Group cognitive behavioral therapy with interoceptive exposure for drug-refractory irritable bowel syndrome: a randomized controlled trial

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Supplemental

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**Supplemental Table 1: The components of GCBT-IE**

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| **Components of GCBT-IE** | | **Details of component** |
| A. | Psychoeducation of IBS | Psychoeducation of the IBS psychological model focusing on the brain-gut interaction and the relationship between anxiety and the abdomen. Participants learn self-monitoring techniques to objectively perceive one's thoughts and feelings. |
| B. | Attention control | Attention control for somatosensory hypersensitivity. Participants learn skills to divert excessive attention to unpleasant visceral sensations causing anxiety. |
| C. | Cognitive restructuring | Cognitive restructuring of unhelpful thoughts. Participants learn to revise their unhelpful exaggerated thoughts about IBS with objective evidence. |
| D. | Interoceptive exposure | In interoceptive exposure to unpleasant visceral sensations, participants learn to feel less anxiety about unpleasant sensations through repeated intentional exposure that cause unpleasant sensations.  For example, a person who believes "coldness always causes abdominal pain" is asked to apply ice to their stomach for a short time. Then they experience that "coldness does not always cause abdominal pain." Similarly, a person who believes that "abdominal pressure always causes abdominal pain" is asked to press their abdomen for a while. Then, they experience that "abdominal pressure does not always cause abdominal pain."  Such challenges to unhelpful beliefs promote cognitive restructuring. |
| E. | Exposure practice | Exposure to anxiety provoking situations and reduction of avoidance behaviors. Participants learn to reduce avoidance behaviors such as avoiding certain foods and not going out. They challenge symptom-provoking behaviors (e.g., eating out, riding express trains where one cannot go to the bathroom immediately, etc.) in a graduated step-by-step approach. |
| F. | Relapse prevention | Relapse prevention. Participants learn to anticipate situations where relapse is likely and discuss coping strategies in advance. |
| GCBT-IE, group cognitive behavioral therapy with interoceptive exposure; IBS, irritable bowel syndrome. | | |

**Supplemental Table 2: IBS-SSS domains**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **GCBT-IE** | | | **Waiting list** | | | **GCBT-IE versus Waiting list** | |
|  | n | Mean (SD) | LS mean changesa (95% CI) | n | Mean (SD) | LS mean changesa (95% CI) | Difference in LS mean changesb (95% CI) | *P* value |
