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THE INTERTWINED LIVES: SCHIZOPHRENIA AND QUALITY OF LIFE - A SYSTEMATIC REVIEW

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Abstract: Schizophrenia is a debilitating and complex syndrome that affects around 1% of the global population, ranking among the top ten most disabling diseases according to the World Health Organization. This chronic condition significantly impacts the quality of life for individuals afflicted by it, causing distress not only to the patients themselves but also to their families and caregivers. Typically, the initial signs and symptoms manifest between the ages of 20 and 25, often in the form of psychotic episodes.

Schizophrenia is characterized by its variable course, which can be categorized into four stages: premorbid, prodromal, progression, and stabilization. The premorbid and prodromal phases precede the first episode of psychosis and are marked by low sociability, social anxiety, and cognitive impairments related to memory, attention, and performance.

Following the first episode of psychosis, clinical presentation can be broadly categorized into three domains: negative, positive, and cognitive symptoms. Negative symptoms entail a range of emotional disturbances, including reduced affect, diminished pleasure in daily life, and difficulties in initiating activities. Positive symptoms manifest as psychotic behaviors, where patients struggle to differentiate between reality and hallucination. Cognitive symptoms, similar to negative symptoms, can be elusive but include reduced executive function, impaired information processing and decision-making, attention deficits, and memory problems.

Keywords: Schizophrenia, psychotic behaviors, cognitive symptoms, emotional disturbances, disease stages.

1. Introduction

Schizophrenia is a complex syndrome that affects approximately 1% of the world population, being considered by the World Health Organization as one of the ten most disabling diseases in the globe. This pathology is a chronic and complex disturbance that affects the quality of life and generates suffering, for both the patient and the family members and caregivers. The first signs and symptoms are commonly manifested between 20 and 25 years old, as psychotic outbreaks. This disease doesn't have a fixed course and can be divided into four stages: premorbid, prodromal, progression and stabilization phase. The premorbid and prodromal phases appear before the first episode of psychosis, and the most common manifestation is low sociability, social anxiety, and memory, attention and performance alterations.

Original Article

After the first episode of psychosis, the clinical presentation can be divided into three spheres: negative, positive, and cognitive symptoms. The disturbance of emotions, such as diminished affection, diminished pleasure in daily life, and difficulty starting an activity, represents the negative symptoms sphere[3]. On the other hand, the psychotic behaviors are the manifestation of positive symptoms. Patients with this condition often lose the distinction between reality and hallucination. Finally, the cognitive symptoms, as negative symptoms, are difficult to detect. The patient has a decrease in executive function, the ability to understand information and make decisions, difficulty to have focus or attention, and problems with memorizing things.

The combination of these symptoms with environmental factors causes a lot of suffering to the patient. According to Katschnig (2006), patients with schizophrenia have specific needs to maintain a reasonable quality of life, which makes them dependent on specialized and continuous treatment. The known factors associated with the worsening condition are the use of licit or illicit drugs, social isolation, anxiety, low therapeutic adherence, low self - esteem and stress. Also, these individuals suffer various forms of stigmatization and prejudice that, associated with cognitive, social and labor limitations, impair the ability of communication and satisfaction of this population

For the World Health Organization (WHO), quality of life derives from a personal perception about the position of the individual in their environment, both cultural and values aspects, covering their expectations, concerns, and goals. On the other hand, the expression of *Health-Related Quality of Life* is about the value attributed to the quality of life in the context of changes and adversities. They can be manifested by deficits in the functional, social, and perceptual state of patients, when medical treatments, diseases or health policies are mentioned [5]. To measure this concept several instruments were created to evaluate the patient's quality of life, the WHOQOL-100 was the pioneer launched by the World Health Organization. It counts with one hundred items, divided into seven domains, and was developed based on cultural analysis of factors that could influence the patient's quality of life. Due to the time taken to apply the questionnaire, WHO has developed a second version, the WHOQOL-BREF reducing it to 26 items organized into four domains. (Krägeloh et al, 2011).

