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REVIEW ARTICLE



Health related quality of life in patients having schizophrenia negative symptoms – a systematic review

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ABSTRACT

Background: Schizophrenia negative symptoms (SNS) contribute substantially to poor functional outcomes, loss in productivity and poor quality of life. It is unclear which instruments may be used for assessing quality of life in patients with SNS.

Objective: The objective of this review was to identify instruments assessing health-related quality of life (HRQoL) validated in patients with SNS and to assess their level of validation.

Data sources: We conducted a systematic literature review in Medline and the ISPOR database in March 2016 to identify studies on the quality of life in patients with SNS published by March 2016.

Data extraction: Psychometric properties and validation steps.

Data synthesis: After applying inclusion/exclusion criteria, 49 studies were selected for the analysis of HRQoL instruments; however, none of these instruments only addressed patients with SNS. Of these, 19 HRQoL instruments used in patients with schizophrenia or including patients with SNS among others, in the context of instrument validation, were identified (4 generic, 10 non-specific mental health, 5 schizophrenia-specific).

Conclusion: No HRQoL instrument has been validated in patients with SNS only; for the remaining instruments identified, it remains unclear whether they were intended to capture HRQoL in patients with SNS.

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Health related quality of life; negative symptoms; validation; instruments; psychometric properties; schizophrenia



Introduction

Schizophrenia is a chronic, severe, and disabling brain disorder. Its clinical presentation encompasses symptoms divided into three dimensions: positive, negative, and cognitive. Schizophrenia positive symptoms (SPS) include psychotic manifestations, such as hallucinations and delusions. Schizophrenia negative symptoms (SNS) encompass a loss of thoughts and/or altered behaviours, a lack of motivation, blunted affect, severe social withdrawal, and paucity of speech as well as communication. Cognitive symptoms include memory, attention, and executive functioning disorders [1].

SNS are heterogeneous and have been categorized into distinct subdomains including blunted affect, avolition, asociality, and anhedonia. SNS are also classified as prominent, predominant and/or persistent depending on severity (Table 1). Patients with SNS lose the normal functioning that they had prior to the onset of their illness [2,3].

SNS are associated with a limited response to pharmacotherapies and poor functional outcomes, thus, remain an area of unmet therapeutic need [3,4]. Reports from the literature show that 40% of patients with schizophrenia have SNS during the first psychosis episode [5] while 20% to 30% of patients suffer from persistent SNS [6,7]. Recent reviews reported that prominent SNS affect approximately 40% of people with schizophrenia; clinically relevant cognitive impairment is diagnosed in 80% [7]; and 20% of patients suffer from predominant SNS of moderate severity [8].

SNS are difficult to assess. Patients with schizophrenia are often unaware of the extent of their symptoms and do not report them spontaneously [9]. In addition, even after a long observation period, physicians may not be able to easily recognize the presence of these symptoms without questioning the patients, family, or caregivers. The patient's perception of his or her own health is, however, very important in the diagnosis and recognition of the changes

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 Supplemental data for this article can be accessed [here](#).

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Table 1. Schizophrenia negative symptom qualification.

SNS	Definition
Prominent negative symptoms [7,33,34]	Moderate symptom severity of ≥ 4 on at least 3 negative PANSS subscore items or moderately severe symptom severity of ≥ 5 on at least 2 negative PANSS subscore.
Predominant negative symptoms	<ul style="list-style-type: none"> • If using the SANS: the score of ≥ 60 on the SANS and of ≤ 50 on the SAPS, or if the score corresponds to less than moderately ill on the CGI-S [7,35]. • If using the PANSS: the total negative subscore of >20 including a score of ≥ 4 in at least one of N1–N7 items, reduction of $<10\%$ on PANSS negative subscore, and stable medication for 2 weeks before an intervention [36,37].
Predominant and persistent negative symptoms [38,39]	<ol style="list-style-type: none"> (1) The total negative score of >20 points on the PANSS including a score of ≥ 4 in at least one of the PANSS-negative items – N1–N7 (range 1–7) (at least moderate, clinically relevant negative symptoms) [40]. (2) Stable antipsychotic medication for 2 weeks before an intervention with reduction of $<10\%$ on PANSS negative subscore over this time. (3) The total positive score of <20 points on PANSS including a score of ≥ 5 (“marked” severity or higher) in at least one of the PANSS-positive items – P1–P6 [40]. (4) The total negative score of ≥ 4 on the CGI-S [41]. (5) A score of >9 on the CDSS [42]. (6) A score of ≥ 3 on the clinical global impression of ESRS at screening [43].

