

ORIGINAL ARTICLE/ARTIGO ORIGINAL

Patients with Schizophrenia who Attended a Partial Hospitalization Program of Psychiatry at Médio Tejo Hospital Center: A Descriptive Study

Doentes com Esquizofrenia que Frequentaram o Regime de Internamento Parcial de Psiquiatria no Centro Hospitalar do Médio Tejo: Um Estudo Descritivo

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ABSTRACT

Introduction: The aim is to evaluate a clinical series of patients with schizophrenia who attended a Partial Hospitalization Program of Psychiatry, in order to understand what challenges these patients pose to us in terms of their treatment, relapse prevention and social reintegration.

Methods: We analyzed a cohort of patients diagnosed with schizophrenia, who attended the Partial Hospitalization Program at a Department of Psychiatry, between the years 2016 and 2020. Data was extracted regarding sociodemographic characterization, attendance of the program, pharmacological treatment, comorbidities, readmissions to the acute ward, post-discharge social responses and presence of psychotic symptoms.

Results: Thirty three patients were included. Most of them were male (66.67%), with an average age of 35.09 years, mostly coming from Tomar (51.52%) and living with their parents and/or siblings (75.76%). 42.42% were initially unemployed.

Patients attended partial hospitalization for an average of 68.71 months. Regarding pharmacological treatment, clozapine established itself as the most common oral antipsychotic and paliperidone as the most common injectable antipsychotic. The average number of antipsychotic medications per patient increased over time accompanied by a significant increase in injectable antipsychotic medications, and a slight decrease in the number of oral antipsychotics. There is also a decrease in the utilization of benzodiazepines, but the utilization of medications to treat extrapyramidal and depressive symptoms remains high.

The most frequent medical comorbidity after discharge is overweight/obesity in 30.3% of cases. Acute ward admissions dropped significantly. Regarding post-discharge social responses, unemployment declined significantly; protected jobs and disability pensions increased significantly. Regarding psychotic symptoms, the number of patients presenting with negative and cognitive symptoms remained high at discharge from the program.

Conclusion: The Partial Hospitalization Program seems to translate in the long term into a smaller number of readmissions in the acute ward. It also contributes to improving the social reintegration of the patients. However, the stability of these patients is mostly achieved through a high cumulative dose of antipsychotic medication. These patients present with significant medical comorbidities and a progressive increase in polypharmacy throughout the years, showing us that we still have a long way to go when it comes to treating patients with schizophrenia.

Keywords: Day Care, Medical; Mental Health Services; Psychiatric Rehabilitation; Psychopharmacology; Schizophrenia

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RESUMO

Introdução: Pretende-se avaliar uma série clínica de doentes com esquizofrenia que frequentaram o regime de Internamento Parcial, de forma a perceber quais os desafios que estes nos colocam relativamente ao seu tratamento, prevenção de recaídas e reinserção social.

Métodos: Foi analisada uma coorte de doentes com esquizofrenia, que frequentaram o regime de Internamento Parcial de um Departamento de Psiquiatria, entre 2016 e 2020. Foram extraídos dados relativos à caracterização sociodemográfica, frequência do internamento parcial, tratamento farmacológico, comorbilidades, reinternamentos em enfermaria de agudos, respostas sociais pós-alta e presença de sintomas psicóticos.

Resultados: Trinta e três doentes foram incluídos, sendo a maioria do sexo masculino (66,67%), com idade média de 35,09 anos, maioritariamente provenientes do concelho de Tomar (51,52%) e a residir com os pais e/ou irmãos (75,76%). Do total, 42,42% encontravam-se inicialmente desempregados.

Os doentes frequentaram o internamento parcial em média durante 68,71 meses. Relativamente ao tratamento farmacológico, a clozapina consolidou-se como o antipsicótico oral mais frequente e a paliperidona como o antipsicótico injetável mais frequente. O número médio de medicação antipsicótica por doente aumentou ao longo do tempo, acompanhado por um aumento significativo na medicação antipsicótica injetável e uma ligeira diminuição no número de antipsicóticos orais. Constata-se também uma diminuição na utilização de benzodiazepinas, porém mantendo-se elevada a utilização de fármacos para tratar sintomas extrapiramidais e depressivos.

