



OPEN Alignment between physician and patient perceptions of antidepressant treatment outcomes in routine clinical practice

Luis Caballero-Martínez¹, Francisco J. Campos-Lucas^{2,6}✉, Diana Monge-Martín², Pilar García-García³, Juan Gómez-Salgado^{4,5} & Fernando Caballero-Martínez²

Patient-reported perspectives have become increasingly relevant in the evaluation of psychiatric treatments. In depression, discrepancies between clinician assessments and patients' subjective experiences may arise, particularly in domains related to tolerability and daily functioning. Pragmatic investigations conducted under routine clinical practice conditions may help clarify how treatment outcomes are evaluated by different stakeholders. This observational, cross-sectional, multicentre study conducted in routine clinical practice compared physicians' and patients' opinions on antidepressant treatment outcomes following real-world use of tianeptine. Data were collected using structured self-administered questionnaires with 5-point Likert-type ordinal scales. Paired comparisons were performed using appropriate non-parametric tests. Sixty physicians and 542 patients from multiple clinical settings across Spain participated. Physicians' and patients' evaluations were largely concordant across global domains, with high or full satisfaction reported by 62% of physicians and 55% of patients, alongside similarly positive evaluations of quality of life impact. However, systematic differences were observed in tolerability-related domains. For example, null or low interference with daily life activities was reported by 68% of patients compared with 56% of physicians. The findings indicate a high degree of physician–patient concordance in global evaluations of antidepressant treatment outcomes under routine clinical conditions, alongside domain-specific differences in tolerability assessments. These findings highlight the importance of incorporating patient-reported perspectives when evaluating treatment experience in depression.

Keywords Depression, Tianeptine, Physician–patient concordance, Patient-reported outcomes, Treatment tolerability, Cross-sectional study

Patient-reported outcome measures (PROMs) have increasingly been recognised as an essential component in the evaluation of medical treatments, including psychiatric pharmacotherapy. Regulatory agencies and clinical guidelines emphasise the importance of incorporating patients' perspectives on treatment benefits, tolerability and impact on daily functioning when assessing therapeutic outcomes¹. In mental health care, these perspectives provide complementary information to clinician-rated assessments and contribute to a more comprehensive understanding of treatment effects in routine practice². In depression, the inclusion of the patient's perspective is particularly relevant. Residual symptoms³, adverse effects such as sexual dysfunction, sedation, insomnia or weight changes^{4–7} and drug–drug interactions frequently complicate antidepressant (AD) treatment⁸ and

¹Psychiatry Service, Puerta de Hierro University Hospital, Madrid, Spain. ²Faculty of Medicine, Universidad Francisco de Vitoria, Pozuelo de Alarcón, Madrid, Spain. ³Exeltis Healthcare S.L. Alcobendas, Madrid, Spain. ⁴Department of Sociology, Social Work and Public Health, Faculty of Labour Sciences, University of Huelva, Avda. Tres de Marzo, S/N, Huelva 21007, Spain. ⁵Safety and Health Postgraduate Programme, Universidad Espíritu Santo, Avda. Tres de Marzo, S/N, Guayaquil 092301, Ecuador. ⁶Postgraduate Studies and Institutional Relations, Faculty of Medicine, Universidad Francisco de Vitoria, Carretera Pozuelo-Majadahonda km 1. 800 - 28223, Pozuelo de Alarcón, Madrid, Spain. ✉email: f.campos@ufv.es

may negatively affect adherence, functional recovery and quality of life. Importantly, clinical improvement as judged by healthcare professionals does not always coincide with patients' subjective experience of treatment^{9,10}, especially in domains related to daily functioning and tolerability.

Previous studies have reported a moderate degree of agreement between clinician-rated and patient-reported outcomes in depression, with higher concordance for overall symptom severity than for domains related to tolerability and everyday functioning¹¹. These findings suggest that certain aspects of treatment experience may be perceived differently by patients and clinicians, potentially leading to gaps in shared understanding of treatment benefits and burdens. However, although PROMs are increasingly used in psychiatric research, their routine implementation in clinical practice remains challenging. Time constraints, heterogeneity of available instruments and limited feasibility for longitudinal monitoring in real-world settings complicate their systematic use in everyday care¹¹. As a result, pragmatic approaches that capture patient experience without imposing excessive burden on clinicians or patients are particularly valuable in observational research.

Discrepancies between clinicians' and patients' perceptions appear to be especially relevant for tolerability-related domains, such as sexual functioning, sedation, or interference with daily activities. These aspects are often underreported or insufficiently explored in routine clinical encounters, despite their well-established impact on treatment satisfaction, adherence and quality of life¹². In addition, outcome measures used in depression research are highly heterogeneous, which complicates comparisons across studies and limits the generalisability of findings derived from controlled clinical trials alone. This heterogeneity reinforces the value of pragmatic, real-world investigations that directly explore how treatments are perceived by both patients and clinicians under routine care conditions¹³.

Tianeptine is an antidepressant with a pharmacological profile distinct from that of classical monoaminergic agents^{14–16}. Beyond its antidepressant effects, it has been associated with anxiolytic properties and potential benefits on cognitive functioning^{17–20}. Clinical and observational studies have described a favourable tolerability profile, which may be particularly relevant from the patient's perspective²¹. However, despite its clinical use in Europe for several decades, evidence from real-world studies examining the alignment between physicians' and patients' perceptions of tianeptine remains limited.

Therefore, the objective of the present study was not to assess the clinical efficacy of tianeptine, but to compare physicians' and patients' perceptions of its effectiveness, tolerability and overall impact on quality of life following real-world use. By examining areas of concordance and discordance between both perspectives, this study aims to contribute to a more patient-centered approach to antidepressant treatment and to inform clinical decision-making in routine psychiatric practice²².

