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Alcohol consumption, lifestyle behaviors, and emotional well-being during GLP-1 receptor agonist therapy: a post hoc analysis of the several study

José Seijas-Amigo [a,b,c,d,*], Ángel Salgado-Barreira [e,f,g], Rosana Castelo-Dominguez [h], María Teresa Pérez-Álvarez [i], Belén Ponce-Piñón [j], Marlén Fernández-Silva [k], Marta Rodríguez-Barreiro [l], Mercedes Pereira-Pía [m], Jose Manuel Iglesias-Moreno [n], Mar Gago-García [o], Raquel Montáns-García [p], Agustina Fernandez-Perez [q], Dolores Fraga-Gayoso [r], Montse Fernandez-Montenegro [s], Beatriz Riveiro-Barciela [t], Natalia Rilla-Villar [u], Begoña Cardeso-Paredes [a,b,c], Marta Ribeiro-Ferreiro [a,b], Diego Rodriguez-Penas [a,b], Alberto Cordero [v,w,x], Moisés Rodríguez-Mañero [a,c], José R. González-Juanatey [a,c], Several Investigators

[a] Cardiology Department, Complejo Hospitalario Universidad de Santiago de Compostela, Santiago de Compostela, Spain
[b] Fundación Instituto de Investigación Sanitaria de Santiago de Compostela (FIDIS), Spain
[c] Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain
[d] Universidade de Santiago de Compostela, Spain
[e] Department of Preventive Medicine and Public Health, University of Santiago de Compostela, Santiago de Compostela, Spain
[f] Health Research Institute of Santiago de Compostela (IDIS), Santiago de Compostela, Spain
[g] Consortium for Biomedical Research in Epidemiology and Public Health (CIBER en Epidemiología y Salud Pública CIBERESP), Carlos III Health Institute, Madrid, Spain
[h] Centro de Salud, Ribeira, A Coruña, Spain
[i] Centro de Salud de Culleredo, A Coruña, Spain
[j] Centro de Salud de Fene, A Coruña, Spain
[k] Centro de Salud O Ventorillo, A Coruña, Spain
[l] Centro de Salud. Virxe Peregrina, Pontevedra, Spain
[m] Centro de Salud de San Roque, Lugo, Spain
[n] Centro de Salud de Val Miñor, Nigrán, Pontevedra, Spain
[o] Centro de Salud de Ribadeo, Lugo, Spain
[p] Centro de Salud de Cee, A Coruña, Spain
[q] Centro de Salud Vilalba, Lugo, Spain
[r] Centro de Salud de Sarria, Lugo, Spain
[s] Centro de Salud de O Carballiño, Ourense, Spain
[t] Centro de Salud O Temple, A Coruña, Spain
[u] Centro de Salud de Arriondas, Asturias, Spain
[v] Cardiology Department, Hospital General Universitario Alicante Dr. Balmis, Alicante, Spain
[w] Grupo de Investigación Cardiovascular (GRINCAVA), Universidad Miguel Hernández, Elche, Spain
[x] Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain

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ABSTRACT

Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been associated with alcohol-related and other behavioral outcomes, although much of the observational evidence derives from retrospective studies. We prospectively evaluated longitudinal changes in self-reported alcohol-consumption categories, lifestyle behaviors, and emotional well-being during GLP-1 RA therapy in routine clinical practice.

Methods: This post hoc analysis of the prospective multicenter SEVERAL study included adults with obesity and type 2 diabetes receiving GLP-1 RAs over 44 weeks. Alcohol consumption categories, dietary adherence, and

* Corresponding author at: Cardiology Department, Complejo Hospitalario Universidad de Santiago de Compostela, Santiago de Compostela, Spain; Universidade de Santiago de Compostela (USC), Santiago de Compostela, Spain.
E-mail addresses: jose.seijas.amigo@sergas.es, jose.seijas@rai.usc.es (J. Seijas-Amigo).

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physical activity were assessed at baseline and weeks 4, 12, and 44. Emotional well-being was evaluated using the EuroQol 5-Dimension questionnaire (EQ-5D) and the 12-Item Short Form Health Survey (SF-12). Paired comparisons were performed using Wilcoxon signed-rank and McNemar tests.

Results: A total of 135 participants were included. At baseline, 87.7% of participants with available alcohol data (114/130) were already in the lowest alcohol-consumption category (0–1 standard drink units/day; 1 unit = 10 g of pure alcohol). This proportion increased to 96.2% at week 44, while the proportion reporting more than 2 units/day decreased from 5.4% to 0%, indicating a statistically significant shift toward lower categories ($p = 0.003$). Dietary adherence increased from 47.7% to 63.2% ($p = 0.001$). No significant long-term change was observed in physical activity ($p = 0.392$). Neither the SF-12 Mental Component Summary (MCS) score ($p = 0.114$) nor the EQ-5D anxiety/depression dimension ($p = 0.055$) changed significantly. Exploratory item-level analyses showed an increase in the proportion reporting feeling calm and peaceful all or most of the time (51.9% to 69.2%; $p = 0.002$)..

Conclusions: During 44 weeks of GLP-1 RA therapy, a shift toward lower self-reported alcohol-consumption categories and improved dietary adherence were observed. Changes in selected emotional well-being items were exploratory and were not accompanied by significant improvements in global mental health measures. These observational findings warrant confirmation in studies designed to assess alcohol-related behaviors and their potential underlying mechanisms.

1. Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have transformed the management of type 2 diabetes and obesity by producing substantial improvements in glycemic control, body weight, and cardiovascular risk factors (Committee, 2026; McGuire et al., 2025; Davies et al., 2021). Beyond their established metabolic effects, increasing evidence suggests that GLP-1 receptors are widely distributed throughout the central nervous system, including brain regions involved in reward processing, motivation, impulsivity, and addictive behaviors (Seijas-Amigo et al., 2026; Kabahizi et al., 2022). These findings have generated growing interest in the potential influence of GLP-1 RAs on lifestyle-related behaviors and emotional well-being. Although reward processing, craving, and impulsivity were not directly assessed in the present study, this neurobiological framework provides a rationale for examining longitudinal changes in self-reported alcohol-consumption categories, dietary adherence, physical activity, and emotional well-being during GLP-1 RAs therapy. Experimental studies have demonstrated that GLP-1 signalling modulates mesolimbic dopaminergic pathways and attenuates reward-seeking behavior. In animal models, GLP-1 receptor activation reduces alcohol intake, alcohol-seeking behavior, and relapse-like responses, supporting a potential role for these agents in the treatment of addictive disorders (Aranäs et al., 2023; Herman and Schmidt, 2024). More recently, observational studies and emerging clinical evidence have suggested that GLP-1 RAs may be associated with reductions in alcohol consumption, food craving, and other reward-driven behaviors, although findings remain heterogeneous across study designs and populations (Cai et al., 2026; Klausen et al., 2026). The present study adds a prospective, multicenter, real-world perspective by examining longitudinal changes in alcohol-consumption categories alongside dietary adherence, physical activity, and emotional well-being over 44 weeks of follow-up.

These observations support further investigation of measurable behavioral outcomes in routine clinical practice, without assuming that changes in these outcomes necessarily reflect alterations in reward-related mechanisms.

Lifestyle-related behaviors represent major determinants of long-term cardiometabolic health. Excessive alcohol consumption, poor dietary adherence, physical inactivity, and psychological distress contribute substantially to cardiovascular morbidity and mortality among individuals with obesity and type 2 diabetes (World Health Organization. Global status report on alcohol and health and treatment of substance use disorders. Geneva: World Health Organization;, 2024; Wu et al., 2025). In parallel, growing evidence suggests that unhealthy lifestyle patterns and addictive behaviors share common neurobiological pathways involving reward processing, stress responses, and executive control, potentially providing a mechanistic link between metabolic disease, behavioral health, and cardiovascular risk (Seijas-Amigo et al., 2026).

Interest has also emerged regarding the impact of GLP-1 RAs on emotional well-being and health-related quality of life. Previous studies have reported improvements in physical functioning, self-perceived health status, and overall quality of life during GLP-1 RA treatment, although their effects on specific emotional domains remain less well characterized (Seijas-Amigo et al., 2026). Previous reports from the prospective multicenter SEVERAL study have examined the effectiveness and safety of GLP-1 RA therapy (Seijas-Amigo et al., 2022); cardiometabolic outcomes and estimated cardiovascular risk (Seijas-Amigo et al., 2025), and health-related quality of life (Seijas-Amigo et al., 2026). In an analysis of 105 participants without established cardiovascular disease, estimated 10-year cardiovascular risk decreased from 24.38% to 21.10% over 44 weeks of follow-up (Seijas-Amigo et al., 2025). A separate analysis reported improvements in health-related quality of life, although changes in the SF-12 Mental Component Summary score were not statistically significant (Seijas-Amigo et al., 2026). However, longitudinal changes in alcohol-consumption patterns, dietary adherence, physical activity, and specific emotional well-being outcomes have not previously been examined together in this cohort.

Therefore, the aim of this post hoc analysis of the SEVERAL study was to evaluate longitudinal changes in self-reported alcohol-consumption categories, dietary adherence, physical activity, and emotional well-being during 44 weeks of GLP-1 RA therapy in routine clinical practice.

2. Participants and methods

2.1. Study design and population

This was a post hoc analysis of the SEVERAL study, a prospective multicenter real-world observational study conducted in individuals with obesity and type 2 diabetes receiving treatment with glucagon-like peptide-1 receptor agonists (GLP-1 RAs). The design, inclusion criteria, and primary outcomes of the SEVERAL study have been previously reported (Seijas-Amigo et al., 2022).

Briefly, adult participants with type 2 diabetes and obesity who initiated or intensified treatment with a GLP-1 RA according to routine clinical practice were followed for 44 weeks. The present analysis included all participants with available baseline and follow-up information regarding lifestyle behaviors and emotional well-being.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Research Ethics Committee. All participants provided written informed consent before study inclusion.

2.2. Variables and assessments

Lifestyle-related behaviors were assessed at baseline and during follow-up visits (weeks 4, 12, and 44).

Alcohol consumption was assessed using three mutually exclusive, predefined categories of self-reported daily intake: 0–1, exactly 2, and >2 standard drink units (UBE/day). Participants reporting exactly 1 UBE/day were included in the first category. These categories were used for descriptive purposes and were not intended to represent guideline-based alcohol-risk thresholds. One Unidad de Bebida Estándar (UBE; standard drink unit) was defined as 10 g of pure alcohol.

Dietary adherence was assessed by participant self-report and classified as a binary variable ("Yes" or "No"). When a valid response could not be obtained, the assessment was recorded as "Do not know", indicating unavailable information rather than a separate category of dietary adherence. Physical activity was also assessed by participant self-report and classified as a binary variable ("Yes" or "No"). The electronic case report form (eCRF) used in the SEVERAL study, including the assessments of alcohol consumption, dietary adherence, physical activity, and emotional well-being, is provided as Supplementary Material S1.