| **Severity of abdominal pain, score 0–100** | | | |  |  |  |  |  |
| Baseline | 54 | 48.2 (26.8) | ·· | 60 | 50.7 (28.9) | ·· | ·· | ·· |
| 4 weeks | 52 | 44.9 (24.7) | −4.8 (−11.2 to 1.6) | 59 | 48.7 (23.3) | −1.6 (−7.6 to 4.5) | −3.2 (12.1 to 5.6) | 0.47 |
| 9 weeks | 49 | 38.3 (26.0) | −11.5 (−18.4 to −4.6) | 58 | 49.8 (24.5) | −0.5 (−6.9 to 5.9) | −11.0 (−20.4 to −1.6) | 0.022 |
| 13 weeks | 49 | 30.8 (22.0) | −19.0 (−25.3 to −12.8) | 58 | 51.7 (22.7) | 1.5 (−4.3 to 7.2) | −20.5 (−29.0 to −11.9) | <0.0001 |
| 27 weeks | 48 | 30.6 (21.6) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Frequency of abdominal pain, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 60.6 (33.6) | ·· | 60 | 63.8 (33.9) | ·· | ·· | ·· |
| 4 weeks | 52 | 47.3 (30.0) | −15.1 (−22.9 to −7.2) | 59 | 52.5 (29.2) | −10.4 (−17.8 to −3.0) | −4.7 ( −15.4 to 6.1) | 0.39 |
| 9 weeks | 49 | 38.2 (28.2) | −23.5 (−31.8 to −15.2) | 58 | 51.0 (31.7) | −12.3 (−20.0 to −4.6) | −11.1 (−22.4 to 0.1) | 0.053 |
| 13 weeks | 49 | 33.2 (29.2) | −28.5 (−36.7 to −20.2) | 58 | 53.9 (32.1) | −9.4 (−17.0 to −1.7) | −19.1 (−30.4 to −7.9) | 0.0010 |
| 27 weeks | 48 | 32.1 (25.1) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Distension, score score 0–100** | | |  |  |  |  |  |  |
| baseline | 54 | 41.0 (32.9) | ·· | 60 | 43.3 (32.1) | ·· | ·· | ·· |
| 4 weeks | 52 | 37.4 (30.5) | −4.8 (−12.6 to 2.9) | 59 | 38.5 (31.8) | −4.0 (−11.2 to 3.3) | −0.9 (−11.5 to 9.8) | 0.87 |
| 9 weeks | 49 | 36.0 (29.7) | −5.9 (−13.7 to 1.9) | 58 | 42.4 (32.3) | 0.1 (−7.2 to 7.3) | −5.9 (−16.5 to 4.7) | 0.27 |
| 13 weeks | 49 | 28.1 (25.7) | −13.8 (−21.3 to −6.3) | 58 | 40.2 (31.8) | −2.1 (−9.1 to 4.8) | −11.7 (−21.9 to −1.4) | 0.026 |
| 27 weeks | 48 | 27.0 (26.6) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Bowel dysfunction, score 0–100** | | | | |  |  |  |  |
| baseline | 54 | 71.0 (25.5) | ·· | 60 | 65.8 (28.5) | ·· | ·· | ·· |
| 4 weeks | 52 | 59.2 (26.8) | −9.8 (−17.3 to −2.2) | 59 | 57.5 (28.4) | −10.9 (−17.9 to −3.8) | 1.1 (−9.3 to 11.4) | 0.84 |
| 9 weeks | 49 | 56.2 (22.8) | −12.5 (−19. to −5.0) | 58 | 53.5 (28.6) | −14.9 (−21.7 to −8.0) | 2.4 (−7.7 to 12.5) | 0.64 |
| 13 weeks | 49 | 47.2 (23.7) | −21.4 (−29.1 to −13.7) | 58 | 55.9 (30.3) | −12.5 (−19.6 to −5.4) | −8.9 (−19.4 to 1.6) | 0.096 |
| 27 weeks | 48 | 48.4 (26.1) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Impact on quality of life, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 81.9 (17.8) | ·· | 60 | 78.2 (20.5) | ·· | ·· | ·· |
| 4 weeks | 52 | 73.1 (21.2) | −8.5 (−14.2 to −2.8) | 59 | 72.2 (23.9) | −7.0 (−12.4 to −1.7) | −1.5 (−9.3 to 6.4) | 0.71 |
| 9 weeks | 49 | 57.4 (24.5) | −24.0 (−30.5 to −17.6) | 58 | 70.1 (24.6) | −9.2 (−15.2 to −3.2) | −14.8 (−23.7 to −6.0) | 0.0012 |