Methods

Study design and setting

This was an observational, cross-sectional, multicentre study conducted under routine clinical practice conditions. The study was designed to compare physicians' and patients' perceptions of antidepressant treatment outcomes following real-world use, without any intervention or modification of usual clinical care.

The study was carried out in outpatient and hospital-based clinical settings across Spain, including psychiatric and geriatric care services. Data collection took place over a predefined recruitment period, during which participating clinicians consecutively enrolled eligible patients as part of their usual clinical activity. The study did not include prospective follow-up or retrospective data collection beyond the information routinely available at the time of assessment.

Participants and sampling

Eligible participants were adult patients (≥ 18 years) with a clinical diagnosis of major depressive disorder who had been receiving treatment with tianeptine for at least 8 weeks prior to inclusion, according to routine prescribing criteria. There were no restrictions regarding concomitant pharmacological treatments. Patients treated for depressive episodes in the context of bipolar disorder were excluded.

Participating physicians were specialist clinicians (psychiatrists or geriatric medicine specialists) responsible for the clinical management of the included patients. Physicians were recruited from all Spanish autonomous regions, with the aim of achieving broad geographical representation proportional to regional population size.

An intentional sampling strategy was used to recruit physicians, who agreed voluntarily to participate in the study. Each participating physician was asked to consecutively include a predefined number of eligible patients attending routine follow-up visits during the recruitment period. This consecutive, non-random sampling approach was chosen to minimise selection bias and to reflect routine clinical practice as closely as possible.

All patients who fulfilled eligibility criteria were invited to participate, and inclusion was conditional on providing written informed consent. Physicians completed their questionnaires without prior knowledge of their patients' responses, in order to reduce potential information bias.

Study instruments and data collection

Data were collected using a structured, self-administered questionnaire specifically developed for the purposes of this study. The same questionnaire framework was used for physicians and patients, with parallel items adapted to each respondent group, in order to allow direct comparison of perceptions regarding antidepressant treatment outcomes. The full English translation of the physician and patient questionnaires is provided in Supplementary Table S1.

The questionnaire was designed to capture subjective perceptions of treatment experience rather than objective clinical outcomes. Items assessed perceived effectiveness (antidepressant, anxiolytic and relief of somatic symptoms), convenience of dosage, perceived speed of onset, tolerability (including effects on alertness,

daily activities, sleep, sexual functioning and appetite), perceived quality of life, overall satisfaction with treatment and the degree of fulfilment of initial treatment expectations.

Variables were measured using 5-point Likert-type ordinal scales, with clearly defined semantic anchors ranging from “null” to “full” effect or satisfaction. The wording of items was deliberately non-technical to ensure comprehensibility for patients with different educational backgrounds and to minimise response bias.

The questionnaire was developed by the study team based on clinical relevance and prior experience with antidepressant treatment and underwent external review by independent experts in psychiatry and clinical pharmacology. Items were selected to represent domains considered most relevant for capturing potential discrepancies between patients’ and physicians’ perceptions of treatment outcomes. Given the comparative and exploratory objectives of the study, a full psychometric validation was not performed. Before study implementation, the instrument was pilot tested in a small mixed sample of participants to evaluate item clarity and acceptability. Test–retest reliability was examined by re-administering the questionnaire after 7 days, in the absence of clinically meaningful changes, to assess score stability and the consistency of item interpretation. This preliminary assessment was considered sufficient to support face validity and to justify use of the instrument in the present study.

Data collection took place during routine clinical visits. Patients completed their questionnaires independently and anonymously, without assistance from the prescribing physician. Physicians completed their corresponding questionnaires separately, based on their clinical judgement of each included patient, and without access to the patient’s responses.

In addition to perception-based variables, physicians provided descriptive clinical information regarding treatment discontinuation, reasons for discontinuation and work incapacity related to the depressive episode when applicable. Patient questionnaires also included basic demographic and clinical descriptors relevant for subgroup analyses.

Sample size and statistical analysis

Sample size

The sample size was determined a priori to ensure sufficient precision in the estimation of physicians’ and patients’ responses to the study questionnaire. The primary objective of the study was descriptive and comparative, focusing on the distribution of perception scores and on the differences between paired physician–patient assessments.

In the absence of prior data allowing more specific assumptions, sample size calculation was based on a conservative approach for the estimation of proportions, assuming the most unfavourable scenario ($p = 0.5$). Under this assumption, a maximum margin of error of 3% around point estimates was targeted, with a confidence level of 95%.

Based on these criteria, a minimum sample of approximately 550 patients was required. To achieve this target while maintaining feasibility in routine clinical practice, the study design planned the participation of 60 physicians, each consecutively recruiting the first 10 eligible patients who agreed to participate among those attending their routine consultations from the study start date.

The final study sample included 542 patients, which was considered sufficient to meet the predefined precision and confidence requirements for the descriptive and comparative analyses.

Statistical analysis

Descriptive statistics were used to summarise physician and patient characteristics, as well as questionnaire responses. Qualitative variables were expressed as absolute and relative frequencies, and quantitative variables as means and standard deviations.

Differences between independent groups were assessed using Student’s *t*-test or the Mann–Whitney *U* test, as appropriate, depending on data distribution. Differences in proportions were analysed using the chi-squared test.

The main comparative analysis of the study focused on the comparison of perception scores between physicians and their corresponding patients. As these assessments were paired by case and based on ordinal Likert-type scales, comparisons were performed using the Wilcoxon signed-rank test for paired data.

Statistical significance was defined as a two-sided *p* value < 0.05 . In addition to *p* values, mean differences in scores between physicians and patients were calculated to provide an objective quantification of the magnitude of observed differences.

