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Health-related quality of life in patients treated with atypical antipsychotics

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Objective: To assess health-related quality of life and associated factors in patients treated with atypical antipsychotics, as well as to determine utility values using the EuroQol-5D-3L instrument.
Methods: A cross-sectional study was conducted at a state-run pharmacy in the Brazilian National Health System. Individuals were included if they were using a single atypical antipsychotic and completed the EuroQol-5D-3L. Sociodemographic, behavioral, and clinical data were collected. The dependent variable was the EuroQol-5D-3L utility score. Associations between the independent variables and the dependent variable were analyzed in a multiple linear regression model.
Results: A total of 394 patients were included, and their mean utility score was 0.664 ± 0.232. Patients treated with clozapine had the highest mean score (0.762 [0.202]), followed by olanzapine (0.687 [0.230]), risperidone (0.630 [0.252]), ziprasidone (0.622 [0.234]), and quetiapine (0.620 [0.243]). The following variables were related to higher utility scores: income, employment, clozapine use, no illicit psychoactive substance use, no suicide attempts, and no comorbidities.
Conclusion: Evaluating health-related quality of life differences in the available atypical antipsychotics can facilitate the choice of treatment, improve health outcomes, and ensure rational prescriptions.

Keywords: Quality of life; antipsychotic agents; mental disorders

Introduction

Quality of life (QoL) is a multidimensional concept that was first considered a complement to traditional concepts of health and functionality. An ideal and complete measurement of health would assess an individual's physical, functional, social, and psychological health.[1] This concept has become more prominent in health care as new technologies have extended life, sometimes at the expense of QoL, or have improved QoL without extending life. Therefore, measuring outcomes such as death rates and life expectancy alone is no longer sufficient, and the need to assess health-related QoL (HRQoL) has emerged.[2] HRQoL is a measure of perceived physical and mental health, including functional status, social support, and socioeconomic status, as part of the multidimensional construct of health status.[3]

The practice of evaluating HRQoL in chronic diseases has become well established, and it has also gained prominence in severe mental illness since the deinstitutionalization and reintegration of psychiatric patients in the community.[4] Such an evaluation is essential for these patients because it measures not only the direct benefits (i.e., reduced psychotic symptoms) of antipsychotics,[5] but other related factors in their lives.[6] New antipsychotic agents, although more effective, also have a range of adverse effects[7,8] that could negatively affect health outcomes such as QoL. Since the focus of atypical antipsychotic treatment is not only symptom reduction, but improvement of QoL,[8] it is important to evaluate this outcome.

Different instruments for measuring HRQoL have been developed and/or validated in Brazil,[9] including the EuroQol-5D-3L (EQ-5D-3L).[10] The EQ-5D-3L is a generic HRQoL measurement instrument that is divided into two stages: a five-dimension descriptive system and a visual analog scale. The EQ-5D-3L's descriptive system includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of the five dimensions has three levels: no problems, some problems, and extreme problems. A five-digit number, generated from the individual's self-assessment in the five dimensions, describes the respondent's health status, and this number is referred to as the utility score.[10]

The Brazilian Unified Health System provides drug treatments, including atypical antipsychotics for patients with mental disorders.[11,12] The use of such drugs must comply with criteria established in the Brazilian Ministry of Health's Clinical Protocol and Therapeutic Guidelines for rational drug therapy.[11-13]

The therapeutic guidelines indicate atypical antipsychotics for schizophrenia, schizoaffective disorder, and type 1 bipolar disorder. For schizophrenia and schizoaffective disorder, the available atypical antipsychotics include clozapine, risperidone, ziprasidone, quetiapine, and olanzapine. Except for clozapine, there is no preferred order of treatment with these atypical antipsychotics.[11,12] For bipolar disorder type I, the protocol describes a sequence of antipsychotics for mania treatment: risperidone, followed by olanzapine, haloperidol, and quetiapine, if necessary.[13] Clozapine is indicated in the three protocols when other antipsychotics are ineffective.[11-13]

HRQoL is a useful tool in psychiatry since it evaluates the impact of mental illness and the possible benefits of therapeutic interventions.[14] This study aims to evaluate HRQoL and associated factors in patients with mental disorders who are being treated with atypical antipsychotics, as well to calculate their utility scores. The results of this study could lead to further research and could help determine which drugs have the greatest clinical benefits for QoL in people with psychotic disorders.

