Health equity and the usage of atypical antipsychotics within the Brazilian national health system: findings and implications

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ABSTRACT

Background: There is a need to evaluate the health equity of atypical antipsychotics users who obtain their medicines from the Brazilian National Health System (SUS) through the identification of key factors that influence their health status due to concerns with equity of care. **Research design and methods:** Cross-sectional study among patients attending state pharmacies in Brazil. Individuals were included if they used atypical antipsychotics, aged ≥18 years, and answered the EQ-5D-3L questionnaire. Sociodemographic, behavioral, and clinical data were collected. The dependent variable was health status. Associations between the independent variables and the dependent variable were analyzed by

adjusting a linear regression model. **Results:** Overall, 388 individuals met the eligibility criteria and were included in the analysis. The final multiple linear regression model demonstrated a statistically significant association between VAS and suicide attempts, private care, current antipsychotics, comorbidities, and perceived family support. **Conclusions:** The study identified several factors both individual and collective that correlate with the health status of atypical antipsychotic users, and confirmed the importance of providing medicines for treating psychotic disorders. However, other factors are involved including social support. Our results suggest additional activities and policies are necessary including strategies to address the differences in private and public health care.

Keywords: Antipsychotic Agents, Psychotic Disorders, Schizophrenia Spectrum and Other Psychotic Disorders, Health Equity, Health Status Disparities

1. INTRODUCTION

The level of social justice in a society affects the way people live and, consequently, their chances of becoming ill and dying [1]. Health inequity, that is, avoidable inequalities in health, is shaped by political, social, and economic forces, which have a determining impact on the possibility of individuals developing their full potential and living a full life [2]. This is particularly important in low- and middle-income countries (LMICs) where there is low access to public healthcare or unaffordable co-payment for private healthcare with potentially catastrophic consequences for the patient and their family once members become ill [3]. Access to essential medicines should be seen as a central component of social inclusion as well as a core component to address when strengthening healthcare systems to provide universal healthcare [4].

Health equity in Brazil has been identified as a long-term goal of the National Health System (SUS) in order to minimize inequities in health status and/or access of individuals to health care [5]. In this sense, SUS applies the principle of social justice, prioritizing the development of public policies and the implementation of different activities that can help reduce inequalities where these exist. As a result, reducing the vulnerability of groups in situations of risk as well as their exposure to health problems including concerns with the provision of appropriate medicines [4]. Whilst SUS aims to achieve equity, published studies have shown that some patients access both the public and private health systems, with 21.4% of the Brazilian population currently purchasing private health insurance to address concerns with access in the public system [4, 6].

Mental, neurological and substance abuse disorders are responsible for nine of the 20 leading causes of years lived with disability (YLD) worldwide (representing 25% of all disabilities measured) and 10% of the total global burden of disease [7], with schizophrenia contributing 13.4 million years of lives lived with disability to the burden of disease globally [8, 9].

The spectrum of schizophrenia and other psychotic disorders comprise a class of psychiatric disorders characterized by the presence of psychosis. Psychosis is a relatively common mental illness, with schizophrenia being the principal diagnosis among psychotic disorders, with a prevalence of 0.3 to 1% of the world's population, averaging 0.28% [8]. Recent studies suggest an incidence of 31.7 cases per 100,000 person-years for psychosis [10]; and 21.4 cases per 100,000 person-years for schizophrenia [11]. In the last decades, the prevalence of schizophrenia rose from 13.1 million in 1990 to 20.9 million cases in 2016 [8]. The economic costs of mental health disorders can be substantial. This is illustrated by the estimated spend on schizophrenia in the USA of US$155.7 billion in 2013, including both direct costs, non-healthcare direct costs, and mental disorder-related indirect costs [12]. Overall, the mean monthly costs per patient with schizophrenia are generally more than four times higher than for patients with similar demographics but without schizophrenia [13]. An analysis by the World Economic Forum estimated that the cumulative global impact of mental disorders in terms of lost economic output will be $16 trillion by 2030 [14]. Consequently, the adequate provision of mental health services should be a priority across countries.