To facilitate interpretation of potential clinical relevance, score differences were also examined in relation to the semantic categories of the response scale, assessing whether observed differences reflected a change in category between physician and patient perceptions.

All statistical analyses were performed using SPSS software (version 21.0; SPSS Inc., Chicago, IL, USA).

Ethical considerations

The study was conducted in accordance with the ethical principles set out in the Declaration of Helsinki and complied with applicable national regulations for observational research involving human participants.

The study protocol FUF-TIA-2016-01 (JUS-EXP-2016-01), together with all study materials, was reviewed and approved by the Research Ethics Committee of Hospital Universitario Puerta de Hierro Majadahonda (Madrid), prior to study initiation.

All participating patients provided written informed consent before being included in the study. Physicians also provided their explicit consent to participate and to contribute anonymised data through the study’s electronic data collection platform.

	Researcher physicians (n = 60)
Age(years)	
Mean (CI _{95%})	49.5 (47.1–51.9)
Median	51
Range	32–63
Sex	
Men-Female	73.3%-26.7%
Speciality	
Psychiatry	90%
Geriatrist	2%
Other	8%
Health care setting	
Outpatient Centre	63.3%
Hospital	30.0%
Private consultancy (with/without previous categories)	13.7%
Previous Professional Experience(years)	
Range	1–37
Mean (CI _{95%})	19.3 (16.7–21.8)
Median	20
Daily healthcare activity	
Average number of patients treated/day	18.6
Patients with depression diagnostic	39.7%
N° prescriptions of antidepressant treatment (<i>last week</i>)	
Mean (CI _{95%})	31 (25.2–37.3)
Experience with tianeptine(months)	
Mean (CI _{95%})	10.7 (9.1–12.2)
Median	10
Range	2–24
	Patients (n = 542)
Age (years)	
Mean (CI _{95%})	52.3 (51.0-53.7)
Median	52
Range	19–102
Sex	
Male-Female	33%-67%
Mean age (years) male-female	48.9–54.1
Educational level patients	
Reads/writes	11%
Primary education	21%
Secondary education	20%
Baccalaureate	17%
Intermediate university studies	15%
Higher university studies	14%
Evolution of depressive disease	
First episode	41.8%
Recurrent disease	58.2%
Previous episodes Mean (CI _{95%})	3.8 (3.5–4.1)
Previous episodes Median	3
N° recurrences maxims	15
Time of evolution of present episode (months)	
Mean (CI _{95%})	6.8 (6.3–7.2)
Median	6
Range	1–48
Duration of tianeptine treatment (months)	
Mean (CI _{95%})	3 (2.8–3.1)
Median	2
Continued	

	Patients (<i>n</i> = 542)
Range	1–16
Indication of tianeptine treatment during episode	
As first treatment	35.6%
As second treatment	40.8%
Due to bad tolerance to previous treatment	72.5%
Due to bad adherence to previous treatment	25%
As concomitant treatment (insufficient response to first treatment)	23.6%
Patients with concomitant treatment with Tianeptine	82.5%
Benzodiazepines	68%
Others antidepressant	33%
Antipsychotics	7%
Euthymics	6%
Others	5%
Antiepileptics	4%
Psychostimulants	1%

Table 1. Study subjects: Professional profile of research specialists and clinic- therapeutic profile of patient surveyed.

Patient data were collected and analysed in anonymised form, and no information allowing individual identification was recorded. Participation in the study did not involve any modification of prescribed treatments or additional clinical procedures beyond routine care.

Results

Study population

All invited specialists agreed to participate in the study ($N = 60$). These physicians, predominantly psychiatrists, consecutively included a total of 542 patients diagnosed with a depressive episode and treated with tianeptine for at least 8 weeks prior to study inclusion. All physician questionnaires and 538 patient questionnaires were completed in full. Four patients provided only sociodemographic information and did not complete the remaining questionnaire sections; these cases were therefore not included in the comparative analyses. No specific reasons for non-completion were reported.

The mean age of the patient sample was 52.3 years. The professional profile of the participating physicians and the clinical and therapeutic characteristics of the patients are summarised in Table 1.

Treatment expectations and discontinuation

At treatment initiation, physicians most frequently reported therapeutic intentions related to the elimination of depressive symptoms (98.7%), avoidance of cognitive adverse effects (91.3%) and minimisation of potential drug–drug interactions (76.4%). Patients reported similar expectations, most commonly the elimination of depressive symptoms (98.3%), avoidance of cognitive disturbances (85.5%), potential interactions with other treatments (69.3%) and preservation of sexual functioning (68.4%).

At the time of assessment, 42 of 542 patients (7.8%) had discontinued treatment with tianeptine. The most frequently reported reasons for discontinuation were insufficient improvement of symptoms, poor adherence, emergence of adverse effects and relapse or recurrence.

A total of 110 patients (20.3%) reported a previous period of work incapacity related to the depressive episode, with a mean duration of 87 days (median: 60 days).

Table 2 summarises the distribution of perception scores reported by physicians and patients across all survey items.

Physicians' perceptions of treatment outcomes

Most physicians reported high or full satisfaction with tianeptine's perceived effectiveness in relieving depressive symptoms (58%), anxiety symptoms (57%) and somatic symptoms (54%). Perceived satisfaction with the speed of onset of action was also rated as high or full by 51% of physicians, whereas satisfaction with the recommended dosage regimen was comparatively lower, with 38% of physicians reporting high or full satisfaction. With regard to tolerability, the majority of physicians rated the impact of treatment on daily activities (56%), level of alertness (55%), sleep quality (52%), appetite (47%) and sexual functioning (45%) as null or low.

