Supplementary Table 2. Change in physical characteristics from baseline to MRF, excluding subjects who became fatigued during

follow-up.

| Characteristic | Fatigued, N=1,470 | Not Fatigued, N=868 | OR (95% CI) | Characteristi c | Fatigued, N = 1,470 | Not Fatigued, N = 868 | OR (95% CI) |
|-----------------------|-----------------------------|---------------------------|-----------------------------|----------------------|-----------------------------|-----------------------------|-----------------------------|
| Get up Worsened | 232 (16.0%) | 103 (12.0%) | 1.4 (1.1- 1.8)* | Bladder Worsened | 346 (24.0%) | 123 (14.3%) | 1.9 (1.5- 2.3)* |
| Stable Stairs | 1214 (84.0%) | 756 (88.0%) | 1.00 (Ref) | Stable Vision | 1096 (76.0%) | 736 (85.7%) | 1.00 (Ref) |
| Worsened | 233 (16.1%) | 98 (11.4%) | 1.5 (1.2- 2.0)* | Worsened | 300 (20.6%) | 89 (10.3%) | 2.2 (1.7- 2.8)* |
| Stable Stand | 1215 (83.9%) | 763 (88.6%) | 1.00 (Ref) | Stable Loneliness | 1157 (79.4%) | 772 (89.7%) | 1.00 (Ref) |
| Worsened | 186 (12.9%) | 101 (11.7%) | 1.1 (0.9-1.5) | Worsened | 177 (12.2%) | 55 (6.4%) | 2.0 (1.4- 2.7)* |
| Stable Drive | 1256 (87.1%) | 759 (88.3%) | 1.00 (Ref) | Stable Pessimism | 1273 (87.8%) | 810 (93.6%) | 1.00 (Ref) |
| Worsened Stable | 205 (14.2%) 1239 (85.8%) | 96 (11.2%) 764 (88.8%) | 1.3 (1.0-1.7) 1.00 (Ref) | Worsened Stable | 148 (10.2%) 1301 (89.8%) | 70 (8.1%) 792 (91.9%) | 1.3 (0.9-1.7) 1.00 (Ref) |
| Pain Worsened | 184 (12.7%) | 135 (15.8%) | 0.8 (0.6-1.0) | Tense Worsened | 174 (12.1%) | 75 (8.7%) | 1.4 (1.1- |
| Stable Pain extent | 1262 (87.3%) | 721 (84.2%) | 1.00 (Ref) | Stable Panic | 1265 (87.9%) | 785 (91.3%) | 1.9)* 1.00 (Ref) |
| Worsened | 76 (11.1%) | 31 (16.3%) | 0.6 (0.4-1.0) | Worsened | 88 (6.1%) | 18 (2.1%) | 3.1 (1.9- 5.2)* |
| Stable Upper Limbs | 611 (88.9%) | 159 (83.7%) | 1.00 (Ref) | Stable Annoyed | 1355 (93.9%) | 846 (97/9%) | 1.00 (Ref) |
| Worsened | 381 (26.9%) | 168 (19.6%) | 1.5 (1.2- 1.8)* | Worsened | 154 (10.7%) | 64 (7.5%) | 1.5 (1.1- 2.0)* |
| Stable | 1061 (73.1%) | 691 (80.4%) | 1.00 (Ref) | Stable | 1289 (89.3%) | 7994 (92.5%) | 1.00 (Ref) |

| Lower Limbs | | | | Morbid Mood | | | |
|--------------------|--------------|-------------|---------------------|-----------------|--------------|-------------|---------------------|
| Worsened | 412 (28.7%) | 218 (25.5%) | 1.2 (1.0-1.4) | Worsened | 120 (8.3%) | 39 (4.5%) | 1.9 (1.3- 2.7)* |
| Stable | 1026 (71.3%) | 637 (74.5%) | 1.00 (Ref) | Stable Guilt | 1324 (91.7%) | 822 (95.5%) | 1.00 (Ref) |
| Bowel Worsened | 334 (23.1%) | 115 (13.4%) | 1.9 (1.5- | Worsened | 136 (9.4%) | 38 (4.4%) | 2.2 (1.5- |
| Stable | 1115 (76.9%) | 746 (86.6%) | 2.4)* 1.00 (Ref) | Stable | 1314 (90.6%) | 822 (95.6%) | 3.2)* 1.00 (Ref) |

Ref=Reference; Odds ratios and 95% confidence intervals for logistic regression models analyzing differences between those who reported fatigue at baseline and most recent follow-up, compared to those who reported no fatigue at baseline or most recent follow-up, adjusted for age, sex, baseline EDSS and MS type, DMT use and disease duration. P-values are adjusted for multiple comparisons. *p-value<0.05.