

Effect of Omega-3 Polyunsaturated Fatty Acids on Depressive Symptoms in Patients with Major Depressive Disorder with and without Overweight/Obesity: Preliminary Results of a Double-Blind, Placebo-Controlled, Randomized Clinical Trial

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ABSTRACT

Background: Research suggests that omega-3 polyunsaturated fatty acids (n-3 PUFAs) have demonstrated protective effects in both individuals with major depressive disorder (MDD) and those who are overweight/obese. However, limited studies explored the combined effect of n-3 PUFAs and weight status specifically in patients with MDD. This study aimed to investigate the interaction between n-3 PUFAs and weight status on clinical outcomes in patients with MDD.

Methods: A total of 78 patients with MDD participated in this 12-week double-blind randomized controlled trial. Patients were randomly assigned to receive either n-3 PUFAs (3g eicosapentaenoic acid, EPA per day) or a placebo (3g soybean oil per day). Demographic data and body mass index (BMI) were collected at baseline. Depression severity was evaluated using the Hamilton Depression Rating Scale (HAM-D) and Beck's Depression Inventory (BDI) at baseline, week 2, 4, 8 and 12. Blood samples were collected for assessment of high sensitivity C-reactive protein (hs-CRP) levels at baseline and week 12.

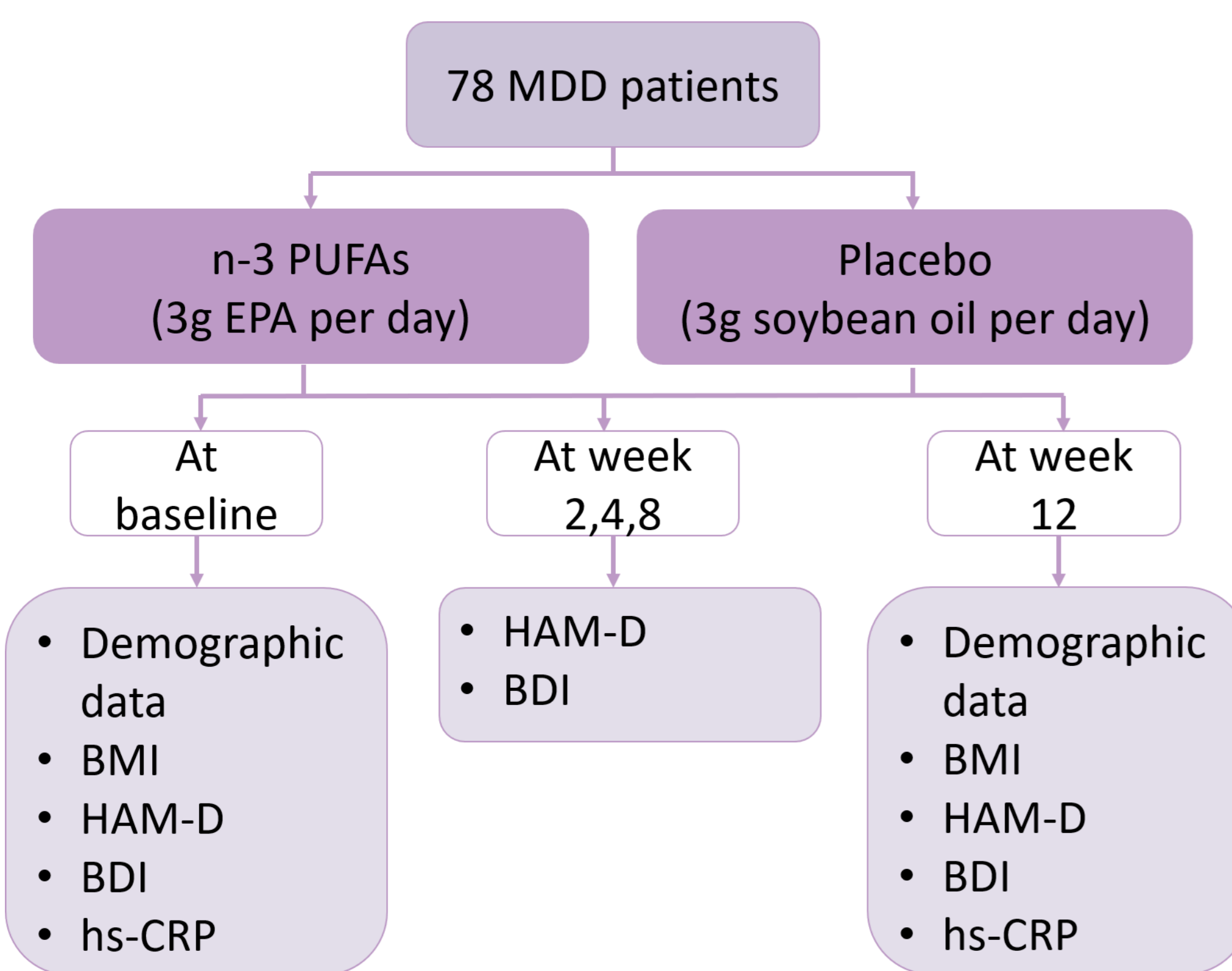
Results: Less than half of our patients (n=36, 46.2%) are overweight/obese (BMI ≥ 24 kg/m²). Our results indicated a positive correlation between hs-CRP levels and BMI (r=0.804, p<0.001). In the 12-week trial, there was no significant difference in the improvement of depression among MDD patients across BMI groups (p=0.421 for HAM-D, p=0.410 for BDI). N-3 PUFA supplementation significantly improved depressive symptoms in MDD patients compared to the placebo group, as indicated by reductions in both HAM-D (p<0.001) and BDI (p<0.001) scores. Moreover, n-3 PUFA intervention notably reduced HAM-D scores (week 4: p=0.014, week 12: p=0.006) and BDI scores (week 8: p=0.032, week 12: p=0.012) in non-overweight/obese MDD patients.