A comorbilidade médica mais frequente após a alta é o excesso de peso/obesidade em 30,3% dos casos. Os internamentos em enfermaria de agudos desceram significativamente. Relativamente às respostas sociais pós-alta, o desemprego diminuiu significativamente; os empregos protegidos e as reformas por invalidez aumentaram significativamente. Relativamente aos sintomas psicóticos, o número de doentes com sintomas negativos e cognitivos permaneceu elevado até à alta do programa.

Conclusão: O regime de internamento parcial parece traduzir-se a longo prazo num menor número de reinternamentos em enfermaria de agudos, contribuindo também para melhorar a reinserção social dos doentes. No entanto, a estabilidade é alcançada sobretudo através da utilização de uma alta dose cumulativa de medicação antipsicótica. Estes doentes apresentam comorbilidades médicas importantes e um aumento progressivo da polifarmácia ao longo dos anos, mostrando-nos que ainda temos um longo caminho a percorrer no que diz respeito ao tratamento das pessoas com esquizofrenia.

Palavras-chave: Esquizofrenia; Hospital de Dia; Psicofarmacologia; Reabilitação Psiquiátrica; Serviços de Saúde Mental.

INTRODUCTION

Schizophrenia is characterized by psychotic symptoms and in many cases by social and occupational decline, remaining a therapeutic challenge.1 Schizophrenia has been long considered to be a life-shortening disease. Recent evidence indicates that life expectancy in patients with severe mental disorders² maybe 10-20 years shorter than in the general population and a study conducted in the Danish population encountered a life expectancy that was 18.7 years shorter for schizophrenic men compared to men in the general population.³ In patients with schizophrenia, the so-called natural causes (mostly cardiovascular disease) account for the majority of deaths, being unnatural deaths (suicide and accidents) accountable for 20%–25% of the total number of deaths in patients with schizophrenia.⁴ Factors associated with mortality by natural causes in patients with schizophrenia include unhealthy lifestyle (e.g., diet, smoking, and other drug use), poor compliance with treatment, risky behaviors, stigma, negative symptoms and cognitive dysfunction, socioeconomic factors, and medication adverse effects. However, long-term antipsychotic use (including clozapine and long-acting injectables) is associated with substantially decreased all-cause mortality, including suicide and cardiovascular mortality, in patients with schizophrenia, despite the well-known cardiometabolic adverse effects of second-generation agents.5

A review conducted by Shek E *et al* (2009)⁶ comparing day hospital versus outpatient care for people with schizophrenia, showed dated and limited evidence. According to a review conducted by Marshall M *et al* (2011)⁷ there is no robust difference between day hospital care and inpatient care for being unemployed at the end of the study, for quality of life, or for treatment satisfaction. Overall, we noticed a shortage in publications regarding Partial Hospitalization Programs for people with schizophrenia, namely what is the profile of the patient attending this modality of treatment and what are the possible outcomes of these programs for patients.

The Department of Psychiatry at Médio Tejo Hospital Center (CHMT) is located in a non-tertiary center that serves a population of approximately 266 000 inhabitants, mainly living in rural areas and small cities. The team working at the Partial Hospitalization Program is composed by a psychiatrist, a social educator, an occupational therapist, a social worker, a psychologist, and two nurses with specialization in mental health. The program includes: a multidisciplinary consultation for the integration of the patient, follow-up in a weekly Psychiatry consultation with medication adjustment, individual psychotherapeutic follow-up in a weekly Psychology consultation for selected cases, group psychotherapy and other group activities, family intervention for

selected cases, weekly reunions of the therapeutic team to discuss all patients and personalized social referral. The individual psychotherapy follows the cognitive behavioral therapy model. The group activities offered by this team include sociodrama, a psychomotricity group, a group aimed at emotional regulation based on cognitive-behavioral therapy techniques, a group directed by a family therapist aimed at discussing family problems, a group aimed at financial management and other daily life tasks and a group providing metacognitive training for psychosis.⁸ Another component of this program integrates the day area with occupational activities such as cooking and manual work. This team also participates in the training of psychiatry residents, general and family medicine residents, and students of psychology, nursing, and psychomotricity.

