Patient Preference and Adherence

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ORIGINAL RESEARCH

Exploring the Impact of Schizophrenia and Its Pharmacological Treatment on Health-Related Quality of Life and Treatment Preferences

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Purpose: Pharmacological treatments play an important role in managing symptoms of schizophrenia but can also be associated with side effects. The aim of this study was to understand the impact of schizophrenia and its pharmacological treatment on patients' health-related quality of life (HRQoL) and to explore patient preferences around treatment benefits and side effects.

Patients and Methods: This study employed a mixed methods approach with two stages of recruitment of adult patients in Spain. Stage 1 included qualitative and quantitative elements (including included two validated patient-reported outcome measures: PETiT and EQ-5D-5L) administered in telephone interviews with people with schizophrenia. Stage 2 consisted of a quantitative online survey completed by people with schizophrenia attending outpatient clinics. Responses to quantitative items across both stages were combined for analysis.

Results: Twenty respondents completed the mixed methods interviews (stage 1), and 25 participants completed the online survey (stage 2). Results from stages 1 and 2, showed that participants perceived treatments to have a beneficial impact on controlling their symptoms. However, cognitive side effects were reported to have a detrimental impact on respondents' daily life and were considered a primary reason for treatment cessation in the past. Qualitative findings further showed that most participants hoped future treatments would minimise the impact of cognitive symptoms of schizophrenia.

Conclusion: The findings suggest that patients' expectation around treatment efficacy and their acceptability of treatment side effects may indicate their capacity to maintain long-term treatment adherence. Trade-offs that patients may be willing to make between these components may prove useful to consider in clinical practice to improve treatment adherence and hence treatment effectiveness in people with schizophrenia.

Keywords: schizophrenia, health-related quality of life, treatment burden, preferences

Introduction

Schizophrenia, a chronic psychiatric disorder, is caused by an array of complex genetic and neurobiological factors that influence early brain development.[1] Globally, it is estimated that around 7 per 1000 individuals will develop

Received: 23 October 2024
Accepted: 19 May 2025
Published: 27 August 2025

schizophrenia during their lifetime, with onset of symptoms typically occurring before age 30.[2,3] Schizophrenia is estimated to affect around 24 million people or 1 in 300 people (0.32%) worldwide.[4] Between 1990 and 2019, there was a 65% increase of schizophrenia prevalence (14.2 to 23.6 million) and 37% rise of schizophrenia incidence globally (941,000 to 1.3 million).[5] Epidemiological studies further estimate a mean prevalence in the Spanish population of 3 per 1000 persons per year in men, with this figure slightly lower in women.[6]

The condition is typically characterised by positive, negative, and cognitive symptoms that occur episodically, evolving into cycles of relapses and remissions.[1,7–9] This symptom profile results in a substantial clinical burden and detriments to the health-related quality of life (HRQoL) of both patients and their caregivers.[7,10–14]

In the absence of a cure for schizophrenia, chronic pharmacological management plays a fundamental role in reducing symptoms and the overall burden on patients.[15] Research has shown that the spectrum of first- and second-generation antipsychotics used in clinical practice demonstrate efficacy in positive symptom reduction, with minor differences in efficacy across the available pharmacological treatments.[16] However, there are notable differences in associated side-effects between these antipsychotic treatments.[17]

The severity of side-effects can potentially be one driver of poor treatment adherence,[18] with 74% of patients found to discontinue their pharmacological treatment before 18 months, on average.[18,19] Therefore, the consideration of the patient perspective and preferences in addition to the wider efficacy and side effect profiles of pharmacological treatments is essential to improve the understanding of how patients' experiences of pharmacological treatments impact tolerability and adherence to those treatments, as well as any subsequent impact on HRQoL in schizophrenia.[20,21] The aim of this study was to explore and understand the impact of schizophrenia and its pharmacological treatment on patients' HRQoL, including the benefits and impacts of those treatments, through use of a mixed methods approach.

Materials and Methods

Study Design and Sample

This non-interventional, observational research study was conducted in two stages. Stage 1 (n=20) employed a mixed methods survey with quantitative and qualitative elements, that was administered via semi-structured web-assisted telephone interviews (WATIs). This stage was designed as a pilot phase to test the means of data collection and to establish if any changes in the survey were needed prior to the main recruitment (stage 2). Stage 2 (n=25) was then conducted using only quantitative components from stage 1 as part of an online survey.

This study was conducted in accordance with the Declaration of Helsinki. All participants provided informed consent, including for publication of anonymized responses. The survey included initial screening questions to record participants' eligibility for the study. Study inclusion criteria are listed in Table 1.

Following initial screening, respondents were asked about their sociodemographic background, height, weight and presented with questions relating to their previous experiences of pharmacological treatment(s) for schizophrenia/psychosis, including rankings of treatment benefits and side effects.

Table 1 Inclusion Criteria

Number	Criteria
1	Confirmed diagnosis of schizophrenia or psychosis* by a clinician
2	Adult (>18 years)
3	Not currently experiencing an acute episode§
4	Experience of taking pharmacological treatment for schizophrenia or psychosis* management
5	Not currently enrolled in any clinical trial of investigational medicinal products (cTIMPs)

Notes: *A diagnosis of psychosis may be given by clinicians to avoid intensifying stigmas associated with schizophrenia in young people.[§]Defined as a schizophrenia/psychotic episode within the last 3 months.

In addition, the survey included two validated patient-reported outcome measures (PROMs): the disease-specific PETiT (Personal evaluation of transitions in treatment) questionnaire and the EQ-5D-5L as a generic HRQoL measure. The PETiT is a self-report tool for evaluating quality of life in patients with acute or persistent psychotic disorder.[22] It assesses adherence-related attitude and psychosocial functioning across 29 items across 12 domains. The PETiT total score ranges from 0 to 54 for the Spanish version, with domain scores including social functioning (0–16), cognitive functioning (0–18), medicines adherence (0–12) and activities (0–8), where higher scores denote better HRQoL. The EQ-5D-5L questionnaire includes a descriptive system with five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with five severity levels, and a visual analogue scale (VAS) for patients to rate their health on a scale between 0 and 100.[23] Responses to the EQ-5D-5L questionnaire are used to calculate health-related utility values, where 1 indicates perfect health and 0 death.