Conclusion: N-3 PUFA intervention effectively alleviated depressive symptoms in MDD patients, particularly among those who were non-overweight/obese.

INTRODUCTION

- Depression and obesity have emerged as significant public health concerns due to their increasing prevalence.
- Several studies suggest the relationship between MDD and obesity, with evidence for both BMI impacting depression and vice versa (Fanelli et al., 2022; Luppino et al., 2010; Tyrrell et al., 2019).
- Recent study revealed that individuals with comorbid MDD and overweight/obesity were at risk for worse clinical outcomes (Kraus et al. 2023)
- Several recent studies explored n-3 PUFA effects in populations with high inflammation, including MDD with type 2 diabetes (Mazaherion et al. 2018) and overweight/obese individuals (Mischoulon et al. 2022).
- However, limited studies examined the impact of n-3 PUFAs on depression severity among MDD patients with varying weight statuses.
- Therefore, this study aimed to investigate the effect of omega-3 polyunsaturated fatty acids on depressive symptoms in patients with major depressive disorder with and without overweight/obesity.

METHODOLOGY



CONCLUSION

n-3 PUFA intervention effectively alleviated depressive symptoms in MDD patients, particularly among those who were non-overweight/obese.

References:
 Fanelli et al. *Am J Med Genet B Neuropsychiatr Genet.* 2022 Apr;189(3-4):74-85.; Luppino FS. *Arch Gen Psychiatry.* 2010 Mar;67(3):220-9.; Tyrrell J et al. *Int J Epidemiol.* 2019 Jun 1;48(3):834-848.; Mazaherion et al. *Iran J Public Health.* 2018 Apr;47(4):575-583.; Kkeli, N., & Michaelides, M. P. *European Journal of Environment and Public Health.* 2023 7(3), em0134.; Mischoulon D. et al. *J Clin Psychiatry.* 2022 Aug 22;83(5):21m14074.; Borsini, A., Nicolaou, A., Camacho-Muñoz, D. et al. (2021) *Mol Psychiatry* 26, 6773–6788.; Liao Y. et al. *Trans Psychiatry.* 2019 Aug 5;9(1):190.