In this study we intend to evaluate a clinical series of patients with schizophrenia who attended the Partial Hospitalization Program at the Department of Psychiatry, to understand their sociodemographic profile, clinical evolution and what challenges these patients pose to us with regard to their treatment, relapse prevention and social reintegration.

MATERIAL AND METHODS

A retrospective observational study was carried out, to analyze a cohort of patients diagnosed with schizophrenia who attended the Partial Hospitalization Program of Psychiatry (PHPP) at the Department of Psychiatry of Médio Tejo Hospital Center (CHMT), between the years 2016 and 2020. All the patients with the diagnosis of 6A20 – Schizophrenia, according to the *International Classification of Diseases, version 11* (ICD-11), were included. Patients' clinical files were consulted for data acquisition, and the following variables were collected:

- Age at the time of entrance in the PHPP.
- Gender of the patients.
- Geographical origin: the location in which the patient lived at the time of entrance in the PHPP.
- Marital status at the time of entrance in the PHPP.
- Household at the time of entrance in the PHPP.
- Drug consumption at the time of entrance in the PHPP.
- Employment status at the time of entrance in the program versus at final discharge from the PHPP.
- Modality of attendance of the PHPP Day Hospital (included individual and/or group psychotherapy) versus Day Area (occupational activities) versus both.
- Since some patients had multiple entrances and exits from the program, especially due to acute ward readmissions, we decided to assess the patient's pharmacological treatment at three different times: at the first entrance of the PHPP, at the last entrance of the program and at the discharge from the program. We calculated the cumulative dose of antipsychotic medication for each patient using an online tool developed by Northwood K *et al* (2020). Medical comorbidities presented by the patients at the time of discharge.
- Number of admissions to the acute psychiatry ward, assessed at three different periods: during the 12 months

- before the first admission to the PHPP; from the first admission until the final discharge from the PHPP; during the 12 months after the discharge from the PHPP.
- Social responses obtained from the PHPP.
- Presence of psychotic symptoms (according to ICD-11) at the first entrance of the PHPP, at the last entrance of PHPP and at discharge from the program. We assessed the presence of positive symptoms (including persistent delusions, persistent hallucinations, disorganized thinking, grossly disorganized behavior and experiences of passivity and control), negative symptoms (including constricted, blunted, or flat affect, alogia or paucity of speech, avolition, asociality and anhedonia), cognitive symptoms (cognitive impairment in any of the following domains: speed of processing, attention/concentration, orientation, judgment, abstraction, verbal or visual learning, and working memory) and psychomotor symptoms (psychomotor agitation or excessive motor activity, usually manifested by purposeless behaviors such as fidgeting, shifting, fiddling, inability to sit or stand still, wringing of the hands, psychomotor retardation, or a visible generalized slowing of movements and speech, and catatonic symptoms such as excitement, posturing, waxy flexibility, negativism, mutism, or stupor).

Statistical analysis was performed using the software Microsoft® Excel and IBM® SPSS® Statistics, version 26. Categorical variables were described as absolute (n) and relative (%) frequencies, and continuous variables were described using the mean. For inferential statistics, the Student's t-test for independent samples was used to compare continuous variables. For the comparison of proportions, a non-parametric test for proportions of 2 two populations was used. A statistical significance level of 0.05 was considered for all comparisons.