Methods

This study is part of the Schizophrenia Economics and Effectiveness Assessment (SCHEEA) project[15] of the Universidade Federal de Minas Gerais, Brazil. In this project, patients were recruited from a state pharmacy of the Specialized Component of Pharmaceutical Service (Componente Especializado da Assistência Farmacêutica [CEAF]) in Belo Horizonte, state of Minas Gerais. Individuals using only one atypical antipsychotic (clozapine, olanzapine, ziprasidone, quetiapine, or risperidone) and who completed the QoL questionnaire (EQ-5D-3L) were eligible for inclusion. Before their antipsychotic drugs were dispensed, the patients were invited to participate in the study, and those who agreed to participate were referred for face-to-face interviews. Along with the HRQoL assessment, a structured questionnaire was used to collect data on sociodemographics, medication use, and behavioral and clinical variables. The study was conducted between September 2017 and March 2018.

The sample size was calculated to compare HRQoL among patients treated with different drugs. A mean of 5,800 patients used the selected drugs at the CEAF pharmacy per month (according to the means from June and July 2017). The primary outcome in this study was the EQ-5D-3L utility score, which ranges from 0 to 1. Since 0 is related to death and 1 to better health, the amplitude was considered 0.9 (range 0.05 to 0.95). Considering 6 standard deviations (SD) (with normal distribution), the sample SD was 0.15 (0.9/6). We expected to detect a minimum difference between the mean utility values between treatments of at least 0.1, with a 5% significance level and 90% power. Using analysis of variance (ANOVA), we calculated n=71 patients per treatment type.

HRQoL was assessed using the EQ-5D-3L, an instrument developed by the EuroQol Group that has been validated for Brazilian Portuguese.[16] The EQ-5D-3L is a generic questionnaire that assesses QoL by identifying 243 possible states of health based on five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Three alternatives exist for each dimension: no problems, some problems, and severe problems. The possible health states range from 11111 (no problems in any dimension) to 33333 (severe problems in all dimensions), and each state has a corresponding utility score (registration ID: L-29510).[17]

We compared the percentage of patients in our sample who had moderate or extreme problems in the EQ-5D-3L dimensions with scores from the general population of the state of Minas Gerais found by Andrade & Noronha.[10] These authors interviewed 3,363 individuals from different locations, which were representative of the entire geographic area of the state. Comparing these two samples highlighted the differences between them.

In our study, the dependent variable was the utility score for patients treated with atypical antipsychotics. The independent variables were: sociodemographic characteristics (gender, age, marital status, education level, employment status, and race),[18-21] clinical characteristics (comorbidities such as hypertension, diabetes, heart disease, human immunodeficiency virus, thyroid dysfunction, respiratory diseases, chronic liver diseases, and chronic kidney diseases),[22] and behavioral characteristics (psychoactive substance use, suicide attempts, and use of mental health services).[23,24]

The statistical analysis included absolute and relative frequency for qualitative variables and measures of central tendency (mean and median) and variability (SD and coefficient of variation) for quantitative variables. A normality test (Kolmogorov-Smirnov) was used to verify Gaussian distribution. For nonparametric distribution (according to the Mann Whitney U and Kruskal-Wallis test), ANOVA was used to verify differences in mean utility scores among treatment groups. Dunn's test was used for multiple comparisons.

Associations among independent variables (gender, age, marital status, education level, and employment status), clinical variables (comorbid diseases), and HRQoL (utility scores) were evaluated in univariate ANOVA with a significance level < 10%. The identified variables were included in a multiple linear regression model with a significance level of 0.05. Statistical analyses were performed in SPSS version 22.0.

Ethics statement

Research personnel at the recruitment sites provided information about the study protocol. All individuals who expressed interest in participating received a full explanation of the study procedures and provided written informed consent. The study protocol and the interview procedures were approved by the relevant UFMG ethics committee (CAAE 57420616.9.0000.5149).

Results

The majority of the 394 interviewed patients were men (54.8%), except in the ziprasidone and quetiapine groups. The predominant age range was 30-59 years (80.5%). The clozapine group had the highest percentage of young adults (32.3%), while the quetiapine group had the highest percentage of older adults (19.4%) (Table 1).

Of the patients in our sample, 32.2% had completed some higher education and 16.5% were employed at the time of the interview. The risperidone group had the lowest percentages among all groups, with 11.1% having completed some higher education and 8.9% currently employed. Concerning marital status, 77.7% of the patients did not have a partner, and the quetiapine group had the highest percentage of patients with a partner (27.8%). Regarding self-reported race, 55.1% of were mixed race or Afro-Brazilian. The ziprasidone group had the highest percentage of Afro-Brazilians and individuals of mixed race (62%), while the quetiapine group had the highest percentage of Caucasians and Asians (47.2%).