In Brazil, mental disorders currently account for 1.1% of adjusted disability years and 2.8% of YLD [15], with a recent study identifying that the costs of atypical antipsychotics account for nearly 80% of the total costs of treating patients with schizophrenia within SUS [16]. Since the promulgation of the Brazilian constitution in 1988 guarantees the right to health for the entire population, it was agreed that SUS should be structured in order to guarantee comprehensive health care including Mental Health and Pharmaceutical Services [5, 17, 18]. Public policies were developed with the purpose of improving the health care of patients with mental health issues, promoting the guarantee of integral care, and access to pertinent treatments. The National Drug Policy and the National Pharmaceutical Services Policy were structured to improve individuals' access to medicines, the Specialized Component of Pharmaceutical Services (CEAF) being one of the strategies created to guarantee access to high-cost treatments in the care of patients with chronic diseases [19]. CEAF under the SUS is responsible for dispensing atypical

antipsychotics used in the treatment of patients with psychotic disorders including schizophrenia, and more recently bipolar disorders [15, 16, 20].

Considering the presence of social inequalities in Brazil, the greater vulnerability of individuals with psychotic disorders, their high incidence and prevalence, and the social and economic impact caused by mental health disorders, it is necessary to research these issues within a unified healthcare system for the economic development and the social well-being of society [21]. Assessing the current health equity of atypical antipsychotic users in SUS could help identify factors that influence the health of these individuals and improve understanding of the relationship between these factors and social equity to help guide future policies. Consequently, this study was undertaken to assess health inequities surrounding the provision of atypical antipsychotics and associated factors to patients in Brazil. We chose to concentrate on atypical antipsychotics, sometimes called second-generation antipsychotics, as these are currently considered high-cost or specialized medicines in Brazil, provided by the CEAF. The findings can subsequently be used as a basis for suggesting possible future initiatives to the Ministry of Health and other key stakeholders in Brazil to help improve the care of patients with psychotic disorders. This builds on earlier studies conducted in Brazil [16, 22–24].

2.   PATIENTS AND METHODS

2.1.   Characterization of the study

This study is part of the Schizophrenia Economics and Effectiveness Assessment (SCHEEA) project undertaken in Minas Gerais, Brazil. SCHEEA is an open prospective cohort whose objective is to evaluate the economic and effectiveness of schizophrenia treatment and other psychotic disorders. The project was conducted among State pharmacies of the CEAF, which dispense atypical antipsychotics under SUS. The data used to obtain the results presented in this article were obtained in the first interview of the SCHEEA cohort. The SCHEEA research project was approved by the Ethics and Research Committee on August 23, 2016, obtaining the necessary registration. It was conducted in agreement with the Brazilian legislation, under the resolution 466/2012 of the National Health Council. The patients answered the questionnaire only after agreeing to participate in the study and signing the informed consent form. In order to comply with the principle of confidentiality, each participant of the study was assigned a unique identification number. The participation of individuals in the study was voluntary, without financial incentives and the participants were informed that, if they did not agree to participate, their access to medicines would not be affected.

2.2. Design of the study

2.2.1. Inclusion criteria

The inclusion criteria of this cross-sectional study were individuals using only one atypical antipsychotic available at SUS (clozapine, olanzapine, ziprasidone, quetiapine, or risperidone), aged 18 years or older and who fully answered to the quality of life (QOL) questionnaire (EQ-5D-3L). These atypical antipsychotics were chosen as they are currently the only ones covered by CEAF, under SUS [15]. The EQ-5D-3L is an instrument developed to provide a generic measure of health-related QOL in adults and has been validated in Brazil [25, 26]. Patients prescribed more than one atypical antipsychotic at the time of the interview were excluded from the study in order to evaluate the impact of each medication individually on the user's health status. Patients who did not fully answer the EQ-5D-3L questionnaire were also excluded once this became the dependent variable of the study. The study was conducted between September 2017 and March 2018.