Another well-diffused questionnaire is the "Medical Outcomes Study 36-Item Short-Form Health Survey" (SF-36). It may be applied to more than 200 diseases and translated in 40 countries. The SF-36 serves the researcher as a measure of the patient's health status profile, consisting of eight dimensions: functional capacity, physical limitation, pain, general state, and vitality, social, mental, emotional, and overall quality of life. The eight dimensions can be used to generate a summary score of the individual's physical and mental health so that higher scores denote better health status. The time to complete the questionnaire ranges from five to ten minutes and can be performed independently by the patient, with reliability and validity levels that go beyond the minimum recommended standards, making this utility extremely relevant for population studies[6].

Given these considerations, this study aimed to conduct a literature review on the theme: quality of life of patients with schizophrenia, answering the question: "What are the factors that interfere with the quality of life of patients diagnosed with schizophrenia?".

2. Methods

The strategy for constructing the research question of this systematic review was the PVO - population, variable, and expected results. Therefore, the population covered by this study was schizophrenic patients, the researched variable was the quality of life, and the expecting results were the factors that change this patient's quality of life. Cochrane guidelines and PRISMA-P checklist guided the construction of this research. This systematic review was submitted and published at PROSPERO with the following identification code CRD42020138764.

First, we searched at the Cochrane database to verify if it has another systematic review in progress regarding this subject, and no paper was found in progress or published. Whereas the vast majority of systematic reviews addressing pharmacological and non - pharmacological therapeutic suggestions for these patients, reaffirming, therefore, the importance of this work, as it aims to identify factors that may likely be targets of these treatments.

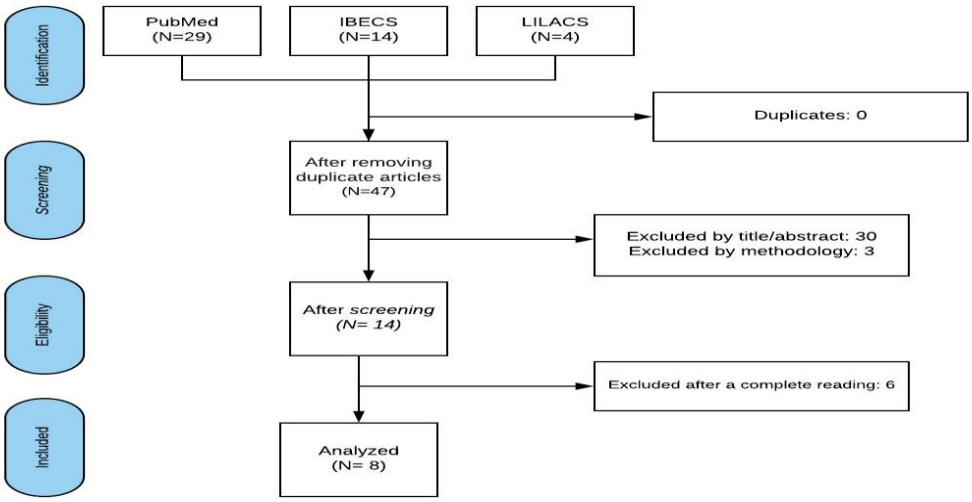
Original Article

The descriptors schizophreni, and quality of life were selected after Mesh and DECS search. These were combined and apply with "the last five years" filter in searches performed at PubMed, IBECS, and LILACS databases. This database choice aimed to cover as many countries as possible, so we selected international and national databases.

This search resulted in 47 articles, summing the three bases used. A peer review was performed to exclude articles that did not meet the criteria of this research. The inclusion criteria were: the type of study (cohort, casecontrol, randomized, cross-sectional study); if both descriptors were at title or abstract; if it was published less than five years from now; if it used validated diagnostic instruments. While the exclusion ones were: other review works, editorials, opinion texts, magazine columns, or experience reports; papers that were not approved by the Research Ethics Committee; and if had participants under 18 in the survey.

After this, the remaining ones were analyzed in full. The last selection was made based on the analysis of the study content and whether or not they contributed to the answer to the research question. The researchers performed a flowchart to illustrate (Figure 1).

FIGURE 1: ARTICLE SELECTION



A tablewas organized (TABLE 1) to facilitate the analysis of the results containing: the author, year of publication. The country where the study was performed, the research method, the applied questionnaires, and the main results obtained.