| 13 weeks | 49 | 48.2 (26.7) | −33.2 (−39.9 to −26.6) | 58 | 71.8 (24.3) | −7.5 (−13.6 to −1.3) | −25.8 (−34.9 to −16.7) | <0.0001 |
| 27 weeks | 48 | 47.3 (28.5) | ·· | ·· | ·· | ·· | ·· | ·· |
| Data are mean (SD) unless otherwise specified.  aLS means of change scores from baseline to each assessment point are from restricted maximum likelihood-based mixed-model repeated measures.  bBetween-group differences in LS means, *P* value < 0.025 (two-sided).  GCBT-IE, group cognitive behavioral therapy with interoceptive exposure; IBS-SSS, the Irritable Bowel Syndrome Symptom Severity Score; LS, least squares. | | | | | | | | |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **GCBT-IE** | | | **Waiting list** | | | **GCBT-IE versus Waiting list** | |
|  | n | Mean (SD) | LS mean changesa (95% CI) | n | Mean (SD) | LS mean changesa (95% CI) | Difference in LS mean changesb (95% CI) | *P* value |
| **Dysphoria, score 0–100** | | | |  |  |  |  |  |
| Baseline | 54 | 15.2 (26.2) | ·· | 60 | 16.5 (26.8) | ·· | ·· | ·· |
| 4 weeks | 52 | 22.5 (25.8) | 7.6 (3.0 to 12.1) | 59 | 18.8 (27.7) | 1.9 (−2.3 to 6.2) | 5.6 (−0.6 to 11.9) | 0.075 |
| 9 weeks | 49 | 37.6 (24.2) | 22.2 (17.2 to 27.2) | 58 | 22.2 (27.3) | 4.8 (0.2 to 9.4) | 17.4 (10.6 to 24.2) | <0.0001 |
| 13 weeks | 49 | 46.2 (21.7) | 30.8 (25.9 to 35.8) | 58 | 18.8 (28.3) | 1.4 (−3.2 to 5.9) | 29.4 (22.7 to 36.2) | <0.0001 |
| 27 weeks | 48 | 41.4 (25.0) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Interferences with activity, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 20.5 (22.7) | ·· | 60 | 18.2 (19.8) | ·· | ·· | ·· |
| 4 weeks | 52 | 21.4 (21.7) | 1.5 (−2.7 to 5.6) | 59 | 20.0 (23.1) | 1.5 (−2.4 to 5.4) | −0.1 (−5.8 to 5.6) | 0.98 |
| 9 weeks | 49 | 37.0 (21.6) | 16.1 (11.5 to 20.6) | 58 | 19.9 (23.8) | 1.4 (−2.8 to 5.6) | 14.7 (8.5 to 20.9) | <0.0001 |
| 13 weeks | 49 | 43.6 (21.7) | 22.6 (17.9 to 27.4) | 58 | 20.2 (24.3) | 1.7 (−2.7 to 6.1) | 20.9 (14.4 to 27.4) | <0.0001 |
| 27 weeks | 48 | 39.3 (21.1) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Body image, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 52.4 (17.6) | ·· | 60 | 49.2 (22.0) | ·· | ·· | ·· |
| 4 weeks | 52 | 53.8 (17.6) | 2.1 (−1.1 to 5.2) | 59 | 48.4 (22.9) | −1.5 (−4.5 to 1.5) | 3.6 (−0.8 to 8.0) | 0.11 |
| 9 weeks | 49 | 58.9 (15.0) | 6.9 (3.3 to 10.6) | 58 | 48.5 (21.8) | −1.6 (−5.0 to 1.7) | 8.5 (3.6 to 13.5) | 0.0009 |
| 13 weeks | 49 | 61.5 (13.6) | 9.4 (5.4 to 13.3) | 58 | 46.7 (24.5) | −3.4 (−7.1 to 0.2) | 12.8 (7.4 to 18.2) | <0.0001 |
| 27 weeks | 48 | 59.2 (13.5) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Health worry, score 0–100** | | | | |  |  |  |  |
