

2. Objective information. A corresponding objective change in the neurologic exam performed by the neurologist, for example the patient complains their leg became weaker 3 days ago and the exam today shows less strength than the previous study visit. The EDSS is a rating scale that summarizes and quantifies the findings on the neurologic exam. Most definitions in trials stipulate the amount of change on the EDSS that is required for the event to qualify as a relapse.

Moreover, according to Dr. J.A. Cohen (53) to constitute a confirmed relapse, the symptoms must have been accompanied by an increase of at least half a point in the EDSS score, of one point in each of two EDSS functional-system scores, or of two points in one EDSS functional-system score (excluding scores for the bowel, bladder, or cerebral functional systems). Higher EDSS scores mean a more severe disability.

The EDSS scoring scheme appears in Table 19.1. As reviewed by John F. Kurtzke (54) the Kurtzke EDSS score has an origin in studies from the early 1950s (55).

e. Multiple sclerosis functional composite (MSFC) score

Another primary endpoint used in the Kappos et al. (56) study was the Multiple Sclerosis Functional Composite (MSFC) score, as set forth by a manual authored by Fischer et al. (57). This test includes a 25-foot walk, a 9-hole peg test, and a listening test. Regarding the 25-foot walk, for example, the manual states that the patient is instructed to walk 25 feet as quickly as possible. The task is immediately administered again by having the patient walk back the same distance. The instruction manual of Fischer et al. (58) also states that patients may use assistive devices when doing the walk, and that materials needed are a stopwatch, clipboard, *Timed 25-Foot Walk Record Form*, and a marked 25-foot distance in an unobstructed hallway.

f. Secondary endpoints

The main secondary endpoint was the time to confirmed **disability progression**. Time to confirmed disability progression is defined as an increase of one point in the EDSS score, with an absence of relapse at the time of assessment and with all EDSS scores measured during that time meeting the criteria for disability progression.

⁵³ Cohen JA. E-mail of September 2, 2010.

⁵⁴ Kurtzke JE Historical and clinical perspectives of the expanded disability status scale. *Neuroepidemiology*. 2008;31:1–9.

⁵⁵ Kurtzke JE A new scale for evaluating disability in multiple sclerosis. *Neurology*. 1955;5:580–583.

⁵⁶ Kappos L, Radue EW, O'Connor P, et al. A placebo-controlled trial of oral fingolimod in relapsing multiple sclerosis. *New Engl J Med*. 2010;362:387–401.

⁵⁷ Fischer JS, Jak AJ, Kniker JE, Rudick RA. Multiple Sclerosis Functional Composite (MSFC) Administration and Scoring Manual. 2001 (41 pages).

⁵⁸ Fischer JS, Jak AJ, Kniker JE, Rudick RA. Multiple Sclerosis Functional Composite (MSFC) Administration and Scoring Manual. 2001 (41 pages).