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Original Article

Comparative Efficacy and Safety of Apple Cider Vinegar Versus Orlistat in reducing Weight and improving aspects of Metabolic Parameters in Overweight and Obese Individuals: A Pilot Trial in Sulaimani City

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Abstract

Background and Objectives: Obesity constitutes a significant public health issue, necessitating the development of effective and safe therapies. This study attempts to investigate the efficacy and safety of apple cider vinegar (ACV) and Orlistat, either individually and in combination, for weight loss and metabolic enhancement in overweight and obese individuals in Sulaimani.

Methods: from September 2024 to April 2025, 183 adults (BMI ≥25 kg/m²) were assigned to Orlistat, ACV, or combination therapy in addition to a standardized individualized diet implemented based on their needs. Body composition parameters (weight, BMI, percentage of body fat, visceral fat, waist-hip ratio, basal metabolic rate), metabolic markers (lipid profile), and adverse events were measured at baseline and after the intervention.

Results: Following the intervention, weight, BMI, PBF, VF, CHOL, TGS, LDL, and WHR all decreased substantially ($p \leq 0.001$). Orlistat uniquely increased HDL (44.4 ± 10.5 to 48.0 ± 9.4, $p \leq 0.001$) and reduced LDL (109.4 ± 32.8 to 92.6 ± 24.5, $p \leq 0.001$). Post-intervention, HDL and LDL levels values differed significantly across groups ($p \leq 0.001$). Constipation (Vinegar: 11 cases; Combine: 0 case) and decreased appetite (Orlistat: 10 cases) were among the adverse effects.

Conclusion & Recommendation: Compared to Orlistat, ACV is a safer, more cost-effective treatment for metabolic health and weight loss, while combination therapy enhanced BMI reduction, it increased gastrointestinal adverse effects. Larger, longer-term trials are required to validate the findings that ACV is a useful adjuvant for managing obesity in comparable groups.

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1. Introduction

One of the biggest global health issues is obesity., defined as a build-up of extra fat that throws off metabolic equilibrium and raises the risk of long-term conditions such type II diabetes, heart disease, and high blood

pressure(1,2). The World Health Organization reports that 12.5% of people worldwide suffered from obesity in 2022, with Iraq having notably high prevalence rates 40.1% among women and 26.5% among men (3). Obesity has a complex aetiology that includes dietary practices, sedentary lifestyles, environmental variables, and genetic predisposition (4). Over 12% of people worldwide suffer from obesity, which has more than doubled since 1990 (5). Similar concerning trends have been noted in Iraq (6,7). With an emphasis on weight loss and changes in metabolic markers, this study compared the safety and effectiveness of ACV, Orlistat, and their combination in overweight and obese people. Body Mass Index (BMI) is used to categorize obesity; a BMI of ≥30 kg/m² is considered obese, and higher classes are linked to increased health risks (6). Insulin resistance, dyslipidemia, and elevated cardiovascular risk are all consequences of obesity's disruption of metabolic homeostasis (8.9). A multidisciplinary approach, including dietary modifications, behavioral therapies, medication, and surgery, is necessary for effective management (10,11). Orlistat, an FDA-approved lipase inhibitor, is recommended for people with a BMI of ≥30 kg/m² or ≥27 kg/m² with comorbidities. It inhibits dietary fat absorption by 30%.(12, 13) It is effective for weight loss but may cause gastrointestinal side effects mainly steatorrhea (13). Apple cider vinegar (ACV), rich in acetic acid, along with bioactive compounds such as polyphenols (chlorogenic acid, gallic acid), trace amount of vitamins (C, B1, B2, B6), minerals (potassium, magnesium, calcium) and, amino acids.(14,15)ACV has shown potential for weight loss through the primary active compound of Acetic acid through different mechanisms and metabolic improvement by enhancing satiety (delay gastric emptying), improving glycemic control, and modulating lipid metabolism and gut microbial influences (15). Effective doses in clinical studies range from 15–30 mL/day (diluted in water), with most trials using 15 mL once or twice daily. (16) The present study applied 15 mL twice daily diluted in 200 mL water after meals, consistent with the higher end of the therapeutic range. Adverse effects, primarily gastrointestinal discomfort, esophageal irritation, and dental erosion, are more common with >30 mL/day undiluted intake or prolonged contact with teeth (16). Contraindications include known allergy to ACV, gastrointestinal issues, and caution in patients with chronic kidney disease due to possible potassium loss. (16,17) Despite promising results from ACV studies regarding weight loss and metabolic health, most research is limited by small scale trial, leaving efficacy and safety uncertain. Additionally, few studies compare ACV with other interventions or explore combination strategies. Therefore, the present study aimed to compare the efficacy and safety of ACV and Orlistat, alone and in combination, for weight loss and metabolic improvement in overweight and obese individuals in Sulaimani, Kurdistan region.