RESULTS

Between 2016 and 2020, 173 patients attended the Partial Hospitalization Program at the Department of Psychiatry. Of those, 33 patients (19.08%) with the diagnosis of 6A20 – Schizophrenia (according to the ICD-11) were included. Regarding the sociodemographic characterization at entry (Table 1), most of these patients were male, single, and living with their parents and/or siblings. Most lived in Tomar, that is the city were the Department of Psychiatry is located. Most of the patients had at least 10 years of scholarity. We observed a high prevalence of substance use disorders among these patients. Initially, almost 50% were unemployed (Table 2).

Patients attended the PHPP for an average of 68.71 months (5.7 years), with a minimum time of permanence of 1 month and a maximum time of permanence of 166 months. Patients participated in an average number of 93.91 treatment days and attended the Day Hospital (included individual and/or group psychotherapy) in 36.36% of cases, the Day Area (occupational activities) in 33.33% of cases and both in 30.3% of cases.

Table 1. Sociodemographic characterization at entry of the program of the patients with schizophrenia who attended the PHPP between the years 2016 and 2020.

Feature	Absolute number (percentage)	
Gender:		
Feminine	11 (33.33%)	
Masculine	22 (66.67%)	
Age (categories):		
18-30	13 (39.39%)	
31-40	9 (27.27%)	
41-50	7 (21.21%)	
51-60	4 (12.12%)	
Average age	35.09	
Residence:		
Tomar	17 (51.52%)	
Torres Novas	3 (9.09%)	
Entroncamento	3 (9.09%)	
Abrantes	4 (12.12%)	
Ourém	3 (9.09%)	
Vila Nova da Barquinha	1 (3.03%)	
Ponte de Sor	1 (3.03%)	
Vila Real	1 (3.03%)	
Marital status:		
Single	27 (81.82%)	
Married	3 (9.09%)	
Divorced	3 (9.09%)	
Household:		
Alone	3 (9,09%)	
Parents and/or siblings	25 (75.76%)	
Children	1 (3.03%)	
Partner and children	3 (9.09%)	
Uncles	1 (3.03%)	
Scholarity:		
4 or less	0 (0%)	
5 or 6 years	4 (12.12%)	
7 or 8 years	4 (12.12%)	
9 years	6 (18,18%)	
10 or 11 years	4 (12.12%)	
12 years	12 (36.36%)	
College degree	3 (9.09%)	
Substance use disorder:		

Feature	Absolute number (percentage)	
Alcohol	7 (21.21%)	
Cannabinoids	10 (30.30%)	
Cocaine	3 (9.09%)	
Heroine	2 (6.06%)	
Other psychoactive drugs	0 (0%)	

Table 2. Employment status at the time of first entrance in the PHPP versus at final discharge from the program. A non-parametric test for proportions of 2 two populations was used

Employment status (absolute number of patients (%)):	At first entrance of PHPP	At discharge of the PHPP	Test value and p -value (statistically significant for p <0.05)
Student	6 (18.18%)	2 (6.06%)	NSS (z=1.5086; p=0.13104)
Employed	4 (12.12%)	8 (24.24%)	NSS (z=-1.2766; p=0.20054)
- Protected employment	0 (0%)	4 (12.12%)	SS (z=-2.0635; p=0.0394)
Unemployed	14 (42.42%)	2 (6.06%)	SS (z=3.4467; p=0,00056)
Disability pension	7 (21.21%)	16 (48.48%)	SS (z=-2.325; p=0.02034)
Housewife	1 (3.03%)	1 (3.03%)	NSS (z=0; p=1)
Professional training course	1 (3.03%)	4 (12.12%)	NSS (z=-1.3955; p=0.16152)

SS – statistically significant; NSS – not statistically significant.