2.2.2. Patient selection and data collection

The recruitment of individuals occurred at the state pharmacies of CEAF before the dispensing of antipsychotic medications by approaching patients and inviting them to participate in the study. All patients who agreed to participate signed the Informed Consent Form and were taken for a face-to-face interview. The data collection form included sociodemographic, behavioral, and clinical information. The study was conducted by postgraduate students and trained health professionals who previously participated in training sessions and administered the questionnaire on a sample of patients at the survey site.

2.3. Variables

The dependent variable defined in the study was the self-reported health status of the patients as measured by the EQ-5D-3L Visual Analogue Scale (EVA) response. As mentioned, the EQ-5D-3L has been validated in Brazil [25, 26]. It is divided into two stages. The first stage defines the health status via a descriptive system of five dimensions (mobility, self-care, habitual activities, pain/discomfort and anxiety/depression), each with three levels of severity (no problems, moderate problems, extreme problems). The second contains a vertical visual analogue scale (VAS) calibrated from 0 to 100 - 0 being the worst and 100 being the best imaginable state of health - in which the patient chooses which value best defines his or her health at that moment. The VAS scale was used in this paper in order to evaluate the self-reported health status of the individuals rather than the utility score provided by the EQ-5D. This

decision was supported by a paper recently published by Almeida et al. [27], which evaluated the influence of atypical antipsychotic usage on QOL and revealed that the VAS scale could be useful to address further factors influencing the self-perceived health status of the patients.

The independent variables selected to identify potential factors influencing the patients' health were: socio-demographic characteristics (age, gender, marital status, skin color, work status, schooling, per capita monthly income), behavioral characteristics (physical activity practice, religion, reports of suicide attempts, and perceived family support) as well as health care variables (type of medical assistance - public/private, comorbidities, antipsychotic prescribed). These variables are known to be related to the health status of the individuals and consequently were selected to describe the patients' health status [23, 28–32].

The variables collected in the study were categorized into two or three categories. The marital status was redefined as "with partner" or "without partner." The population was classified into five age groups: 19 to 29, 30 to 39, 40 to 49, 50 to 59 and over 60 years. Regarding skin color, subjects were divided into two categories: black/brown, and others. The variable educational level was categorized into "until high school" and "higher or higher education". The variable "household income" was transformed into "household income per capita" by dividing the income reported in the questionnaire by the number of dependents. From this, participants were categorized into those who received up to one, one to two or more than two minimum wages. The employment status was also redefined in "employed" or "unemployed". For the location of the psychiatric consultations, the three categories included "public sector", "private sector" and "public/private sector" in line with the current situation. Comorbidities were divided according to the number of reported diseases besides the psychotic disorder. The variables "suicide attempt", "abortion", "family support", "religious" and "physical activity practice" were dichotomized in "yes" or "no".

2.4 Comparative analysis

A comparative analysis was performed between patients in the SCHEEA cohort, patients with psoriatic arthritis [22] and the general population in Minas Gerais [26] and Brazil [33]. The aim of this comparison was to evaluate the sociodemographic, behavioral, and clinical characteristics of different populations and their impact on the individuals' QOL. The psoriatic arthritis cohort was chosen both because it was conducted at the same state pharmacy as the SCHEEA cohort and because of the profile of the diseases, which are chronic, disabling and compromise QOL [7–9, 16, 34, 35]. The comparison

between patients in the SCHEEA cohort and the general population in Minas Gerais (the state in which the research was conducted) and in Brazil was carried out in order to highlight the potential impact of psychotic disorders on the QOL of individuals, as well as on socioeconomic aspects.

2.5.   Statistical analysis

The descriptive analysis was be performed by frequency distribution for categorical variables, and measures of central tendency (mean) and variability (standard deviation - SD) for the quantitative variables. The Kolmogorov-Sminorv test was applied to test the normality hypothesis of the dependent variable.

To analyze the individual association of each qualitative independent variable with the dependent variable, the numbers in the VAS (quantitative), the ANOVA test was performed to compare the means and the Tuckey multiple comparison test was conducted when applicable. Variables with p-value less than or equal to 0.20 in the individual analysis were included in the initial multiple linear regression model; and in the final model variables were kept with a p-value equal to or less than 0.05.

Statistical analyzes were performed using Statistical Package for Social Sciences (SPSS) software version 22.0 and data will be organized in the form of tables and graphs.

