

**Supplementary Table 1.** Baseline characteristics of 192 Crohn's disease subjects with univariate and multivariate analysis of demographic and clinical factors associated with disability.

| Variable  | Univariate analysis |                    | Multivariate analysis              |         |
|---|---------------------|--------------------|------------------------------------|---------|
|   | IBD-DI (IQR)        | P value            | B (95% CI)                         | P value |
| (Constant)  |                     |                    | 20.48 (3.62 to 37.36)              | .018    |
| Age ≤35 years (n=110)                             | 26 (14-39)          | .961 <sup>a</sup>  | 0.01 (-0.26 to 0.27) <sup>b</sup>  | .968    |
| Age >35 years (n=82)                              | 27 (13-39)          |                    |                                    |         |
| Male (n=98)                                       | 21 (12-38)          | .007 <sup>a</sup>  | -                                  | -       |
| Female (n=94)                                     | 31 (17-40)          |                    | 4.97 (0.22 to 9.73)                | .040    |
| Body mass index <25 (n=85) <sup>c</sup>           | 25 (13-39)          |                    | -                                  | -       |
| Body mass index 25-29 (n=76)                      | 27 (15-39)          | .952 <sup>d</sup>  | 0.18 (-0.35 to 0.70) <sup>b</sup>  | .503    |
| Body mass index ≥30 (n=28)                        | 27 (13-40)          |                    |                                    |         |
| Disease duration ≤ 5 years (n=85)                 | 27 (11-38)          | .394 <sup>a</sup>  | -0.06 (-0.44 to 0.32) <sup>b</sup> | .749    |
| Disease duration > 5 years (n=107)                | 25 (14-43)          |                    |                                    |         |
| Small bowel disease (n=49) <sup>e</sup>           | 29 (13-43)          |                    | -                                  | -       |
| Colonic disease (n=53)                            | 23 (13-38)          | .546 <sup>d</sup>  | 0.22 (-6.52 to 6.95)               | .949    |
| Small bowel and colonic disease (n=89)            | 27 (16-39)          |                    | 0.33 (-5.33 to 5.99)               | .907    |
| No perianal disease (n=160)                       | 27 (13-39)          | .925 <sup>a</sup>  | -                                  | -       |
| Perianal disease (n=32)                           | 28 (13-41)          |                    | -0.49 (-7.03 to 6.04)              | .882    |
| Student (n=32)                                    | 29 (13-43)          |                    | -                                  | -       |
| Employed/Homemaker (n=103)                        | 25 (13-38)          | .007 <sup>d</sup>  | -4.09 (-11.11 to 2.94)             | .252    |
| Unemployed (n=44)                                 | 36 (18-48)          |                    | -1.58 (-9.98 to 6.83)              | .712    |
| Retired (n=13)                                    | 14 (6-27)           |                    | -19.62 (-33.63 to -5.60)           | .006    |
| Education to 16 years (n=43) <sup>c</sup>         | 32 (21-46)          |                    | -                                  | -       |
| Education to 18 years (n=52)                      | 27 (14-41)          | .067 <sup>d</sup>  | -3.68 (-10.38 to 3.02)             | .280    |
| Third level (University) education (n=94)         | 23 (13-38)          |                    | -4.97 (-11.47 to 1.53)             | .133    |
| No current anti-depressant (n=276) <sup>b</sup>   | 25 (13-38)          | .007 <sup>a</sup>  | -                                  | -       |
| Current anti-depressant (n=44)                    | 39 (19-53)          |                    | 10.27 (3.45 to 17.09)              | .003    |
| No current cigarette smoking (n=270) <sup>b</sup> | 25 (13-38)          | .065 <sup>a</sup>  | -                                  | -       |
| Current cigarette smoking (n=57)                  | 32 (18-43)          |                    | 1.15 (-4.65 to 6.96)               | .695    |
| No resectional surgery (n=111)                    | 23 (13-36)          |                    | -                                  | -       |
| Previous bowel resection (n=63)                   | 30 (17-43)          | .035 <sup>d</sup>  | 4.88 (-0.55 to 10.30)              | .078    |
| Permanent stoma surgery (n=18)                    | 37 (10-54)          |                    | 2.50 (-6.48 to 11.48)              | .583    |
| No current steroid (n=160)                        | 25 (13-38)          | .008 <sup>a</sup>  | -                                  | -       |
| Current steroid (n=32)                            | 36 (22-46)          |                    | 8.35 (1.96 to 14.73)               | .011    |
| No current immune modulator (n=124)               | 29 (13-42)          | .286 <sup>a</sup>  | -                                  | -       |
| Current immune modulator (n=68)                   | 23 (14-37)          |                    | -1.85 (-6.60 to 2.89)              | .442    |
| No current biologic (n=230)                       | 26 (14-38)          | .550 <sup>a</sup>  | -                                  | -       |
| Current biologic (n=99)                           | 27 (11-46)          |                    | 3.03 (-1.98 to 8.05)               | .234    |
| Inactive disease (n=241)                          | 23 (13-36)          | <.001 <sup>a</sup> | -                                  | -       |
| Active disease (n=88)                             | 36 (24-46)          |                    | 7.62 (2.38 to 12.86)               | .005    |