RESULTS

Table 1. Demographic and clinical outcomes of patients with MDD

	Total (n=78)	PLA (n=41)	EPA (n=37)	P value
Age	41.9 ± 14.57	39.53 ± 14.76	44.60 ± 14.07	0.126
Gender ^b				0.196
Male, n (%)	20 (25.6)	13 (31.7)	7 (18.9)	
Female, n (%)	58 (74.4)	28 (68.3)	30 (81.1)	
Education ^b				0.510
High school & below, n (%)	27 (35.1)	13 (31.7)	14 (38.9)	
College & above, n (%)	50 (64.9)	28 (68.3)	22 (61.1)	
Smoking ^b				0.648
Never, n (%)	60 (77.9)	32 (80.0)	28 (75.7)	
Smoker, n (%)	17 (22.1)	8 (20.0)	9 (24.3)	
Alcohol ^b				0.972
Never, n (%)	61 (78.2)	32 (78.0)	29 (78.4)	
Alcoholic, n (%)	17 (21.8)	9 (22.0)	8 (21.6)	
BMI Category ^b				0.675
BMI < 24 kg/m ² , n (%)	42 (53.8)	23 (56.1)	19 (51.4)	
BMI ≥ 24 kg/m ² , n (%)	36 (46.2)	18 (43.9)	18 (48.6)	
BMI	23.90 ± 5.83	23.53 ± 6.71	24.33 ± 4.74	0.549
Hs-CRP, mg/dL (Week 0)	0.22 ± 0.53	0.29 ± 0.72	0.13 ± 0.14	0.317
Hs-CRP, mg/dL (Week 12)	0.17 ± 0.23	0.14 ± 0.19	0.21 ± 0.27	0.413
HAM-D (Week 0)	22.92 ± 4.73	23.42 ± 4.73	22.40 ± 4.73	0.391
HAM-D (Week 12)	16.72 ± 6.88a	18.17 ± 7.28a	15.11 ± 6.10a	0.049
BDI (Week 0)	27.39 ± 11.38	27.90 ± 10.13	26.83 ± 12.72	0.689
BDI (Week 12)	19.44 ± 13.91a	23.09 ± 14.67a	15.11 ± 11.79a	0.027

T-test (PLA vs EPA) is significant at p<0.05; Paired t-test^a (Week 12 vs Week 0) is significant at p<0.001; chi-square^b is significant at p<0.05.
 Abbrev: MDD, Major depressive disorder; PLA, placebo; EPA, Eicosapentaenoic acid; BMI, Body Mass Index; HAM-D, Hamilton Depression Rating Scale; BDI, Beck's Depression Inventory.