When examining the fulfilment of physicians' initial expectations, the highest mean scores were observed for avoidance of drug–drug interactions (mean = 4.1) and preservation of cognitive functioning (mean = 4.0), followed by effects on sexual functioning (mean = 3.86) and relief of depressive symptoms (mean = 3.57).

Overall, 62% of physicians reported high or full satisfaction with tianeptine treatment and 56% reported high or full satisfaction with its perceived impact on patients' quality of life.

	Null 1	Low 2	Medium 3	High 4	Full 5	Punctuation (average)	<i>p</i> (Wilcoxon signed-rank test)
1. Tianeptine efficacy							
Control of depressive symptoms							
Patients	2%	12%	35%	44%	6%	3.40	<0.001
Physicians	2%	12%	27%	49%	9%	3.52	
Control of anxiety symptoms							
Patients	2%	10%	32%	45%	9%	3.50	0.009
Physicians	1%	11%	28%	46%	11%	3.57	
Control of somatic depressive symptoms							
Patients	3%	14%	30%	41%	8%	3.38	<0.001
Physicians	2%	12%	27%	44%	10%	3.51	
2. Usability and response time of tianeptine							
Patient satisfaction with prescribed posology							
Patients	1%	26%	40%	28%	4%	3.07	<0.001
Physicians	2%	18%	42%	33%	5%	3.21	
Satisfaction with rapid action of drug							
Patients	2%	13%	39%	42%	4%	3.33	<0.001
Physician	2%	11%	35%	46%	5%	3.42	
3. Tianeptine Tolerability							
Interference with alert level (sedation)							
Patients	35%	34%	17%	13%	2%	2.13	<0.001
Physician	12%	43%	18%	11%	16%	3.25	
Interference with dairy life activities							
Patients	36%	32%	16%	15%	1%	2.14	<0.001
Physician	13%	43%	17%	12%	15%	3.28	
Interference with sleep quality (insomnia)							
Patients	37%	27%	19%	15%	2%	2.19	<0.001
Physician	13%	39%	21%	13%	14%	3.24	
Interference with sexual function (inappetence or dysfunction)							
Patients	40%	27%	20%	11%	1%	2.06	<0.001
Physicians	13%	32%	23%	11%	20%	3.07	
Interference with appetite changes (increased or decrease appetite)							
Patients	38%	28%	21%	11%	1%	2.09	<0.001
Physician	12%	35%	23%	13%	17%	3.14	
4. Health outcomes of tianeptine treatment							
Quality of life achieved by this patient							
Patients	2%	11%	36%	46%	5%	3.42	0.011
Physician	1%	12%	32%	49%	7%	3.48	
Global satisfaction with treatment							
Patients	2%	12%	31%	48%	7%	3.48	<0.001
Physician	1%	9%	28%	52%	10%	3.60	
5. Compliance of expectations on needs that induced tianeptine treatment							
To eliminate depressive symptoms (*) <i>n</i> = 531 cases							
Patients	3%	14%	32%	38%	13%	3.45	<0.001
Physicians	3%	11%	28%	43%	15%	3.57	
Avoid interactions with other drugs (*) <i>n</i> = 411 cases							
Patients	2%	5%	23%	43%	27%	3.80	<0.001
Physicians	1%	2%	15%	50%	32%	4.09	
Avoid intellectual and consciousness impairment. (*) <i>n</i> = 491 cases							
Patients	1%	6%	25%	44%	24%	3.79	<0.001
Physicians	0%	4%	20%	48%	28%	4.00	
Avoiding disruption of sex life. (*) <i>n</i> = 386 cases							
Patients	5%	9%	23%	39%	24%	3.66	<0.001
Physicians	4%	4%	20%	44%	27%	3.86	

Table 2. Patients' and physicians' perceptions and opinions of antidepressant treatment with tianeptine. *n* = 538, except for (*).

Patients’ perceptions of treatment outcomes

Patients’ perceptions of tianeptine effectiveness were predominantly distributed within the medium-to-high range of the scale for depressive, anxiety and somatic symptoms, with proportions ranging from 71% to 79%. Satisfaction with the prescribed dosage regimen and perceived speed of therapeutic effect were also mainly rated in the medium-to-high range (68% and 79%, respectively). Regarding tolerability, the majority of patients (65–69%) reported null or low interference of tianeptine with alertness, daily activities, sleep, sexual functioning and appetite.

The fulfilment of patients’ initial treatment expectations was also predominantly rated in the high-to-full range of the scale (51–70%), with the highest mean scores corresponding to avoidance of drug–drug interactions (mean = 3.80) and preservation of cognitive functioning (mean = 3.79), followed by minimisation of sexual side effects (mean = 3.66) and relief of depressive symptoms (mean = 3.45).

Overall, 55% of patients reported high or full satisfaction with tianeptine treatment and 51% reported high or full satisfaction with its perceived impact on quality of life.

Subgroup analyses

Sex-related differences were observed in patient-reported satisfaction, with male patients reporting slightly higher overall satisfaction scores than female patients (mean = 3.54 vs. 3.36; $p = 0.011$, Mann–Whitney U test). Male patients more frequently reported an expectation of preserved sexual functioning at treatment initiation compared with female patients (84.4% vs. 60.4%; $p < 0.001$, chi-squared test).

Additional subgroup analyses comparing patients experiencing a first depressive episode with those with recurrent episodes are presented in Table 3. Patients with first episodes reported higher ratings for relief of depressive symptoms, preservation of sexual functioning, avoidance of drug–drug interactions, overall satisfaction and quality of life.

Comparison between physicians’ and patients’ perceptions

Overall, physicians and patients reported comparable perceptions of treatment effectiveness, satisfaction with practical aspects of treatment and perceived impact on quality of life, with no statistically significant differences observed for these domains (Fig. 1).