Health-related quality of life was assessed using the EuroQol 5-Dimension questionnaire (EQ-5D) and the 12-Item Short Form Health Survey (SF-12) at baseline and week 44. In addition to the SF-12 Mental Component Summary (MCS) score, individual emotional domains were analyzed, including limitations due to emotional problems (questions 6 and 7), feelings of calmness and tranquility (question 9), and feelings of sadness or discouragement (question 11).

2.3. Outcomes

The primary outcome of this post hoc analysis was the longitudinal change in alcohol consumption from baseline to week 44.

Secondary outcomes included changes in dietary adherence, physical activity, EQ-5D anxiety/depression dimension, SF-12 emotional domains, and health-related quality of life measures.

2.4. Statistical analysis

Continuous variables are presented as mean ± standard deviation or median (interquartile range), according to distribution. Categorical variables are expressed as frequencies and percentages.

Changes between baseline and follow-up assessments were analyzed using paired statistical tests. Ordinal variables, including alcohol consumption categories and SF-12 emotional domains, were evaluated using the Wilcoxon signed-rank test. Paired binary variables were analyzed using McNemar's test.

For dietary adherence, "Do not know" responses were treated as unavailable data and excluded from paired comparisons. McNemar's test was performed using participants with valid "Yes" or "No" responses at both visits being compared.

Missing data were assessed by comparing baseline characteristics between participants with and without available follow-up information. As a sensitivity analysis, multiple imputation was performed using sex, age, baseline body mass index (BMI), and available baseline and week-44 values of the variables of interest. Five imputed datasets were generated, and McNemar's test was applied separately to each dataset to assess the robustness of the findings for dietary adherence and physical activity.

A two-sided p value < 0.05 was considered statistically significant. Given the exploratory nature of this post hoc analysis, no adjustment for multiple comparisons was performed.

Statistical analyses were performed using R software version 4.4.1.

3. Results

3.1. Baseline characteristics

A total of 135 participants were enrolled in the SEVERAL study. The present post hoc analysis included patients with available information regarding lifestyle behaviors and emotional well-being at baseline and follow-up assessments. The number of participants included in each analysis varied slightly according to data availability for individual study variables.

Baseline characteristics were consistent with a population of individuals with obesity and type 2 diabetes managed in routine clinical practice. Mean age was 61.6 years, 54.1% were male, mean body mass index was 36.2 kg/m^2, and cardiovascular risk factors were highly prevalent, including hypertension (75.6%) and dyslipidemia (77.0%). Baseline treatment distribution included subcutaneous semaglutide (29.6%), oral semaglutide (31.1%), dulaglutide (34.8%), and other GLP-1 Ras (4.4%) (Table 1).

During follow-up, 58 patients (43.0%) experienced an adverse drug reaction (ADR), of which more than 80% were gastrointestinal. Among patients experiencing an ADR, treatment was temporarily interrupted in 14 (24.1%), permanently discontinued in 4 (6.9%), and the dose was reduced in 2 (3.4%); no treatment modification was required in the remaining 38 (65.5%). No statistically significant differences in ADR incidence were observed across GLP-1 RA agents, although dulaglutide was associated with the lowest proportion of ADRs and the highest proportion of patients reaching the maximum dose. Further details on treatment exposure, dose adjustments, and safety outcomes have been reported previously (Seijas-Amigo et al., 2023).

3.2. Changes in alcohol consumption

At baseline, self-reported alcohol consumption was predominantly concentrated in the lowest category (0–1 UBE/day), comprising 114 of 130 participants (87.7%). Only 16 participants (12.3%) reported consumption of 2 or more UBE/day. The proportion of participants in the lowest alcohol-consumption category (0–1 UBE/day) increased from 87.7% at baseline to 96.2% at week 44, whereas the proportion reporting more than 2 UBE/day decreased from 5.4% to 0%.

Paired analysis confirmed a statistically significant shift toward lower alcohol-consumption categories between baseline and week 44 (Wilcoxon signed-rank test, $p = 0.003$) (Table 2, Fig. 1).

Missing-data sensitivity analyses were performed using five imputed

Table 1
Baseline Characteristics of Participants Included in the Post Hoc Analysis of the SEVERAL Study.

Characteristic	Total (n = 135)
Age (years); mean ± sd	61.6 ± 10.6
Male; n (%)	73 (54.1)
BMI (kg/m^2); mean ± SD	36.2 ± 5.4
Comorbidities; n (%)	
Hypertension	102 (75.6)
Dyslipidemia	104 (77.0)
Obstructive sleep apnea	17 (12.6)
Asthma or COPD	18 (12.9)
Acute coronary syndrome	24 (17.8)
Heart failure	14 (10.4)
Baseline GLP-1 RA treatment; n (%)	
Subcutaneous semaglutide	40 (29.6)
Oral semaglutide	42 (31.1)
Dulaglutide	47 (34.8)
Other GLP-1 RA (liraglutide, exenatide)	6 (4.4)

Data are presented as mean ± standard deviation (SD) or number (%), as appropriate.
Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

Table 2
Longitudinal changes in alcohol-consumption categories, dietary adherence, and physical activity during 44 weeks of GLP-1 RA therapy.