For the additional qualitative component in stage 1, participants were asked a series of questions to prompt spontaneous reports of the value they placed on benefits and side effects associated with pharmacological treatments for schizophrenia. A discussion guide including open-ended questions/discussion prompts to encourage spontaneous responses was designed to explore the value participants placed on pharmacological treatment side effects and benefits. The discussion guide covered three areas:

1. Identifying the symptoms that participants experience
2. How previous treatments have impacted those symptoms
3. Which of those impacts are most important to participants

The online survey was programmed using the Qualtrics XMTM[24] platform where all quantitative responses were recorded and stored. The study was reviewed by two independent ethics boards. Ethical approval for stage 1 was obtained on 7th August 2022 from the association of research managers and administrators (ARMA), an independent body in the UK. Review for stage 2 was completed by the hospital ethics board at Gregorio Marañón General University Hospital.

Recruitment and Study Procedure

Participants for stage 1 were recruited by a specialist recruitment agency through digital social media campaigns and an existing health consumer research panel in Spain.[25] One-to-one WATIs were conducted with participants by trained healthcare researchers at the specialist recruitment agency. For stage 2, an online cross-sectional questionnaire was developed, containing only quantitative components of the survey from stage 1. Participants were identified and recruited by medical staff at outpatient clinics in Spain at three university hospitals: Clinic Barcelona Hospital, Virgen del Rocio University Hospital, Príncipe de Asturias University Hospital. Clinic staff received training on consent and survey procedures before the start of stage 2 recruitment. Participants self-completed the survey with staff available to aid, if required. Participants' responses were recorded on the online platform (Qualtrics XM)[24] and were only identifiable by means of a unique, anonymised identification number.

Analysis Procedure

Analysis of Qualitative Data

Qualitative data was analysed using content analysis processes in accordance with best practice guidelines for qualitative interviews in health economics.[26] Transcripts were analysed by an experienced qualitative researcher with a background in health outcomes research and mixed-methods analysis. The coding process used both deductive and iterative elements, beginning with a structured coding framework aligned with the interview guide, which was then adapted as new categories and patterns were identified during the content analysis. The coding framework was reviewed by a second experienced qualitative researcher to enhance rigour and consistency.

All transcripts were first read to establish familiarity with the content. Each transcript was then sequentially coded for each survey item using a flexible grouping process. The coding structure was refined iteratively across transcripts to reflect the frequency and relevance of emerging content. The frequency of each code was counted only in relation to

a single survey item. Irrelevant information, such as moderator explanations, was disregarded. Data were coded using qualitative analysis software (MAXQDA).[27]

All identifying information, such as names and locations, was removed from transcripts prior to analysis to protect participant confidentiality. As such, no investigators or analysts had access to personally identifiable information beyond the direct recruitment contacts.

Analysis of Quantitative Data

Data was pooled from the quantitative components from stage 1 interviews and the survery from stage 2, it was then checked and cleaned prior to all analyses in Stata 17.[28] Quantitative survey data were analysed using standard descriptive methods. Frequencies, simple counts, percentages, means/medians (and distributional statistics such as standard deviation (SD) and interquartile range (IQR)) across all survey items were generated. For data obtained from validated PROMs, the PETiT scale and the EQ-5D-5L, recommended methodological approaches for each instrument were applied to generate scores.[22,29] For the valuation of responses to the EQ-5D-5L questionnaire, the Spanish tariff was used for the study.[30] Exploratory subgroup analysis used a two-sample *t*-test to evaluate the relationship between the reasons for past cessation of treatment (eg, side effects, perceived treatment benefit, treatment burden and who (patient or doctor) decided to stop medication treatment) on current medicines adherence as measured by the PETiT scale.

Results

Respondent Characteristics

Table 2 provides a summary of all participant characteristics. There were proportionally fewer women (44%) in the sample. The mean age of participants was 57.4 years (SD = 14.3). The majority were classified as overweight (66%), based on a BMI >25 calculated from self-reported height and weight, using categories defined by the World Health Organization (WHO). Most participants were also not economically active (81%).

Table 2 Sample Characteristics

	Overall (n=45)	**Phase 1 (n=20)**	**Phase 2 (n=25)**
	Mean (Standard Deviation, Min:Max)	**Mean (Standard Deviation, Min:Max)**	**Mean (Standard Deviation, Min:Max)**
Age (years)	57.4 (11.8, 34:83)	58.4 (11.1, 34:74)	56.6 (12.6, 38:83)
	Count (percent)	**Count (percent)**	**Count (percent)**
Male	25 (56%)	13 (65%)	13 (48%)
Nationality			
Spanish	41 (91%)	19 (95%)	22 (88%)
Non-Spanish, but other European	4 (9%)	1 (5%)	3 (12%)
BMI			
BMI 20-25	14 (31%)	5 (25%)	9 (32%)
BMI 25-29	18 (40%)	9 (45%)	9 (32%)
BMI 30 and above	18 (40%)	6 (30%)	7 (28%)
Geographical area			
Urban	40 (88%)	16 (80%)	24 (96%)
Rural	5 (12%)	4 (20%)	1 (4%)

(*Continued*)

Table 2 (Continued).