3.   RESULTS

3.1.   Sociodemographic, behavioral and clinical characteristics of the individuals included in the study

Of the 448 individuals included in the SCHEEA cohort, 388 met the eligibility criteria and were included in this cross-sectional study. 43 subjects were excluded because they did not fully respond to the EQ-5D-3L and 16 because they were prescribed more than one atypical antipsychotic. For the sociodemographic characteristics, the majority were male (55.2%), and the mean age was 46.1 (SD=11.8) years, with a predominance of those aged between 30 and 59 years (80.9%). Most of the interviewees had no spouse/partner (77.3%), studied until high school (68.0%), self-declared as brown/black (55.2%), were unemployed at the time of interview (83.8%) and had a mean per capita household income of up to one times the minimum wage (49.0%) (Table 1). The great majority of individuals reported being religious (93.6%); 69.3% always said they felt supported by the family and 41.2% stated that they practiced physical activities at least twice a week (Table 1).

Table 1: Baseline characteristics of the users of atypical antipsychotics included in the study, n=388

		N (%)	VAS mean (SD)	*ANOVA p*-value
Gender	Female	174 (44.8)	65.4 (27.1)	0.107
	Male	214 (55.2)	64.4 (21.3)	
Age (y)	19 a 29	27 (7.0)	73.5 (20.1)	
	30 a 39 ‡	95 (24.5)	71.6 (25.0)	
	40 a 49 ‡	115 (29.6)	64.6 (24.7)	0.142
	50 a 59	104 (26.8)	65.5 (24.8)	
	≥ 60	47 (12.1)	68.5 (20.7)	
Marital status	With partner	88 (22.7)	65.5 (23.2)	0.343
	Without partner	300 (77.3)	68.3 (24.4)	
Educational level	Until high school	264 (68.0)	65.6 (25.3)	0.017
	Higher education or more	124 (32.0)	71.9 (21.1)	
Skin color	Brown/black	214 (55.2)	64.9 (26.6)	0.014
	Others	174 (44.8)	70.9 (20.4)	
Household income per capita (in minimum wages)*	< 1 £	190 (49.0)	63.9 (25.4)	
	1 - 2	88 (22.7)	69.6 (20.4)	0.002
	≥ 2 £	45 (11.6)	77.0 (19.6)	
Employment status	Employed	63 (16.2)	75.3 (18.3)	0.006
	Unemployed	325 (83.8)	66.2 (24.9)	
Funding of psychiatric consultations	Public £	192 (50.3)	63.0 (25.5)	
	Private £ †	164 (42.9)	73.9 (20.5)	0.000
	Public/private†	26 (6.8)	62.9 (27.8)	
Atipycal antipsychotic	Clozapine £ †	65 (16.8)	75.2 (19.9)	
	Olanzapine ‡	138 (35.6)	68.8 (24.0)	
	Quetiapine †	72 (18.6)	65.2 (24.4)	0.011
	Risperidone	42 (10.8)	67.5 (22.9)	
	Ziprasidone £ ‡	71 (18.3)	60.9 (26.9)	
Presence of comorbidities	Yes	198 (51.0)	65.5 (23.2)	0.074
	No	190 (49.0)	69.9 (25.0)	
Number of comorbidities	0 £	190 (49.0)	69.9 (25.1)	
	1 †	121 (31.0)	68.3 (21.4)	0.025
	≥ 2 £ †	77 (20.0)	61.1 (25.2)	
Use of alcohol or tobacco at least once in a lifetime	Only alcohol † ‡	92 (23.7)	72.3 (23.8)	
	Only tobbaco ‡	16 (4.1)	58.2 (27.4)	0.040
	Both †	198 (51.0)	65.4 (24.3)	
	Neither	82 (21.1)	69.7 (22.9)	
Use of illicit drugs at least once in a lifetime	Yes	84 (22.0)	69.4 (20.6)	0.555
	No	295 (88.0)	67.7 (24.7)	
Suicide attempt	Yes	135 (35.0)	59.3 (26.4)	0.000
	No	250 (65.0)	72.7 (20.8)	
Abortion	Yes	36 (20.7)	66.0 (26.5)	0.896
	No	138 (79.3)	65.3 (27.4)	
Family support	Yes	269 (69.3)	72.4 (22.0)	0.000
	No	119 (30.7)	56.8 (25.3)	
Religiosity	Yes	363 (93.6)	68.4 (23.6)	0.021
	No	25 (6.4)	56.8 (29.5)	
Physical activity[1]	Yes	160 (41.2)	70.7 (21.6)	0.036
	No	228 (58.8)	65.5 (25.6)	