The clinical and behavioral characteristics of patients using atypical antipsychotics are shown in Table 2. In total, 47.5% reported no comorbidities, 30.7% reported one, and 19.5% reported two or more. The olanzapine group had the highest percentage who reported no comorbidities (50.4%), while the risperidone group had the highest percentage of those who reported two or more associated diseases (24.4%). A total of 34.5% of the patients reported having attempted suicide. The risperidone group had the highest percentage of patients with no suicide attempts (77.8%), while the ziprasidone group had the highest percentage of patients who had attempted it three or more times (28.2%). A total of 21.8% of the patients reported having used illicit psychoactive substances at some point in their lives. The ziprasidone group had the highest percentage of patients who had never used them (83.1%), while the risperidone group had the highest percentage of those who had used three or more types (8.7%). Data was collected on the use of psychosocial care centers (Centros de Atenção Psicossocial [CAPS]) and mental health referral centers (Centros de Referência em Saúde Mental [CERSAM]), with 53.3% of the patients reporting that they had used them. The quetiapine group had the highest percentage of patients who reported using all types of mental health services.

Responses for each EQ-5D-3L dimension differed according to antipsychotic type (Table 3). The olanzapine,

Table 1 Sociodemographic characteristics of patients treated with atypical antipsychotics provided by the CEAF pharmacy in the state of Minas Gerais, 2017-2018[15]

	Clozapine	Olanzapine	Quetiapine	Risperidone	Ziprasidone	Global
Gender						
Female	18 (27.7)	53 (37.6)	43 (59.7)	15 (33.3)	49 (69.0)	178 (45.2)
Male	47 (72.3)	88 (62.4)	29 (40.3)	30 (66.7)	22 (31.0)	216 (54.8)
Age, years						
18-29	2 (3.1)	8 (5.7)	3 (4.2)	7 (15.6)	3 (4.2)	23 (5.8)
30-39	19 (29.2)	25 (17.7)	12 (16.7)	10 (22.2)	17 (23.9)	83 (21.1)
40-49	22 (33.8)	42 (29.1)	23 (31.9)	14 (31.1)	21 (29.6)	121 (30.7)
50-59	17 (26.2)	47 (33.3)	20 (27.8)	9 (20.0)	20 (28.2)	113 (28.7)
> 60	5 (7.7)	19 (13.5)	14 (19.4)	5 (11.1)	10 (14.1)	53 (13.5)
Education						
Primary education	25 (38.5)	40 (28.3)	16 (22.2)	20 (44.4)	14 (19.7)	115 (29.2)
Secondary education	28 (43.1)	44 (31.2)	29 (40.3)	20 (44.4)	31 (43.7)	152 (38.6)
Higher education	12 (18.5)	57 (40.4)	27 (37.5)	5 (11.1)	26 (36.6)	127 (32.2)
Labor activity						
Working	11 (16.9)	30 (21.3)	10 (13.9)	4 (8.9)	11 (15.5)	65 (16.5)
Unemployed/unplaced/retiree	54 (83.1)	111 (78.7)	62 (86.1)	41 (91.1)	58 (81.7)	329 (83.5)
Marital status						
With a partner	13 (19.12)	28 (19.8)	20 (27.8)	10 (22.2)	18 (25.4)	88 (22.3)
Without a partner	52 (80.88)	113 (80.1)	52 (72.2)	35 (77.8)	53 (74.6)	306 (77.7)
Family income						
Up to 4 x the minimum salary	42 (64.6)	89 (63.1)	52 (72.2)	34 (75.6)	51 (71.8)	368 (68.0)
4 to 8 x	4 (6.2)	20 (14.2)	5 (6.9)	2 (4.4)	8 (11.3)	39 (9.9)
More than 8 x	5 (7.7)	8 (5.7)	3 (4.2)	1 (2.2)	4 (5.6)	21 (5.3)
Don't know	14 (21.5)	17 (17.0)	12 (16.7)	8 (17.8)	8 (11.3)	66 (16.8)
Race						
Caucasian/Asian	24 (36.9)	65 (46.1)	34 (47.2)	14 (31.1)	25 (35.2)	162 (41.1)
Mixed/Afro-Brazilian	40 (61.5)	72 (51.1)	34 (47.2)	27 (60.0)	44 (62.0)	217 (55.1)
Did not answer	1 (1.5)	4 (2.8)	4 (5.6)	4 (8.9)	1 (1.4)	15 (3.8)
Total	65 (100.0)	141 (100.0)	72 (100.0)	45 (100.0)	71 (100.0)	394 (100.0)

Data presented as n (%).
CEAF = Componente Especializado da Assistência Farmacêutica (Specialized Component of Pharmaceutical Service).