Outcome / response	Baselinen (%)	95% CI	Week 4n (%)	95% CI	Week 12n (%)	95% CI	Week 44n (%)	95% CI	Baseline vs Week 4p-value	Baseline vs Week 12p-value (paired n)	Baseline vs Week 44p-value (paired n)
Alcohol-consumption category, n (%)									**0.015**[a] **(n = 130)**	**0.015**[a] **(n = 129)**	**0.003**[a] **(n = 130)**
0–1 UBE/day	114 (87.7)	81.7–93.7	120 (92.3)	87.3–97.3	122 (93.8)	89.3–98.4	125 (96.2)	92.5–99.8			
Exactly 2 UBE/day	9 (6.9)	2.2–11.7	7 (5.4)	1.1–9.6	5 (3.8)	0.2–7.5	5 (3.8)	0.2–7.5			
>2 UBE/day	7 (5.4)	1.1–9.6	3 (2.3)	0.0–5.3	3 (2.3)	0.0–5.3	0 (0.0)	0.0–0.0			
Dietary adherence, n (%)									**<0.001**[b] **(n = 125)**	**0.029**[b] **(n = 113)**	**0.001**[b] **(n = 124)**
Yes	63 (47.7)	38.8–56.6	84 (66.7)	58.0–75.3	65 (57.5)	48.0–67.1	79 (63.2)	54.3–72.1			
No	64 (48.5)	39.6–57.4	33 (26.2)	18.1–34.3	39 (34.5)	25.3–43.7	35 (28.0)	19.7–36.3			
Do not know	5 (3.8)	0.2–7.4	9 (7.1)	2.2–12.0	9 (8.0)	2.5–13.4	11 (8.8)	3.4–14.2			
Physical activity, n (%)									**0.029**[b] **(n = 125)**	**0.016**[b] **(n = 105)**	**0.392**[b] **(n = 118)**
Yes	58 (43.9)	35.1–52.8	67 (52.3)	43.3–61.4	60 (56.1)	46.2–65.9	61 (50.4)	41.1–59.7			
No	74 (56.1)	47.2–64.9	61 (47.7)	38.6–56.7	47 (43.9)	34.1–53.8	60 (49.6)	40.3–58.9			

Data are presented as n (%). The 95% CIs describe proportions at each visit. Paired n refers to the number reported for each baseline-versus-follow-up comparison; p-values are nominal and unadjusted for multiple comparisons.
"Do not know" indicates that a valid dietary-adherence response could not be obtained and is not a separate adherence category. It was excluded from the primary paired binary comparisons, as described in Methods.
Alcohol-consumption categories (0–1, exactly 2, and > 2 UBE/day) are descriptive and do not represent guideline-based risk thresholds.
Abbreviations: CI, confidence interval; GLP-1 RA, glucagon-like peptide-1 receptor agonist; UBE, Unidad de Bebida Estándar (standard drink unit; 10 g of pure alcohol).
[a] Wilcoxon signed-rank test for ordinal alcohol-consumption categories.
[b] McNemar test for paired binary outcomes.

datasets. For dietary adherence, 8 missing observations at baseline and 21 at week 44 were imputed; the results remained statistically significant across all five datasets (all $p < 0.001$). For physical activity, 3 missing observations at baseline and 14 at week 44 were imputed, with p-values ranging from 0.165 to 0.391 across datasets. These analyses did not materially change the interpretation of the primary findings.

3.3. Changes in lifestyle behaviors

Dietary adherence improved significantly during follow-up. The proportion of participants reporting adherence to dietary recommendations increased from 47.7% at baseline to 63.2% at week 44 ($p = 0.001$).

Physical activity increased during the early phases of treatment, with higher participation rates at weeks 4 and 12; however, these improvements were not maintained at week 44 and no significant long-term changes were observed ($p = 0.392$) (Table 2, Fig. 1).

3.4. Emotional well-being

No significant changes were observed in the global SF-12 Mental Component Summary score (baseline 50.3 vs. week 44 52.2; $p = 0.114$). Similarly, changes in the EQ-5D anxiety/depression dimension did not reach statistical significance ($p = 0.055$), although a numerical reduction in anxiety/depression problems was observed.

Analysis of individual emotional domains of the SF-12 revealed improvements in selected aspects of emotional well-being. A numerical decrease in limitations in daily activities due to emotional problems was observed for both accomplishing less than desired (Question 6, $p = 0.050$) and carrying out activities less carefully than usual (Question 7, $p = 0.076$). These findings should be interpreted cautiously given their borderline or nonsignificant p-values and the exploratory nature of the analyses.

The most pronounced improvement was observed in feelings of calmness and tranquility (Question 9), which significantly improved during follow-up ($p = 0.002$), with the proportion of participants reporting being calm and peaceful all or most of the time increasing from 51.9% to 69.2%. In contrast, no significant changes were observed in feelings of sadness or discouragement (Question 11, $p = 0.797$) (Table 3, Fig. 2).

4. Discussion

In this post hoc analysis of the prospective multicenter SEVERAL study, treatment with GLP-1 RAs was associated with significant reductions in alcohol consumption and improvements in dietary adherence during 44 weeks of follow-up. In addition, patients experienced favorable changes in selected domains of emotional well-being, particularly feelings of calmness alongside numerical reductions in emotional limitations affecting daily activities. In contrast, no significant changes were observed in the global SF-12 Mental Component Summary score or in feelings of sadness and discouragement.

4.1. Alcohol consumption and reward-related behaviors

The main finding of the present study was a statistically significant shift toward lower self-reported alcohol-consumption categories during follow-up. This observation is compatible with emerging evidence of associations between GLP-1 RA therapy and alcohol-related behaviors. Although experimental studies suggest a potential role for reward-related pathways, the present study did not directly assess these mechanisms (Seijas-Amigo et al., 2026; Klausen et al., 2026; Vallöf et al., 2016; Hendershot et al., 2025; Klausen et al., 2022; Klausen et al., 2025).