	Overall (n=45)	Phase 1 (n=20)	Phase 2 (n=25)
	Mean (Standard Deviation, Min:Max)	**Mean (Standard Deviation, Min:Max)**	**Mean (Standard Deviation, Min:Max)**
Education			
Primary school	7 (16%)	3 (15%)	4 (16%)
Secondary school	17 (38%)	8 (40%)	9 (36%)
Higher secondary/university preparation	4 (9%)	1 (5%)	3 (12%)
University	6 (13%)	1 (5%)	5 (20%)
Vocational training	11 (24%)	7 (35%)	4 (16%)
Economic activity			
Working full time	6 (13%)	2 (10%)	4 (16%)
Working part time	2 (4%)	1 (5%)	1(4%)
Student	6 (13%)	3 (15%)	3 (12%)
Retired	3 (7%)	3 (15%)	
Unemployed	6 (13%)	2 (10%)	4 (16%)
Permanent disability/subsidy	20 (44%)	8 (40%)	12 (48%)
Other	2 (4%)	1 (5%)	1 (4%)

Qualitative Results

Sample

Nineteen of the 20 qualitative interview transcripts were included for analysis. One transcript was excluded as the interview deviated significantly from the interview guide. Response rates for analysed survey items ranged from seven to 19 respondents, as some participants did not provide answers to those items, or they were not asked by the interview moderator. In 10 of the 19 analysed transcripts, respondents had difficulty understanding or misinterpreted questions. Three participants had someone with them during the interview to help them, by explaining specific questions or the general purpose of the interview. Full qualitative responses are available in supplementary materials and proportions of responses to interview questions available in Tables S1-S10).

Symptoms Experienced

In total 53 symptoms were reported by 19 participants. The most commonly reported symptoms were "delusions/paranoia" reported by 14 respondents, followed by "hallucinations" (n=9) and "anxiety" (n=8). The most severe symptom at its worst reported by participants was experiencing "delusions" (n=6) followed by "hallucinations" (n= 4).

Impact of Treatment

Participants described the impact of treatments on their symptoms, their daily function and quality of life. The most reported impact on symptoms experienced was a reduction in hallucinations (n=5), followed by "feeling more stable/calmer" (n=4), "positive influence" (n=3), and "increased drowsiness" (n=3).

Participants reported a variety of benefits (n=9) from receiving pharmacological treatments for their schizophrenia. Being "more sociable/better relationships with people" (n=2) and more "lucid/clearer head" (n=2) were the most reported benefits. Two participants reported that their medication increased their ability to engage in everyday activities, such "taking a shower everyday" and "finding it easier to read". The ability to control weight was considered important by 9 out of 18 respondents. Although important, controlling the effects of schizophrenia took preference for one participant.

It is important for me. Stabilizing my head comes first and takes priority over my body, but I do mind putting on weight. (Interview 15)

Improvements in cognition (n=7) such as "better concentration" and "feeling more alert" were the most reported items where participants hoped future treatments would be improved, followed by items for "more satisfying sex" (n=4) and 'reduced auditory hallucination's (n=3). Three respondents reported that they were happy with their current treatment and did not suggest areas that future treatment might improve.

Quantitative Results

Figure 1 shows the frequencies of experienced treatment benefits and side effects in the survey. The most frequently reported treatment benefit was "decreases in delusions and usual beliefs" (n=32). This was followed by "decreases restlessness" (n=28) and "decreases mistrust/hostility" and "helps me think clearer" (n=27).

The least frequently experienced treatment benefits were "increases my interest in socialising", "helps me to feel or control my emotions", and "decreases anxiety", "irritability" and "interest and energy for life".

Among the available responses for experienced side effects (Figure 2), the most frequently experienced side effects were "feeling tired" (n=36), "difficulties in concentrating" and "passing urine frequently" (n=33), and "thirsty/dry mouth" and "difficulty concentrating" (n=31). The least frequently experienced side effects were "vertigo" (n=15) and "loss of sex drive" (n=18).

Figure 3 shows the summary statistics of the importance scores attached to both experienced and unexperienced treatment benefits on a scale from 1 (not important) to 10 (extremely important). The highest mean score for experienced benefits was attached to "decreases anxiety" (mean=9.2, SD=1.4). This was followed by "decreases in hallucinations" (mean=8.7, SD=1.7), and a "decrease in restlessness" (mean=8.5, SD=1.6). The highest mean score for benefits that participants had not previously experienced was attached to "decreases mistrust/hostility" (mean=7.1, SD=2.7). This was followed by "helps me to feel or control my emotions" (mean=6.6, SD=3.2) and "increases interest and energy for life" (mean=6.6, SD=3.18).

Figure 4 shows the summary statistics of the importance scores attached to both experienced and unexperienced side effects. The highest mean score for experienced side effects was attached to "feel like a zombie" (mean=8.6, SD=2.2). This was followed by "restlessness" (mean=8.5, SD=1.7), and "memory issues" (mean=8.3, SD=1.9). The three highest mean scores for unexperienced side effects slightly deviated from this pattern, here "feeling tired" (mean=6.7, SD=3.4)

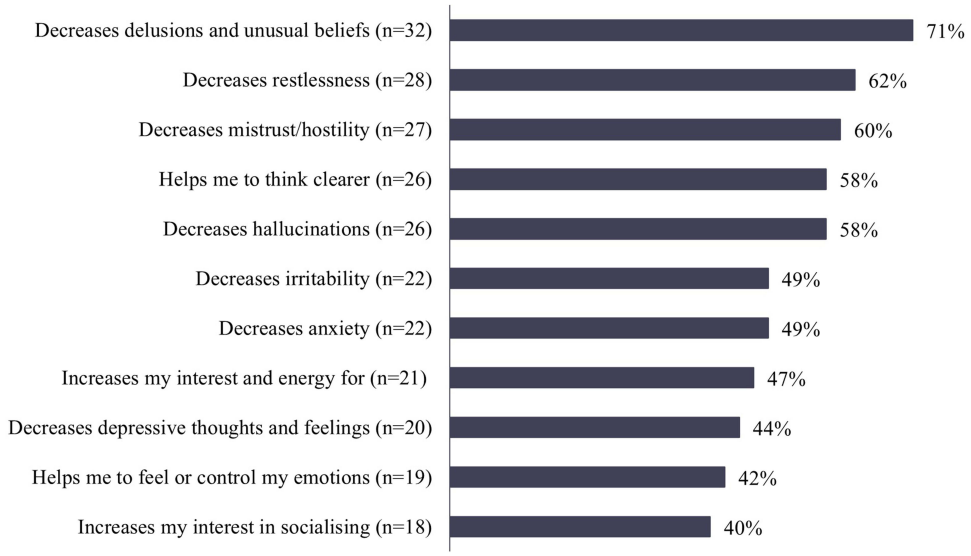

Figure 1 Percentage of respondents experienced treatment benefits.