Dummy variables for the multivariate analysis included male sex, Small bowel Crohn's, no perianal disease, retired subjects, Education to 16 years, no current antidepressant use, no cigarette smoking, no resectional surgery, no exposure to steroid medications, immune modulators or biologic agents, and disease remission. Univariate data are presented as medians and interquartile ranges (IQR) and multivariate data as B and 95% confidence intervals (CI).

<sup>a</sup>Mann-Whitney U test.

<sup>b</sup>Entered into multivariate model as a continuous variable.

<sup>c</sup>Data not available for all cases.

<sup>d</sup>Kruskal-Wallis test.

<sup>e</sup>A single Crohn's disease subject had only perianal disease.

**Supplementary Table 2.** Baseline characteristics of 137 ulcerative colitis subjects with univariate and multivariate analysis of demographic and clinical factors associated with disability.

| Variable  | Univariate analysis |                             | Multivariate analysis               |                 |
|---|---------------------|-----------------------------|-------------------------------------|-----------------|
|   | IBD-DI (IQR)        | P value                     | B (95% CI)                          | P value         |
| (Constant)  |                     |                             | 18.21 (-0.38 to 36.80)              | .055            |
| Age ≤35 years (n=58)                                | 21 (14-34)          | .303 <sup>a</sup>           | -0.27 (-0.50 to -0.05) <sup>b</sup> | <b>.019</b>     |
| Age >35 years (n=79)                                | 21 (9-32)           |                             |                                     |                 |
| Male (n=73)   | 20 (9-29)           | <b>.037<sup>a</sup></b>     | -                                   | -               |
| Female (n=64)                                       | 24 (14-35)          |                             | 4.37 (-0.39 to 9.14)                | .071            |
| Body mass index <25 (n=52) <sup>c</sup>             | 20 (10-33)          |                             | -                                   | -               |
| Body mass index 25-29 (n=48)                        | 22 (9-32)           | .983 <sup>d</sup>           | 0.09 (-0.34 to 0.51) <sup>b</sup>   | .684            |
| Body mass index ≥30 (n=33)                          | 23 (11-32)          |                             |                                     |                 |
| Disease duration ≤ 5 years (n=70)                   | 21 (10-32)          | .703 <sup>a</sup>           | 0.06 (-0.29 to 0.42) <sup>b</sup>   | .729            |
| Disease duration > 5 years (n=67)                   | 21 (11-32)          |                             |                                     |                 |
| Ulcerative proctitis (n=13)                         | 23 (4-30)           |                             | -                                   | -               |
| Ulcerative colitis left colon (n=67)                | 23 (11-32)          | .465 <sup>d</sup>           | 1.33 (-6.89 to 9.55)                | .749            |
| Ulcerative colitis total colon (n=57)               | 18 (10-29)          |                             | -1.53 (-10.03 to 6.97)              | .723            |
| Student (n=9)                                       | 20 (8-42)           |                             | -                                   | -               |
| Employed/Homemaker (n=100)                          | 18 (9-30)           | <b>.021<sup>d</sup></b>     | 1.48 (-9.41 to 12.37)               | .789            |
| Unemployed (n=16)                                   | 32 (25-48)          |                             | 13.10 (0.59 to 26.62)               | <b>.040</b>     |
| Retired (n=12)                                      | 24 (16-33)          |                             | 12.99 (-2.84 to 28.82)              | .107            |
| Education to 16 years (n=26) <sup>c</sup>           | 27 (7-34)           |                             | -                                   | -               |
| Education to 18 years (n=39)                        | 18 (7-31)           | .453 <sup>d</sup>           | -1.07 (-8.59 to 6.45)               | .779            |
| Third level (University) education (n=70)           | 20 (14-33)          |                             | 2.10 (-5.43 to 9.63)                | .582            |
| No current anti-depressant use (n=121) <sup>c</sup> | 20 (10-30)          | <b>.045<sup>a</sup></b>     | -                                   | -               |
| Current anti-depressant use (n=13)                  | 30 (21-47)          |                             | 7.31 (-0.94 to 15.56)               | .082            |
| No cigarette smoking (n=121) <sup>c</sup>           | 20 (9-32)           | .406 <sup>a</sup>           | -                                   | -               |
| Cigarette smoking (n=15)                            | 23 (13-52)          |                             | 4.69 (-2.82 to 12.20)               | .218            |
| No resectional surgery (n=122)                      | 22 (11-32)          |                             | -                                   | -               |
| Previous bowel resection (n=9)                      | 20 (9-46)           | .573 <sup>d</sup>           | 0.82 (-9.77 to 11.41)               | .878            |
| Permanent stoma surgery (n=6)                       | 13 (5-29)           |                             | -7.31 (-19.05 to 4.44)              | .220            |
| No current steroid (n=104)                          | 18 (9-30)           | <b>.001<sup>a</sup></b>     | -                                   | -               |
| Current steroid (n=33)                              | 29 (19-39)          |                             | 6.61 (0.88 to 12.33)                | <b>.024</b>     |
| No current immune modulator (n=95)                  | 23 (9-32)           | .688 <sup>a</sup>           | -                                   | -               |
| Current immune modulator (n=42)                     | 20 (14-33)          |                             | 1.90 (-3.37 to 7.17)                | .476            |
| No current biologic (n=108)                         | 21 (13-32)          | .862 <sup>a</sup>           | -                                   | -               |
| Current biologic (n=29)                             | 23 (9-36)           |                             | 0.01 (-6.03 to 6.06)                | .997            |
| Inactive disease (n=101)                            | 18 (8-27)           |                             | -                                   | -               |
| Active disease (n=36)                               | 37 (21-51)          | <b>&lt;.001<sup>a</sup></b> | 15.48 (9.92 to 21.05)               | <b>&lt;.001</b> |