2. Methods and Materials

2.1 Study design and setting

This pilot trial was conducted in SulaImani, Iraq, between September 2024 to April 2025.

2.2 Participants

Participants were adults aged 18–65 years with a BM of 25 kg/m² or higher. Recruitment was achieved through flyers, social media campaigns, and referrals from primary care

physicians. Interested individuals underwent structured screening by study physicians to confirm eligibility. Block randomization, stratified by baseline BMI and sex, was used to allocate participants into one of three intervention groups, ensuring balanced distribution for the duration of 10 weeks.

Eligible participants were those aged 18 years or older, with a BMI of at least 25 kg/m² as measured by the InBody 770 device, and who had maintained a stable weight (±2 kg) for at least one month prior to enrollment. Requirements were to receive written informed consent and a commitment to comply with the set diet and intervention routines. Exclusion criteria included being pregnant and nursing, preexisting weight-related diseases (i.e., hypothyroidism or Cushing's syndrome), being allergic/acutely hypersensitive to ACV or orlistat, experiencing gastrointestinal dysfunction, or suffering from ongoing use of weight-affecting medication, drinking alcohol since, considered an extra source of calorie or taking drugs known to affect body mass index. One hundred eighty-three patients were randomized into three groups (61 in each group): combination group, the Orlistat group, and the ACV group. The ACV group ingested 15 mL of apple cider water. The extracts were given as vinegar in water (200 mL), two times a day after meals. The Orlistat group was given 120 mg of the drug three times a day, before meal and combination group receive both formula at the same time and dosage for the 8 -week. At a moderate effect size (f = 0.25), 80% statistical power, a significance level of 0.05, with an additional 15% to account for possible attrition, the sample size was determined using G*Power software (version 3.1)(18).

2.3 Data collection

To guarantee dependability and reproducibility across all study sites, data collecting methods were strictly standardized and carried out by qualified research specialists. The ACV used in the intervention underwent thorough safety and quality evaluations before to participant recruitment. Nutritional profile, antioxidant capacity evaluation using DPPH and ABTS assays, and heavy metal screening using Fourier-Transform Infrared Spectroscopy (FTIR) were all included of these assessments. Both the procedure of preparation and batch uniformity were described in great detail. Following a run-in of 2 weeks, baseline assessments were carried out for hydration, physical activity, and sleep standardization. By using the validated InBody 770 bioelectrical impedance analyzer (Kyle et al., 2004), anthropometric parameters were obtained, i.e., weight, BMI, waist-hip ratio (WHR) estimated visceral fat area (VFA), basal metabolic rate, and body fat %. All measurements were taken fasting after an overnight fast. Participants were asked to void their bladder prior to the test, and not perform physical activity for 12 hours before the test. The instrument was calibrated daily as per the manufacturer's protocol. Lipid profiles (Total Cholesterol, Serum Triglyceride, HDL-C, and LDL-C) were analyzed with the Roche Cobas c501 analyzer after 5 mL fasting venous blood was collected into serum-separating tubes, centrifuged for ten minutes at 3,000 rpm. Intervention compliance was assessed by the number of Orlistat tablets remaining, returned bottles of ACV, and compliance diaries kept by participants. To be included in the PP (per-protocol analysis),

compliance should be ≥80%. Systematically recorded baseline and follow-up documentation of any gastrointestinal symptom or adverse event using standardized questionnaires at fortnightly, ≥ biweekly consultations were scored according to the Common Terminology Criteria for Adverse Events (CTCAE v5.0). All of the data was stored in a secure, password-protected database for use in further research.