Experimental studies have demonstrated that GLP-1 receptor signaling regulates neural circuits involved in reward processing,

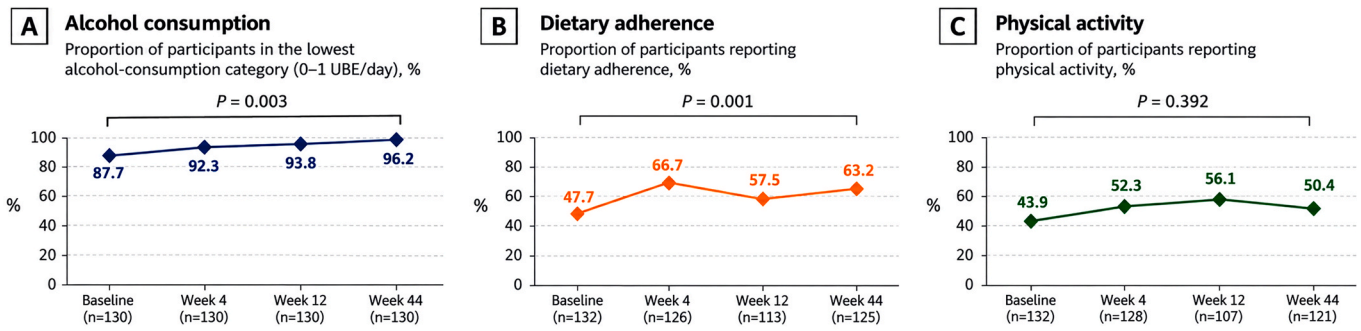


Fig. 1. Longitudinal changes in self-reported lifestyle behaviors during GLP-1 receptor agonist therapy. Data are presented as percentages of participants with available information at each assessment. Sample sizes are indicated below each time point. P-values correspond to paired comparisons between baseline and week 44, using the Wilcoxon signed-rank test for the ordinal alcohol-consumption categories (panel A) and McNemar's test for binary variables (panels B and C). UBE, Unidad de Bebida Estándar (standard drink unit), equivalent to 10 g of pure alcohol. Alcohol-consumption categories were defined as 0–1, exactly 2, and >2 UBE/day for descriptive purposes and do not represent validated alcohol-risk thresholds.

Table 3
Changes in emotional well-being and mental health outcomes during 44 weeks of GLP-1 RA therapy.

Outcome/response	Baseline	95% CI	Week 44	95% CI	Paired n	p-value
EQ-5D anxiety/depression dimension, n (%)					**116**	**0.055**[b]
No anxiety or depression	76 (57.1)	48.4–65.9	83 (70.9)	62.3–79.6		
Moderately anxious or depressed	47 (35.3)	26.8–43.8	26 (22.2)	14.3–30.2		
Severely anxious or depressed	10 (7.5)	2.7–12.4	8 (6.8)	1.8–11.8		
SF-12 Mental Component Summary (MCS), mean ± SD	**50.3 ± 12.6**	**47.9–52.6**	**52.2 ± 11.6**	**47.9–52.6**	**112**	**0.114**[c]
SF-12 Q6. Accomplished less because of emotional problems, n (%)					**116**	**0.050**[b]
Yes	42 (31.6)	23.3–39.9	23 (19.7)	12.0–27.3		
No	91 (68.4)	60.1–76.7	94 (80.3)	72.7–88.0		
SF-12 Q7. Worked less carefully than usual because of emotional problems, n (%)					**116**	**0.076**[b]
Yes	33 (24.8)	17.1–32.5	16 (13.7)	7.0–20.3		
No	100 (75.2)	67.5–82.9	101 (86.3)	79.7–93.0		
SF-12 Q9. Felt calm and peaceful, n (%)					**116**	**0.002**[a]
All of the time	39 (29.3)	21.2–37.4	45 (38.5)	29.2–47.7		
Most of the time	30 (22.6)	15.1–30.0	36 (30.8)	22.0–39.6		
A good bit of the time	11 (8.3)	3.2–13.3	9 (7.7)	2.4–12.9		
Some of the time	24 (18.0)	11.1–25.0	18 (15.4)	8.4–22.3		
A little of the time	21 (15.8)	9.2–22.4	5 (4.3)	0.2–8.4		
None of the time	8 (6.0)	1.6–10.4	4 (3.4)	0.0–7.1		
SF-12 Q11. Felt downhearted and blue, n (%)					**116**	**0.797**[a]
All of the time	4 (3.0)	0.0–6.3	4 (3.4)	0.0–7.1		
Most of the time	15 (11.3)	5.5–17.0	8 (6.8)	1.8–11.8		
A good bit of the time	14 (10.5)	4.9–16.1	6 (5.1)	0.7–9.6		
Some of the time	22 (16.5)	9.9–23.2	25 (21.4)	13.5–29.2		
A little of the time	19 (14.3)	8.0–20.6	24 (20.5)	12.8–28.3		
None of the time	59 (44.4)	35.5–53.2	50 (42.7)	33.3–52.1		

Data are presented as mean ± standard deviation (SD) or n (%). Percentages and 95% CIs refer to available observations at each visit; paired n refers to the reported number of paired observations for the corresponding comparison.
Abbreviations: EQ-5D, EuroQol 5-Dimension questionnaire; SF-12, 12-Item Short Form Health Survey; MCS, Mental Component Summary; CI, confidence interval; GLP-1 RA, glucagon-like peptide-1 receptor agonist.
[a] Wilcoxon signed-rank test across the ordinal response scale.
[b] McNemar test, as reported by the statistician.
[c] Paired Student's *t*-test. All p-values are nominal and unadjusted for multiple comparisons.

including the ventral tegmental area, nucleus accumbens, lateral septum, and other mesolimbic structures implicated in reinforcement and craving (Seijas-Amigo et al., 2026; Kabahizi et al., 2022; Seijas-Amigo et al., 2022; Vallöf et al., 2016; Klausen et al., 2022; Alhadeff et al., 2012; Dickson et al., 2012; Badulescu et al., 2024; Edvardsson et al., 2025; Völker et al., 2026).