Dummy variables for the multivariate analysis included male sex, ulcerative proctitis, retired subjects, Education to 16 years, no current antidepressant use, no cigarette smoking, no resectional surgery, no exposure to steroid medications, immune modulators or biologic agents, and disease remission. Univariate data are presented as medians and interquartile ranges (IQR) and multivariate data as B and 95% confidence intervals (CI).

<sup>a</sup>Mann-Whitney U test.

<sup>b</sup>Entered into multivariate model as a continuous variable.

<sup>c</sup>Data not available for all cases.

<sup>d</sup>Kruskal-Wallis test.

**Supplementary Table 3.** Factor loadings of principle component analyses.

| One-factor model <sup>a</sup> |                |
|-------------------------------|----------------|
| Question                      | Factor loading |
| 1 General Health              | 0.636          |
| 2 Sleep                       | 0.670          |
| 3 Energy                      | 0.736          |
| 4 Depression                  | 0.745          |
| 5 Anxiety                     | 0.661          |
| 6 Body Image                  | 0.571          |
| 7 Abdominal pain              | 0.669          |
| 8 Bowel function              | 0.588          |
| 9 Health and diet             | 0.710          |
| 10 Personal relationships     | 0.652          |
| 11 Community participation    | 0.716          |
| 12 Work/study activities      | 0.785          |
| 13 Liquid stools              | 0.400          |
| 14 Arthralgia/arthritis       | 0.244          |

**Supplementary Table 4.** Final Cox backward regression models identifying baseline factors significantly and independently related to short-term and long-term disease activity.

| Short-term disease activity with treatment escalation |                     |                |   |         |
|---|---------------------|----------------|---|---------|
|   | Coefficient $\beta$ | Standard error | Relative Risk<br>(95% confidence intervals) | P value |
| Disease remission baseline                            | -                   | -              | 1   | -       |
| Active disease baseline                               | 1.883               | 0.220          | 6.575 (4.274-10.116)                        | <.0001  |
| Disease duration <sup>a</sup>                         | -0.053              | 0.017          | 0.948 (0.917-0.981)                         | .002    |
| IBD-DI at baseline <sup>a</sup>                       | 0.017               | 0.006          | 1.017 (1.005-1.029)                         | .004    |

  

| Long-term disease activity with treatment escalation |                     |                |   |         |
|--|---------------------|----------------|---|---------|
|  | Coefficient $\beta$ | Standard error | Relative Risk<br>(95% confidence intervals) | P value |
| IBD-DI at baseline <sup>a</sup>                      | 0.016               | 0.004          | 1.016 (1.008-1.024)                         | <.001   |
| Participant age <sup>a</sup>                         | -0.015              | 0.006          | 0.985 (0.974-0.996)                         | .007    |

<sup>a</sup>Entered into multivariate model as a continuous variable.