Abbreviations: CDSS – Calgary Depression Scale for Schizophrenia; CGI-S – Clinical Global Impressions-Severity; ESRS – Parkinsonism of the Extrapyrimal Symptom Rating Scale; PANSS – Positive and Negative Syndrome Scale; SANS – Scale for the Assessment of Negative Symptoms; SAPS – Scale for the Assessment of Positive Symptoms

occurring over time in the patient’s behavior, even with such a disabling disease [10,11].

Health-related quality of life (HRQoL) is a subjective concept that has been measured since the 1980s [12]. The FDA and EMA defined it ‘as the patient’s subjective perception of the impact of his disease and its treatment(s) on his daily life, physical, psychological, and social functioning and well-being’ [13,14]. However, HRQoL is not just a subjective and multidimensional concept, but it is also an encompassing physical and occupational function, a psychological state, a social interaction, and a somatic sensation [15,16]. HRQoL is frequently used in psychotic diseases and especially in schizophrenia as a functional assessment of a medical condition and/or its consequent therapy upon a patient [15,16]. HRQoL instruments may be generic or disease-specific. A generic instrument is designed to assess quality of life in a wide range of diseases and interventions. Disease-specific HRQoL instruments are intended to be used in a specific population of patients having the same disease and take into consideration the specific attributes of this disease [17].

The use of HRQoL instruments is increasing in clinical practice as it supports decision-making. With this increased popularity, choosing an instrument that will best measure the assessed concept becomes of paramount importance. We believe that a review of evidence on HRQoL in the scope of SNS would be beneficial and insightful. Therefore, the objective of this review was to identify instruments assessing HRQoL that have been validated in patients with SNS and to evaluate their level of validation. We assumed that the number of those instruments would be low; thus, we performed our research on quality of life in

patients with schizophrenia in general, although specifically targeting SNS.

Methods

Search strategy

A systematic literature review was conducted in Medline and the ISPOR database in March 2016. Additional reports were selected through searching the citations in the identified studies. No restrictions were applied to the date of publication or geographical region; although, papers written in English and French only were included. Two reviewers independently assessed titles and abstracts of collected publications for possible inclusion in the study; disagreements were resolved by consensus.

Selection criteria

Studies were included when they addressed the application of the HRQoL instruments along with their consequent results; furthermore, the studies included details on the development and/or validation processes of HRQoL instruments validated in patients with schizophrenia and/or SNS.

Extraction

We extracted general characteristics of selected instruments including the name, the type (generic, mental illness-specific, or schizophrenia-specific), the number of domains, and the number of items along with their psychometric properties, such as the type of validity (construct validity, face validity, content validity and

Table 2. Definitions of psychometric properties and subcategories.

	Definition
The validity of an instrument	<p>It is the most important property of an instrument. The validity is the state that proves that the instrument is able to measure what it is aimed to measure. Several types of validity exist [18,44,45].</p> <p>Construct validity is the ability of a test to measure a theoretical construct. It is about generalization of a construct or results from a study to the large concept of this study. It includes convergent and discriminant validity.</p> <p>Face validity addresses time of filling of an instrument, the missing rate, the ceiling and floor effect, etc. It is a general impression determining if the operationalization seems like a good translation of the construct or not.</p> <p>Content validity checks the relationship between the content domain and the purpose of the instrument. The aim of this validation is to have a good description of the content.</p> <p>Criterion-related validity is the ability to test if a measure is able to predict a variable that is designated as a criterion or not.</p> <ul style="list-style-type: none"> • Predictive validity is the fact of predicting the future measure or a result from a current measurement. It measures the extent to which a future level of a variable can be predicted from a current measurement. This includes correlation with measurements made with different instruments. • Concurrent validity is the fact of measuring the existing relationship between the new measure and an existing test which is the criterion.
Reliability of an instrument	<p>It is the degree to which assessed tool produces stable and consistent measurements. It includes the internal consistency and the test retest reliability [18,46,47].</p> <p>Reproducibility or test-retest reliability is obtained by administering the same instrument twice over a period of time (this period varies from one instrument to another). To evaluate the stability of the test retest reliability over time, a correlation between the first and the second score is calculated.</p> <p>Internal consistency is a method of reliability measure evaluating the degree to which all items included in the same domain evaluate the same construct and produce a score. The combination of this score with the score of the other domains of the same instrument produces an overall score.</p>
Ability to detect change	<p>It is the ability to measure the degree and the latency of the change between two measurements and to give the evidence that the tool is equally sensitive to the change independently of the duration of break between them [18,48,49].</p>

criterion-related validity), the type of reliability (internal consistency and reproducibility), and the ability to detect change.