Importantly, emerging clinical evidence supports the translational relevance of these mechanisms. Randomized studies with semaglutide have reported reductions in alcohol self-administration, heavy drinking days, craving intensity, and alcohol-related reward responses in individuals with alcohol use disorder (Klausen et al., 2026; Klausen et al., 2025). More recently, large observational studies have suggested a reduced incidence of substance use disorders and substance-related adverse outcomes among individuals receiving GLP-1 RAs (Cai et al., 2026).

Our findings are consistent with previous clinical and observational evidence linking GLP-1 RA therapy to alcohol-related outcomes. However, much of the existing observational evidence derives from retrospective analyses of electronic health records or administrative databases. A recent nationally representative US survey (Uscher-Pines et al., 2026) found that 44.2% of respondents who were drinking when they initiated GLP-1 RA therapy retrospectively reported reduced alcohol consumption during the first three months of treatment.

The present study contributes complementary prospective,

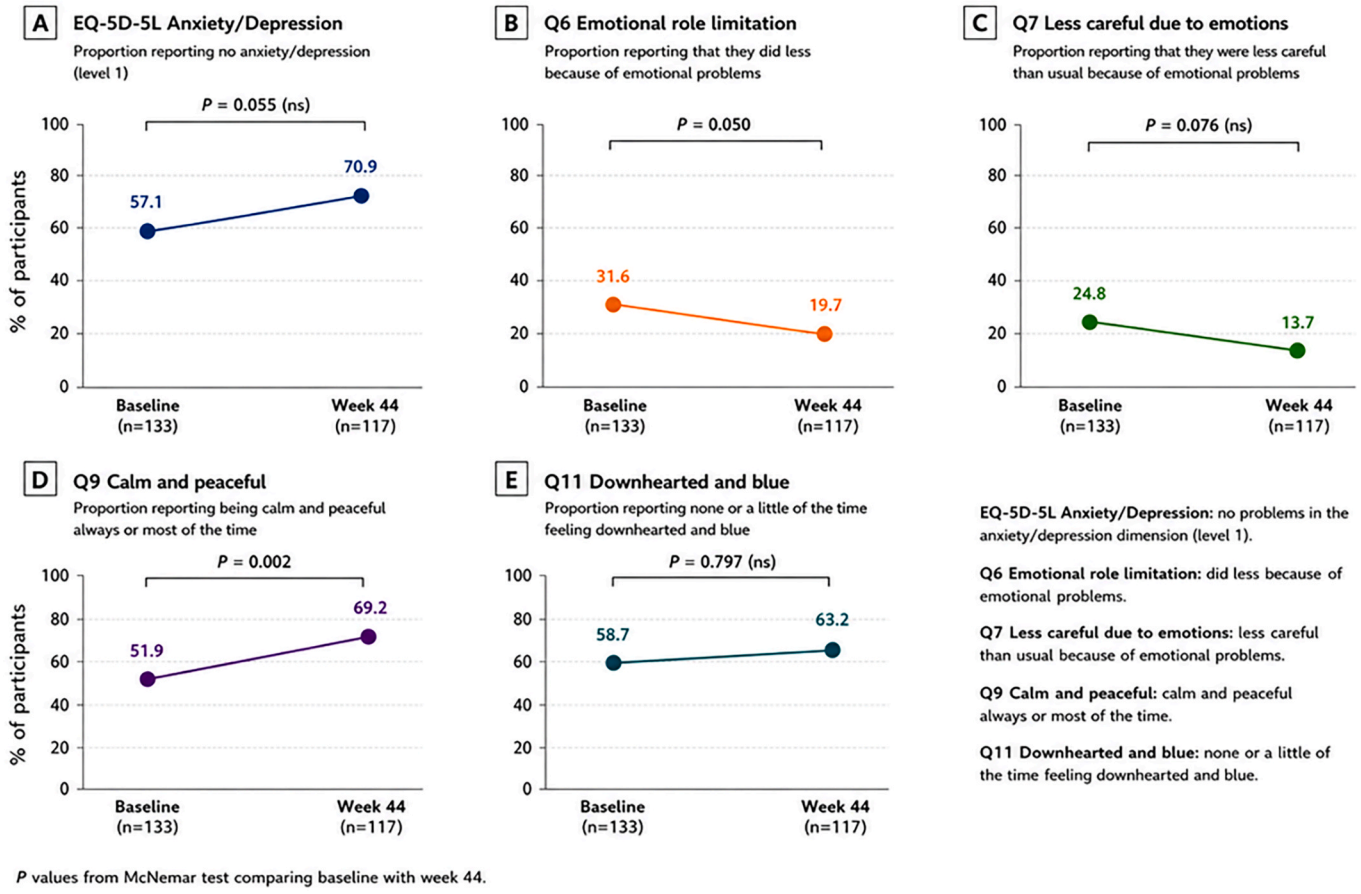


Fig. 2. Evolution of patient-reported outcomes and emotional well-being during GLP-1 receptor agonist therapy. P values from McNemar test comparing baseline with week 44.

multicenter, real-world data based on repeated assessments of self-reported alcohol-consumption categories over 44 weeks in a population with obesity and type 2 diabetes receiving GLP-1 RAs for metabolic indications. Unlike the retrospective assessment of perceived changes in the US survey, SEVERAL prospectively collected alcohol-consumption categories at predefined follow-up visits. Nevertheless, differences in study populations and alcohol-consumption measures preclude direct quantitative comparisons.