Figure 1. Positive correlation between hs-CRP levels and BMI in MDD patients

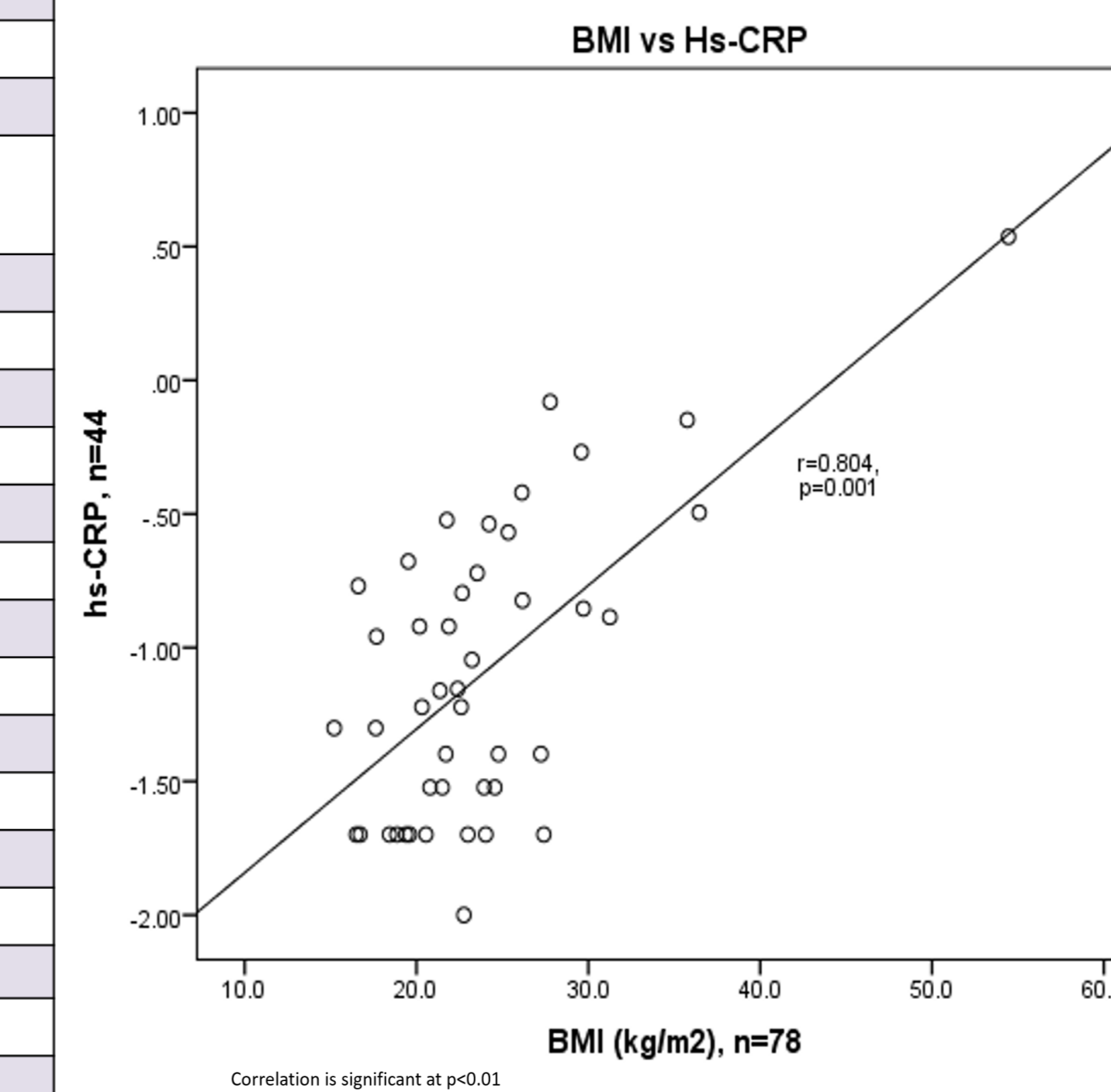


Figure 2. The interaction effects of n-3 PUFAs on HAM-D scores within 12 weeks in MDD patients

