Effect of Multinutrient Supplementation and Food-Related Behavioral Activation Therapy on Prevention of Major Depressive Disorder Among Overweight or Obese Adults With Subsyndromal Depressive Symptoms The MooDFOOD Randomized Clinical Trial

Key Points

**Question** What is the effect of multinutrient supplementation and food-related behavioral activation therapy on prevention of a new episode of major depressive disorder among overweight or obese adults with subsyndromal depressive symptoms?

**Findings** In this $2 \times 2$ factorial randomized clinical trial that included 1025 adults, there was no significant difference in episodes of major depressive disorder over 1 year of follow-up with multinutrient supplementation vs placebo (54 [10.5%] vs 51 [9.9%]) or with food-related behavioral activation therapy vs no therapy (48 [9.4%]) vs 57 [11.1%]).

**Meaning** These findings do not support the use of multinutrient supplementation or food-related behavioral activation therapy for prevention of major depressive disorder.

Abstract

**Importance** Effects of nutritional interventions on the prevention of major depressive disorder (MDD) in overweight adults are unknown.
Objective To examine the effect of 2 nutritional strategies (multinutrient supplementation, food-related behavioral activation therapy) and their combination for prevention of a new MDD episode in overweight adults with subsyndromal depressive symptoms.

Design, Setting, and Participants This multicenter 2 × 2 factorial randomized clinical trial included overweight adults (body mass index, 25-40) with elevated depressive symptoms (Patient Health Questionnaire-9 [PHQ-9] scores ≥5) and no MDD episode in the past 6 months from 4 European countries. A total of 1025 adults were randomized (July 30, 2015-October 12, 2016) and followed up for 1 year (October 13, 2017).

Interventions Daily multinutrient supplements (1412-mg omega-3 fatty acids, 30-µg selenium, 400-µg folic acid, and 20-µg vitamin D₃ plus 100-mg calcium) vs placebo and 21 individual or group therapy sessions vs none (blinded to researchers) for 1 year. Participants were allocated to placebo without therapy (n = 257), placebo with therapy (n = 256), supplements without therapy (n = 256), and supplements with therapy (n = 256).

Main Outcome and Measures Cumulative 1-year onset of MDD via the Mini International Neuropsychiatric Interview at 3, 6, and 12 months. Logistic regression using effect-coded variables (−1 indicating control, 1 indicating intervention) evaluated intervention effects both individually and in combination (interaction) on MDD onset.

Results Among 1025 participants (mean age, 46.5 years; 772 women [75%]; mean BMI, 31.4), 779 (76%) completed the trial. During the 12-month follow-up, 105 (10%) developed MDD: 25 (9.7%) patients in the placebo without therapy, 26 (10.2%) in the placebo with therapy, 32 (12.5%) in the supplement without therapy, and 22 (8.6%) in the supplement with therapy group. None of the treatment strategies affected MDD onset. The odds ratio (OR) for supplements was 1.06 (95% CI, 0.87-1.29); for therapy, 0.93 (95% CI, 0.76-1.13); and for their combination, 0.93 (95% CI, 0.76-1.14; P for interaction, .48). One person in the supplementation with therapy group, died. Twenty-four patients in each of
the placebo groups and 24 patients in the supplementation with therapy group were hospitalized, and 26 patients in the supplementation-only group were hospitalized.

**Conclusions and Relevance** Among overweight or obese adults with subsyndromal depressive symptoms, multinutrient supplementation compared with placebo and food-related behavioral activation therapy compared with no therapy did not reduce episodes of major depressive disorder during 1 year. These findings do not support the use of these interventions for prevention of major depressive disorder.

**Trial registration** ClinicalTrials.gov Identifier: [NCT02529423](https://clinicaltrials.gov/ct2/show/NCT02529423)