2.4 Ethical Considerations

The ethical consideration for this research was approved by the College of Medicine Ethics Committee at the University of Sulaimani (No.: 318, date: 13/10/2024). All participants granted written informed consent, and anonymized data coding was employed to maintain anonymity.

2.5 Statistical Analysis

Data was analyzed with SPSS version 28.0. Categorical variables were expressed as frequency and percentage, and continuous values as mean ± standard deviation or median. Between-group comparisons were done using one-way ANOVA or Kruskal-Wallis tests, being $p < 0.05$ considered statistically significant.

3. Results

DPPH and ABTS tests were employed to evaluate antioxidant property of ACV which demonstrated concentration dependent raise in radical scavenging for both the methods. The scavenging of ABTS was significantly higher than DPPH at all volume treatments: the ABTS gradually increased from about 45% to above 80% and for DPPH from 20% to just below 70%, respectively, as the volume grew from 10 µL to 100 µL (Figure 1).

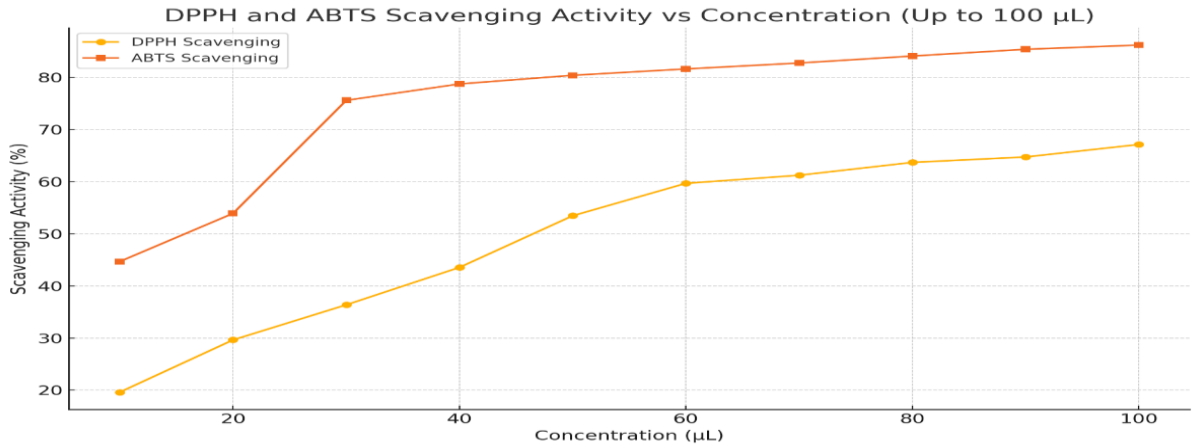

Figure 1. DPPH and ABTS scavenging activity of ACV (ABTS was seen to have higher activity as compared to DPPH, with the two increasing in a concentration-dependent manner.

During simulated gastrointestinal digestion, a rapid release of phenolic compounds was observed in the gastric phase, rising from 455 µg/mL to 741 µg/mL within 90 minutes, followed by a slower increase in the intestinal phase, reaching 221 µg/mL at 240 minutes. With an average of 6.59 mg/g gallic acid equivalent, the total phenolic content of ACV stayed constant across all doses, suggesting uniform phenolic distribution and reliable

extraction (Figure 2).