TABLE1: Search in databases

	AUTHOR	COUNTRY	POPULATION	METHOD	APPLIED QUESTIONNAIRES	CONCLUSION

1	(SAN; MILAWATY ; JIMMY, 2019)	Singapore	340 individuals from 2012 to 2015, of which only 297 completed the study and 1 outlier was removed from the statistical analysis.	Quantitati ve crosssectional study	*Clinical Global Impression - Severity scale* ; *Global Phsysical Activity Questionaire; RAND-36; Health Status Inventory; Positive and negative syndrome scale* (PANSS);	In this article, the authors found that disease severity was the variable that most affected the quality of life index, in contrast to physical exercise that did not correlate. The authors also concluded that strategies for exploring motivational values are important for these patients' quality of life index.
2	(HOFER et al., 2018)	Austria	189 individuals, of which 52 were patients with schizophrenia, 60 patients with bipolar disorder and 77 healthy patients who were used as a control group .	Quantitati ve casecontrol study	*WHOQL-BREF; The mini international neuropsychiatric interview* (MINI); *25-resilience scale* (RS-25); *Positive and negative syndrome scale* (PANSS)	Both patient groups had lower quality of life and resilience compared to controls. Another significant finding was that those patients with higher resilience also had higher quality of life. Thus, the authors concluded that both disease remission

						and patient resilience shaped the results of QOL.
3	(DOMENECH; BERNASCONI; *et al.* , 2008)	Austria	1379 outpatients with schizophrenia From September 2012 to December 2013.	Documentary quantitativ e study	*PANSS;; Clinical Global Impression – Schizophrenia; Schizophrenia quality of life (SQLS); Short Form-36 (SF-36); EuroQol-5 Dimension (EQ5D).*	Men reported higher HRQoL at all scales. HRQoL is influenced by different psychiatric symptoms in women and men, with more importance for negative symptoms in men and positive symptoms in women . This can have significant implications when deciding the main treatment target in patients with schizophrenia.

4	(DOMENECH; HEIGHT; *et al.* , 2018)	Germany	1345 patients were included, of which 1196 were followed for 12 months.	Documentary quantitative study	*Positive and negative syndrome scale* (PANSS); *Clinical Global Impression - Schizophrenia* (CGI-SCH); *Schizophrenia quality of life* (SQLS); *Short Form-36* (SF-36); *EuroQol-5 Dimension* (EQ5D).	It was concluded that positive and negative symptoms are probably the most important therapeutic targets for improving the quality of life of patients with schizophrenia.
5	KANCHANATAWAN; SRISWASDI; MAES, 2018)	Thailand	120 individuals, 80 schizophrenic patients and 40 controls.	Study quantitative casecontrol	*Mini-international neuropsychiatry interview*; *Schedule for the Deficit Syndrome*; PANSS;	Decreased quality of life in schizophrenic patients was associated with higher levels of TRYCATLV, as it caused memory changes (semantic and episodic), as well as symptoms such as anxiety and psychosomatic symptoms.
6	(LIM; LEE, 2018)	Singapore	157 outpatients with schizophrenia	Cross-sectional quantitative study	RAND-36, PANSS, GAS	The most important factor that decreased patients' quality of life was depressive symptoms. Positive symptoms and other psychiatric comorbidities

						also impacted, but with less relevance.
7	SECADES; TIRAPU, 2017)	Spain	41 patients divided into two groups according to clinical severity level	Quantitati ve crosssectional study	Index Interpersonal Reactivity (IRI); Scale GEOPTE Social Cognition to psychosis; WHOQOL-BREF; PANSS.	Positive symptoms affect these patients' quality of life more than negative and environmental factors. However, it points out that the severity of the disease should be considered and that not evaluating it becomes an important research bias.
8	(CHOU; MA; YANG, 2014)	Taiwan	120 patients diagnosed with schizophrenia	Cross-sectional quantitativ e study	PANSS, S- QoL -C, SIS	Mostly depressive symptoms negatively interfered with the quality of life of patients with schizophrenia.

Regarding the bias of these researches, the following were identified as the use of different Health Related Quality of Life (HRQoL) assessment instruments; the fact that these instruments are not all specific to the pathology; the diagnostic evaluation of psychiatric illness still be subjective. In an attempt to solve the bias, only articles that used at least one validated instrument were selected, in addition to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) or the International Classification of Diseases and Problems

Related to (ICD 10), to establish it. Furthermore, as the use of different instruments is a research bias too, we organized a table (TABLE 2), which will be presented below, aiming an equivalence between different domains of each questionnaire. Therefore, we choose the eight domains of the 36-item Short-Form Health Survey (functional capacity, physical limitation, pain, general health, vitality, social, mental and emotional capacity) to structure the columns of the table.