* Value in the year of research: US$ 283.25.

[1] Physical activity practice defined as performing physical exercise at least twice a week.

£ Statistically significant differences s at 5%; † statistically significant differences at 10%; ‡ statistically significant difference at 20% (Tukey multiple comparisons test).

For the clinical characteristics, 51.0% of the interviewees reported having another disease besides a psychotic disorder, and 20.0% had two or more associated diseases. Regarding substance abuse, 51.0% of the interviewees reported having used alcohol and tobacco at least once in their lives, 22.0% reported illicit drug use at least once in their lifetime, and 3.6% reported illicit drug use in the last 6 months. 35% had already performed at least one suicide attempt and 20.7% of women had already undergone an abortion (Table 1).

The distribution of individuals who reported having psychiatric consultations in either the public and private sectors was well balanced between the two groups, and the most prescribed atypical antipsychotic was olanzapine (35.6%) (table 1).

3.2. Factors associated with the self-perception of health of individuals interviewed in the study

In the individual analysis of the relationship between the VAS and the sociodemographic, behavioral, and clinical factors of the interviewees, there was a statistically significant association between higher health status VAS (i.e. better) score and female gender; age under 39 years; higher level of education; average per capita household income greater than two times the minimum wage; being employed; not being black/brown; conducting psychiatric consultations in the private health sector; not being on ziprasidone; having no comorbidities; not having attempted suicide; having family support; being religious and practicing physical activity (Table 1). Marital status, alcohol/tobacco/illicit drug use and abortion did not have a statistically significant association with VAS at a significance level of 20% and therefore were not included in the initial multiple linear regression model.

In the multiple linear regression analysis of factors associated with higher health status VAS, statistical significance was identified for age up to 39 years, no suicide attempt, use of private care for psychiatric consultations, use of clozapine, absence of comorbidities and family support (Table 2). The final multiple model demonstrated a statistically significant association between higher health status VAS and no suicide attempt, private care consultations, not using ziprasidone, absence of other diseases and the presence of perceived family support (Table 3).

Table 2: Initial linear regression model of the multiple analysis of the association between sociodemographic, behavioral and clinical factors and health status of atypical antipsychotic users, n=388

Variables		Coefficient	SE	p-value
Constant		60.136	6.670	0.000
Gender	Female	1.227	2.448	0.616
	Male	-		
Age (y)	19 - 29	-		
	30 - 39	-3.612	4.844	0.456
	40 - 49	-9.179	4.692	0.051
	50 - 59	-9.773	4.950	0.049
	≥ 60	-7.980	5.545	0.151
Educational level	Until high school	-		
	Higher education or more	-0.118	2.770	0.966
Household income per capita*	< 1	-		
	1 to 2	0.505	2.844	0.859
	> 2	3.786	3.946	0.338
Employment status	Employed	-		
	Unemployed	-1.840	3.118	0.556
Skin color	Brown/black	-2.488	2.344	0.289
	Others	-		
Use of alcohol or tobacco at least once in a lifetime	Only alcohol	5.970	3.503	0.089
	Only tobacco	-0.988	6.094	0.871
	Alcohol/tobbaco	0.832	2.998	0.782
	Neither	-		
Suicide attempt	Yes	-10.070	2.444	0.000
	No	-		
Funding of psychiatric consultations	Public	-		
	Private	6.549	2.679	0.015
	Public/private	0.682	4.653	0.884
Atypical antipsychotic	Clozapine	2.999	3.390	0.377
	Olanzapine	-		
	Quetiapine	-1.576	3.212	0.624
	Risperidone	-0.523	4.008	0.896
	Ziprasidone	-7.010	3.268	0.033
Number of comorbidities	0	-		
	1	-0.241	2.624	0.927
	≥ 2	-7.897	3.094	0.011
Family support	Yes	12.489	2.535	0.000
	No	-		
Religiosity	Yes	8.867	4.567	0.053
	No	-		
Physical activity[1]	Yes	1.326	2.285	0.562
	No	-		

R^2 (adjusted)=0.255. SE: Standard Error.