In contrast, physicians consistently rated the negative impact of tianeptine on various aspects of daily functioning and tolerability higher than did patients (Fig. 2), indicating a systematic difference in perceived tolerability between the two groups.

Physicians’ ratings of the fulfilment of initial expectations motivating treatment prescription were also systematically higher than patients’ ratings, although the magnitude of these differences was small.

When considering the overall benefit–risk balance, physicians’ and patients’ assessments of general treatment satisfaction (80% vs. 79%) and perceived impact on quality of life (81% vs. 82%) largely overlapped and were predominantly located within the medium-to-high range of the response scale.

Discussion

This observational, cross-sectional study examined the alignment between physicians’ and patients’ perceptions of antidepressant treatment outcomes following real-world use of tianeptine. Overall, the findings indicate a substantial degree of concordance between both groups regarding perceived effectiveness, satisfaction with practical aspects of treatment and impact on quality of life, suggesting that, in routine clinical practice, physicians’ global impressions of treatment outcomes are generally consistent with patients’ subjective experiences. Notably, the main area of discordance identified in this study concerned tolerability-related domains, as physicians systematically rated the negative impact of treatment on daily functioning, alertness, sleep, sexual functioning and appetite higher than did patients. This pattern was consistent across multiple domains and contrasts with the frequent assumption that clinicians tend to underestimate treatment burden compared with patients.

Previous research has shown that agreement between clinician-rated and patient-reported outcomes in depression is often domain-specific, with higher concordance for overall symptom severity and lower concordance for functional and tolerability-related outcomes¹¹. The present findings are consistent with this

Aspect	Type of episode	n	Mean	p-value
Results of quality of life	First episode	225	3.56	< 0.001
	Recurrent	309	3.31	
Personal satisfaction with treatment	First episode	225	3.60	0.004
	Recurrent	309	3.38	
To eliminate depressive symptoms	First episode	225	3.61	< 0.001
	Recurrent	309	3.30	
Avoid interactions with other drugs	First episode	225	3.36	0.047
	Recurrent	309	3.61	
Avoiding disruption of sex life	First episode	225	3.44	0.009
	Recurrent	309	3.14	

Table 3. Influence of the type of current depressive episode on some patients’ perceptions after their experience of tianeptine use.

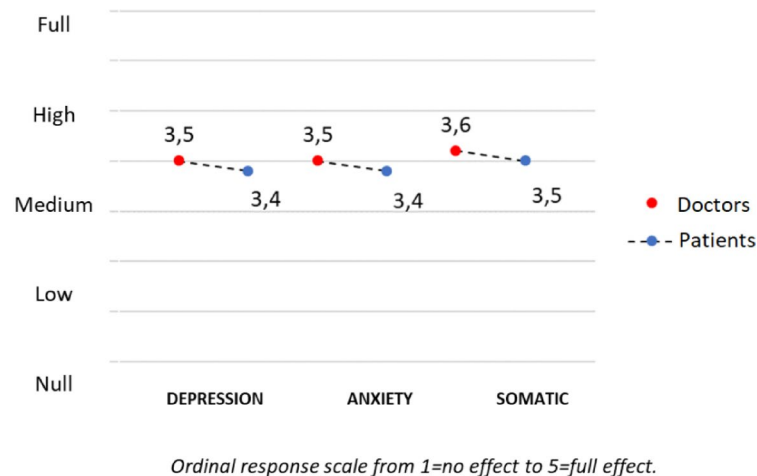


Fig. 1. Perception of the efficacy of tianeptine in the control of depressive, anxiety and somatic symptoms.

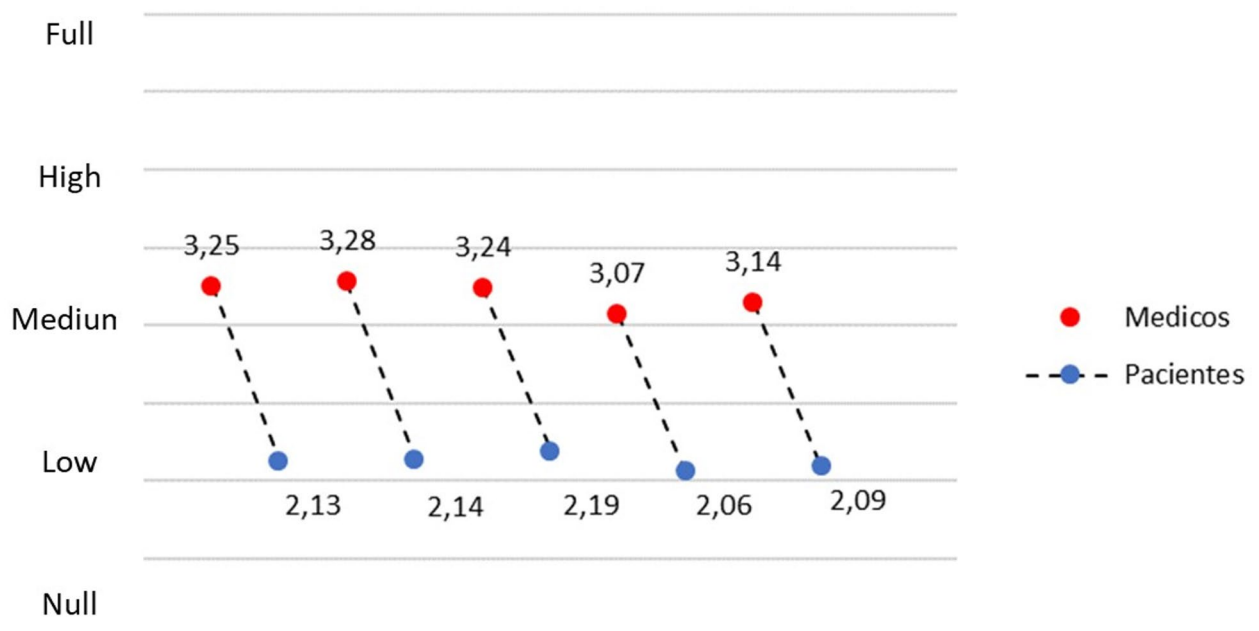


Fig. 2. Tolerability of tianeptine (degree of interference with the indicated functions).