Table 2 Clinical and behavioral characteristics of patients treated with atypical antipsychotics provided by the CEAF pharmacy in the state of Minas Gerais, 2017-2018[15]

	Clozapine	Olanzapine	Quetiapine	Risperidone	Ziprasidone	Global
Other diseases						
None	32 (49.2)	71 (50.4)	29 (40.3)	21 (46.7)	34 (47.9)	187 (47.5)
One	22 (33.8)	34 (24.1)	26 (36.1)	13 (28.9)	26 (36.6)	121 (30.7)
Two or more	10 (15.4)	29 (20.6)	16 (22.2)	11 (24.4)	11 (15.5)	77 (19.5)
Did not answer	1 (1.5)	7 (5.0)	1 (1.4)	-	-	9 (2.3)
Suicide attempts						
None	46 (70.8)	94 (66.7)	45 (62.5)	35 (77.8)	38 (53.5)	258 (65.5)
Once	4 (6.2)	21 (14.9)	11 (15.3)	2 (2.4)	7 (9.9)	45 (11.4)
Twice	5 (7.7)	5 (3.5)	5 (6.9)	4 (8.9)	6 (8.5)	25 (6.3)
Three or more times	10 (15.4)	21 (14.9)	11 (15.3)	4 (8.9)	20 (28.2)	66 (16.8)
Psychoactive substance use						
None	48 (73.82)	107 (75.9)	49 (68.1)	35 (78.2)	59 (83.1)	298 (75.6)
One type	8 (12.3)	12 (8.5)	11 (15.3)	5 (10.9)	2 (2.8)	38 (9.6)
Two types	4 (6.2)	6 (4.3)	6 (8.3)	1 (2.2)	3 (4.2)	20 (5.1)
Three or more types	3 (4.6)	10 (7.1)	5 (7.0)	4 (8.7)	6 (8.4)	28 (7.1)
Did not answer	2 (3.1)	6 (4.3)	1 (1.4)	-	1 (1.4)	10 (2.5)
Frequency of CAPS/CERSAM use						
None	28 (43.1)	71 (50.4)	30 (41.7)	22 (48.9)	33 (46.5)	184 (46.7)
Visits or group activities	17 (26.2)	33 (23.4)	19 (26.4)	13 (28.9)	19 (26.8)	101 (25.6)
Stays all day	11 (16.9)	22 (15.6)	13 (18.1)	8 (17.8)	13 (18.3)	67 (17.0)
Overnight stays or hospitalization	9 (13.8)	15 (10.6)	10 (13.9)	2 (4.4)	6 (8.5)	42 (10.7)
Total	65 (100.0)	141 (100.0)	72 (100.0)	45 (100.0)	71 (100.0)	394 (100.0)

Data presented as n (%).
CAPS = Centro de Atenção Psicossocial (phychosocial care center); CEAF = Componente Especializado da Assistência Farmacêutica (Specialized Component of Pharmaceutical Service); CERSAM = Centro de Referência em Saúde Mental (mental health referral center).

Table 3 EuroQol-5D-3L dimension scores of patients treated with atypical antipsychotics provided by the CEAF pharmacy in the state of Minas Gerais, 2017-2018[15]