When it comes to pharmacological treatment, we observed a predominance of polypharmacy from the moment of entry into the PHPP. We observed a predominance of second-generation antipsychotics, either in oral or injectable formulations. Over time, clozapine established itself as the most frequent oral antipsychotic and paliperidone as the most frequent long-acting injectable (LAI) (Table 3 and Fig. 1), with a utilization that tripled from initial admission to discharge from the program. We also noted the introduction of LAI aripiprazole, a third-generation antipsychotic (partial D2 receptor agonist). The average number of antipsychotic medications per patient increased over time at the expense of a statistically significant increase in injectable antipsychotic medication, accompanied by a slight decrease in the number of oral antipsychotics. At discharge, 42, 42% of the patients were taking a high cumulative dose of antipsychotics. A decrease in the need for the use of benzodiazepines is observed over time. However, the need for drugs to treat extrapyramidal symptoms and depressive symptoms remains high (Table 3).

The most frequent medical comorbidities after discharge were overweight/obesity in 30.3% of cases, dyslipidemia in 27.27% of cases, arterial hypertension in 15,15% of cases, thyroid pathology in 15,15% of cases and osteoarticular pathology in 12,12% of cases.

Admissions to the acute care ward dropped significantly in the 12 months after discharge from the PHPP (Fig. 2). Regarding employment status, unemployment had a statistically significant decline; accordingly, protected employment and disability pensions increased significantly (Table 2).

As far as social responses are concerned, at the time of discharge from the PHPP, 54% of the patients had a specific social response: a reintegration in the workplace for 24% of the patients; a rehabilitation in a specialized center for 9% of the patients; a professional course or internship for 9% of the patients; voluntary work for 9% of the patients; a master's degree for 3% of the patients.

When it comes to the description of psychotic symptoms in these patients (Fig. 3), we can observe an evolution towards a decrease in the number of patients with positive symptoms, while the number of patients with negative and cognitive symptoms remains high at discharge from the program.

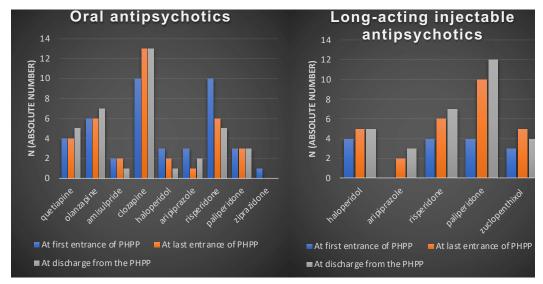


Figure 1. Oral and long-acting injectable antipsychotic medication used to treat the patients with schizophrenia who attended the PHPP between the years 2016 and 2020.

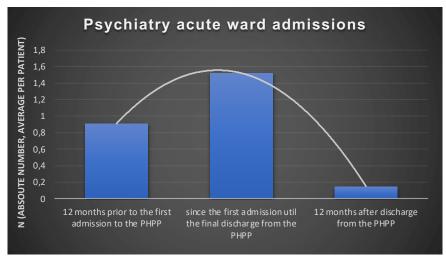
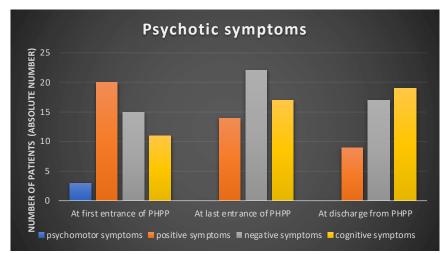


Figure 2. Psychiatry acute ward admissions per patient, of the patients with schizophrenia who attended the PHPP between the years 2016 and 2020. We found a statistically significant decrease in inpatient admissions (t=2.31621; p=0.011881).



and cognitive psychotic symptoms, attending the PHPP between the years 2016 and 2020. We found a statistically significant decrease in the number of patients with positive symptoms (z=2.7281; p=0.00634) and a statistically significant increase in the number of patients with cognitive symptoms (z=1.9777; p=0.0477).

