Supplementary Table 1. Classification of individual symptoms into depressive symptom profiles.

|  |  |  |
| --- | --- | --- |
|  | **Mood/cognition symptom profile** | **Somatic symptom profile** |
| **Energy-related symptom profile** | Leaden paralysis | Increased appetite |
|  | Low energy level/fatigue | Increased weight |
|  |  | Sleeping too much |
| **Other symptoms** | Feeling sad | Problems falling asleep |
|  | Feeling irritable | Problems sleeping during the night |
|  | Feeling anxious or tense | Early morning awakenings |
|  | Mood reactivity | Decreased weight |
|  | Quality of mood | Decreased appetite |
|  | Concentration/decision making problems | Psychomotor agitation |
|  | Self-criticism and blame | Aches and pains |
|  | Future pessimism | Other bodily symptoms |
|  | Suicidal thoughts | Panic/phobic symptoms |
|  | Diminished interest in people/activities | Constipation/diarrhea |
|  | Diminished capacity for pleasure/enjoyment |  |
|  | Reduced interest in sex |  |
|  | Psychomotor retardation |  |
|  | Interpersonal sensitivity |  |

Supplementary Table 2. *Effect modification by age, sex and baseline body mass index (BMI).*

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Mood/cognition** | | |  | **Somatic** | | |  | **Energy-related** | | |
|  |  | B | SE | *p* |  | B | SE | *p* |  | B | SE | *p* |
| Model 1 | F-BA × BMI | -0.07 | 0.08 | .357 |  | 0.04 | 0.05 | .382 |  | -0.01 | 0.03 | .762 |
|  | Supplements × BMI | 0.09 | 0.08 | .246 |  | 0.07 | 0.05 | .126 |  | 0.06 | 0.03 | **.043** |
| Model 2 | F-BA × Age | -0.04 | 0.03 | .107 |  | -0.02 | 0.01 | .232 |  | -0.013 | 0.01 | .180 |
|  | Supplements × Age | 0.0008 | 0.03 | .976 |  | -0.001 | 0.01 | .950 |  | 0.003 | 0.01 | .791 |
| Model 3 | F-BA × Sex | -1.01 | 0.71 | .156 |  | -0.36 | 0.39 | .357 |  | 0.04 | 0.26 | .180 |
|  | Supplements × Sex | -0.26 | 0.72 | .716 |  | -0.60 | 0.39 | .124 |  | -0.48 | 0.27 | .791 |

Models were adjusted for F-BA therapy, supplements, time, baseline symptom profile score, recruitment site and history of depression. P-values < .05 are highlighted in bold.

Supplementary Table 3. *GEE sensitivity analyses on a subset with complete symptom profile data at all follow-up measurements (n = 687, nobservations = 2061)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | B | SE | *p-*value |
|  | **Mood/cognition** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.01 | 0.02 | .598 |
|  | Supplements vs. placebo | 0.04 | 0.02 | .**047a** |
| Model 2 | Supplements x F-BA | 0.01 | 0.04 | .819 |
|  | **Somatic** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.03 | 0.01 | **.047b** |
|  | Supplements vs. placebo | 0.01 | 0.02 | .620 |
| Model 2 | Supplements x F-BA | -0.007 | 0.03 | .981 |
|  | **Energy-related** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.06 | 0.03 | **.026c** |
|  | Supplements vs. placebo | 0.06 | 0.03 | **.013d** |
| Model 2 | Supplements x F-BA | 0.04 | 0.05 | .474 |

Intervention effects are modelled over 3, 6 and 12-month follow-up measurements. Intervention variables are dummy coded (supplements/F-BA = 1; placebo/no intervention = 0). Model 1: adjusted for time, baseline symptom profile score, recruitment site and history of major depressive disorder. Model 2: adjusted for model 1, F-BA therapy, and supplements. P-values < .05 are highlighted in bold. aCohen’s d (95% CI) = 0.08 (-0.004 to 0.17); bCohen’s d (95% CI) = -0.08 (-0.17 to 0.003); cCohen’s d (95% CI) = -0.09 (-0.18 to -0.01); dCohen’s d (95% CI) 0.10 (0.02 to 0.19).