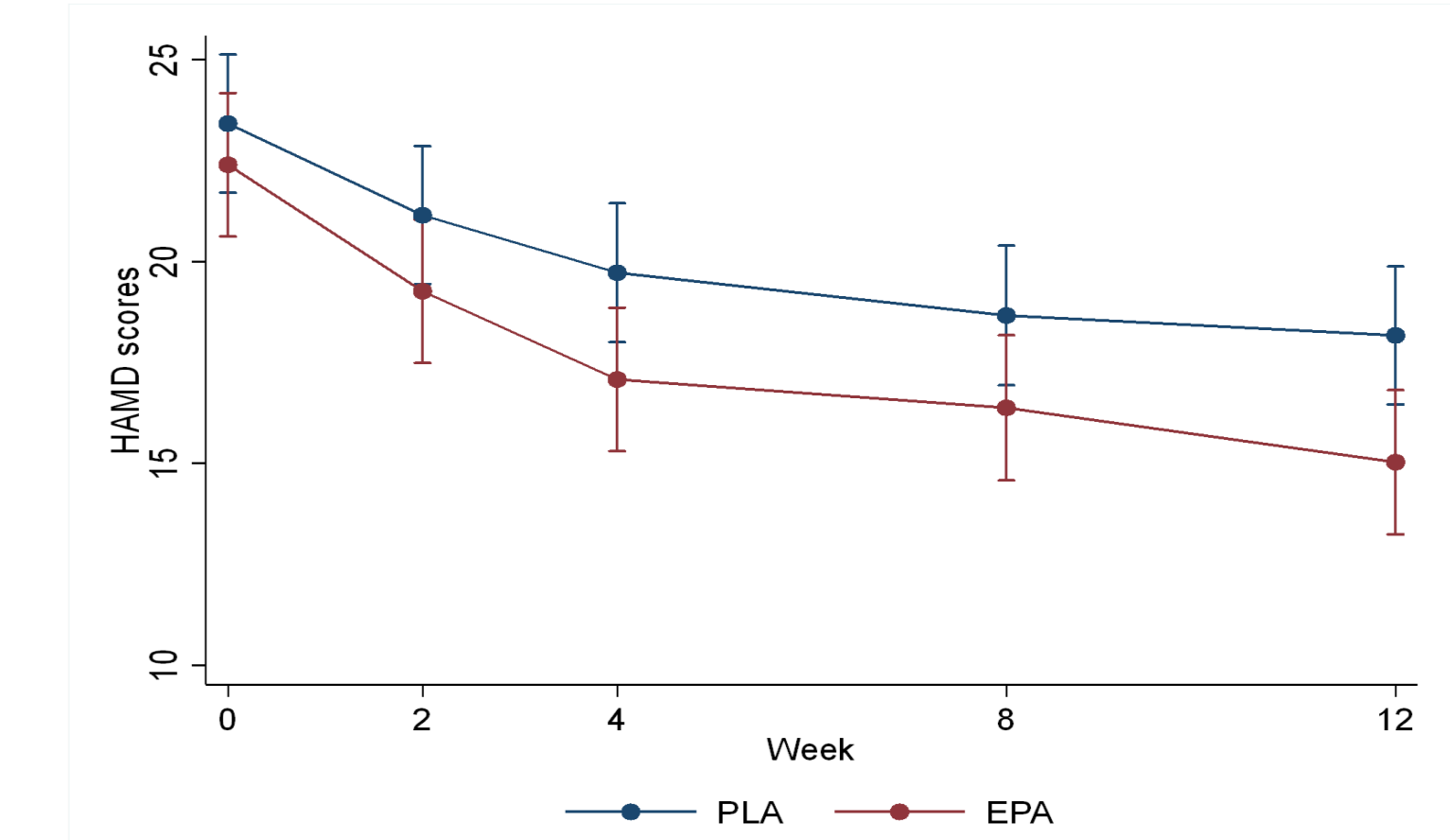


Figure 3. The interaction effects of n-3 PUFAs on BDI scores within 12 weeks in MDD patients