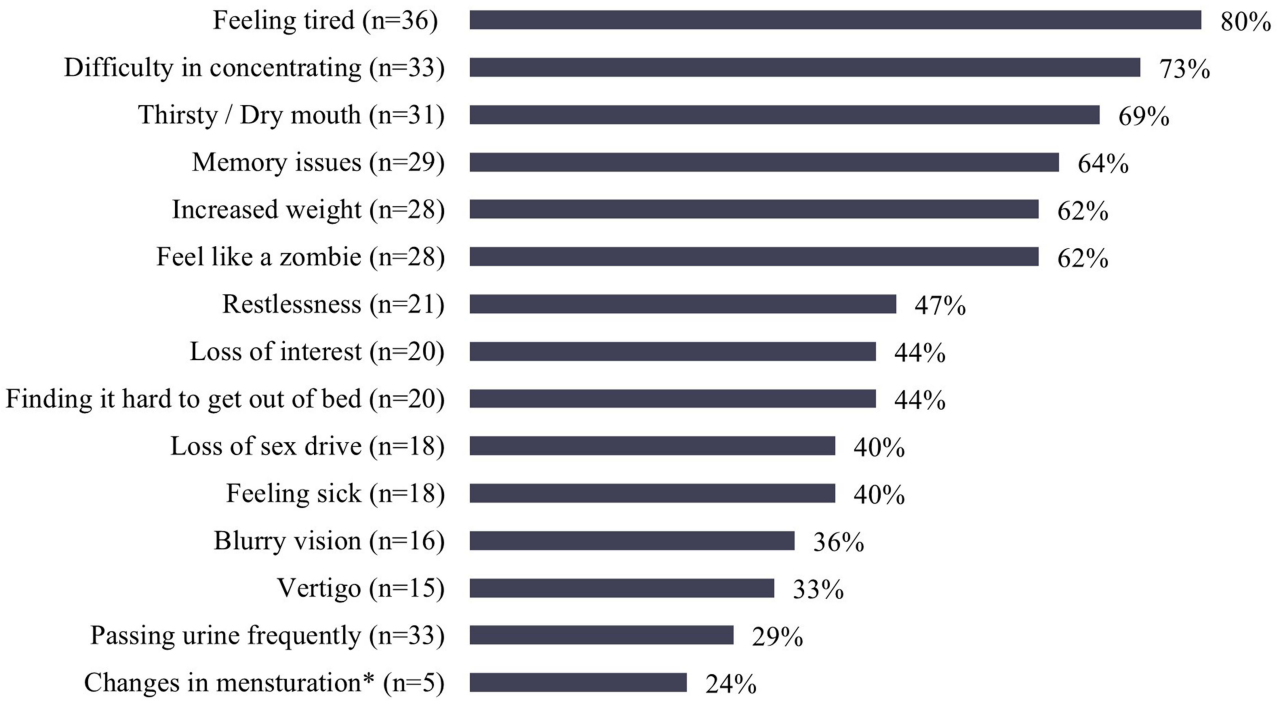

Figure 2 Percentage of respondents that experienced side effects.

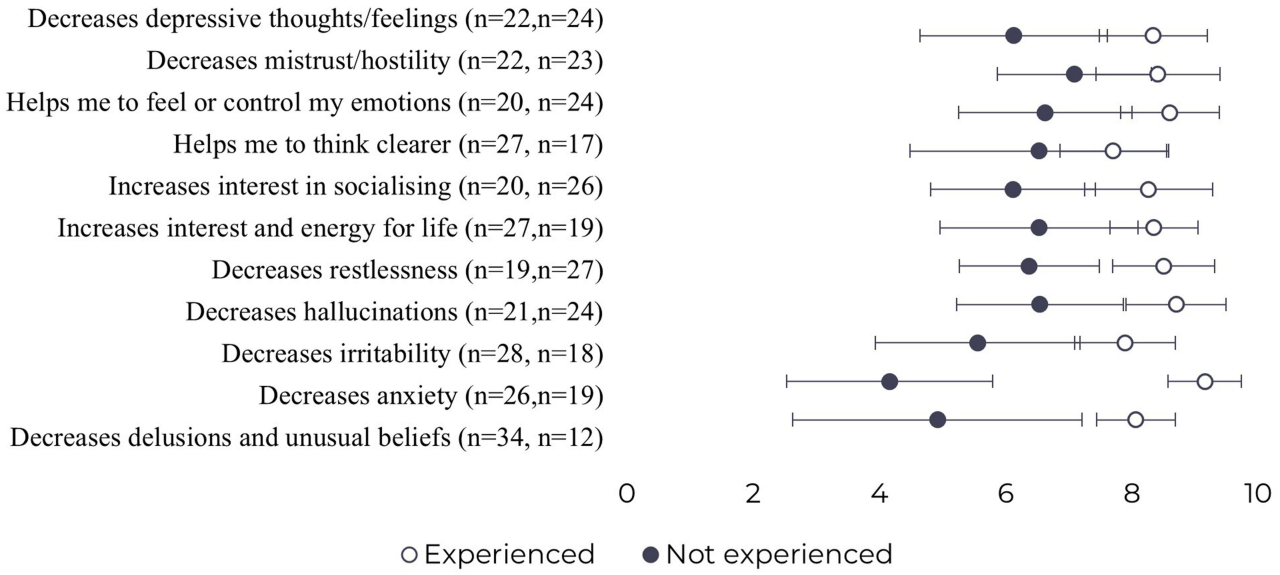

Figure 3 The importance of experienced and unexperienced treatment benefits (mean rating and confidence intervals). Score range: 0–10. A score of 10 represents high importance while a score of 0 represents low importance.

was ranked second to "feels like a zombie" (mean=6.9, SD=4.1) and followed by "memory issues" (mean=6.4, SD=3.00).