Supplementary Table 4.1 *Adherence to the interventions*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Placebo | F-BA + Placebo | Supplements | F-BA + Supplements |
|  | *n* = 247 | *n* = 254 | *n* = 244 | *n* = 248 |
| ≥ 8 sessions F-BA, *n*(%) | - | 184 (72.4%) | - | 180 (72.6%) |
| ≥70% multi-nutrient supplement, *n*(%) | 135 (77.1%) | 134 (79.3%) | 126 (76.4%) | 119 (78.8%) |
| ≥70% omega 3 fatty acid supplement, *n*(%) | 133 (76.0%) | 133 (79.2%) | 126 (76.4%) | 119 (79.3%) |

Supplementary Table 4.2 *Per protocol GEE analyses on a subset with good adherence to the supplements (n = 510, nobservations = 1530)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | B | SE | *p-*value |
|  | **Mood/cognition** |  | | |
| Model 1 | F-BA therapy vs. no intervention | 0.002 | 0.03 | .933 |
|  | Supplements vs. placebo | 0.05 | 0.02 | .**038a** |
| Model 2 | Supplements x F-BA | 0.05 | 0.05 | .335 |
|  | **Somatic** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.03 | 0.02 | .090**b** |
|  | Supplements vs. placebo | 0.03 | 0.02 | .129 |
| Model 2 | Supplements x F-BA | 0.02 | 0.04 | .522 |
|  | **Energy-related** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.05 | 0.03 | .080c |
|  | Supplements vs. placebo | 0.10 | 0.03 | **.0005d** |
| Model 2 | Supplements x F-BA | 0.07 | 0.06 | .191 |

Good adherence was defined as receiving 70% of the supplements over a period of 12 months. Intervention effects are modelled over 3, 6 and 12-month follow-up measurements. Intervention variables are dummy coded (supplements/F-BA = 1; placebo/no intervention = 0). Model 1: adjusted for time, baseline symptom profile score, recruitment site and history of major depressive disorder. Model 2: adjusted for model 1, F-BA therapy, and supplements. P-values < .05 are highlighted in bold. aCohen’s d (95% CI) = 0.10 (-0.01 to 0.20); bCohen’s d (95% CI) = -0.09 (-0.18 to 0.02); cCohen’s d (95% CI) = -0.08 (-0.18 to 0.02); dCohen’s d (95% CI) = 0.17 (0.07 to 0.27).

Supplementary Table 4.2 *Per protocol GEE analyses on a subset with good adherence to F-BA therapy (n = 795, nobservations = 2565)*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | B | SE | *p* |
|  | **Mood/cognition** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.01 | 0.02 | .561 |
|  | Supplements vs. placebo | 0.05 | 0.02 | .**038a** |
| Model 2 | Supplements x F-BA | 0.02 | 0.04 | .665 |
|  | **Somatic** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.04 | 0.01 | **.011b** |
|  | Supplements vs. placebo | 0.02 | 0.01 | .205 |
| Model 2 | Supplements x F-BA | -0.02 | 0.03 | .534 |
|  | **Energy-related** |  | | |
| Model 1 | F-BA therapy vs. no intervention | -0.07 | 0.02 | **.002c** |
|  | Supplements vs. placebo | 0.08 | 0.02 | **.002d** |
| Model 2 | Supplements x F-BA | 0.0002 | 0.05 | .996 |

Good adherence was defined as receiving ≥8 of 21 therapy sessions. Intervention effects are modelled over 3, 6 and 12-month follow-up measurements. Intervention variables are dummy coded (supplements/F-BA = 1; placebo/no intervention = 0). Model 1: adjusted for time, baseline symptom profile score, recruitment site and history of major depressive disorder. Model 2: adjusted for model 1, and F-BA therapy, and supplements. P-values < .05 are highlighted in bold. aCohen’s d (95% CI) = 0.10 (-0.01 to 0.19); bCohen’s d (95% CI) = -0.11 (-0.19 to -0.02); cCohen’s d (95% CI) = -0.13 (-0.21 to -0.04); dCohen’s d (95% CI) = 0.13 (0.04 to 0.22).