Dimensions	Clozapine	Olanzapine	Quetiapine	Risperidone	Ziprasidone	Global
Mobility						
1	51 (78.5)	108 (76.6)	46 (63.9)	29 (65.9)	50 (70.4)	284 (72.3)
2	13 (20.0)	30 (21.3)	21 (29.2)	12 (27.3)	17 (23.9)	93 (23.7)
3	1 (1.5)	3 (2.1)	5 (6.9)	3 (6.8)	4 (5.6)	16 (4.1)
Self-care						
1	60 (92.3)	121 (85.8)	55 (76.4)	34 (77.3)	58 (81.7)	328 (83.5)
2	4 (6.2)	15 (10.6)	17 (23.6)	8 (18.2)	12 (16.9)	56 (14.2)
3	1 (1.5)	5 (3.5)	0 (0)	2 (4.5)	1 (1.4)	9 (2.3)
Usual activities						
1	43 (66.2)	82 (58.2)	34 (47.2)	23 (52.3)	29 (40.8)	221 (53.7)
2	17 (26.2)	33 (23.4)	26 (36.1)	16 (36.4)	30 (42.3)	122 (31.0)
3	5 (7.7)	26 (18.4)	12 (16.7)	5 (11.4)	12 (16.9)	60 (16.3)
Pain/discomfort						
1	47 (72.3)	89 (63.1)	36 (50.0)	23 (52.3)	38 (53.5)	233 (59.3)
2	17 (26.2)	30 (21.3)	26 (36.1)	15 (34.1)	22 (31.0)	110 (28.0)
3	1 (1.5)	22 (15.6)	10 (13.9)	6 (13.6)	11 (15.5)	50 (12.7)
Anxiety/depression						
1	26 (40.0)	46 (32.6)	36 (50.0)	12 (27.3)	16 (22.5)	119 (30.3)
2	30 (46.2)	62 (44.0)	26 (36.1)	16 (36.4)	27 (38.0)	165 (42.0)
3	9 (13.8)	32 (22.7)	10 (13.9)	16 (36.4)	28 (39.4)	109 (27.7)
Total	65 (100.0)	141 (100.0)	72 (100.0)	45 (100.0)	71 (100.0)	394 (100.0)

Data presented as n (%).
CEAF = Componente Especializado da Assistência Farmacêutica (Specialized Component of Pharmaceutical Service).
1 = no problems; 2 = some problems; 3 = extreme problems.
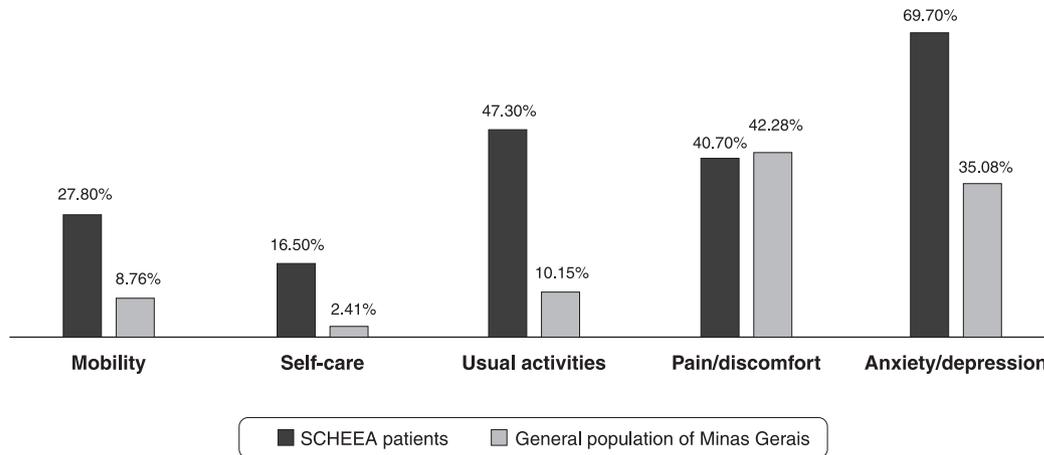
Figure 1 A comparison of people who reported problems in each dimension of the EuroQol-5D-3L: patients treated with atypical antipsychotics provided by the Specialized Component of Pharmaceutical Service (Componente Especializado da Assistência Farmacêutica [CEAF]) pharmacy vs. individuals from the general population of the state of Minas Gerais. SCHEEA = Schizophrenia Economics and Effectiveness Assessment project.

quetiapine, risperidone, and ziprasidone groups had the highest proportions who reported "extreme problems." The quetiapine (6.9%) and risperidone (6.8%) groups reported the most problems in the mobility dimension. The risperidone group (4.5%) reported the most problems in the self-care dimension. The olanzapine group (18.4%) reported the most problems in the usual activities dimension. The olanzapine (15.6%) and ziprasidone (15.5%) groups reported the most problems in the pain/discomfort dimension. Finally, the risperidone (36.4%) and ziprasidone (39.4%) groups reported the most problems in the anxiety and depression dimension. The clozapine group had the most patients who reported "no problems" in four of the five dimensions (mobility, self-care, usual activities, and pain/discomfort), and the quetiapine group was the most frequent to report "no problems" in the depression/anxiety dimension.

Figure 1 compares patients from the SCHEEA project with individuals from the statewide sample who reported problems in the EQ-5D-3L dimensions. SCHEEA project patients had the highest percentages in every dimension except pain/discomfort, in which both groups were similar.