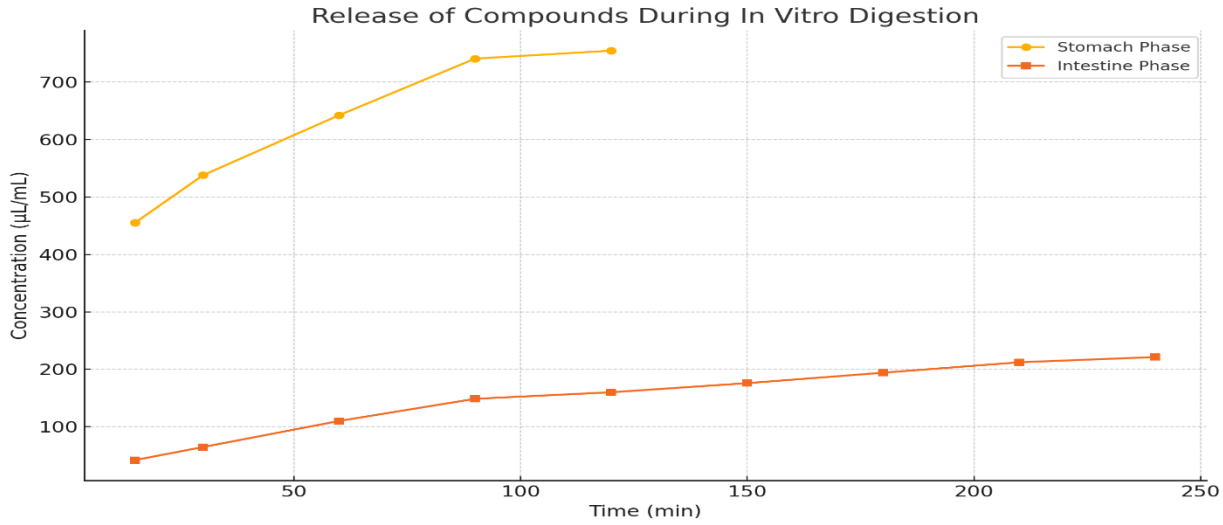

Figure 2. Phenolic compound that was produced from ACV throughout the in vitro digestion process.

According to CHN elemental analysis, the composition of ACV was 36.39% carbon, 7.24% hydrogen, and 0.43% nitrogen by weight. Acetic acid, water, and trace levels of organic and bioactive compounds are all consistent with these results. An estimated protein content of 2.69% (weight/wight) was linked to the nitrogen concentration, which is a sign of the existence of protein and amino acids. FTIR spectroscopy verified the existence of phenolic chemicals, water, and acetic acid by detecting significant functional groups including O–H, C–H, C=O, and C–O.

The average age was 32.721 ± 9.983 years for the Orlistat group, 32.693 ± 10.731 years for the Vinegar group, and 33.332 ± 11.7489 years for the Combine group. There was no statistically significant difference in the participants' mean age between the three groups. Of the 61 participants, 9 (14.8%) were males and 52 (85.2%) were women in the Orlistat group; 11 (19.4%) were men and 50 (80.6%) were women in the Vinegar group; and 6 (11.3%) were men and 55 (88.7%) were women in the Combine group. Similarly, there was no statistically significant difference in the distribution of genders across the three groups. These results are shown in (Table 1).

Table 1. Socio-demographic's Characteristics in participant's study.

Characteristics		Orlistat group (n=61)	Vinegar group (n=61)	Combine group (n=61)	P-value[#]
Age		32.721 ± 9.983*	32.693 ± 10.731	33.332 ± 11.7489	0.934
Sex	Male	9 (14.8%)**	11 (19.4%)	6 (11.3%)	0.454
	Female	52 (85.2%)	50 (80.6%)	55 (88.7%)	

*Mean ± SD, **Frequency (Percent), [#]P-value calculated t-test and Chi-square

All three interventions resulted in significant reductions in body weight, BMI, percent body fat (PBF), visceral fat (VF), total cholesterol (CHOL), triglycerides (TGS), LDL, and waist-hip ratio (WHR) after two months ($p \leq 0.001$ for most comparisons). Basal metabolic rate (BMR) did not change significantly in any group. HDL increased significantly only in the Orlistat and combined groups (Table 2).

Table 2. Changes in Metabolic Health Markers Before and After Intervention.