[1] Physical activity practice defined as performing physical exercise at least twice a week.

* In minimum wages. Value in the year of research: US$ 283.25.

Table 3: Final linear regression model of the multiple analysis of the association between sociodemographic, behavioral and clinical factors and health status of atypical antipsychotic users

Variables		Coefficient	SE	p-value
Constant		67.980	4.793	0.000
Age (y)	19 - 29	-		
	30 - 39	-1.473	4.754	0.423
	40 - 49	-8.174	4.660	0.053
	50 - 59	-8.631	4.858	0.059
	≥ 60	-6.598	5.459	0.201
Suicide attempt	Yes	-10.158	2.356	0.000
	No	-		
Funding of psychiatric consultations	Public	-		
	Private	8.901	2.371	0.000
	Public/private	1.617	4.522	0.721
Atypical antipsychotic	Clozapine	2.140	3.275	0.514
	Olanzapine	-		
	Quetiapine	-2.325	3.172	0.464
	Risperidone	-2.108	3.897	0.589
	Ziprasidone	-7.239	3.145	0.022
Number of comorbidities	0	0.081	2.582	0.975
	1	-8.242	3.071	0.008
	≥ 2	-		
Family support	Yes	12.632	2.485	0.000
	No	-		

R^2(adjusted): 0.227. SE: Standard Error.

As mentioned, a comparative analysis was performed between the health status and characteristics of the study population, the health status and characteristics of people with psoriatic arthritis [22] and the general population in Minas Gerais [26] and Brazil [33] (Table 4). This analysis showed that the population with psychotic disorders have the worst self-reported health status despite a higher average per capita income, a higher proportion of health plan beneficiaries, a higher proportion of individuals without partners and with the majority of unemployed people.

Table 4: Comparison of sociodemographic and clinical characteristics of atypical antipsychotic users (SCHEEA), individuals with psoriatic arthritis and general population in Minas Gerais and Brazil

	SCHEEA (n=388)	Psoriatic Arthritis (n=122)	Minas Gerais		Brasil	
			Santos, 2015[23] (n=3363)	PNAD, 2015[31] (n= 32933)	Santos, 2015[23] (n=9148)	PNAD, 2015[31] (n= 356904)
Age (y)*	46.0	51.5	36.4	34.3	37.8	32.6
Household income per capita (R$)*	1,404.84	-	-	1,322.00	-	1,373.00
VAS of EQ-5D-3L*	67.6	70.0	83.8	-	82.1	-
Gender (%) Female	44.8	59.1	50.6	50.8	52.6	51.5
Male	55.2	40.9	49.4	49.2	47.4	48.5
Marital status (%) With partner	22.7	57.5	51.0	48.3	50.8	51.7
Without partner	77.3	42.5	49.0	51.7	49.2	48.3
Educational level (%) < high school	68.0	64.2	-	86.0	-	83.9
≥ high school	32.0	35.8	-	14.0	-	16.1
Employment status (%) Employed	16.2	-	-	67.6	-	64.8
Unemployed	83.8	-	-	32.4	-	35.2
Skin color (%) Brown	44.6	30.3	-	46.8	-	45.1
Others	52.4	69.6	-	53.1	-	54.6
Health insurance (%) Yes	50.3	-	-	31.0	-	27.9
No	49.7	-	-	69.0	-	72.1

*Mean. VAS: visual analogue scale.
Source: Database of the project Schizophrenia Economics and Effectiveness Assessment (SCHEEA, 2018).