The participants' utility scores were calculated according to their EQ-5D-3L responses. The mean score was 0.664±0.232. The clozapine group had the highest mean score (0.762±0.202), followed by the olanzapine group (0.687±0.230) and the risperidone group (0.630±0.252). The lowest scoring groups were ziprasidone (0.622± 0.234) and quetiapine (0.620±0.243).

Table 4 shows the relationship between sociodemographic, clinical, and behavioral variables and utility scores. Gender, education, income, employment, and race were significantly associated with utility score. All other clinical and behavioral variables were also significant (suicide attempts, psychoactive substance use, use of mental health services – CAPS/CERSAM, and comorbid diseases). Medication type was also significantly associated with utility score.

A multiple linear regression model was used to determine which variables were associated with higher utility scores (Table 5). The final model contained variables whose significance level was 5% or less. The variables that remained in the model were: income, employment, comorbid diseases, psychoactive substance use, suicide attempts, and medication type.

According to the model, the mean utility score of patients who earned more than eight times the federal minimum salary was 0.128 units higher than that of patients who earned less than four times the minimum salary. The mean score of employed patients was 0.122 units higher than that of unemployed or retired patients. The mean score of patients without comorbidities was 0.069 units higher than that of patients with comorbidities. The mean score of those who had never used illicit psychoactive substances was 0.102 units higher than that former or current users. The mean score of those who had not attempted suicide was 0.157 units higher than that of those who had. Moreover, the mean score of clozapine users was higher than all other medication types: 0.113, 0.110, 0.113, and 0.070 units higher than ziprasidone, risperidone, quetiapine, and olanzapine, respectively.

Discussion

Our sample was predominantly male, aged 30-59 years, unemployed, without a partner, and with a low education level, which corroborates other research.[21,25] Although most of the patients are in the economically active age group, they are largely unemployed[21] due to mental illness. Mental disorders affect individuals at an early age, before they have finished school. Due to the disease, stigma or both, their school attendance is irregular, reducing the possibility of employment. They are also unable to achieve stable relationships.[19,21]

Most SCHEEA antipsychotic users self-reported their race as Afro-Brazilian or mixed (55.1%). Studies have found that blacks are three times more likely than whites to use psychosis services.[20]

More than 20% of the participants have used illicit psychoactive substances. The use of these substances

Table 4 Utility scores stratified according to patient characteristics in a sample of patients treated with atypical antipsychotics provided by the CEAF pharmacy in the state of Minas Gerais, 2017-2018[15]

Variables	Mean utility (SD)	Median (1st quartile; 3rd quartile)	p-value
Gender			
Male	0.693 (0.222)	0.704 (0.578; 0.801)	0.070
Female	0.639 (0.248)	0.663 (0.519; 0.801)	
Age, years			
18-29	0.674 (0.190)	0.704 (0.588; 0.801)	0.339
29-39	0.668 (0.307)	0.736 (0.536; 1.000)	
39-49	0.694 (0.213)	0.691 (0.572; 0.801)	
49-59	0.639 (0.223)	0.673 (0.519; 0.786)	
Over 60	0.677 (0.198)	0.731 (0.494; 0.794)	
Marital status			
Single/divorced/widowed	0.671 (0.236)	0.691 (0.572; 0.801)	0.564
Married	0.661 (0.236)	0.681 (0.503; 0.801)	
Education			
Primary education*	0651 (0.227)	0.662 (0.519; 0.797)	0.061
Secondary education	0.657 (0.245)	0.704 (0.519; 0.801)	
Higher education	0.712 (0.207)	0.736 (0.616; 0.801)	
Income			
Up to 4 x the minimum salary†	0.650 (0.228)	0.659 (0.519; 0.801)	0.000
From 4 to 8 x	0.741 (0.179)	0.736 (0.624; 0.801)	
More than 8 x	0.837 (0.179)	0.801 (0.704; 1.000)	
Employment			
Unemployed/retired	0.645 (0.238)	0.666 (0.519; 0.801)	0.000
Employed	0.798 (0.176)	0.801 (0.686; 1.000)	
Suicide attempts			
None	0.722 (0.207)	0.736 (0.619; 0.801)	0.000
One‡	0.591 (0.263)	0.637 (0.451; 0.756)	
Two‡	0.584 (0.200)	0.592 (0.463; 0.704)	
Three or more‡	0.549 (0.266)	0.539 (0.405; 0.754)	
Comorbid diseases			
None	0.700 (0.229)	0.704 (0.583; 0.801)	0.005
One disease	0.656 (0.230)	0.691 (0.520; 0.801)	
Two or more disease§	0.606 (0.227)	0.626 (0.456; 0.786)	
Race			
Caucasian/Asian	0.700 (0.205)	0.704 (0.594; 0.801)	0.063
Mixed/Afro-Brazilian	0.645 (0.256)	0.681 (0.503; 0.801)	
Psychoactive substance use			
Never used	0.677 (0.228)	0.704 (0.571; 0.801)	0.072
Former of current user	0.664 (0.212)	0.692 (0.520; 0.801)	
CAPS/ CERSAM use			
None	0.703 (0.219)	0.704 (0.592; 0.801)	0.068
Group activities/visits	0.658 (0.228)	0.666 (0.571; 0.801)	
All day stays‖	0.618 (0.276)	0.642 (0.452; 0.801)	
Overnight/hospitalization (> 24 h)	0.626 (0.240)	0.675 (0.458; 0.790)	
Medication			
Clozapine¶	0.762 (0.202)	0.786 (0.662; 1.000)	0.001
Olanzapine	0.687 (0.230)	0.704 (0.572; 0.801)	
Quetiapine	0.620 (0.243)	0.659 (0.478; 0.786)	
Risperidone	0.630 (0.252)	0.640 (0.539; 0.763)	
Ziprasidone	0.622 (0.234)	0.639 (0.491; 0.786)	