literature and further suggest that, in some contexts, clinicians may adopt a more cautious or conservative appraisal of potential adverse effects than patients themselves. Several factors may contribute to this discrepancy, including clinicians' broader experience across patient populations and their awareness of known adverse effect profiles, whereas patients' evaluations are grounded in their individual lived experience and may prioritise perceived benefits over mild or expected adverse effects. This divergence highlights the importance of explicitly exploring patient-reported experiences during clinical encounters, particularly for domains that may not be spontaneously disclosed^{23,24}.

Tolerability-related outcomes, such as sexual functioning and interference with daily activities, have been identified as key determinants of adherence and long-term treatment success, yet these domains are not always systematically assessed in routine care despite their relevance to patient satisfaction and quality of life¹². In this context, the present findings reinforce the clinical value of incorporating patient perspectives when evaluating

antidepressant treatments beyond symptom reduction alone. In addition, the observed alignment between physicians and patients regarding overall satisfaction and quality of life suggests that global evaluations may mask meaningful differences in specific experiential domains. This observation is consistent with reports highlighting the heterogeneity of outcome measures used in depression research and the limitations of relying on single summary indicators to capture treatment impact¹³. Pragmatic studies that disaggregate treatment experience into distinct domains may therefore provide more clinically actionable insights.

Interpretation of specific outcome domains

With respect to tianeptine specifically, the favourable perceptions reported by both physicians and patients across multiple domains provide a coherent framework for the domain-specific analyses presented below. These findings are in line with previous clinical and observational studies describing its effectiveness and tolerability profile²¹. However, the present study extends existing knowledge by focusing on the degree of alignment between physician and patient perspectives under routine practice conditions, rather than on efficacy outcomes per se.

Both physicians and patients reported medium-to-high perceived effectiveness of tianeptine across depressive, anxiety and somatic symptom domains. This overall convergence supports the clinical plausibility of the findings and is consistent with previous studies describing the effectiveness of tianeptine in depressive disorders, including its effects on anxiety and neurocognitive symptoms^{25,26}. Importantly, these perceptions reflect real-world clinical experience rather than controlled efficacy assessments.

Perceptions of practical aspects of treatment, such as speed of onset and dosage regimen, were also broadly aligned between physicians and patients. Although physicians tended to provide slightly higher ratings in these domains, the magnitude of these differences was small and unlikely to be clinically meaningful. Nevertheless, this pattern may suggest that certain sources of patient dissatisfaction, even when mild, are not always fully captured during routine clinical evaluation²⁷.

With regard to tolerability, patients consistently reported low interference of treatment with key aspects of daily functioning, including alertness, sleep, appetite, sexual functioning and overall activity. These findings are in line with previous reports highlighting the favourable tolerability profile of tianeptine¹⁷. At the same time, physicians systematically perceived greater interference across these domains, particularly in relation to daily activities. This discrepancy may reflect clinicians' heightened awareness of potential adverse effects and underscores the importance of systematically exploring patient-reported experiences to avoid overestimation or misinterpretation of treatment burden.

Expectations, satisfaction and subgroup patterns

Overall satisfaction with treatment and perceived impact on quality of life were remarkably similar between physicians and patients and were predominantly rated in the medium-to-high range. This convergence is consistent with the generally favourable benefit–risk profile of tianeptine described in previous literature²⁸ and supports the internal coherence of the study findings.

The fulfilment of initial therapeutic expectations was also rated positively by both groups, particularly with respect to preservation of cognitive functioning and avoidance of drug–drug interactions. These domains are clinically relevant, as cognitive impairment and functional limitations are known to substantially affect occupational and social outcomes in patients with depression. The comparatively lower ratings observed for relief of depressive symptoms and avoidance of sexual dysfunction suggest that these areas may warrant closer attention during follow-up consultations.

Subgroup analyses indicated slightly higher satisfaction and expectation fulfilment among patients experiencing a first depressive episode compared with those with recurrent episodes (Table 3), as well as among male patients compared with female patients (Table 2). Although these differences should be interpreted cautiously, they are consistent with previously reported clinical and epidemiological patterns in depression and may reflect factors such as illness chronicity, treatment resistance, or gender-related differences in symptom perception and communication^{29–31}.

Contextual validity and representativeness of the study population

The characteristics of both participating clinicians and patients support the contextual validity and representativeness of the study findings. Most participating physicians were psychiatrists working in outpatient settings, which reflects routine clinical practice in Spain and is consistent with patterns reported in other developed healthcare systems^{32,33}. The clinical and demographic profile of the patient sample also aligns with epidemiological data on depression, including the predominance of middle-aged women and the observed mean age^{34–37}, as well as the duration of depressive episodes reported in comparable studies³⁸.

Although this study was not designed to estimate lifetime recurrence, the observed clinical characteristics are compatible with published data on the recurrent nature of depressive disorders in middle-aged populations³⁹. Prescribing patterns and the use of concomitant treatments were consistent with routine clinical practice and established safety considerations^{40,41}, and the minimum treatment duration required for inclusion was considered sufficient for patients to form informed perceptions of treatment outcomes⁴².