3. Results

Of the eighth articles analyzed, four were performed using the quantitative cross-sectional research method, two were case-control and two were an observational study. Considering these articles 12.5% was published in 2019, 62.5% in 2018, 12.5% in 2017, none in 2016 or 2015, and 12.5% in 2014. The average sample population of the studies was 456 participants, and the study by Domenech, Bernasconi, et al. (2018) had 1379 patients diagnosed with schizophrenia. Eighty schizophrenic patients and forty controls, in turn, attended the study conducted by Kanchanataw et al. (2018). Regarding the countries of publication of these articles, most were published in Singapore (2) and Austria (2).

Regarding the instruments used, seven authors applied the scale for the evaluation of positive and negative symptoms of schizophrenia (PNASS). Regarding the analysis of the life quality, only the authors Domenech, Bernasconi et al. (2018), Domenech, Altamura et al. (2018) and Chou et al. (2014) used a specific questionnaire for the pathology: *Schizophrenia quality of life* (SQLS). The other researchers used the non-specific ones, namely: *World Health Organization Quality of Life Brief* (WHOQOL-BREF), *Short Form Health Survey* of 36 items (SF-36), RAND-36 (Quality of Life Perception Questionnaire, based on SF-36). All instruments were duly validated for the language of the countries in which they were applied.

Overall, all authors found a diminished quality of life in the schizophrenic population. San et al. (2019) aimed to assess the relationship between body weight, physical inactivity, and disease severity with the quality of life of patients with schizophrenia. Therefore, they applied the *Clinical Global Impression - Severity Scale and Global Physical Activity Questionaire*, in addition to the RAND-36, which assessed the reported quality of life (HRQoL) of these patients. At the end of the study, the authors identified that only the severity of the disease brought a significant impairment to quality of life, while physical activity did not appear directly related.

As found by his study, Domenech Altamura et al. (2018), also did not identify statistical differences in HRQoL of obese schizophrenic patients when compared to those with normal BMI. For these authors, negative and positive symptoms should be the main therapeutic targets when the goal is to improve the quality of life of this population.

In contrast, Domenech Bernasconi et al. (2018) found a statistically significant difference ($p < 0.005$) in the obesity range, so it was considered one of the factors that reduce the patient's quality of life. The authors also assessed the difference in life quality between the sexes and concluded that as regards the global assessment of the scales, the male population had a higher quality of life than the female.

However, when it considers only cognitive symptoms, HRQoL was lower in men in the domains of mental and emotional state. Age was also an assessed issue and had the biggest negative impact on HRQoL in the female population in almost all domains, except for the global scale and social capacity.

Corroborating with those results, Secades et al. (2017) also focus on the social capacity and empathy of patients with schizophrenia. The authors showed that positive symptoms affect these patients' quality of life more than negative symptoms and environmental factors. However, it points out that the severity of the disease should be considered, and do not evaluate it becomes an important research bias. It is emphasized that Domenech, Bernasconi, et al. (2018), and Chou et al. (2014) used a specific questionnaire to access life quality in schizophrenic patients. So it is probably because of that, they found different results from Secades et al. (2017), once they identified a worsen HRQoL in those patients who presented predominance of negative symptoms.

Original Article

to the individual, and the spheres of the symptoms of schizophrenia.

Table 2: Variables that interfered in the different domains assessed by the quality of life

AUTHOR	FACTORS	FC	PL	P	GS	V	SC	E	M	GL
(San, Milawaty, and Jimmy 2019)	Age, material status, antipsychotic dose	X	X	X	X	X	X	X	X	
	Smoking and education level	X	X	X	X	X	X			
	Disease severity	X	X	X	X	X	X	X	X	X
	Body mass index	X	X							
(HOFER et al. 2018)	Unemployed	< Control	< Control		< Control	< Control	< Control	< Control	< Control	< Control
	Resilience									X
	Symptoms Remission									X
(Domenech, Bernasconi, et al. 2018)	Age	X	X	X		X		Women	Women	
	Obesity	X	X			X				

On the other hand, Lim and Lee (2018) aimed to find the relationship between depression and HRQoL, considering the clinical and functional variables of this population. The results found were consistent with expectations, that depressive symptoms showed a statistically significant impact on patients' quality of life when compared to positive symptoms and other psychiatric comorbidities. In addition, Hofer et al. (2018) compared the quality of life of patients with Bipolar Disorder and Schizophrenia, mainly evaluating the influence of symptom remission and resilience on HRQoL. As expected by the authors, quality of life was modulated by these two comorbidities and was better in Bipolar patients when compared to schizophrenics ones. However, overall, both disorders decrease HRQoL when compared to the control group.