For variables with two categories, the Mann Whitney U test was performed, for three or more, the Kruskal-Wallis test was performed followed by the Dunn test.
CAPS = Centro de Atenção Psicossocial (phychosocial care center); CEAF = Componente Especializado da Assistência Farmacêutica (Specialized Component of Pharmaceutical Service); CERSAM = Centro de Referência em Saúde Mental (mental health referral center); SD = standard deviation.
* Significant difference compared to patients with a higher education level.
† Significant difference compared to patients whose income is four to eight times the minimum salary and patients whose income is over eight times the minimum salary.
‡ Significant difference compared to patients who have not attempted suicide.
§ Significant difference compared to patients with no comorbid disease.
‖ Significant difference compared to patients not do not use CAPS/CERSAM services.
¶ Significant difference compared to the quetiapine, risperidone, and ziprasidone groups.

Table 5 Multiple linear regression of variables for patient taking atypical antipsychotics provided by the CEAF pharmacy in the state of Minas Gerais, 2017-2018[15]

Variables	Coefficient	Standard error	p- value
Constant	0.597	0.079	0.000
Income			
Over 8 x/up to 4 x the minimum salary	0.128	0.048	0.008
Labor activity			
Employed/unemployed	0.122	0.031	0.000
Comorbid diseases			
None/two or more	0.069	0.031	0.026
Psychoactive substance use			
Never/former or current user	0.102	0.046	0.027
Suicide attempts			
None/ three or more	0.157	0.032	0.000
Medicine			
Clozapine/ziprasidone	0.113	0.038	0.003
Clozapine/risperidone	0.110	0.043	0.011
Clozapine/quetiapine	0.113	0.038	0.003
Clozapine/olanzapine	0.070	0.034	0.040

CEAF = Componente Especializado da Assistência Farmacêutica (Specialized Component of Pharmaceutical Service).

among patients with psychotic disorders is high, and Wilson & Cadet[26] believe that the rate may be up to twice as high as that of the general population.

Among our sample, 34.5% had attempted suicide at least once. Suicide attempts among patients with psychotic disorders is a matter of concern, since it adversely affects HRQoL.[24,27] In the general population, suicide attempts are around 1%; among schizophrenic patients, this rate can reach 50%.[28]

In this study, 50.2% of the patients reported at least one comorbidity. The incidence of diseases, such as diabetes and cardiovascular disease, in patients with mental disorders is high and may be twice as high as that of the general population.[29]

Of this study's total sample, 53.3% currently use or have used CAPS/CERSAM for medical visits, group activities, or hospitalization. These patients arrive at CAPS/CERSAM units through self-referral or referral from other health services and, according to a study conducted in Belo Horizonte, their mean stay is 7.7 months.[30]

Overall, more than half of our sample reported no problems in the EQ-5D-3L dimensions mobility, self-care, usual activities, and pain/discomfort dimensions. On the other hand, 69.7% of the sample reported moderate or extreme problems with anxiety and depression, which is consistent with other studies.[29,36]

Clozapine users more frequently reported "no problems" for the EQ-5D-3L dimensions mobility, self-care, usual activities, and pain/discomfort, although in the anxiety and depression domain, quetiapine users reported the fewest problems. Clozapine has a lower incidence of extrapyramidal effects than other atypical antipsychotics due to its low affinity for D2 receptors.[31] Quetiapine, however, has a greater affinity for 5-HT2 receptors,[5] which improves depressive symptoms and could partly explain the HRQoL results.