Finally, the methodological approach used to compare physician and patient perceptions is supported by the clarity and interpretability of the assessment instruments. The use of a structured 5-point ordinal scale with explicit semantic anchors facilitated meaningful comparison between groups, and the statistical methods applied were appropriate for the type of data and sample size, as detailed in the Methods section.

These considerations provide an appropriate context in which to interpret the strengths and limitations of the present study.

Strengths and limitations

This study has several strengths, including its multicentre design, large sample size, and focus on paired physician–patient assessments collected concurrently in real-world clinical settings. The use of parallel questionnaires allowed direct comparison of perceptions while minimising recall bias and temporal discrepancies.

Several limitations should also be acknowledged. First, the cross-sectional design precludes assessment of changes in perceptions over time and limits causal interpretation. Second, treatment duration varied among participants, which may have influenced individual evaluations of effectiveness and tolerability. Third, the questionnaire used was specifically developed for this study and was not intended as a psychometrically validated instrument; however, it was designed to be pragmatic, clinically relevant and feasible for routine use, and was pilot-tested to ensure clarity and interpretability.

Finally, as with all observational studies conducted in routine practice, the possibility of residual confounding and selection bias cannot be fully excluded. Nevertheless, the consecutive recruitment strategy and broad inclusion criteria were intended to enhance representativeness and ecological validity.

Clinical implications and conclusions

In conclusion, this study demonstrates a high degree of alignment between physicians' and patients' perceptions of antidepressant treatment outcomes in routine clinical practice, alongside systematic differences in the appraisal of tolerability-related domains. These findings underscore the importance of incorporating patient perspectives into treatment evaluation and decision-making, particularly for domains that directly affect daily functioning and quality of life.

Greater awareness of potential discrepancies between clinician and patient perceptions may facilitate more effective communication, shared decision-making, and individualised treatment planning. Future research may benefit from longitudinal designs and from the integration of standardised patient-reported measures to further explore the dynamics of physician–patient alignment over time.

Data availability

Data are available upon reasonable request to the corresponding author.

Received: 16 March 2026; Accepted: 12 May 2026

Published online: 21 May 2026

References

- Guidance for industry. patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual. Life Outcomes*. **4**, 79 (2006).
- IsHak, W. W. et al. Patient-reported outcomes before and after treatment of major depressive disorder. *Dialog. Clin. Neurosci.* **16** (2), 171–183 (2014).
- Kennedy, N. & Paykel, E. S. Residual symptoms at remission from depression: impact on long-term outcome. *J. Affect. Disord.* **80** (2–3), 135–144 (2004).
- Bet, P. M., Hugtenburg, J. G., Penninx, B. W. & Hoogendijk, W. J. Side effects of antidepressants during long-term use in a naturalistic setting. *Eur. Neuropsychopharmacol.* **23** (11), 1443–1451 (2013).
- Jantarantotai, N., Mosikanon, K., Lee, Y. & McIntyre, R. S. The interface of depression and obesity. *Obes. Res. Clin. Pract.* **11** (1), 1–10 (2017).
- Thase, M. E. Depression and sleep: pathophysiology and treatment. *Dialogues Clin. Neurosci.* **8** (2), 217–226 (2006).
- Werneke, U., Northey, S. & Bhugra, D. Antidepressants and sexual dysfunction. *Acta Psychiatr. Scand.* **114** (6), 384–397 (2006).
- Preskorn, S. & Werder, S. Detrimental antidepressant drug–drug interactions: are they clinically relevant? *Neuropsychopharmacology* **31** (8), 1605–1612 (2006).
- Gibson, K., Cartwright, C. & Read, J. Patient-Centered perspectives on antidepressant use: a narrative review. *Int. J. Mental Health.* **43** (1), 81–99 (2014).
- Aikens, J. E., Nease, D. E. Jr. & Klinkman, M. S. Explaining patients' beliefs about the necessity and harmfulness of antidepressants. *Ann. Fam. Med.* **6** (1), 23–29 (2008).
- Hershenberg, R. et al. Concordance between clinician-rated and patient reported outcome measures of depressive symptoms in treatment resistant depression. *J. Affect. Disord.* **266**, 22–29 (2020).
- Zeiss, R. et al. Sexual dysfunction induced by antidepressants—a pharmacovigilance study using data from VigiBase(TM). *Pharmaceuticals (Basel)* **17**(7). (2024).
- Veal, C. et al. Heterogeneity of outcome measures in depression trials and the relevance of the content of outcome measures to patients: a systematic review. *Lancet Psychiatry.* **11** (4), 285–294 (2024).
- Álamo, C., García-García, P., López-Muñoz, F. & Zaragoza, C. Tianeptine, an atypical pharmacological approach to depression. *Revista de Psiquiatría y Salud Mental (English Edition)*. **12**. (2019).
- Wilde, M. I., Benfield, P. & Tianeptine A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in depression and coexisting anxiety and depression. *Drugs* **49** (3), 411–439 (1995).
- McEwen, B. S. et al. The neurobiological properties of tianeptine (Stablon): from monoamine hypothesis to glutamatergic modulation. *Mol. Psychiatry.* **15** (3), 237–249 (2010).
- Kasper, S. & McEwen, B. S. Neurobiological and Clinical Effects of the Antidepressant Tianeptine. *CNS Drugs.* **22** (1), 15–26 (2008).
- Jeon, H. J. et al. Improvement in subjective and objective neurocognitive functions in patients with major depressive disorder: a 12-week, multicenter, randomized trial of tianeptine versus escitalopram, the CAMPION study. *J. Clin. Psychopharmacol.* **34** (2), 218–225 (2014).
- Kasper, S. & Olié, J. P. A meta-analysis of randomized controlled trials of tianeptine versus SSRI in the short-term treatment of depression. *Eur. Psychiatry.* **17** (Suppl 3), 331–340 (2002).
- Wagstaff, A. J., Ormrod, D. & Spencer, C. M. Tianeptine: a review of its use in depressive disorders. *CNS Drugs.* **15** (3), 231–259 (2001).
- García-Alberca, J. M., Gris, E., de la Guía, P. & Mendoza, S. Effects of tianeptine treatment on depression and cognitive function in patients with Alzheimer's disease: a 12-month retrospective observational study. *J. Alzheimers Dis.* **88** (2), 707–720 (2022).
- Mezzich, J. E. World Psychiatric Association perspectives on person-centered psychiatry and medicine. *Int. J. Integr. Care.* **10** (Suppl(Suppl), e003 (2010).