| baseline | 54 | 41.4 (22.8) | ·· | 60 | 33.8 (25.7) | ·· | ·· | ·· |
| 4 weeks | 52 | 46.8 (20.2) | 6.6 (1.9 to 11.2) | 59 | 34.3 (26.5) | −0.7 (−5.1 to 3.7) | 7.2 (0.8 to 13.7) | 0.028 |
| 9 weeks | 49 | 55.4 (19.5) | 13.7 (8.9 to 18.6) | 58 | 36.8 (26.4) | 1.3 (−3.2 to 5.8) | 12.4 (5.7 to 19.1) | 0.0004 |
| 13 weeks | 49 | 57.7 (19.5) | 16.0 (10.9 to 21.1) | 58 | 34.3 (29.0) | −1.1 (−5.8 to 3.6) | 17.1 (10.2 to 24.1) | <0.0001 |
| 27 weeks | 48 | 57.5 (17.1) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Food avoidance, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 19.9 (31.3) | ·· | 60 | 19.0 (31.6) | ·· | ·· | ·· |
| 4 weeks | 52 | 21.0 (28.9) | 1.4 (−3.4 to 6.3) | 59 | 17.8 (29.5) | −0.6 (−5.1 to 3.9) | 2.0 (−4.6 to 8.6) | 0.55 |
| 9 weeks | 49 | 34.9 (26.1) | 15.0 (9.3 to 20.6) | 58 | 16.7 (30.9) | −2.2 (−7.4 to 3.0) | 17.2(9.5 to 24.8) | <0.0001 |
| 13 weeks | 49 | 42.5 (12.1) | 22.6 (16.9 to 28.2) | 58 | 17.8 (30.0) | −1.1 (−6.3 to 4.2) | 23.6 (16.0 to 31.3) | <0.0001 |
| 27 weeks | 48 | 39.4 (24.8) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Social reaction, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 48.6 (19.2) | ·· | 60 | 42.4 (27.2) | ·· | ·· | ·· |
| 4 weeks | 52 | 49.5 (19.0) | 2.0 (−1.3 to 5.3) | 59 | 40.8 (26.8) | −1.5 (−4.6 to 1.6) | 3.5 (−1.0 to 8.0) | 0.13 |
| 9 weeks | 49 | 58.5 (15.3) | 6.9 (3.0 to 10.7) | 58 | 43.1 (27.4) | −1.6 (−5.2 to 2.0) | 8.5 (3.2 to 13.8) | 0.002 |
| 13 weeks | 49 | 62.5 (12.1) | 9.3 (5.1 to 13.5) | 58 | 43.2 (27.0) | −3.4 (−7.3 to 0.5) | 12.7 (7.0 to 18.5) | <0.0001 |
| 27 weeks | 48 | 58.9 (16.9) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Sexual, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 56.0 (23.0) | ·· | 60 | 54.8 (25.5) | ·· | ·· | ·· |
| 4 weeks | 52 | 55.8 (25.2) | 5.5 (0.4 to 10.5) | 59 | 52.1 (28.3) | 0.5 (−4.2 to 5.3) | 4.9 (−2.0 to 11.9) | 0.16 |
| 9 weeks | 49 | 55.1 (24.3) | 12.4 (7.1 to 17.7) | 58 | 51.7 (27.0) | 2.4 (−2.5 to 7.4) | 10.0 (2.7 to 17.2) | 0.0073 |
| 13 weeks | 49 | 64.0 (17.2) | 14.7 (9.3 to 20.1) | 58 | 51.5 (29.0) | 0.0 (−5.0 to 5.0) | 14.7 (7.3 to 22.1) | 0.0001 |
| 27 weeks | 48 | 57.3 (25.0) | ·· | ·· | ·· | ·· | ·· | ·· |
| **Relationships, score 0–100** | | | |  |  |  |  |  |
| baseline | 54 | 34.1 (21.9) | ·· | 60 | 29.9 (27.5) | ·· | ·· | ·· |
| 4 weeks | 52 | 34.9 (22.1) | 1.3 (−3.9 to 6.5) | 59 | 31.6 (26.3) | −0.3 (−5.2 to 4.5) | 1.6 (−5.5 to 8.8) | 0.65 |
| 9 weeks | 49 | 46.9 (18.0) | 14.8 (8.5 to 21.0) | 58 | 31.0 (27.3) | −2.0 (−7.8 to 3.7) | 16.8 (8.3 to 25.3) | 0.0002 |
| 13 weeks | 49 | 51.4 (18.7) | 22.4 (16.0 to 28.7) | 58 | 31.3 (31.0) | −0.9 (−6.7 to 5.0) | 23.2 (14.6 to 31.9) | <0.0001 |
| 27 weeks | 48 | 46.2 (21.0) | ·· | ·· | ·· | ·· | ·· | ·· |