Finally, Kanchanataw et al. (2018) investigated biological markers catabolite of tryptophan (TRYCAT LV), nitric oxide, and the production of glutamate, which were related to diminished the patient's life quality. They also considered the three groups of symptoms (positive, negative and cognitive) in addition to their remission. The authors found significantly higher levels of TRYCAT in patients with lower quality of life indices, as this compound interferes in memory, as well as anxiety and psychosomatic symptoms.

From these results, a table was organized (Table 2) containing the factors responsible for negatively impact the quality of life of patients with schizophrenia. The items were grouped into modifiable factors, intrinsic

LEGEND: FUNCTIONAL CAPACITY: FC; PHYSICAL LIMITATION: PL; PAIN: P; GENERAL STATE: GS; VITALITY: V; SOCIAL CAPACITY: SC; MENTAL: M; EMOTIONAL: E; GLOBAL QUALITY OF LIFE: GL

4. Discussion

Within this analysis, the results of this review indicate an important association between intrinsic and environmental factors and HRQoL in patients with schizophrenia, as well as the presence of positive and negative symptoms. In all researched studies, there were relevant data about the domains that interfere in the prognosis

	Positive Symptoms	X	X	X	X	X		X	X	X
	Negative Symptoms							X	X	X
(Chou; Ma; Yang 2014)	Sociodemographic factors							X	X	
	Psychopathological factors	Men	Men	X	X	Men	X	X	X	and
	Clinical factors	X	X	X			X	X	X	
	Psychosocial factors	X	X	X	X	X	X	Men	Men	X
	Positive Symptoms	X	X	X	X	X	X	X	X	X
(DOMENECH; HEIGHT; Et Al. , 2018)	Age	X	X	X		X		X	X	
	Women	X	X	X		X		X	X	
	Abuse of two or more substances	X	X	X		X				
	Years since symptoms onset							X	X	
	Negative symptoms						X	X	X	X
	Obesity	-	-	-	-	-	-	-	-	-
(Kanchanatawan, Sriswasdi, and Maes 2018)	Fibromyalgia					X		X	X	X
	Anxiety and depression						X			X
	Verbal fluency									X
	Negative Symptoms					X	X	X	X	X
	Deficts related to Schizophrenia	X	X	X	X	X				X
	Number of psichoses	X	X	X	X	X				X

well-being of these individuals, emphasizing the importance of scientific survey and analysis of these factors for the correct therapeutic intervention.

(Lim;Lee 2018)	Positive Symptoms	X	X	X		X	X	X		X
	Negative Symptoms									X
	Presence of others psychiatric comorbidities									X
	Depression					X	X	X	X	X
	Cognitive impairment									X
(Secades and Tirapu 2017)	Envioriment									Severe > Light

Although the manifestation of schizophrenia is heterogeneous and depends on each patient, the evaluation regarding the quality of life of these individuals has shown results that converge to a singular conclusion: the factors responsible for the deterioration of these patients' life quality are common and in part, treatable. Within this pathology, it is pertinent, therefore, to investigate the interaction of classical symptoms with social, environmental, contextual, physical and psychological factors, which may add considerable suffering and worsening of the general condition of these patients, as well as the acute exacerbation of underlying diseases.

4.1 Environmental factors and quality of life

Most authors found unemployment and sedentary behavior as the main environmental factors that decrease the quality of life of schizophrenic patients. Both studies by San, Millawaty, and Jimmy (2019) and Domenech's, Bernasconi et al (2018) identified that higher body mass index (BMI) results in a lower level of quality of life, especially in the physical domains. Corroborates to this idea, the study by Chou (2014) discusses an important association between psychosocial factors, obesity, and depressive symptoms - present in 80.7% of this population. In this context, self-reported depressive symptoms seemed to be a strong individual factor for the development of obesity. These findings explain the lower overall HRQoL index of patients since there is a decrease in their self-care and self-esteem. In contrast, for Domenech, Altamura et al (2018), obesity did not significantly alter the quality of life index.