The majority of respondents 61% stated that they had ceased taking medication at one point in time. The most frequently stated reasons for cessation were that the "medication had caused unpleasant side effects" and the "patient decided to stop taking it" (Figure 5).

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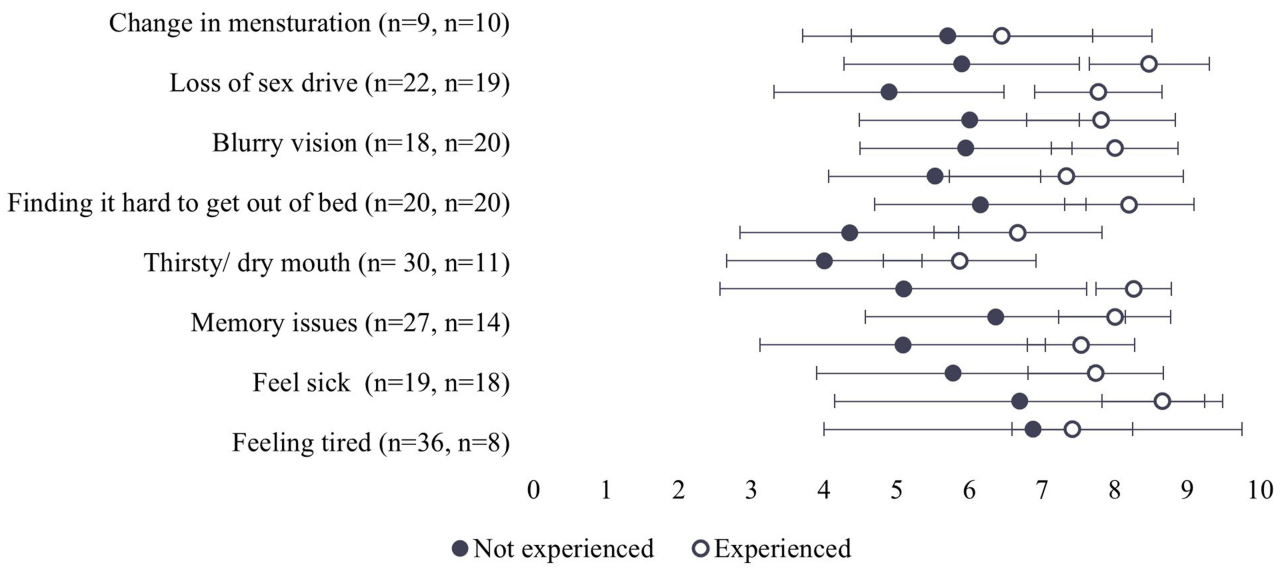

Figure 4 The importance of experienced and unexperienced side-effects (mean ratings and confidence intervals). Score range: 0–10. A score of 10 represents high importance while a score of 0 represents low importance.

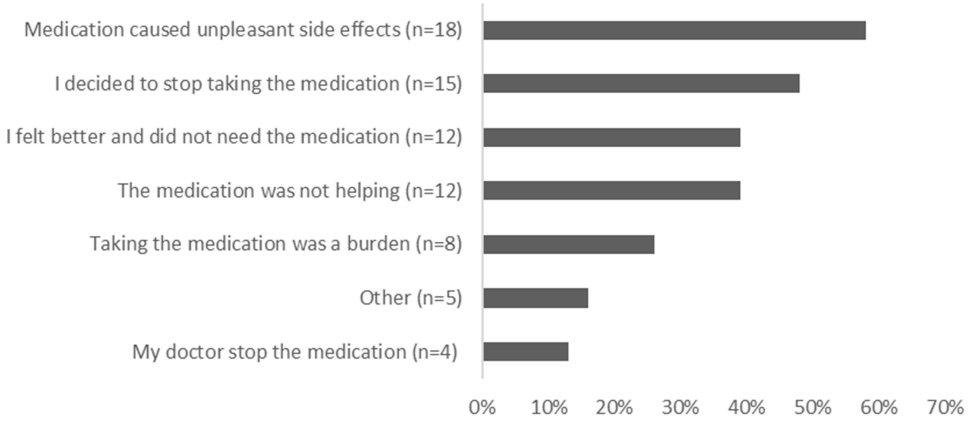

Figure 5 Reasons for respondents to stop medications.

The mean total PETiT scale score of respondents in this study was 35.47 (SD=11.88). The other domains are highlighted in Table 3 with the maximum range detailed for each component. Figure 6 details the distribution of the total PETiT and the individual domain scores, and full proportions of responses available in Figure S1.

Table 3 Personal Evaluation of Transitions in Treatment (PETiT) by Domains

PETiT (Score Range)	Frequency	Mean	SD	Min	Max
Total score (0–58)	45	35.47	11.88	13	55
Social function (8 items, 0–16)	45	9.89	3.63	2	16
Cognitive function (9 items, 0–18)	45	9.09	3.72	2	15
Medicine adherence (6 items, 0–12)	45	8.96	2.84	1	12
Activities (4 items, 0–8)	45	5.29	2.15	1	8

