Evidence Report

Chapter 1. Introduction

Purpose

The purpose of this project, nominated by the Social Security Administration (SSA) and contracted through the Agency for Healthcare Research and Quality (AHRQ), was to determine whether current medical knowledge supports the SSA's stated policies regarding MS. In January 2003, the Duke Evidence-based Practice Center began work on this 13-month task to review evidence from the medical literature for use in updating SSA's listing of impairments for multiple sclerosis (MS) and for revising its disability policy (if indicated).

Background

The Social Security Administration runs the world's largest disability program and processes more than 3.5 million claims each year. Multiple sclerosis is the third most common neurological diagnosis cited as the cause for disability. SSA uses the most stringent criteria of any disability program in the world to define disability.[1]

Knowledge of the terms used in the SSA disability evaluation process, components of that process, and Medical Listing criteria related to MS is critical to the reader's understanding of this report. To assist in the preparation of the report, SSA provided explanations of terms and processes as currently defined by SSA regulations and rulings. The terms cited below, as well as other terms and processes used by SSA for disability determination, are defined and described in the SSA publication, *Disability Evaluation Under Social Security 2003*.[2]

The statutory definition of "Disability" is: The inability to engage in any substantial gainful activity by reason of a medically determinable physical or mental impairment(s) which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months. This definition differs from the clinically used definition of the World Health Organization's *International Classification of Impairments, Disabilities and Handicaps* (1980),[3] which defines disability as "any restriction or lack of ability to perform an activity in a manner or within the range considered normal for a human being." While much of the medical literature uses the latter, broader definition, the reader must be aware that the goals of this report relate to the statutory definition.

The following terms are defined by current (2003) SSA regulations:

"Claimant" is anyone who has filed a disability claim.

"Substantial Gainful Activity" is the ability to earn an average of $800 per month.

"Medically Determinable Impairment" is a physical or mental impairment that results from anatomical, physiological, or psychological abnormalities which can be shown by medically acceptable clinical and laboratory diagnostic techniques.

"Evidentiary Requirements" for disability determination are described by SSA regulation. An acceptable medical source must report signs, symptoms, and laboratory findings diagnostic of an impairment. Although a claimant's reported signs and symptoms are not sufficient to meet the evidentiary requirements for establishing the presence of a medically determinable impairment, all available evidence including the claimant's report of symptoms is used to

Note: Appendixes and Evidence Tables cited in this report are provided electronically at http://www.ahrq.gov/clinic/epcindex.htm.

evaluate the impact of any documented impairment(s) on the claimant's ability to carry out work tasks.

"Severe Impairment" is defined by the agency as any "impairment that more than minimally limits the claimant's ability to do basic work activities."

The regulations include a Listing of Impairments for each body system that define disability. Often referred to as the "medical listings," this list allows quick disability determinations to be made on the basis of medical criteria alone. The SSA publication, *Disability Evaluation Under Social Security 2003*,[2] under the neurological category of impairments, includes Listing 11.09.

11.09 Multiple Sclerosis with:

A. Disorganization of motor function as described in 11.04; or

B. Visual or mental impairment as described under the criteria in 2.02, 2.03, 2.04, or 12.02: or

C. Significant, reproducible fatigue of motor function with substantial muscle weakness on repetitive activity, demonstrated on physical examination, resulting from neurological dysfunction in areas of the central nervous system known to be pathologically involved by the multiple sclerosis process.

All pages pertinent to the Medical Listing for multiple sclerosis, including the imbedded references to sections 2, 11, and 12, are found in Appendix A.

"Residual Functional Capacity" is assessed when a claimant is determined to have a "severe" impairment that does not meet or equal the intent of the medical listings. Physical capacity (lifting, carrying, walking, standing, sitting, pedaling, etc.) and mental capacity (cognitive and behavioral, thought processing, concentration, pace, behavior) are assessed in determining residual functional capacity.

In order to adjudicate claims by individuals with MS for disability benefits, SSA must determine whether the claims file includes information from an acceptable medical source that documents the signs, symptoms, and laboratory findings that are diagnostic of a physical or mental impairment. SSA adjudicators also determine whether the impairment would be expected to more than minimally interfere with the claimant's capacity to carry out basic work activities for at least 12 consecutive months or end in death. If a severe impairment is identified, the adjudicator determines whether the medical findings meet or equal an impairment in the medical listings. If the documented impairment does not meet or equal a listed impairment, the adjudicator must determine the claimant's residual functional capacity and consider vocational factors prior to making a final disability determination.

Research Questions

This evidence report covers five major topic areas framed within seven research questions, all of which are targeted to the adult population with MS. Our primary goal was to identify, review, and evaluate the published literature to answer the research questions; our secondary goal was to identify areas where no evidence exists or where the evidence has important limitations and then describe the type of data that would be needed to more fully address the question.

The questions are listed below by topic area, along with a brief description of our analytical approach, including interventions and outcomes of interest.