In literature, the majority of the authors associate an increase at BMI with low vitality, so these patients spend less time doing physical exercises. On average, schizophrenic patients spend eight hours per day with sedentary behavior, maybe because of antidepressant or antipsychotic prescription due to medication side effects, like fatigue. Moreover, other associated factors were male gender, unemployment, non-tobacco use, and being single. 14,15

The authors San, Millawaty, and Jimmy (2019) discussed in their research the negative impact on the life quality of smokers and alcoholics, especially concerning chronic manifestations of the use of these substances. The integrative review by Oliveira and Furegato (2011) reported an average of 59% of smokers among patients diagnosed with the disease. The reason for this alarming incidence is historical and cultural, in the 1950s, scientific studies pointed a low prevalence of cancer among smokers with schizophrenia in comparison to the

general population, and it was hypothesized that this population would be more resistant to their growth and development. With this data, the tobacco industry had for 30 years this population as a target of their campaigns. Therefore, it has developed a popular belief that smoke would have a self-medication effect on these patients; added to this, the attempt to cease addiction would aggravate the psychiatric condition, and could contribute to the difficulty of establishing dependence mitigation strategies.[16].

Another factor considered as one of those that changed most of the patient's life quality was unemployment. In spite of almost all authors discuss how it can interfere with the general index just Hofer et al (2017) evaluated the effect on each domain. The employment rate is too variable, depends on many cultural and circumstantial conditions. A literature review found an average of 30% of schizophrenic patients employed since those who already had a job before the first outbreak or who started in the first year after the onset of psychosis is the ones who easily keep the job[17]. When it comes to the factors that increase the unemployment rate, the positive symptoms are the firsts, followed by severe manifestations of negative symptoms. The cognitive sphere was associated with the difficulty of these patients found a competitive job.

Finally, in addition to the level of study of these patients being a hindrance when it comes to getting a job, it is in itself a factor that decreases the quality of life in almost all HRQoL domains - except the mental, emotional, and global spheres - as identified by San, Millawaty, and Jimmy (2019).

4.2 Symptomatology and life quality

Instead of we expected most authors identified the sphere of negative symptoms as being the most detrimental to patients' quality of life. A cross-sectional survey with 7678 schizophrenic patients analyzed that 41% of them had at least one of these symptoms: low motivation, diminished affection, decreased eye contact, or poor expression of emotions. For these authors, this patient profile is a man, single, and with 20 to 29 years [19]. However, the Domenech, Bernasconi, et al. (2018) study founded that the females had their HRQoL more impaired by this sphere of symptoms. At their studies, Domenech, Altamura, et al. (2018), Domenech, Bernasconi, et al. (2018), and Kanchanatawa, et al. (2018) identified that the presence of negative symptoms impacts on life quality, mainly in the domain of emotional and mental capacity, in addition to reducing the overall HRQoL index.

The expression of negative symptoms may be associated with impairment of the cognitive sphere, since memories alterations, and the presence of anxious and psychosomatic symptoms, intensify the manifestation of this condition. In their research, Kanchanatawa et al. (2018) identified variation in the level of some biological markers that result in neurotoxic products, causing an oxidative and inflammatory response in neurons. It contributes to the appearance of physical and cognitive symptoms, consequently in a worse quality of life.

The research conducted by Domenech, Altamura et al. (2018) corroborates these findings, for them, the main cause would be the decrease in social relations and, therefore, this could be one of the improvement targets for this population. Lim and Lee (2018) found that depressive symptoms are also linked to social isolation and self-report dissatisfaction and therefore impact more significantly the HRQOL.

Also according to the results found by Lim and Lee (2018), the positive symptoms cause an impaired HRQoL in physical and emotional domains. Many studies fail to establish statistical relevance between psychotic symptoms and HRQoL, it because of the low sensitivity of generic scales for this type of symptom; and the fact that studies are often conducted in hospitals, where the patients evaluated are under the medication effect. Another issue is the heterogeneity and intensity of clinical presentations, so it would be interesting to identify if there are some symptoms that most actively interfere with one domain when compared to others.