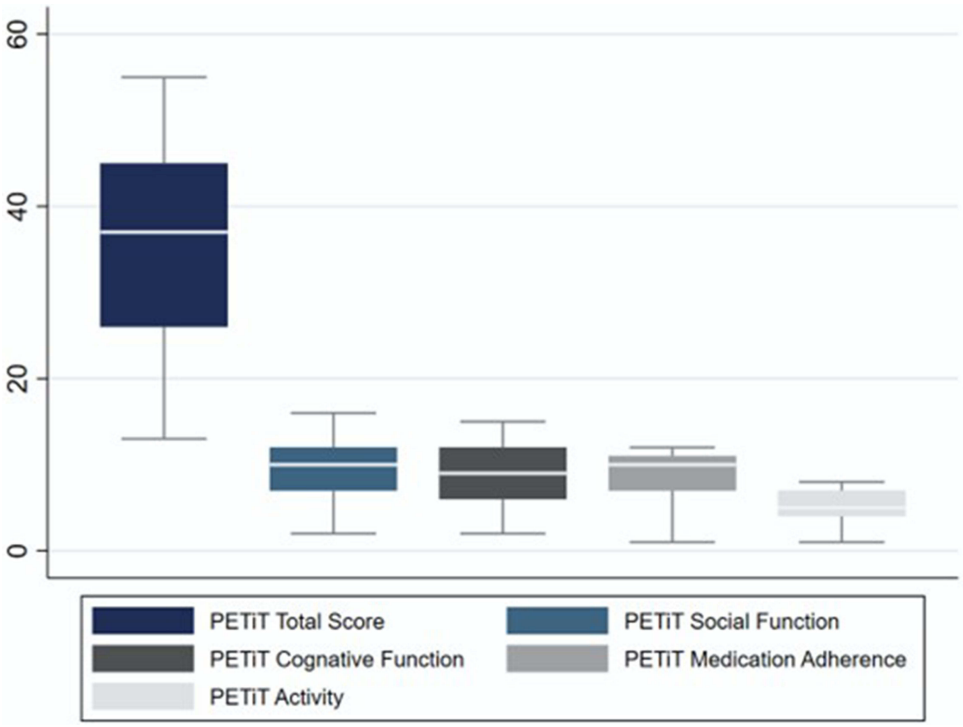

Figure 6 Boxplots of PETiT total and domain scores. PETiT scores by domain, with higher scores indicating better outcomes in each domain.

Subgroup analyses examined treatment adherence as measured by the PETiT scale for those participants who stopped their medication use, accounting for reasons for discontinuation (Table 4). Statistically significant lower scores were observed for those who experienced unpleasant side effects (−2.51, $p < 0.05$), where the persons with schizophrenia perceived the medication as not helping (as measured on the PETiT scale (−2.78, $p < 0.05$) and where the medication was considered a burden to take (−2.23, $p < 0.05$). One explanation for this finding may be that participants who perceived a better experience with pharmacological treatments had been more adherent to treatments compared to those who did not.

The overall mean EQ-5D-5L utility score was 0.78 (SD 0.17) with a range of 0.36 to 1, with a mean EQ-VAS score of 62 (SD 20) out of a range between 0–100, where a score of 100 indicates perfect health and 0 death. Figure 7 graphically depicts the EQ-5D-5L distribution of EQ-5D-5L utility values within the sample. Full EQ-5D-5L responses are available in Figure S2.

Table 4 Subgroup Analysis (Discontinued Treatment) of the Medication Adherence Scores of the PETiT Measure

Reasons for Stopping Treatment	Difference in Medication Adherence Score	P-value
Medication caused unpleasant side effects	−2.51	<0.05
Medication was not helping	− 2.78	<0.05
I felt better and did not need the medication	−0.96	0.32
Taking the medication was a burden to me	−2.23	<0.05
My doctor stopped the medication	1.15	0.44
I decided to stop taking the medication	−0.933	0.30

Note: $p<0.05$ was statistically significant at 5%.

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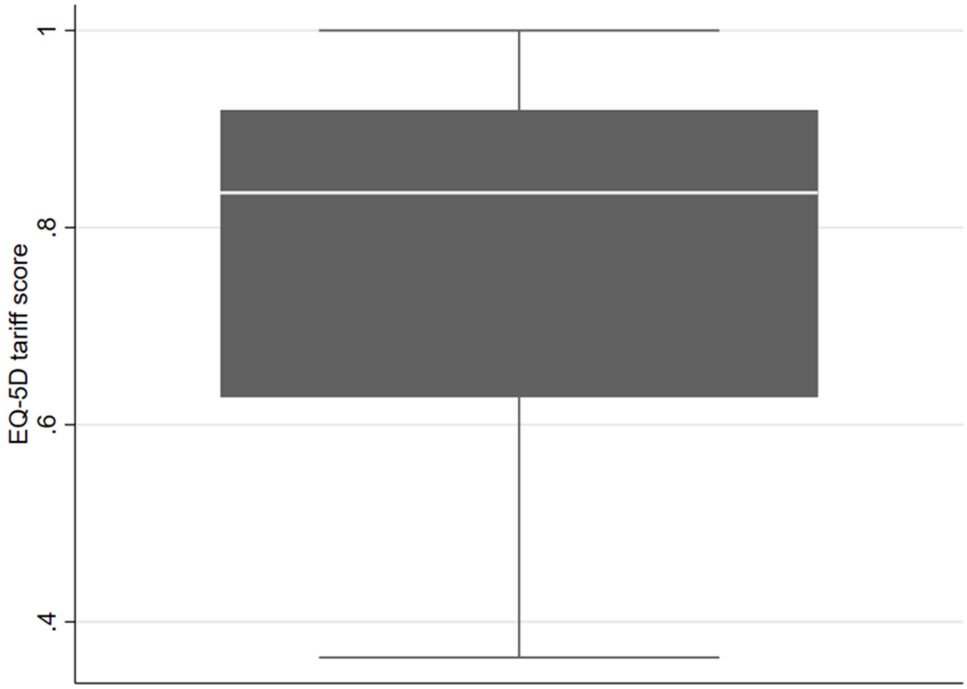

Figure 7 Boxplot of EQ-5D-5L score. Distribution of EQ-5D tariff scores among participants, with higher scores indicating higher health-related quality of life.