Based on the definition of validity, reliability, and sensitivity to the change of each study presented in Table 2, psychometric properties were rated independently by the analysts, as robust (when all evidence was provided in the publication and suggested to be of high quality), moderate (when partial evidence was provided) or poor (when not all analyses were performed). As established in the Millier et al. study [18], psychometric properties rating was based on the number, type, and results of the analyses.

Extraction of criteria assessing SNS

The following was extracted: 1) the HRQoL instrument specific to schizophrenia, 2) the scale used to assess SNS, 3) the correlation between items of this scale and items of the HRQoL instrument, 4) the proportion of items on SNS, and 5) the proportion of patients with SNS.

Results

Overview of instruments validated in patients with SNS

A total of 238 abstracts were identified from Medline (n = 202) and from ISPOR (n = 36) databases. After applying the search criteria, 49 studies were selected

for further analysis; however, none of the HRQoL instruments included in these studies were validated in patients with SNS only. Figure 1 shows the study selection process.

As presented in Table 3, 19 HRQoL instruments were validated in 22 studies for schizophrenia, including patients with and without SNS. Out of these 19 instruments, 4 were generic, 10 were dedicated non-specific mental health, and 5 were schizophrenia-specific. Five instruments were developed before 2000, 12 between 2000 and 2010, and 2 after 2010. Nearly half of these validated HRQoL instruments (n = 10) were validated in patients with schizophrenia in general without any information about patients with SNS; the 9 other studies including 6 non-specific mental health and 3 schizophrenia-specific instruments were validated in patients with schizophrenia in general, although including patients with SNS.

Psychometric validation of schizophrenia-specific HRQoL instruments

Table 4 presents the summary of the psychometric validation of the 3 schizophrenia-specific instruments. More information is available in the supplement material.

Results show that HRQoL instruments were validated in several languages. Almost all instruments evaluate dimensions such as health in general and/or physical and mental health, social relationship, economic or