Although alcohol consumption was assessed using a simplified behavioral questionnaire rather than validated alcohol use disorder instruments, the observed shift toward lower alcohol-consumption categories suggests that changes in reported alcohol-related behavior may occur even when treatment is initiated outside addiction-specific settings. However, these findings do not establish whether such changes are related to alterations in alcohol craving, reward processing, or other neurobehavioral mechanisms.

An important consideration is the predominantly low level of self-reported alcohol consumption at baseline, with 87.7% of participants classified in the lowest consumption category (0–1 UBE/day). This distribution suggests a potential floor effect, as most participants had limited opportunity to move to a lower category. Nevertheless, a statistically significant shift toward lower alcohol-consumption categories was observed during follow-up. This finding should be interpreted cautiously, given the small number of participants in the higher baseline categories, the ordinal nature of the assessment, and the absence of an untreated comparator.

4.2. Lifestyle behaviors beyond alcohol

In addition to alcohol consumption, dietary adherence improved significantly during follow-up. This finding is biologically plausible given the established role of GLP-1 signaling in appetite regulation, satiety, food reward, and eating behavior (O'Connor, 2026; Guo J, Hayes MR, Leggio L, Oru E, Rinaman L. GLP-1 Receptor Agonists and Research to Treat Overeating and Substance Use Disorders. J Neurosci., 2025; Da Porto et al., 2020; Richards et al., 2023).

Previous studies have demonstrated that GLP-1 receptor activation reduces the motivational value of highly palatable foods and modifies reward-driven eating behaviors through actions on neural pathways that overlap substantially with those implicated in addiction (Dickson et al., 2012; O'Connor, 2026; Guo J, Hayes MR, Leggio L, Oru E, Rinaman L. GLP-1 Receptor Agonists and Research to Treat Overeating and Substance Use Disorders. J Neurosci., 2025). Consistent with this concept, randomized and observational studies have shown reductions in binge-eating episodes, compulsive eating behaviors, and food craving among individuals treated with GLP-1 RAs (Da Porto et al., 2020; Richards et al., 2023; Radkhah et al., 2025).

Interestingly, improvements in dietary adherence persisted throughout the 44-week follow-up period, whereas improvements in physical activity were not sustained Although these findings may be considered in the context of the established role of GLP-1 signaling in appetite regulation, the present study cannot determine whether the observed differences between dietary adherence and physical activity reflect reward-related mechanisms or other factors.

4.3. Emotional well-being during GLP-1 therapy

Exploratory analyses of individual SF-12 emotional well-being items suggested favorable changes in selected domains, particularly feelings of calmness and tranquility. The proportion of participants reporting

feeling calm and peaceful all or most of the time increased by more than 17 percentage points during follow-up ($p = 0.002$). However, no statistically significant change was observed in the overall SF-12 Mental Component Summary score ($p = 0.114$). Given the number of secondary outcomes examined and the absence of adjustment for multiple comparisons, these item-level findings should be interpreted cautiously as hypothesis-generating rather than confirmatory evidence of improved emotional well-being.

These findings are particularly interesting when interpreted alongside the results of the original SEVERAL quality-of-life study, in which improvements in overall quality of life were observed despite relatively modest changes in global mental health measures (Seijas-Amigo et al., 2026). These findings raise the possibility of domain-specific changes in self-reported emotional well-being; however, the absence of a significant change in the global SF-12 Mental Component Summary score and the exploratory nature of the item-level analyses preclude firm conclusions regarding broader mental health benefits.

Current evidence regarding the psychiatric effects of GLP-1 RAs remains heterogeneous. While some studies have reported improvements in well-being, quality of life, cognitive function, or patient-reported outcomes, evidence for direct antidepressant or anxiolytic effects remains inconsistent (Seijas-Amigo et al., 2026; Ballum et al., 2026; Pierret et al., 2025; Kim, 2025). Our findings align with this emerging literature, suggesting that specific aspects of emotional functioning may improve during treatment even in the absence of measurable changes in broader mental health constructs.

4.4. Potential mechanisms and clinical implications

The mechanisms underlying these observations are likely multifactorial. Weight loss, improvements in metabolic health, and better self-perceived health status may all contribute to favorable behavioral and emotional outcomes. However, accumulating experimental and translational evidence indicates that GLP-1 receptor signaling directly influences reward processing, motivation, impulsivity, stress responsiveness, neuroimmune pathways, and affective regulation, supporting its role as a neurometabolic modulator with potential therapeutic implications for addictive and affective disorders (Seijas-Amigo et al., 2026; Alhadeff et al., 2012; Dickson et al., 2012; Badulescu et al., 2024; O'Connor, 2026; Marquez-Meneses et al., 2025; Amorim Moreira Alves et al., 2025; Seijas-Amigo et al., 2026).

The convergence of metabolic and neurobehavioral pathways provides a plausible theoretical framework for investigating changes in alcohol-consumption patterns, dietary behaviors, and selected emotional outcomes. However, reward processing, craving, impulsivity, and related neurobehavioral constructs were not directly assessed in this study. Therefore, the observed associations should not be interpreted as evidence of reward-pathway modulation or other specific neurobiological mechanisms. From a clinical perspective, these findings support the growing hypothesis that GLP-1 RAsmay exert effects extending beyond traditional metabolic endpoints and may influence broader health-related behaviors relevant to long-term clinical outcomes (Seijas-Amigo et al., 2026).

Although numerous observational studies have investigated associations between GLP-1 RA therapy and alcohol-related outcomes, many have relied on retrospective healthcare databases. By prospectively assessing alcohol-consumption categories alongside dietary adherence, physical activity, and emotional well-being at multiple time points, the present study provides complementary longitudinal evidence from routine clinical practice.