In conclusion, control the psychotic symptoms could improve HRQoL, so management is an important piece in this scenario. Many studies discuss these medication use and how it can affect a patient's life but have many determinants to be considered, such as side effects, daily dose; treatment time; tolerability of the drug; and adherence. Hence, there is disagreement in the literature regarding the best class of medication, most of the

authors found that the prescription of atypical antipsychotics improves the quality of life in comparison with the use of the common antipsychotic. But at Guo's, et al (2012) research they didn't found statistics difference between the two medication classes, they observed that Olanzapine and Quetiapine treated patients improve significantly than Clorhomazepine treated patients. Furthermore, San, Milawaty, and Jimmy (2019) identify that higher doses of antipsychotics reduce in all domains the patients' quality of life.

Disease severity was a topic addressed by San, Milawaty, and Jimmy (2019) that found a negative impact caused by the greater intensity of symptoms presentation, be they in any of the spheres. Besides, Hofer et al. (2018) discussed in their study that remission and periods of disease stability cause the improvement of life quality. In this study, it stressed the importance of continued medical attention for schizophrenic patients, as many of them still have their HRQoL affected by depressive symptoms, even though the disease is considered stabilized.

4.3 Intrinsic factors and quality of life

The last group of factors that modify patients' quality of life includes other psychiatric comorbidities, gender, and age of patients. The authors Chou, Ma, and Yang (2014) identified that the presence of other psychiatric disorders has a direct impact on the physical domains, social capacity, and global quality of life index. In turn, Lim and Lee stated that this factor would only affect the global index. The study by Kanchanatawa, et al. (2018) concluded that the presence of anxiety or depression in association with schizophrenia causes a decrease in the general HRQoL, and at the social capacity domain.

The literature that associates psychiatric comorbidities highlights the difficulty in making a clear separation between the diagnoses of schizophrenia with anxiety and depression. Unipolar depression has an even more tenuous distinction, once the negative symptoms and antipsychotic medication can cause manifestations such as anhedonia and akathisia. However, some studies claim that the presence of depressive symptoms can worsen psychotic symptoms in the long-term. [21,22]

The anxiety symptoms, in turn, are more clearly associated with schizophrenia; some researchers have already identified genes in common between the two pathologies. The most common anxiety disorder is a panic disorder - that is three times more prevalent in the population with schizophrenia compared to the general population. This association is due to the presence of paranoid symptoms intrinsic to the pathology itself, which eventually triggers panic attacks in up to 20% of patients. In addition to a large number of patients who are abused both in the pre-morbid phase and after the first psychotic break, which can result in post-traumatic stress disorder.

Domenech, Altamura, et al. (2018) concluded that women have a diminished quality of life index in almost all domains, except for general state and social capacity. These findings go against the literature data, a study with 300 schizophrenic patients demonstrated that woman has a better prognosis in comparison with men, may because they have a smaller suicide index and generally are less violent. Furthermore, these patients have a higher rate of employment and social relationship, justifying the expectation of a better quality of life for the female population [23]. Domenech, Bernasconi, et al. (2018) also compared the male and female HRQoL and identified that negative and cognitive symptoms affect more men's quality of life at functional capacity, physical limitation, vitality, mental, and emotional domains. Other domains and variables affect equally both sex, except for age, that diminishes more women's quality of life in emotional and mental domains.

The age of the patients is strongly linked to the time of the disease's evolution, so as long the patient lives with the symptoms, lower is their quality of life in practically all domains. Besides, the time of medication use also has a strong impact on HRQoL, since they are more subject to side effects, such as cognitive symptoms, bradykinesia, and diminution of affective expression.

From this study, we reiterated the importance of encouraging the practice of physical activity and smoking cessation, once these would nullify the main environmental factors that diminish the life quality of schizophrenic patients. Although more difficult to handle, the intrinsic factors found can be anticipated and somewhat mitigated

by encouraging continued psychotherapy, even in periods of symptom stabilization. This practice is beneficial because it increases resilience and improves self-perception, which positively affects patients' quality of life. Finally, when it comes to symptom spheres, this research brought an alarming situation that may be a consequence of the neglect of negative and cognitive symptoms in the therapeutic planning of these patients.
In conclusion, this systematic review allowed to compile the main factors that influence the life quality of patients with schizophrenia and thus more effectively target therapeutic from the division of these into three groups: environmental, intrinsic to the individual, and the symptoms presented.

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