The percentage of SCHEEA project patients who reported moderate or extreme problems was higher in all dimensions than in the statewide sample of Andrade & Noronha,[10] which shows that patients on atypical antipsychotics have greater impairment in mobility, self-care, habitual activities, and anxiety/depression than other individuals. Since only the pain/discomfort dimension responses were similar in both groups, it can be concluded that patients on atypical antipsychotics have no more self-perceived pain and discomfort than the general population.

The participants'EQ-5D-3L responses were used to calculate utility scores, which reflect different health states. We compared the estimated values from the statewide population with those of our sample. The mean utility score for patients with psychotic disorders was 0.664 (SD: 0.232). The clozapine group had the highest mean utility score of any atypical antipsychotic.[32,33] One factor in this result is the decrease in suicide attempts in patients unresponsive to other treatments.[34] Another factor is that clozapine users have lower readmission rates than conventional antipsychotic treatments. Significantly higher readmission rates were found in patients who received conventional antipsychotics than clozapine users.[33,35] Another relevant finding was lower illicit psychoactive substance use in the clozapine group than in the other groups. Clozapine also has a lower likelihood of extrapyramidal effects than the other antipsychotics.[31]

Variables such as gender, age, education level, marital status, and race were not associated with HRQoL in our sample, unlike the results Souza & Coutinho's literature review.[36] However other variables, such as employment,

comorbidity, illicit psychoactive substance use, and suicide attempts were associated with HRQoL.

Employment directly affects HRQoL since feelings of competence contribute to mental health.[37,38] Given that patients with mental disorders are generally unemployed, they have low incomes and do not have the resources to meet their daily needs. Thus, they are concerned with the future, feel dependent, and have difficulties dealing with personal finances, which contribute to low HRQoL.[36,39]

Patients with mental disorders can have other chronic diseases, as was the case in 50.2% of our sample. The most commonly reported diseases were hypertension, diabetes, and dyslipidemia, which could have negatively affected utility scores. In fact, the more chronic diseases, the more significant the impact on HRQoL.[22,38]

Our results indicate that illicit psychoactive substance use is adversely associated with HRQoL. This could be due to the fact that these substances have a considerable impact on treatment, such as poor response and non-compliance, which hinders patient recovery.[40]

According to the multiple linear regression model, variables that were significantly related to higher utility scores included: income at least eight times the federal minimum salary, employment, no illicit psychoactive substance use, no suicide attempts, no comorbidities, and clozapine use. These variables should be taken into account when developing mental health policies. Psychoactive substance use should be reduced in the general population, since it is related to the onset of psychosis[23] and poor HRQoL.[40] Proper education and training must be provided to patients with mental disorders so they can enter the labor market.[37]

Regarding the Clinical Protocols and Therapeutic Guidelines reported in this paper, patient-specific situations for using clozapine should be evaluated, such as patients with a history of hospital readmissions and current users of illicit psychoactive substances.[11-13] Such evaluations are already performed in patients with a history of suicide attempts, those with significant tardive dyskinesia, and those unresponsive to other antipsychotics (for whom the protocol already recommends clozapine).[11-13]

Although the sample was calculated at 71 patients for each drug group, the clozapine and risperidone groups only had 65 and 45 patients, respectively. To avoid affecting the direction of results, the associations between QoL and sociodemographic, behavioral, and clinical variables should be carefully evaluated. This study did not include patients with mental disorders who are not taking antipsychotics. Furthermore, cross-sectional studies are insufficient to explore causal connections among variables.

In conclusion, clozapine users were more likely to report "no problems" in the mobility, self-care, usual activities, and pain/discomfort dimensions than users of olanzapine, quetiapine, risperidone, and ziprasidone. The drug with the best results for the anxiety/depression dimension was quetiapine.

We found that sociodemographic, clinical, and behavioral variables are associated with utility scores. Thus, individuals with psychotic disorders who are unemployed, use illicit psychoactive substances, have already attempted suicide, and have comorbid diseases have worse HRQoL than other patients. Clozapine use was positively associated with HRQoL.

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Disclosure

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