect costs of illness. We expect that some of the items in the questionnaire might require some extra time and thought. This questionnaire is expected to take 10 to 15 minutes to complete.

7. Assessment of Health Services Utilization (adults and parents of adolescents), including complementary and alternative medicine.

Utilization of health services will be assessed by collecting data from all clinic participants using a questionnaire developed by the CFS research group at CDC. A basic version of The Health Services Utilization Questionnaire was approved by the IRB for use in the *Survey of CFS and Chronic Unwellness in Georgia* (CDC IRB protocol #4121) and was modified to include questions on complementary and alternative medicine use. This instrument will be included in the packet of materials to be completed at home, and collects information regarding number of visits to a health care professional, type of health care professional seen, purpose of visit, and diagnosis received. This instrument takes 10 to 15 minutes to complete at home and will be brought to the clinic.

8. Assessment of provider's knowledge, attitudes and beliefs (Pre-test and Post-test). Knowledge, attitudes and beliefs of providers will be assessed at two time-points, using a 20-item questionnaire. A Pre-Test will be mailed to all providers who indicated their interest in participating in the study. It will be included in the packet of materials sent at the initiation of the study. Providers will be asked to complete the short questionnaire and return it in a stamped, addressed envelope. The same questionnaire (minus the demographic/patient

base information) constitutes the Post-Test, which will be mailed to providers approximately 9 months after initiation of the study. Each questionnaire takes about 5 minutes to complete.

Literature Cited

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