Reliability of MS Diagnostic Criteria

Question 1a. *What is the reliability of new McDonald criteria (incorporating supplementary information from radiologic and laboratory studies including magnetic resonance imaging [MRI], visual evoked potential [VEP], and cerebrospinal fluid [CSF] analyses) compared with long-term follow-up diagnosis of clinically definite MS according to the Poser criteria?*

The major difference between the Poser criteria[4] and the new McDonald criteria[5] is the addition of MRI findings. Our approach to this question was to identify studies in two categories: (1) those that specifically compared the new McDonald criteria with the reference standard of long-term diagnosis of clinically definite MS according to Poser criteria; and (2) those that provided data on the accuracy of various MRI techniques, CSF, and VEP (paraclinical diagnostic techniques incorporated into the criteria) with regard to the diagnosis of MS and thus supported their use as a supplement to clinical diagnosis.

In reporting results, the focus was on both relative measures (e.g., Hazard ratios) and absolute rates (e.g., percentages of patients with or without positive CSF who met Poser criteria at long-term follow up), with a primary focus on the latter.

Question 1b. *What is the inter-rater reliability of diagnosis of MS according to Poser or McDonald criteria among neurologists or between neurologists and non-neurologist physicians?*

The relevant diagnostic criteria were the Poser and new McDonald criteria plus any other clinical, laboratory, neurological exam, MRI, CSF, VEP, or other data supporting the MS diagnosis. Results had to describe data on agreement or disagreement on the MS diagnosis between evaluating physicians. Agreement statistics could include kappa scores, sensitivity and specificity rates, or other data of the type that could be used in completing a two-by-two table.

Predictors of Physical and Mental Impairments at 12 Months

Question 2. *What clinical indicators, including particularly time-course of impairments, predict physical or mental impairment at 12 months?*

There were four main categories of clinical predictors of particular interest to the analysis: (1) clinical characteristics such as exacerbation rates, disease type, age at disease onset, sex, degree of remission after relapse, and type and number of neurological symptoms; (2) imaging studies, particularly MRI; (3) laboratory test results such as apolipoprotein E (APOE) ε4 allele and intrathecal immunoglobulin-M (IgM) synthesis; and (4) self-reported health status using validated scales.

The evaluation of studies for this question was limited to those with a time course of 12 months (SSA's statutory limit), a timeframe which treating physicians would not ordinarily consider an important decision point. For this disease, the course has typically been studied over time horizons of many years.

Effect of Treatment and Symptom Management on Disease Course

Question 3a. *Among patients with MS, do current disease-modifying treatments result in long-term improvements in physical or mental outcomes compared to placebo or usual care?*

Interventions of interest for this question were all current (2003) disease-modifying immunomodulatory treatments (interferons and glatiramer acetate) and immunosuppressive

treatments (e.g., azathioprine, mitoxantrone, cyclophosphamide, intravenous [IV] immunoglobulin-G [IgG]).

Outcomes of interest were physical functioning (primarily Expanded Disability Status Scale [EDSS] scores), proportion of patients with "improvement," relapse frequency, cognitive functioning, quality of life, and adverse events.

Question 3b. *Among patients with MS, do treatments aimed at symptom management result in improvements in physical or mental outcomes compared to usual care?*

The effectiveness of symptomatic therapies for spasticity, rehabilitation, urinary management, fatigue, depression, and cognitive impairment was evaluated. Relevant outcomes were analyzed within six categories: (1) symptom-specific functional status or quality-of-life outcomes; (2) physical functioning (primarily EDSS); (3) cognitive functioning; (4) work or employment outcomes; (5) generic quality-of-life outcomes; and (6) adverse events.

The analysis of studies relevant to Questions 3a and 3b was complicated by issues of definition, particularly for outcomes reporting "improvement," "long-term improvement," and "relapse rates." Our reporting of the results and subsequent analysis are presented within SSA's regulatory definition of "disability," which considers physical or mental impairments that can be expected to result in death or which have lasted or can be expected to last for a continuous period of not less than 12 months.

Association of Clinical Findings with Work Ability

Question 4. *Among individuals with MS, what physical, mental, laboratory, or radiographic findings have been associated with inability to work?*

The phrasing of this question predetermined the outcome of interest as ability to work. Findings reported as absolute and relative measures of physical and mental/cognition function and laboratory and radiographic testing related to work activity were assessed.

Environmental Factors and Work Ability

Question 5. *Among individuals with MS, how does elevated temperature or other environmental factors impair the capacity to work?*

This question was interpreted as the association of workplace environmental conditions and demands (specifically, ambient temperature, individual's body temperature, or exposure to heat or cold) on the ability of an individual with MS to work. Relative and absolute measures of association were assessed.

Limitations of Report

In requesting this evidence report, SSA sought evidence from the medical and scientific literature to determine whether current medical knowledge supports SSA's stated policies regarding MS. Seven specific questions were framed within five topic areas. The information compiled in this report may enable SSA, for example: (1) to improve consistency of disability claims by applying more objective criteria, but only if the criteria are valid; (2) to change the population eligible for disability through a change in the diagnostic criteria for MS; (3) to influence changes in treatment that might reduce the number of people permanently disabled by

MS; and (4) beyond motor and cognitive impairments, to consider how other significant symptoms, such as fatigue and urinary urgency, may be incorporated into considerations of disability status.

We believe the evidence presented in this report could also be used as the basis for a consensus conference of multidisciplinary experts on Listing of Impairments for MS that would employ formal consensus methods to update the current listing, as well as possibly expanding the disability process to include sociocultural factors that impinge upon desiring, seeking, finding, acquiring, and sustaining a job.