4.5. Limitations

Several limitations should be acknowledged. First, this was a post hoc exploratory analysis of a prospective observational study, and the original SEVERAL study was not specifically designed to evaluate alcohol consumption, lifestyle behaviors, or mental health outcomes. Therefore, the findings should be considered hypothesis-generating.

Second, alcohol consumption, dietary adherence, physical activity, and emotional well-being were assessed during routine study visits using investigator-administered questionnaires and patient-reported information. As a result, the findings may still be subject to recall bias and social desirability bias. In particular, alcohol intake was evaluated using a simplified ordinal scale and no validated instruments for alcohol use disorder, alcohol craving, or substance-related behaviors were employed. Furthermore, reward processing, impulsivity, and other proposed neurobehavioral mechanisms were not directly measured, precluding mechanistic interpretations of the observed changes. In addition, the predominance of participants in the lowest alcohol-consumption category at baseline may have introduced a floor effect, limiting the ability to detect further downward shifts.

Third, the observational design precludes causal inference. The observed changes may reflect the combined effects of GLP-1 RA therapy, weight loss, lifestyle counseling, increased clinical follow-up, or other unmeasured factors. In addition, the study was not powered to detect differences in behavioral or mental health outcomes, and subgroup analyses should be interpreted cautiously. Furthermore, multiple secondary outcomes, including individual SF-12 emotional items, were examined without adjustment for multiple comparisons, increasing the possibility of chance findings. Accordingly, statistically significant item-level results should be regarded as exploratory and require confirmation in adequately powered studies with prespecified outcomes.

Finally, the findings may not be generalizable to populations without obesity or type 2 diabetes, or to individuals with diagnosed substance use disorders.

Missing data arose from incomplete follow-up assessments and unavailable questionnaire or clinical information. No statistically significant differences in the baseline characteristics examined were identified between participants with and without available follow-up data. Nevertheless, residual attrition bias cannot be excluded. Sensitivity analyses using imputed datasets yielded findings consistent with the primary analyses.

Despite these limitations, the study has important strengths, including its prospective multicenter design, 44-week follow-up, real-world setting, and the simultaneous assessment of alcohol consumption, lifestyle behaviors, and emotional well-being.

5. Conclusions

In this prospective real-world analysis of individuals with obesity and type 2 diabetes receiving GLP-1 RAs, a statistically significant shift toward lower self-reported alcohol-consumption categories and improved dietary adherence were observed over 44 weeks of follow-up.

Improvements were also observed in selected domains of emotional well-being, particularly feelings of calmness and tranquility, although no significant changes were detected in global mental health measures. Exploratory analyses suggested favorable changes in selected emotional well-being items, particularly feelings of calmness and tranquility, although no significant changes were detected in global mental health measures. These item-level findings require confirmation in future studies.

These findings support the growing evidence supporting the hypothesis that GLP-1 RAs may exert clinically relevant behavioral effects extending beyond their established metabolic benefits. Further prospective studies specifically designed to evaluate alcohol-related behaviors, reward processing, and mental health outcomes are warranted to confirm these observations and clarify the underlying mechanisms.

CRediT authorship contribution statement

José Seijas-Amigo: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources,

Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Ángel Salgado-Barreira:** Formal analysis, Methodology, Investigation, Visualization, Writing – original draft, Writing – review & editing. **Rosana Castelo-Dominguez:** Investigation, Writing – review & editing. **María Teresa Pérez-Álvarez:** Investigation, Writing – review & editing. **Belén Ponce-Piñón:** Investigation, Writing – review & editing. **Marlén Fernández-Silva:** Investigation, Writing – review & editing. **Marta Rodríguez-Barreiro:** Investigation, Writing – review & editing. **Mercedes Pereira-Pía:** Investigation, Writing – review & editing. **Jose Manuel Iglesias-Moreno:** Investigation, Writing – review & editing. **Mar Gago-García:** Investigation, Writing – review & editing. **Raquel Montáns-García:** Investigation, Data curation. **Agustina Fernandez-Perez:** Investigation, Writing – review & editing. **Dolores Fraga-Gayoso:** Investigation, Writing – review & editing. **Montse Fernandez-Montenegro:** Investigation, Writing – review & editing. **Beatriz Riveiro-Barciela:** Investigation, Writing – review & editing. **Natalia Rilla-Villar:** Investigation, Writing – review & editing. **Begoña Cardeso-Paredes:** Investigation, Data curation, Writing – review & editing. **Marta Ribeiro-Ferreiro:** Investigation, Data curation, Writing – review & editing. **Diego Rodriguez-Penas:** Investigation, Writing – review & editing. **Alberto Cordero:** Investigation, Writing – review & editing. **Moisés Rodríguez-Mañero:** Investigation, Writing – review & editing, Supervision. **José R. González-Juanatey:** Investigation, Writing – review & editing, Supervision.

Ethics approval and consent to participate

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Galicia Research Ethics Committee (Registration No. 2021/471). All participants provided written informed consent before study inclusion. The SEVERAL study was registered at ClinicalTrials.gov (NCT05136287).

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT (OpenAI) to assist with language editing and manuscript preparation. The authors reviewed, edited, and validated all generated content and take full responsibility for the content of the publication.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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The electronic case report form (eCRF) used in the SEVERAL study, including the assessments of alcohol consumption, dietary adherence, physical activity, and emotional well-being, is provided as Supplementary Material S1.

This observational study was conducted and reported in accordance with the STROBE recommendations. The completed STROBE checklist is provided as Supplementary Material S2.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.addbeh.2026.108905.

Data availability

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request and subject to institutional approval. De-identified participant data may be shared for academic purposes in accordance with applicable ethical and regulatory requirements.

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