| Data are mean (SD) unless otherwise specified.  aLS means of change scores from baseline to each assessment point are from restricted maximum likelihood-based mixed-model repeated measures.  bBetween-group differences in LS means, *P* value < 0.025 (two-sided).  GCBT-IE, group cognitive behavioral therapy with interoceptive exposure; IBS-QOL, the Irritable Bowel Syndrome-Quality of Life; LS, least squares. | | | | | | | | |

**Supplemental Table 3: IBS-QOL subscales**

**Supplemental Table 4: GSRS subscale**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **GCBT-IE** | | **Waiting list** | | **GCBT-IE versus Waiting list** | |
|  | n | Mean (SD) | n | Mean (SD) | Difference in LS mean changesa (95% CI) | *P* value |
| **Gastric acid reflux, score 1-7** | | |  |  |  |  |
| Baseline | 54 | 2.1 (1.2) | 60 | 2.0 (1.3) | ·· | ·· |
| 4 weeks | 52 | 1.9 (1.1) | 59 | 2.0 (1.1) | −0.2 (−0.5 to 0.2) | 0.32 |
| 9 weeks | 49 | 1.9 (1.2) | 58 | 2.2 (1.3) | −0.4 (−0.8 to 0.0) | 0.062 |
| 13 weeks | 49 | 1.6 (0.8) | 58 | 2.1 (1.1) | −0.6 (−0.9 to −0.2) | 0.0005 |
| **Abdominal pain, score 1-7** | | |  |  |  |  |
| baseline | 54 | 2.2 (1.4) | 60 | 2.2 (1.1) | ·· | ·· |
| 4 weeks | 52 | 2.2 (1.1) | 59 | 2.3 (1.1) | −0.1 (−0.4 to 0.2) | 0.47 |
| 9 weeks | 49 | 2.1 (1.3) | 58 | 2.4 (1.2) | −0.3 (−0.7 to 0.1) | 0.10 |
| 13 weeks | 49 | 1.7 (0.8) | 58 | 2.4 (1.3) | −0.6 ( −1.2 to −0.4) | <0.0001 |
| **Indigestion, score 1-7** | | |  |  |  |  |
| baseline | 54 | 2.6 (1.3) | 60 | 2.7 (1.4) | ·· | ·· |
| 4 weeks | 52 | 2.5 (1.1) | 59 | 2.7 (1.5) | −0.1 (−0.4 to 0.2) | 0.46 |
| 9 weeks | 49 | 2.2 (1.1) | 58 | 2.8 (1.3) | −0.4 (−0.7 to −0.1) | 0.0057 |
| 13 weeks | 49 | 1.9 (0.9) | 58 | 2.6 (1.3) | −0.6 (−0.9 to −0.3) | 0.0003 |
| **Diarrhea, score 1-7** | | |  |  |  |  |
| baseline | 54 | 3.8 (1.7) | 60 | 3.4 (1.5) | ·· | ·· |
| 4 weeks | 52 | 3.7 (1.5) | 59 | 3.5 (1.7) | −0.1 (−0.6 to 0.4) | 0.80 |
| 9 weeks | 49 | 3.1 (1.2) | 58 | 3.8 (1.6) | −0.8 (−1.3 to −0.4) | 0.0005 |
| 13 weeks | 49 | 2.6 (1.1) | 58 | 3.7 (1.6) | −1.2 (−1.7 to −0.7) | <0.0001 |
| **Constipation, score 1-7** | | |  |  |  |  |
| baseline | 54 | 2.9 (1.5) | 60 | 3.1 (1.4) | ·· | ·· |
| 4 weeks | 52 | 2.8 (1.3) | 59 | 2.8 (1.3) | 0.0 (−0.4 to 0.4) | 0.96 |
| 9 weeks | 49 | 2.4 (1.2) | 58 | 3.0 (1.3) | −0.6 (−1.0 to −0.2) | 0.0042 |
| 13 weeks | 49 | 2.3 (1.2) | 58 | 2.9 (1.4) | −0.6 (−1.0 to −0.1) | 0.0089 |
| Data are mean (SD) unless otherwise specified.  aBetween-group differences in LS means of change scores from baseline to each assessment point are from restricted maximum likelihood-based mixed-model repeated measures, *P* value < 0.05 (two-sided).  GCBT-IE, group cognitive behavioral therapy with interoceptive exposure; GSRS, the Gastrointestinal Symptom Rating Scale; LS, least squares. | | | | | | |

