Table e1. Characteristics of participants who did and did not complete the study

| Covariate                  | Non-Completers (n = 129) | Completers (n = 833) | P-value |
|----------------------------|--------------------------|----------------------|---------|
| MS                         | 21 (16.3)                | 234 (28.1)           |         |
| IBD                        | 31 (24.0)                | 216 (25.9)           |         |
| RA                         | 20 (15.5)                | 134 (16.1)           |         |
| DEP/ANX                    | 57 (18.6)                | 249 (29.9)           |         |
| Women, n (%)               | 93 (72.1)                | 636 (76.4)           | 0.29    |
| White, n (%)               | 95 (73.6)                | 693 (83.4)           | 0.007   |
| Age (years), mean (SD)     | 46.6 (14.7)              | 49.6 (14.1)          | 0.028   |
| Diabetes, n (%)            | 11 (8.5)                 | 56 (6.7)             | 0.46    |
| Hypertension, n (%)        | 24 (18.6)                | 198 (23.8)           | 0.22    |
| Hyperlipidemia, n (%)      | 26 (20.2)                | 148 (17.8)           | 0.54    |
| Current smoker, n (%)      | 43 (33.3)                | 142 (17.1)           | <0.001  |
| BMI, mean (SD)<sup>a</sup> | 28.4 (7.1)               | 28.9 (7.2)           | 0.50    |

Symptoms of depression/ anxiety

|                      | Non-Completers (n = 129) | Completers (n = 833) | P-value |
|----------------------|--------------------------|----------------------|---------|
| HADS-D ≥11, n (%)<sup>b</sup> | 28 (21.9)                | 104 (12.5)           | 0.004   |
| HADS-A ≥11, n (%)<sup>c</sup> | 54 (42.2)                | 236 (28.4)           | 0.002   |
| HADS-D, mean (SD)<sup>b</sup> | 7.08 (4.5)               | 5.49 (4.2)           | <0.001  |
| HADS-A, mean (SD)<sup>c</sup> | 9.24 (4.8)               | 7.69 (4.7)           | <0.001  |

Cognitive function Z-scores

|                      | Non-Completers (n = 129) | Completers (n = 833) | P-value |
|----------------------|--------------------------|----------------------|---------|
| SDMT, mean (SD)      | -0.43 (1.1)              | -0.19 (1.1)          | 0.026   |
| CVLT verbal learning, mean (SD) | -0.68 (1.5) | -0.50 (1.4) | 0.19    |
| CVLT delayed recall, mean (SD) | -0.63 (1.4) | -0.35 (1.3) | 0.023   |
| LNS, mean (SD)       | -0.16 (0.96)             | 0.08 (0.90)          | 0.005   |

MS = multiple sclerosis, IBD = inflammatory bowel disease, RA = rheumatoid arthritis, DEP/ANX = depressed or anxious without an immune-mediated inflammatory disease, BMI = body mass index, HADS = Hospital Anxiety and Depression Scale, FSIQ = full scale intelligence quotient, SDMT = Symbol Digit Modalities Test, CVLT = California Verbal Learning Test, LNS = Letter Number Sequencing Test
Table e2. Participant characteristics at the fourth visit

| Covariate                          | MS (N=234) | IBD (N=216) | RA (N=134) | DEP/ANX (N=249) | P-value |
|------------------------------------|------------|-------------|------------|----------------|---------|
| Women, n (%)                       | 193 (82.5) | 131 (60.6)  | 116 (86.6) | 196 (78.7)     | <0.0001 |
| Age (years), mean (SD)             | 53.7 (12.7)| 52.6 (14.7) | 62.8 (11.7)| 47.8 (13.1)    | <0.001  |
| Diabetes, n (%)                    | 19 (8.1)   | 12 (5.6)    | 11 (8.2)   | 21 (8.4)       | 0.64    |
| Hypertension, n (%)                | 59 (25.3)  | 48 (22.2)   | 55 (41.0)  | 65 (26.1)      | 0.001   |
| Hyperlipidemia, n (%)              | 50 (21.4)  | 32 (14.8)   | 42 (31.3)  | 50 (20.1)      | 0.003   |
| Current smoker, n (%)              | 43 (18.4)  | 26 (12.0)   | 17 (12.8)  | 44 (17.7)      | 0.16    |
| BMI, mean (SD)^[a]                 | 29.0 (6.7) | 26.9 (6.0)  | 29.3 (7.2) | 31.1 (8.2)     | <0.001  |
| Symptoms of depression/ anxiety    |            |             |            |                |         |
| HADS-D ≥11, n (%)                  | 30 (12.8)  | 12 (5.6)    | 12 (9.0)   | 40 (16.1)      | 0.003   |
| HADS-A ≥11, n (%)                  | 32 (13.7)  | 33 (15.3)   | 24 (17.9)  | 107 (43.0)     | <0.001  |
| HADS-D, mean (SD)                  | 5.0 (3.9)  | 4.2 (3.7)   | 4.7 (3.8)  | 6.7 (4.5)      | <0.001  |
| HADS-A, mean (SD)                  | 5.6 (4.2)  | 6.4 (4.3)   | 6.1 (4.1)  | 10.0 (4.5)     | <0.001  |
| Cognitive function Z-scores        |            |             |            |                |         |
| SDMT, mean (SD)                    | -0.35 (1.2)| 0.49 (1.1)  | 0.40 (1.0) | 0.33 (1.2)     | <0.001  |
| CVLT verbal learning, mean (SD)    | -0.60 (1.6)| -0.19 (1.4)| -0.33 (1.4)| -0.21 (1.6)    | 0.012   |
| CVLT delayed recall, mean (SD)     | -0.35 (1.4)| 0.04 (1.3)  | 0.11 (1.3) | 0 (1.4)        | 0.0032  |
| LNS, mean (SD)                     | -0.08 (1.0)| 0.21 (1.0)  | -0.35 (0.8)| 0.21 (1.1)     | <0.001  |

MS = multiple sclerosis, IBD = inflammatory bowel disease, RA = rheumatoid arthritis, DEP/ANX = depressed or anxious without an immune-mediated inflammatory disease, BMI = body mass index, HADS = Hospital Anxiety and Depression Scale, FSIQ = full scale intelligence quotient, SDMT = Symbol Digit Modalities Test, CVLT = California Verbal Learning Test, LNS = Letter Number Sequencing Test

^[a] 22 missing for MS, 17 for IBD, 5 for RA, 18 for DEP/ANX
Figure e1. Mean ± standard deviation Hospital Anxiety (A) and Depression (D) Scale scores at each study visit stratified by disease group

Figure e2. Percentage of participants in each cohort with impaired performance on verbal learning, delayed recall memory and working memory at each visit

MS = multiple sclerosis, IBD = inflammatory bowel disease, RA= rheumatoid arthritis, DEP/ANX = depressed/anxious