Table 3. Pharmacological treatment of the patients with schizophrenia who attended the PHPP between 2016 and 2020. A student's t-test for independent samples was used

Feature	At first entrance of PHPP	At last entrance of PHPP	At discharge of the PHPP	Test value and p-value (statistically significant for <i>p</i> <0.05)
Most frequent oral antipsychotic(s)	risperidone (10), clozapine (10)	clozapine (13)	clozapine (13)	N/A
Most frequent injectable antipsychotic(s)	Haloperidol (4), risperidone (4), paliperidone (4)	paliperidone (10) paliperidone (12)		N/A
Average number of oral antipsychotics per patient	1.33	1.12 1.12		NSS (t=1.00709; p=0.158842)
Average number of long-acting injectable antipsychotics per patient	0.45	0.85	0.94	SS (t=-3.08635; p=0.001497)
Average total number of antipsychotics per patient	1.79	1.97	2.1	NSS (t=-1.3775; p=0.086578
Number of patients receiving high cumulative dose of antipsychotics	10 (30.30%)	16 (48.48%)	14 (42.42%)	NSS (z=-1.0235; p=0.30772
	1 st -antipsychotics (57)			
Most frequent drug classes	2 nd -benzodiazepines (20)	1 st -antipsychotics (65)	1 st - antipsychotics (68)	
		2 nd -benzodiazepines (19)	2 nd - biperiden + propranolol	N/A
	3 rd - biperiden + propranolol (16)	3 rd - biperiden + propranolol (16)	(17) 3 rd -antidepressants (16)	
	4 th - antidepressants (15)	4 th - antidepressants (14)	4 th - benzodiazepines (15)	
Average number of psychotropic drugs per patient	3.55	3.79	3.82	NSS (t=-0.66598; p=0.253908)
Average total number of drugs per patient	4	4.21	4.48	NSS (t=-0.93453; p= 0.176771)

SS – statistically significant; NSS – not statistically significant; N/A = not applicable. Note: although propranolol is not strictly considered a psychotropic drug, in this study we chose to consider it within this category, as in these patients it was used strictly to treat psychiatric pathology and side effects of antipsychotics.

DISCUSSION

The sociodemographic profile of the patient that was included in the PHPP corresponds to a male patient in his thirties, single, living with his parents and/ or siblings, and very likely unemployed, despite his high scholarity. This profile seems to indicate a socio-occupational decline that presents in an early stage of the illness. The high prevalence of substance use disorders (cannabis and/or alcohol)

is also of notice and might be one the contributing factors for this decline.

The fact that about half the patients who attended the PHPP lived near the hospital confirmed our impression that the geographical location might be an important factor in accessibility and adherence to this modality of treatment, since it requires patients to travel to the hospital several times a week.

When it comes to psychopharmacological treatment, 39.4% of the patients were taking clozapine at discharge, which indicates a profile of treatment resistance that is consistent with the socio-occupational decline and persistence of psychotic symptoms observed in these patients. A study conducted by Hajj A and colleagues¹⁰ showed that treatment-resistant patients with schizophrenia had specific clinical features/patterns: they were more often men who developed the disease earlier in life and had higher rates of alcohol and substance abuse, which is consistent with the profile of the patients included in our study.

Admissions to the acute care ward dropped significantly in the 12 months after discharge of the PHPP. One factor that very likely contributed to achieving the clinical stabilization was the significant increase in the utilization of LAI antipsychotics, reaching values at the end of the program of one injectable on average per patient. The literature has consistently demonstrated the superiority of LAI in preventing rehospitalizations due to decompensation in patients with schizophrenia.11 Another factor that probably contributed to relapse prevention of these patients was the set of psychosocial interventions provided by this PHPP. A meta-analysis conducted by Bighelli I et al,12 that evaluated psychosocial and psychological interventions for relapse prevention in schizophrenia, revealed robust benefits in reducing the risk of relapse for family interventions, family psychoeducation, and cognitive behavioral therapy.

