**Background:** ROBUST was a 12-month, United States–based, prospective, observational, open-label, single-arm, multicenter outcomes study of patients taking interferon beta-1b (IFNβ-1b) given every other day for relapsing forms of multiple sclerosis (MS). **Objectives:** The objectives of this analysis were to assess work productivity and activity impairment over the course of 12 months among MS patients in a real-world observational study. **Methods:** ROBUST collected, monthly via a web-based data-capture system, responses from patients to the Work Productivity and Activity Impairment questionnaire (WPAI). Higher WPAI scores represent greater impairment, and reductions in WPAI scores over time represent improvement in outcomes. A one-sample t test was used to explore the statistical significance of the changes in WPAI domain scores from their baseline values. A total of 184 patients were included in the final analysis. **Results:** At baseline, the mean WPAI scores among all 184 patients were as follows: absenteeism: 17.84; presenteeism: 33.64; work productivity loss: 43.31; activity impairment: 46.89. Absenteeism (−11.92, P = .0001), presenteeism (−4.36, P = .0931), work productivity loss (−11.39, P = .0005), and activity impairment (−7.65, P = .0036) scores all decreased from baseline to month 12, indicating an improvement after the initiation of IFNβ-1b. The decreases from baseline in the absenteeism, work productivity loss, and activity impairment scores were statistically significant at each and every month (months 1 through 12) throughout the study. The largest mean decrease in presenteeism occurred at the first month following initiation of IFNβ-1b (−4.95, P = .0111); the largest mean decrease in activity impairment occurred at month 11 (−8.62, P = .0013). **Conclusions:** Work productivity and activity impairment improved significantly in the ROBUST study participants, suggesting an effect of IFNβ-1b in these outcome measures.

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