23. Middleton, J. F., McKinley, R. K. & Gillies, C. L. Effect of patient completed agenda forms and doctors' education about the agenda on the outcome of consultations: randomised controlled trial. *Bmj* **332** (7552), 1238–1242 (2006).
24. Starfield, B. et al. The influence of patient-practitioner agreement on outcome of care. *Am. J. Public. Health.* **71** (2), 127–131 (1981).
25. Waintraub, L., Septien, L. & Azoulay, P. Efficacy and safety of tianeptine in major depression: evidence from a 3-month controlled clinical trial versus paroxetine. *CNS Drugs.* **16** (1), 65–75 (2002).
26. Yoo, I. et al. Influence of anxiety symptoms on improvement of neurocognitive functions in patients with major depressive disorder: A 12-week, multicenter, randomized trial of tianeptine versus escitalopram, the CAMPION study. *J. Affect. Disord.* **185**, 24–30 (2015).
27. Hasler, G. et al. Patient satisfaction with outpatient psychiatric treatment: the role of diagnosis, pharmacotherapy, and perceived therapeutic change. *Can. J. Psychiatry.* **49** (5), 315–321 (2004).
28. García-García, P. Tianeptina, antidepresivo con perfil beneficio/riesgo positivo. *Revista de Psiquiatría y Salud Mental.* **9** (4), 234–235 (2016).
29. Fava, G. A., Park, S. K. & Sonino, N. Treatment of recurrent depression. *Expert Rev. Neurother.* **6** (11), 1735–1740 (2006).
30. Lai, C.-H. Major depressive disorder: gender differences in symptoms, life quality, and sexual function. *J. Clin. Psychopharmacol.* **31** (1), 39–44 (2011).
31. Sramek, J. J., Murphy, M. F. & Cutler, N. R. Sex differences in the psychopharmacological treatment of depression. *Dialogues Clin. Neurosci.* **18** (4), 447–457 (2016).
32. Valencia Agudo, F., García Haro, J., Gimeno Peón, A., Pérez Zabalza, A. & Viuda Suárez, M. E. Análisis de la demanda en salud mental en el Principado de Asturias: características de la demanda y respuesta asistencial. *Revista de la. Asociación Española de Neuropsiquiatría.* **34**, 741–752 (2014).
33. Olsson, M. et al. National trends in the outpatient treatment of depression. *Jama* **287** (2), 203–209 (2002).
34. Wang, J. et al. Prevalence of depression and depressive symptoms among outpatients: a systematic review and meta-analysis. *BMJ Open.* **7** (8), e017173 (2017).
35. Steel, Z. et al. The global prevalence of common mental disorders: a systematic review and meta-analysis 1980–2013. *Int. J. Epidemiol.* **43** (2), 476–493 (2014).
36. Lewer, D., O'Reilly, C., Mojtabai, R. & Evans-Lacko, S. Antidepressant use in 27 European countries: associations with sociodemographic, cultural and economic factors. *Br. J. Psychiatry.* **207** (3), 221–226 (2015).
37. Nassan, M. et al. Pharmacokinetic pharmacogenetic prescribing guidelines for antidepressants: a template for psychiatric precision medicine. *Mayo Clin. Proc.* **91** (7), 897–907 (2016).
38. Ten Have, M. et al. Duration of major and minor depressive episodes and associated risk indicators in a psychiatric epidemiological cohort study of the general population. *Acta Psychiatr Scand.* **136** (3), 300–312 (2017).
39. Burcusa, S. L. & Iacono, W. G. Risk for recurrence in depression. *Clin. Psychol. Rev.* **27** (8), 959–985 (2007).
40. Toon, S. et al. Pharmacokinetic and pharmacodynamic interaction between the antidepressant tianeptine and oxazepam at steady-state. *Psychopharmacology* **101** (2), 226–232 (1990).
41. Woo, Y. S. et al. Tianeptine combination for partial or non-response to selective serotonin re-uptake inhibitor monotherapy. *Psychiatry Clin. Neurosci.* **67** (4), 219–227 (2013).
42. Vuković, O. et al. Efficacy, tolerability and safety of tianeptine in special populations of depressive patients. *Psychiatr Danub.* **21** (2), 194–198 (2009).

Acknowledgements

We thank all the physicians and patients who participated in the EXPERTIA study. Editorial assistance in language refinement and consistency checking was provided by an AI-based language model (OpenAI, ChatGPT-5). The authors are solely responsible for the scientific content and interpretation of the study.

Author contributions

LCM, FJCL, DMM, PGG, JGS, and FCM contributed equally to all aspects of this work, including: Conceptualization; Methodology; Software; Validation; Formal analysis; Investigation; Resources; Data curation; Writing – Original Draft; Writing – Review & Editing; Visualization; Supervision; and Project administration.

Funding

The study was conducted independently by the authors, who received financial support from Exeltis Healthcare S.L.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-026-53437-z>.

Correspondence and requests for materials should be addressed to F.J.C.-L.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

© The Author(s) 2026