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 × 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 D_3 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