**Supplemental Table 5: Subgroup Analysis for IBS-SSS**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **GCBT-IE (N=54)** | **Waiting list (N=60)** | **GCBT-IE versus Waiting list** | | |
|  | n (%) | n (%) | Difference in LS mean changesa (95% CI) | *P* value | *P* value for interaction |
| **Disease duration** |  |  |  |  |  |
| 0.5–10 years | 30/54 (55.6) | 23/60 (38.3) | −93.4 (−141.1 to −45.8) | 0.0003 | 0.5045 |
| 10 years ≤ | 24/54 (44.4) | 37/60 (61.7) | −71.9 (−115.9 to −27.8) | 0.0018 |
| **IBS subtypes** |  |  |  |  |  |
| IBS-D | 33/54 (61.1) | 34/60 (56.7) | −93.4 (−136.3 to −50.6) | < 0.0001 | 0.4595 |
| Others | 21/54 (38.9) | 26/60 (43.3) | −71.2 (−112.9 to −29.6) | 0.0013 |
| **Implementation format** | |  |  |  |  |
| Face-to-face | 35/54 (64.8) | 38/60 (63.3) | −105.8 (−145.0 to −66.5) | < 0.0001 | 0.1226 |
| Internet-base | 19/54 (35.2) | 22/60 (36.7) | −55.6 (−107.9 to −3.3) | 0.038 |
| Data are n/N (%) unless otherwise specified.  aBetween-group differences in LS means of change scores from baseline to each assessment point are from restricted-maximum likelihood based mixed-model repeated measures, *P* value < 0.05 (two-sided).  GCBT-IE, group cognitive behavioral therapy with interoceptive exposure; IBS-D, Diarrhea-predominant irritable bowel syndrome; IBS-SSS, IBS-Symptom Severity Score; LS, least squares. | | | | | |

**Supplemental Table6: Subgroup Analysis for IBS-QOL**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **GCBT-IE (N=54)** | **Waiting list (N=60)** | **GCBT-IE versus Waiting list** | | |
|  | n (%) | n (%) | Difference in LS mean changesa (95% CI) | *P* value | *P* value for interaction |
| **Disease duration** |  |  |  |  |  |
| 0.5–10 years | 30/54 (55.6) | 23/60 (38.3) | 21.2 (13.5 to 28.9) | <0.0001 | 0.6526 |
| 10 years ≤ | 24/54 (44.4) | 37/60 (61.7) | 18.4 (11.8 to 25.1) | < 0.0001 |
| **IBS subtypes** |  |  |  |  |  |
| IBS-D | 33/54 (61.1) | 34/60 (56.7) | 18.7 (11.8 to 25.5) | < 0.0001 | 0.4580 |
| Others | 21/54 (38.9) | 26/60 (43.3) | 22.4 (14.6 to 30.3) | < 0.0001 |
| **Implementation format** | |  |  |  |  |
| Face-to-face | 35/54 (64.8) | 38/60 (63.3) | 18.8 (12.0 to 25.6) | < 0.0001 | 0.4601 |
| Internet-base | 19/54 (35.2) | 22/60 (36.7) | 22.8 (14.9 to 30.7) | < 0.0001 |
| Data are n/N (%) unless otherwise specified.  aBetween-group differences in LS means of change scores from baseline to each assessment point are from restricted-maximum likelihood based mixed-model repeated measures, *P* value < 0.05 (two-sided).  GCBT-IE, group cognitive behavioral therapy with interoceptive exposure; IBS-D, Diarrhea-predominant irritable bowel syndrome; IBS-QOL, IBS-Quality of Life; LS, least squares. | | | | | |