4.   DISCUSSION

Patients with psychotic diseases treated at SUS with only one atypical antipsychotic were mostly men, with a mean age of 46.0 years, self-identified as brown/black, had no partner, studied until high school and were not working at the time of the interview. This is similar to the population described in a study conducted among patients prescribed atypical antipsychotics at Rio Grande do Norte, Brazil [23]. The authors documented that more men than women used antipsychotics, the average monthly household income was 1.1–2.1 times the minimum wage ($339–$678), participants had low educational levels (less than 8 years in 80.8–100% of individuals) and the majority (69.2–90.3%) of individuals were unemployed [23]. Another cross-sectional survey conducted among patients with schizophrenia at two public psychiatric services in Rio de Janeiro, Brazil [24], also found the majority were male (52.9%), were single (77.9%), with a low educational level (up to 8 years in 63.3% of individuals) patients, and with a mean age of 41.7 years, which is encouraging.

In our sample, the mean self-reported health status was 67.6, which was lower than those reported in other studies [22, 26, 33]. Compared to the general population in Minas Gerais [26] and Brazil [33], our sample of patients prescribed atypical antipsychotics presented a worse health status as

measured by VAS (83.8 and 82.1 versus 67.6, respectively). Regarding the sociodemographic characteristics, our study population was older, had a higher proportion of men, higher per capita household income, better educational level, higher proportion of unmarried patients, significantly more unemployed, and a higher proportion of individuals with health insurance, compared to the general population in Brazil and Minas Gerais. This is perhaps not surprising given the impact of mental health disorders on the QOL of patients [23, 24, 29–32, 36, 37]. Patients with psoriatic arthritis had a higher average age (51.5 years), with the majority being women (55.9%), white (69.6%), and married (57.5%). The median EQ-5D VAS was 70.0 (interquartile range: 50.0-80.0). This indicates that patients with psoriatic arthritis, although they have a chronic and disabling disease such as psychotic disorders, have not only a better health status, but also a better educational level and marital status compared to those with psychotic diseases (VAS: 67.6 vs. 70.0; education level: 32.0 vs. 35.8 of individuals with higher education; marital status: 22.7% vs 57.5% of married individuals - in the SCHEEA cohort and psoriatic arthritis, respectively). These findings highlight the relevant and important impact of psychotic disorders on individuals' self-reported QOL. Consequently, requiring appropriate treatment.

Interestingly, despite the low income and low rate of employment of the individuals in our study, almost half of the respondents had psychiatric consultations in the private health sector through health insurance or direct payment. Data from 2017 show that only 21.4% of Brazilians had private health insurance at that time [6]. Of these, 80.3% were corporate or membership collective plans, that is, contracts for employment and/or affiliation with professional class councils, unions and cooperatives [6]. Such a finding in our sample was unexpected when the socioeconomic profile of the study population is considered, with 83.8% of individuals without employment and 49% only receiving up to the minimum wage. This may indicate a lag in specialized care for patients with psychotic disorders, who must pay their own money for specialist follow-up. We have started investigating this unexpected finding.

The individual analysis of the health status measured by the VAS and the characteristics of the patients in our study demonstrated statistical significance for gender; age; education level; mean per capita household income; work status; skin color; location of the psychiatric consultation; the antipsychotic prescribed; the number of comorbidities; whether attempted suicide; whether any family support; current religion and physical activity similar to previous studies [23, 28–32].

Regarding the association between the health status of the interviewees and their clinical and behavioral characteristics, a cross-sectional study conducted in the USA identified an association

between exercise and better health status for patients with mental disorders, in all age groups, sexes, race and at all family income levels [32]. Ideation and attempted suicide were associated with poorer health status in the work of Neil et al. [30], as well as in our study. Regarding religion, Urizar and collaborators [28] found that religious involvement was positively related to the QOL of individuals with schizophrenia in Latin America, consistent with studies conducted in high-income countries including the United States, the Netherlands, Denmark, Italy, Spain and Switzerland [36, 38].

Social support was evaluated by Guedes de Pinho et al. [37], who identified that QOL is related to satisfaction with social support: the higher the satisfaction with social support, the better the QOL of the patients. However, in the study of Guedes de Pinho et al, there was no statistical significance for family support but for social support as a whole (friends, affective partners, social activities), unlike our findings. We are not sure of the reasons for this but will be exploring this further.