Discussion

This study demonstrates that most patients with schizophrenia do receive benefits from their medication with regards to controlling positive symptoms, alongside the possibility of HRQoL gains within their wider lives. However, there was a notable proportion of patients that experience detrimental clinical and HRQoL impacts as a side effect of the medication. As such, the findings provide valuable insights into patient perspectives around pharmacological treatments of schizophrenia and the subsequent impact on HRQoL. The qualitative component of included in the mixed methods (stage 1) in this study offers a more contextualized understanding of patient experiences, with each method contributing complementary insights.

Secondary findings from this study are consistent with established research showing an increased risk of obesity for people with schizophrenia.[31] This is shown by the sub-group analysis finding of participants with a high BMI who reported gaining weight related to their treatment. The increased mortality associated with obesity is an additional issue that impacts people with schizophrenia, supported by the current responses showing that the ability to control weight was an important factor when considering pharmacological treatments. Pharmacological and non-pharmacological interventions that address medication-related weight gain could have a consequential impact on quality of life by reducing the risks associated with comorbid obesity and mitigating the psychological impact of weight gain on negative body image and self-esteem.[32]

The core findings highlight both the positive impact of pharmacological interventions for schizophrenia and the treatment burden associated with medication. For example, participants reported that treatments helped reduce the symptoms of schizophrenia, such as reducing hallucinations/delusional beliefs and anxiety, but can also result in feeling tired and sedation, as well as weight gain. Results from the qualitative items support this contrasting perspective of treatment benefits and side effects, as well as identifying a broader impact on participants' lives, including improved interpersonal relationships, feelings of increased stability and more independence. Items relating to participants' functional capacity (usual activities, self-care and mobility) on the EQ-5D-5L showed a high proportion of responses as "no problems". Such responses suggest an improved capacity for participants when the positive symptoms of their condition are managed with medication. As such, support is offered for previous findings demonstrating that patients with fewer symptoms and improved daily functioning tend to have a more positive attitude towards treatment adherence.[33]

The primary function of pharmacological treatments for schizophrenia is to reduce the symptoms of the condition and people with schizophrenia are generally positive about the impact of treatments in the short term and during acute episodes. However, to maintain long-term medication adherence, people with schizophrenia need the opportunity to engage in a process of functional and social recovery alongside a perception of effectiveness the side effect profile of currently available treatments may impede these processes.[34] Our findings support this notion, demonstrating that side effects from pharmacological treatments relating to "weight gain", "fatigue", 'vitality' were found to have a substantial impact on patients' experiences. Such impacts can ultimately influence a patient's medication adherence, as supported by the current findings from the quantitative survey, with discontinuation recognised as a risk factor of relapse and poorer outcomes.[35–37] A key influence on medication adherence in this study was patients' attitudes and beliefs regarding the impact of treatment. For example, we observed a statistically significant relationship between the patients who perceived their treatments not to be helping their condition and adherence (on the PETiT), suggesting a poor perception of medication effectiveness to be a contributing factor to reduced medication adherence, which is consistent with previous studies.[38,39]

Similarly, cognitive side effects such as 'feeling like a zombie' and 'memory/concentration issues' were the most frequently identified across both qualitative and quantitative items. These side effects impacted participants' daily functioning and capacity to work. Additionally, memory issues associated with treatment could directly affect adherence as people may forget to take their medication, and lead to poor medication adherence. Overall, cognitive side effects were identified as the area where most participants hoped future treatments would improve. There is therefore an apparent unmet need in existing treatments to address the cognitive side effects that represent concern for patients and clinicians. While controlling for the primary symptoms, such as delusions and hallucinations, they could exacerbate the impact on cognition already associated with the condition.[40] This dual burden can likely severely impede daily functioning, cognitive performance and quality of life.

The burden associated with treatment was evident in the large proportion of participants who reported that they had ceased taking their medication as a result of side effects.[41] Side effects such as lethargy and weight gain can affect patients' daily functioning and capacity to engage effectively in recovery, including a potential bidirectional relationship between weight gain and poorer cognitive functioning.[42] The cumulative impact of side effects over time is likely to lead to treatment nonadherence and the associated increase in risk for relapse.[43] In this study, the average time since diagnosis for participants was over 10 years, suggesting that participants have been on long-term treatments and, therefore, the cumulative effect of long-term side effects most likely impacted adherence and patient expectations around treatment effectiveness. Findings from this study and recently published research suggest that reducing the treatment burden associated with currently available treatments could reduce barriers to long-term treatment adherence.[44]

Together, our findings describe the detriments and importance in managing pharmacological treatment side effects such as lethargy, weight gain, and cognitive side effects, as well as the hope for improvement in these areas with future treatments. Despite these side effects, patients are potentially willing to accept trade-offs to gain treatment effectiveness with regards to the positive symptoms of schizophrenia. It is therefore likely that such acceptance is governed by individual patient preferences influenced by context, circumstances, previous treatment experiences, and clinical advice.[45,46]

In the current landscape of schizophrenia treatments, a variety of pharmacological options are available. Recent advancements have demonstrated comparable efficacy, with the added benefit of improved metabolic profiles.[16,47] Additionally, there is emerging literature suggesting potential of lurasidone hydrochloride.[48] Additionally, TAAR1 agonists, which show promise in targeting cognitive and negative symptoms of schizophrenia, potentially addressing key concerns identified by patients in this study.[49]

While this study focused on treatment-related factors such as weight gain and lethargy, it is important to acknowledge that broader social determinants (access to medication, socioeconomic status, and healthcare inequality) are also likely to play a significant role in treatment adherence. This reflects an emerging understanding of adherence as a multidimensional issue, and recent reviews have begun to explore the biological and systemic impact of social determinants on treatment engagement in schizophrenia.[50]

To fully understand the scope of patient preferences regarding expected treatment benefits, acceptable side effects, and any acceptable trade-offs between these factors, there is an apparent need for larger scale research beyond the current study's geographic context that can provide more statistically robust results from a larger, representative international sample that would also allow for further sub-group analyses. Such works should aim to provide comprehensive insights into recognising these patient preferences, acknowledging the impact of these factors on treatment adherence, and with the ultimate aim of optimising this adherence and therefore the effectiveness of pharmacological treatments for schizophrenia.