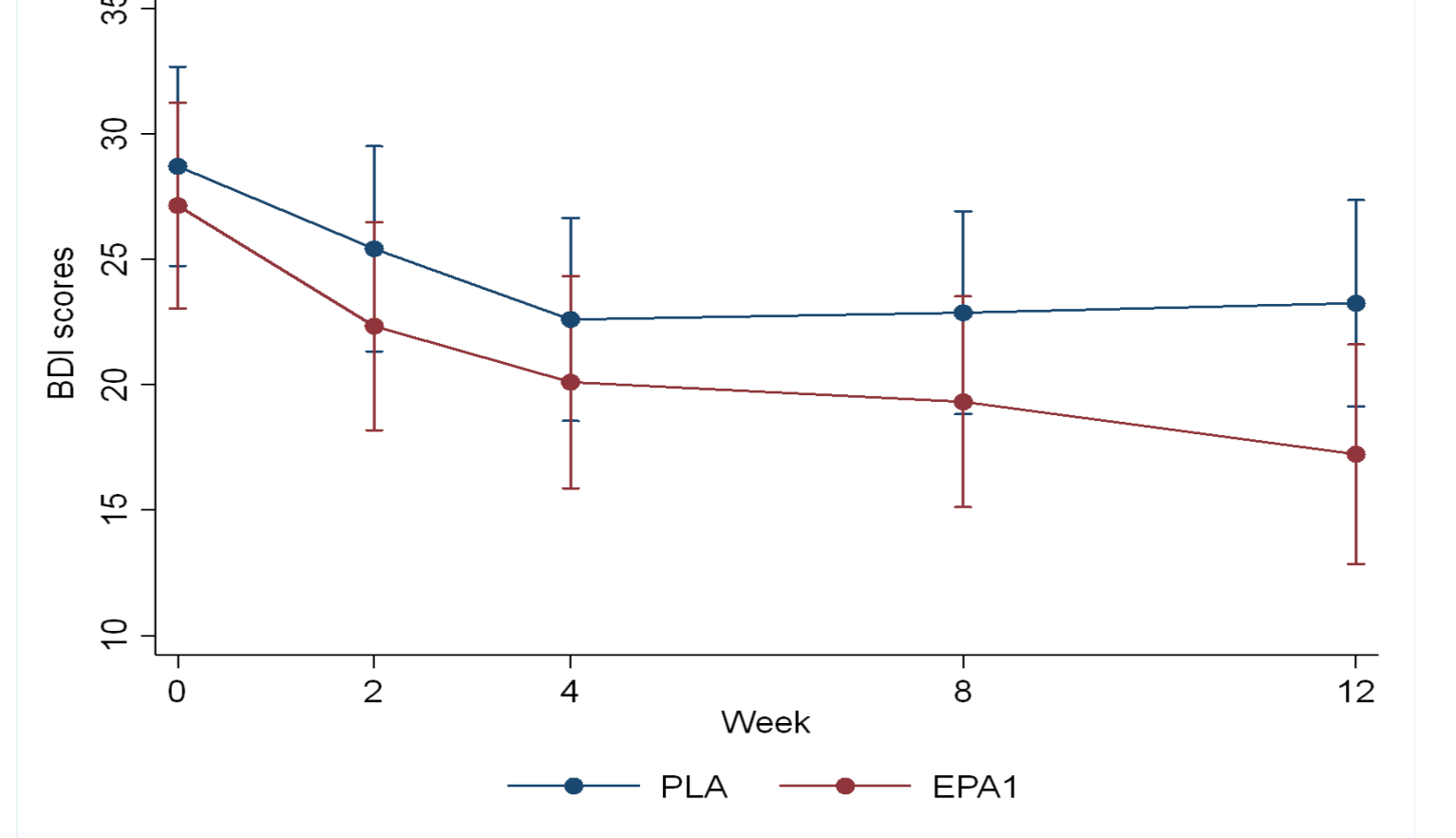
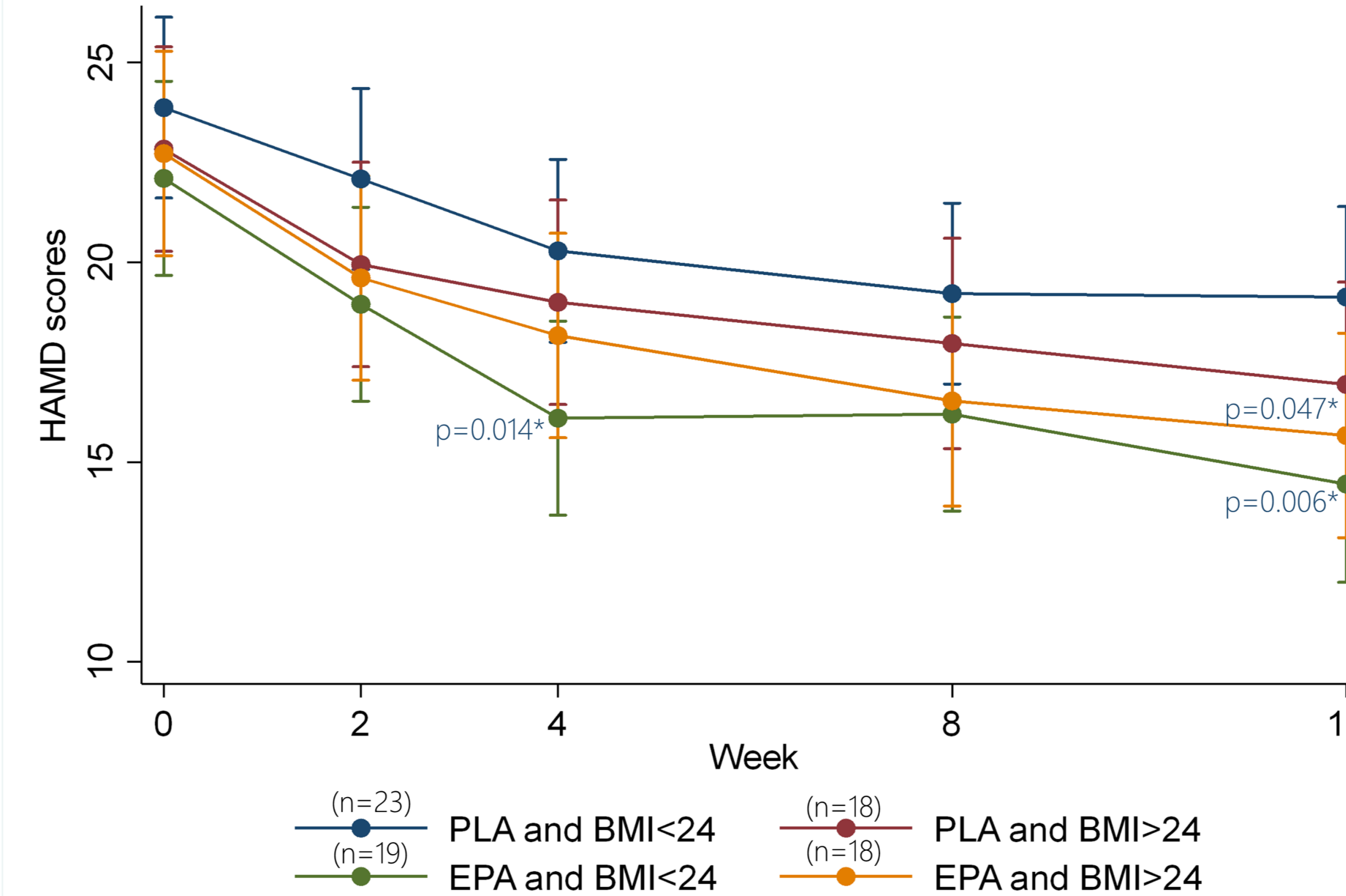
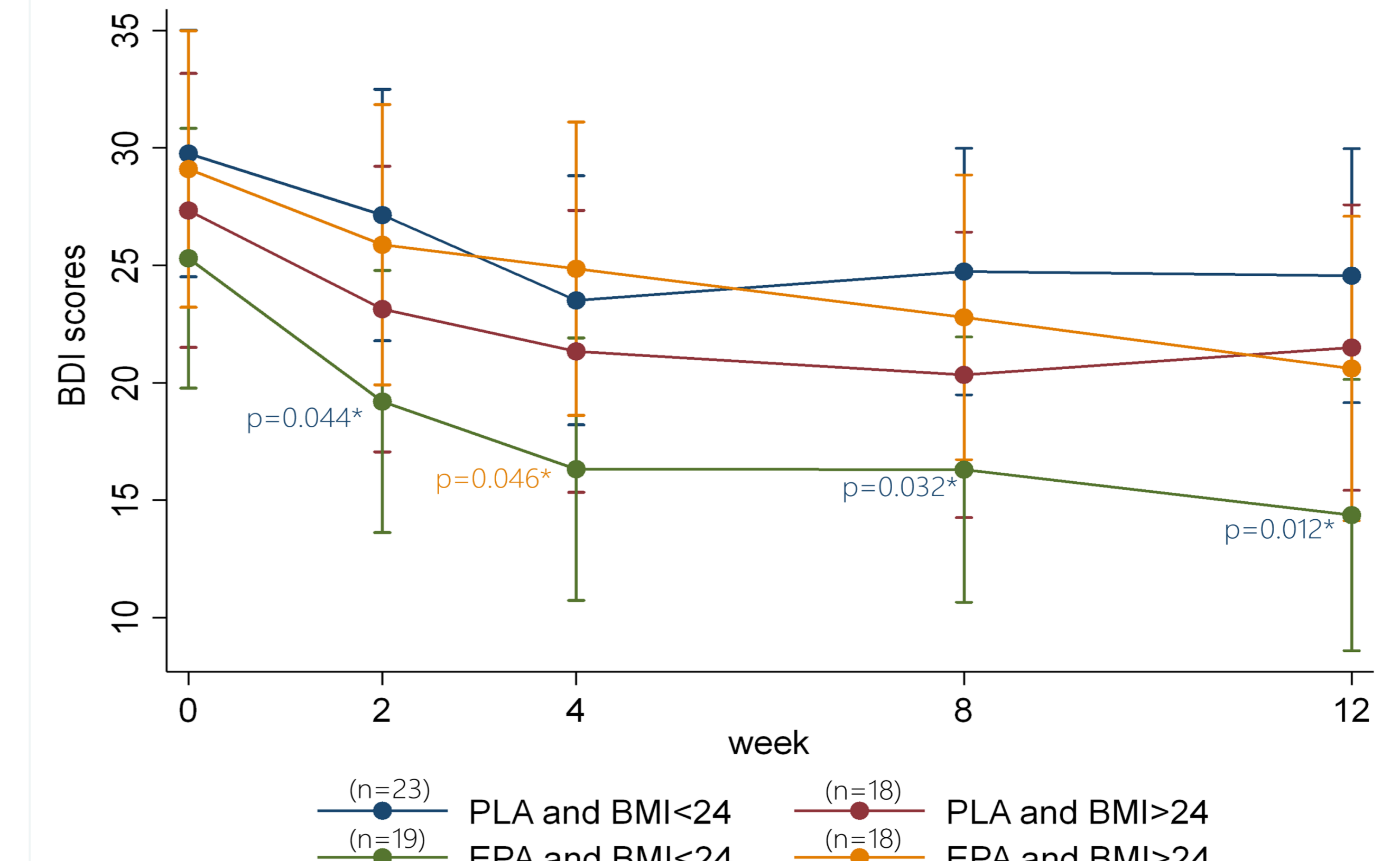


Figure 4. The interaction effects of n-3 PUFAs on HAM-D scores within 12 weeks in MDD patients with/without overweight/obese



Multiple linear mixed model is significant at p<0.05.
 Abbrev: N-3 PUFAs, omega-3 polyunsaturated fatty acids; MDD, Major depressive disorder; PLA, placebo; EPA, Eicosapentaenoic acid; BMI, Body Mass Index; HAM-D, Hamilton Depression Rating Scale.

Figure 5. The interaction effects of n-3 PUFAs on BDI scores within 12 weeks in MDD patients with/without overweight/obese



Multiple linear mixed model is significant at p<0.05.
 Abbrev: N-3 PUFAs, omega-3 polyunsaturated fatty acids; MDD, Major depressive disorder; PLA, placebo; EPA, Eicosapentaenoic acid; BMI, Body Mass Index; BDI, Beck's Depression Inventory.