Marker	Orlistat (n=61)			Vinegar (n=61)			Combine (n=61)		
	Before	After	P	Before	After	P	Before	After	P
BMI	35.74 ± 4.16*	33.44 ± 3.82	0.001	30.77 ± 3.35*	28.79 ± 3.13	0.001	38.36 ± 6.09*	35.80 ± 5.38	0.001
PBF	45.24 ± 4.89	41.80 ± 4.57	0.001	39.99 ± 6.83	36.53 ± 6.31	0.001	47.06 ± 5.36	43.81 ± 4.97	0.001
VF	18.95 ± 3.23	16.55 ± 3.22	0.001	15.01 ± 3.80	13.20 ± 3.12	0.001	19.88 ± 2.98	17.75 ± 2.57	0.001
BMR	1480.131 ± 208.42	1479.327 ± 202.96	0.909	1410.67± 214.76	1426.951 ± 214.561	0.120	1484.129 ± 194.536	1472.225 ± 189.666	0.250
CHOL	173.07 ± 40.01	162.63 ± 36.98	0.001	167.46 ± 38.32	161.32 ± 36.62	0.001	175.077 ± 32.978	161.951 ± 31.948	0.001
TGS	161.63 ± 83.16	145.70 ± 76.68	0.001	126.13 ± 66.78	114.69 ± 50.00	0.029	138.46 ± 77.29	121.82 ± 68.27	0.001
HDL	44.38 ± 10.51	48.02 ± 9.36	0.001	44.45 ± 13.30	45.88 ± 12.51	0.088	43.30 ± 8.14	46.26 ± 8.35	0.001
LDL	109.42 ± 32.81	92.55 ± 24.53	0.001	106.69 ± 32.37	96.16 ± 27.28	0.001	114.69 ± 27.877	105.75 ± 26.32	0.001
WHR	0.980 ± 0.054	0.94 ± 0.04	0.001	0.94 ± 0.06	0.91 ± 0.05	0.001	0.97 ± 0.06	0.93 ± 0.05	0.001

*Mean ± SD, **P-value calculated Paired t-test

A comparison of the three groups' metabolic health indicators is shown in (Table 3)

Table 3. Comparison of metabolic health markers among the three studied groups

		Orlistat group	Vinegar group	Combine group	P-value*
BMI	Before	35.747 ± 4.166*	30.779 ± 3.350	38.361 ± 6.091	0.001
	After	33.447 ± 3.829	28.795 ± 3.138	35.801 ± 5.389	0.001
PBF	Before	45.244 ± 4.897	39.990 ± 6.831	47.066 ± 5.368	0.001
	After	41.803 ± 4.578	36.537 ± 6.318	43.817 ± 4.975	0.001
VF	Before	18.950 ± 3.237	15.016 ± 3.800	19.887± 2.986	0.001
	After	13.209 ± 3.126	13.209 ± 3.126	17.758 ± 2.577	0.001
BMR	Before	1480.131 ± 208.426	1410.677± 214.760	1484.129 ± 194.536	0.086
	After	1479.327 ± 202.961	1426.951 ± 214.561	1472.225 ± 189.666	0.299
CHOL	Before	173.072 ± 40.012	167.464 ± 38.322	175.077 ± 32.978	0.5
	After	162.639 ± 36.980	161.324 ± 36.620	161.951 ± 31.948	0.979
TGS	Before	161.634 ± 83.167	126.138 ± 66.781	138.461 ± 77.296	0.034
	After	145.704 ± 76.687	114.693 ± 50.007	121.822 ± 68.272	0.026
HDL	Before	44.385 ± 10.519	44.451 ± 13.305	43.303 ± 8.145	0.805

	After	48.023 ± 9.367	45.887 ± 12.515	46.262 ± 8.358	0.001
LDL	Before	109.427 ± 32.816	106.693 ± 32.376	114.695 ± 27.877	0.348
	After	92.557 ± 24.538	96.168 ± 27.280	105.754 ± 26.325	0.001
WHR	Before	0.980 ± 0.054	0.941 ± 0.061	0.972 ± 0.061	0.001
	After	0.948 ± 0.049	0.912 ± 0.56	0.939 ± 0.055	0.001

*Mean ± SD, **P-value calculated based on One-Way ANOVA

All groups experienced significant weight loss over the two-month intervention period. The Orlistat group reduced from 92.58 ± 13.87 kg at baseline to 85.88 ± 13.29 kg at two months, the Vinegar group from 80.1 ± 11.95 kg to 74.87 ± 11.4 kg, and the Combine group from 97.65 ± 16.2 kg to 90.15 ± 14.65 kg ($p \leq 0.001$ for all) (Table 4)

Table 4. Comparison of mean weight among the three studied groups

Groups	Weight*			P-value**
	Initial	After one month	After two months	
Orlistat group	92.588 ± 13.878	88.662 ± 13.325	85.885 ± 13.290	0.001
Vinegar group	80.125 ± 11.950	76.940 ± 11.681	74.871 ± 11.401	0.001
Combine group	97.650 ± 16.223	92.806 ± 15.223	90.153 ± 14.651	0.001
P-value	0.001	0.001	0.001	

*Mean ± SD, **P-value calculated based on One-Way ANOVA

Adverse events were generally mild. Constipation was reported in 11 participants in the Vinegar group, likely related to excessive vinegar intake. Ten incidences of decreased appetite were reported by the Orlistat group. The Orlistat and Combined groups had higher rates of steatorrhea. (Table 5).