Study Limitations

This study is not without limitations. While the presented results provide valuable insights into people with schizophrenia's experience of pharmacological interventions, it does not account for the potential impact of alternative non-pharmacological treatments, such as psychological interventions.

This study achieved a relatively small sample size in stage 2, limiting statistical testing of quantitative data, in particular for sub group analysis and robustness of conclusions that could be drawn from the available responses.[51] Generalisability of the findings is limited by as the study was conducted solely in Spain, and results may not fully reflect patient experiences or treatment dynamics in other healthcare systems or cultural contexts. However, the use of qualitative methods alongside the quantitative methods allowed for a magnifying of meaningful concepts such as the importance of treatment benefits and side effects identified by patients. The use of both methodologies together was able to demonstrate similar conceptual trends across the findings, therefore strengthening conclusions compared to a single-method approach, using quantitative and qualitative methodologies in isolation. It would be beneficial to the research literature to further confirm these findings in a larger quantitative study to reduce the uncertainty around the current estimates and determine how preferences might differ across a wider patient population with varying experiences around previous treatments.

Due to the observational study design, no causal relationship can be inferred.[52] The exploratory analysis of both qualitative and quantitative data was mitigated as participants for this study were recruited from both clinical and community settings. This approach allowed for a diverse sample to be included in the analysis, enabling the capturing of a broader spectrum of experiences from people with the condition, enhancing the generalisability of the findings.

Conclusion

This multi-stage study offers insights into patient perspectives around pharmacological treatments of schizophrenia and the subsequent impact on patients' HRQoL. The findings highlight a dual impact of pharmacological interventions, including a beneficial effect on positive symptoms of schizophrenia, yet also a substantial burden associated with treatment side effects. Demonstrated is the presence and perceived importance of managing weight gain, lethargy, cognitive detriments, and reduced functional capacity. Such impacts can likely influence long-term clinical outcomes through interactions with treatment satisfaction and adherence. Future research and clinical practice could benefit from acknowledging this influence on adherence and the patient preferences driving that influence, including any potential trade-offs patients would be willing to make between pharmacological treatment benefits and side effects.

Acknowledgments

IB would like to acknowledge Pons Bartran legacy (FCRB_IPB2-2023) for her support. This study was sponsored by Angelini Pharma Espana. The abstract of this paper was presented at the 36th ECNP Congress 2023 (Barcelona 7-10 October) as a poster presentation with interim findings. The poster's abstract was published in Abstracts of the 36th ECNP Congress 2023 in Neuroscience applied (Vol2, Supplement 2): https://doi.org/10.1016/j.nsa.2023.103062.

Funding

CA has been supported by the Spanish Ministry of Science and Innovation, Instituto de Salud Carlos III (ISCIII), co-financed by the European Union, ERDF Funds from the European Commission, "A way of making Europe", financed by the European Union - NextGenerationEU (PMP21/00051), PI19/01024, PI22-01824.CIBERSAM, Madrid Regional

Government (B2017/BMD-3740 AGES-CM-2), European Union Structural Funds, European Union Seventh Framework Program, European Union H2020 Program under the Innovative Medicines Initiative 2 Joint Undertaking: Project PRISM-2 (Grant agreement No.101034377), Project AIMS-2-TRIALS (Grant agreement No 777394), Horizon Europe, the National Institute of Mental Health of the National Institutes of Health under Award Number 1U01MH124639-01 (Project ProNET) and Award Number 5P50MH115846-03 (project FEP-CAUSAL), Fundación Familia Alonso, and Fundación Alicia Koplowitz. IB has been supported by the Spanish Ministry of Science and Innovation, Instituto de Salud Carlos III (PI21/0391), co-financed by the European Union, Drugs National Plan (2022I053) and Fundación Alicia Koplowitz.

Disclosure

EV has received grants and served as consultant, advisor or CME speaker for the following entities: AB-Biotics, AbbVie, Adamed, Alcediag, Abbott, Angelini, Biogen, Beckley-Psytech, Biohaven, Boehringer-Ingelheim, Cambridge University Press, Casen-Recordati, Celon Pharma, Compass, Dainippon Sumitomo Pharma, Elsevier, Ethypharm, Ferrer, Gedeon Richter, GH Research, Glaxo-Smith Kline, HMNC, Idorsia, Johnson & Johnson, Lundbeck, Luye Pharma, Medincell, Merck, Newron, Novartis, Orion Corporation, Organon, Otsuka, Roche, Rovi, Sage, Sanofi-Aventis, Sunovion, Takeda, Teva, and Viatris, outside the submitted work. CA has been a consultant to or has received honoraria or grants from Abbot, Acadia, Ambrosetti, Angelini, Biogen, Boehringer, Gedeon Richter, Janssen Cilag, Lundbeck, Medscape, Menarini, Minerva, Otsuka, Pfizer, Roche, Sage, Servier, Shire, Schering Plough, Sumitomo Dainippon Pharma, Sunovion, Takeda and Teva. CGR has received grants from/or served as consultant, advisor or speaker for the following entities Adamed, Angelini, Casen-Recordati, Janssen-Cilag, Lunbeck and Newron. IB has received honoraria or support to attend conferences from Angelini and Lundbeck. GL reports personal fees from Angelini Pharma España, during the conduct of the study; personal fees and/or non-financial support from Lundbeck, Adamed, Viatris, Johnson & Johnson, and Otsuka, outside the submitted work. FB reports grants from Angelini Pharma, during the conduct of the study. IGI and EAB are employees of Angelini Pharma. The authors report no other conflicts of interest in this work.

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