It is worth pointing out that, even with the introduction of LAI antipsychotics, polypharmacy seems to be the rule instead of the exception, with a rise in the number of antipsychotic medications per patient over time. While some authors point out the scarce scientific evidence supporting this practice, other authors highlight the rationale and advantages of using several combinations of antipsychotics in clinical practice, combining the ones with different pharmacological profiles to get a better therapeutic response. 13,14 However, the significant percentage of patients taking a high cumulative dose of antipsychotics might raise some concerns. A study conducted by Kanahara N and colleagues¹⁵ suggest a link between cumulative lifetime antipsychotic dosage and progressive brain volume reduction in patients with schizophrenia. On the other hand, in the patients assessed in our study, we observed a high prevalence of side effects derived from antipsychotics, such as extrapyramidal symptoms (proven by high utilization of biperiden and propranolol). The presence of metabolic side effects is also relevant, such as overweight/ obesity, dyslipidemia, and arterial hypertension. A study conducted by Ijaz S et al16 points out conflicting evidence on the association between antipsychotic polypharmacy and metabolic syndrome in schizophrenia, concluding that long-term prospective studies are required for an accurate appraisal of diabetes risk, hypertension and hyperlipidemia in patients exposed to antipsychotic polypharmacy. A meta--analysis conducted by Mitchell AJ et al¹⁷ encountered an overall rate of metabolic syndrome of 32.5% in patients with schizophrenia and the highest rates were seen in those prescribed clozapine.

Regarding employment status, unemployment had a statistically significant decline; accordingly, protected employment and disability pensions increased significantly. A study by Na EY *et al*¹⁸ comparing a sample of unemployed versus employed patients with schizophrenia, concluded that emotional and psychological well-being was significantly higher in employed patients with schizophrenia living in the community.

Considering the persistence of negative and cognitive symptoms in most of these patients at discharge from the program, we consider that it would be important for our PHPP to invest in a cognitive remediation program incorporating multiple domains, besides metacognitive training for psychosis. Cognitive remediation programs showed not only improvement in a variety of cognitive domains affected in patients with schizophrenia but also improved negative symptoms.¹⁹ The review conducted by Barlati S *et al*²⁰ points out some of the most significant intervention programs aimed at improving cognition and social functioning in schizophrenia.

This study has some limitations, namely the low number of participants, since we only assessed patients from our PHPP, not including other centers. Another important limitation arises from the fact that we conducted a retrospective observational study and therefore had a limited amount of data that was available to collect and analyze. A future study regarding PHPP could also include a formal assessment of the symptoms of schizophrenia and the quality of life of these patients, which could add interesting outcomes to this type of study.

CONCLUSION

The Partial Hospitalization Program of Psychiatry seems to translate, in the long-term, into the stabilization of patients diagnosed with schizophrenia, with a smaller number of readmissions in the acute ward after discharge from the program. It also contributes to improving the social reintegration of the patients, namely with a significant decrease in unemployment. These results add an important contribution to the scientific literature that is scarce regarding partial hospitalization programs for patients with schizophrenia.

The typical profile of the patient that is admitted for this treatment modality in our hospital center is a male patient in his thirties, who reveals a rapid socio-occupational decline and difficulty in clinical stabilization. Therefore, the stability of these patients is mostly achieved, on one hand, through a long-term frequency of the program and, on the other hand, through polypharmacy, including a high cumulative dose of antipsychotic medication. Additionally, these patients present with a high prevalence of medical comorbidities, which might translate into an augmented risk for premature death. The challenges these patients pose to us reveal that we still have a long way to go when it comes to treating people with schizophrenia.

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PREVIOUS PRESENTATIONS

This study was presented as one of the finalist posters at Janssen Neuroscience RWE Award 2022/VII Neuroscience Forum, in Lisbon, May 14, 2022.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2024 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

DECLARAÇÃO DE CONTRIBUIÇÃO

TPVA: Colheita, análise dos dados e redação do manuscrito. **LCS, AJCC e LPD:** Redação e aprovação do manuscrito. Todos os autores aprovaram a versão final a ser publicada.

CONTRIBUTORSHIP STATEMENT

TPVA: Collection, analysis of data and writing of the manuscript. **LCS, AJCC and LPD:** Drafting and approval of the manuscript. All the authors approved the final version to be published.

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