Table 5. Intervention adverse effects in the three studied groups.

Groups	After program constipated	Decrease appetite	Overdose vinegar leading to constipation	GI discomfort due to Vinegar	Steatorrhea
Orlistat group	14	10	0	0	61
Vinegar group	23	46	11	12	0
		35		10	61
Combine	17		0		
P-value	0.26	<0.0001			

4. Discussion

The results showed that both ACV and Orlistat significantly reduced weight and improved metabolic markers as body fat percentage, BMI, and lipid profiles. Notably, Orlistat was associated with a higher frequency of gastrointestinal side effects, particularly steatorrhea; nevertheless, ACV by itself decreased visceral fat, BMI, and body fat percentage to a level that was comparable to that of Orlistat. Although this was not consistently shown across all body composition measures, the combination of ACV and Orlistat produced the largest

reduction in BMI, suggesting a possible additive impact. These results are in line with earlier studies showing the positive benefits of ACV on metabolic health and weight. For instance, Jafarirad et al. (2023) and Arjmandfard et al. (2025) found that ACV supplementation improved glycemic and lipid profiles and decreased body weight and waist circumference with few side effects (19,20). Similarly, while benefits on HDL and triglycerides are less noticeable, systematic reviews and meta-analyses have demonstrated that ACV consumption is linked to significant decreases in fasting blood glucose, HbA1c (21,22), and total cholesterol (23,24). These earlier results are consistent with our study's conclusion that the ACV group's HDL did not significantly change (25,26). Sohouli et al. carried out a meta-analysis to assess the impact of vinegar intake on cardiometabolic risk factors because prior research on the association between vinegar consumption and other cardiometabolic parameters has been inconsistent and variable. Their findings indicated that while vinegar consumption had no discernible impact on HDL or triglycerides, it was linked to significant decreases in fasting blood glucose, HbA1c, total cholesterol, and LDL. (27) In order to evaluate the effects of daily ACV supplementation (5, 10, or 15 mL) over a 12-week period, 120 overweight or obese Lebanese adolescents and young adults participated in the study. When compared to a placebo, the study discovered that all ACV doses significantly improved anthropometric and metabolic indicators, including weight, BMI, waist/hip circumference, body fat ratio, fasting glucose, triglycerides, and cholesterol, with no side effects noted (28). Small sample sizes, however, limit the data, and if taken improperly, ACV may result in gastrointestinal distress and teeth erosion (28, 29). According to previous studies, the well-known pharmaceutical medication Orlistat demonstrated the expected efficacy in improving metabolic parameters and reducing weight (30.31). The reported adverse impact profile, particularly gastrointestinal issues, is also consistent with the known mechanism of action of Orlistat (32, 33). One novel aspect of this study was the assessment of combined treatment with ACV and Orlistat. The combination therapy was also related to constipation, thus indicating a possibly undesirable effect that needs further study. Despite the run-in, results cannot be easily translated to long-term efficacy (for 8-week is relatively short in terms of long-term effectiveness, weight maintenance, and persistent metabolic effects) with limited control both on diet and physical activity as adopted in real-life situations. Despite the study's strength these limitations that we have to take into account in interpreting our results. In addition, non-blinding and reports of constipation associated with excessive ingestion of ACV suggest that not all participants may have strictly followed dosing and dilution instructions could increase the risk of bias and non-adherence that could also lead to have an impact on efficacy and safety estimates.

5. Conclusions

In conclusion, this pilot study showed that both ACV and Orlistat are viable treatments for increasing metabolism and aiding overweight/obese individuals with weight loss. Due to its high safety profile, ACV may represent a natural alternative/adjunct for the

management of this condition. The addition of ACV with Orlistat may further reduce BMI, although, due to the increased gastrointestinal side effects, caution is recommended. To validate these findings and provide better guidance for therapeutic options in the management of obesity, long-term follow-up studies with more effective control conditions and large sample sizes are recommended.

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Data availability: Upon reasonable request, the data from the research may be obtained from the corresponding author.

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