Comorbidities, mainly cardiovascular diseases and metabolic disorders, have already been strongly associated with poorer health status and higher mortality in patients with severe mental illness [30, 39, 40]. Adverse health behaviors, including tobacco use, low rates of physical activity, poor diet, substance misuse, and high-risk sexual behavior, are major contributors to the development and worsening of these comorbid conditions. Low socioeconomic status may reduce access to healthy foods and safe environments for exercise. Other social factors, including chronic psychological stress and poor social networks, are also likely to contribute to increase cardiovascular disease and other poor health outcomes. Adverse effects from medication, particularly the metabolic effects of atypical antipsychotics, may also play a role [39–41].

Specifically, in relation to antipsychotics, clozapine demonstrated the best outcome for the individuals' health status, followed by olanzapine, risperidone, quetiapine and ziprasidone. The superior efficacy of clozapine compared to the other antipsychotics has been demonstrated in a number of studies [42, 43]. The focus of treatment with atypical antipsychotics is not only symptom reduction, but also improvement of QOL, and atypical antipsychotics may also increase patients' ability to participate in psychosocial rehabilitation, improving outcomes in health and social life [23]. However, atypical antipsychotics have a range of adverse effects including metabolic and cardiovascular adverse reactions [40, 41]. One study conducted in Rio Grande do Norte, Brazil, found that psychiatric, neurological, and autonomous adverse effects, as well as other side effects, were prevalent among

atypical antipsychotic drugs, especially ziprasidone and clozapine, reducing health-related QOL, with olanzapine being associated with fewer side effects and better health status [23].

Although the initial hypothesis of our study was that socioeconomic inequity among individuals strongly influenced health status [23, 29, 37], household income per capita was not statistically significant in the final multiple regression model of this study. The individual analysis of the socioeconomic variables income and labor situation was though statistically significant; however, this was not maintained in the final model. On the other hand, access to private care was statistically significant regarding individuals' health status in the multiple final model. Individuals who had psychiatric consultations in the private care sector had better health status when compared to those who had consultations in SUS (p <0.001). Whilst this was not defined as the main socioeconomic variable of the study, it can indicate that individuals who have sufficient resources to access private care have the potential to achieve better health status. This is a concern within a universal healthcare system such as Brazil as it may indicate a quality gap between public and private care, and we will be investigating this further in future studies.

Socioenvironmental factors impacting on the overall outcome of psychotic disorders can be classified in individual factors and neighborhood or ecological factors. Individual factors include unemployment, low socioeconomic status, gender, age, and marital status [28, 29], while neighborhood-level factors include urbanity, deprivation, availability of social services, and politics [31, 32]. Our study identified several individual factors associated with the health status of individuals being prescribed atypical antipsychotics; however, not all dimensions described in the literature were explored. This could have contributed to the low power of the final linear regression model (R^2 = 0.227) as only relevant factors were explored in our study.

We accept that there are a number of limitations in our study. One of the limitations of naturalistic studies of complex, multifactorial disorders, and their outcomes, is that the explanatory models identified are not strong, given the limited number of variables that can be explored in each study with feasible sample sizes. In addition, as usually occurs in databases of this nature, we do not have high-level information about a number of variables including the severity of the disease, hospitalizations during treatment, and adherence to prescribed oral medicines. However, having said this, we believe our findings are robust, providing direction for the future, and have not been compromised despite these limitations.

5.   CONCLUSION

The study identified several factors both individual and collective that correlate with the health status of patients prescribed atypical antipsychotics. The importance of providing medicines and care for the treatment of psychotic disorders is undisputed but it does not avoid the health inequities identified in our study. Our results suggest additional actions and policies regarding mental health care treatments should be instigated to address modifiable factors of such inequities. For instance, actions to improve social support, to address the differences between private and public health care, and strategies to help reduce suicides could improve the overall health status of these patients in Brazil. We will be following this up in future research projects.

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(*=of importance, **= of considerable importance)

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