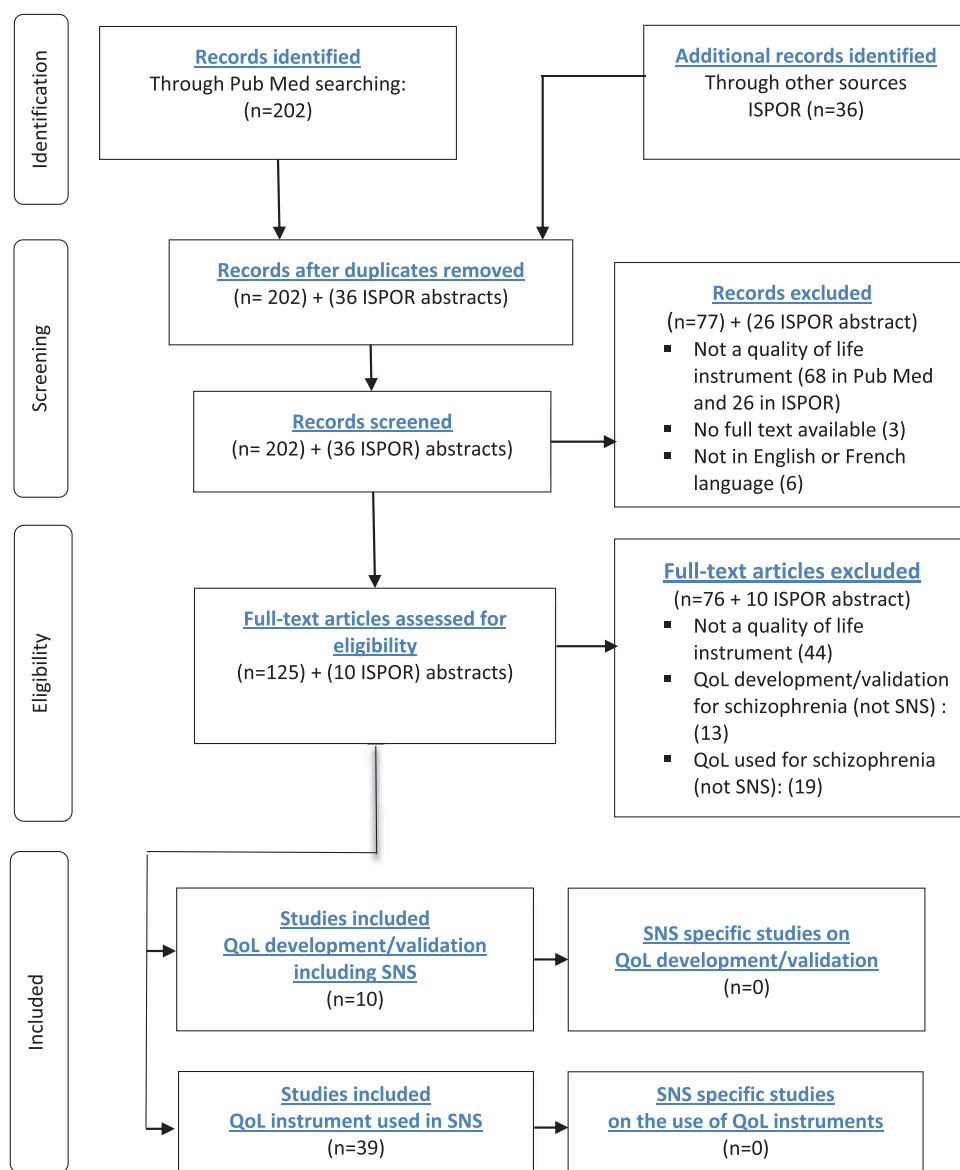


Figure 1. Flow chart.

work/financial situation, living activities, and leisure activities. Three validation studies on the following instruments: the Brief Quality-Of-Life Questionnaire in Schizophrenia (S-QoL-18) [19], the Satisfaction with Life Domains Scale (SLDS) [20], and the schizophrenia-specific Quality-Of-Life Scale (QLiS) [21,22] include evaluations of these instruments' validity in SNS patient populations. The S-QoL-18 is a short form of the S-QoL, which was initially developed by Auquier et al in 2003 [23]. It was then, shortened and validated by Boyer et al. in 2010 [19]. And It demonstrated strong psychometric proprieties (robust validity, moderate reliability, and moderate sensitivity to change). The SLDS was developed by Baker and Intagliata in 1982 [24] for the assessment of HRQoL in patients with several mental illnesses and in 2009, it was validated by

Carlson et al. [20] as a schizophrenia-specific HRQoL instrument. This instrument showed a moderate validity and reliability, while the sensitivity to change was not assessed. Lastly, Franz et al. developed a German version of the QLiS in 2012 [21]. It demonstrated a moderate validity and reliability, but the sensitivity to change was not assessed.

Overview of SNS assessment in HRQoL instruments specific to schizophrenia

SNS were assessed using the Positive and Negative Syndrome Scale (PANSS) [24,25] in 9 studies: 3 schizophrenia-specific HRQoL instruments and 6 severe mental illness instruments – all of these instruments were validated in

Table 3. HRQoL instruments used in patients with schizophrenia.

Acronyms	Complete label	No of items	No of dimensions	Include patients with SNS	Studies
Generic HRQoL instruments					
EQ-5D	EuroQol-5D	5	5	No	Prieto 2003 [50]
SF-36	Short Form 36 Health Survey	36	8	No	Ware 1993 [51]
WHOQOL-100	The World Health Organization Quality of Life Scale	100	6	No	The WHOQOL Group 1998 [52]
WHOQOL-Bref		26	4	No	Skevington 2004 [53]
Severe mental illness HRQoL instruments					
QoLI	The brief Quality of Life Interview	74	8	Yes	Lançon 2000 [54]
LQOLP	Lancashire Quality of Life Profile	24	9	No	Oliver 1996 [55]
MANSA	Manchester Short Assessment of Quality of Life	12	NA	No	Priebe 1999 [56]
SWN	Subjective Well-being under Neuroleptics Scale	38	5	Yes	Naber 2001 [57]
SWN-20		20	5	Yes	de Hann 2002 [58]
TOOL	The Tolerability and Quality of Life questionnaire	8	8	Yes	Montejo 2009/2011 [59,60]
WQLI	Wisconsin Quality of Life Index	47	8	No	Diaz 1991[61]
S.QUA.LA	Subjective Quality of Life Analysis	22	44	Yes	Nadalet 2005 [62]
Q-LES-Q	Quality of Life Enjoyment and Satisfaction Questionnaire	60	7	No	Pitkänen 2012 [63]
Q-LES-Q-18		18	5	Yes	Ritsner 2005 [64]
Schizophrenia specific HRQoL					
S-QoL	Quality-of-life Questionnaire in Schizophrenia	41	8	No	Auquier 2002 [23]
S-QoL-18		18		Yes	Boyer 2010 [19]
SQLS	Schizophrenia Quality of Life Scale	30	3	No	Wilkinson 2000 [65]
		30	3	No	Kaneda 2002 [66]
SLDS	Satisfaction with Life Domains Scale	15	15	Yes	Carlson 2009 [20]
QLIS	Schizophrenia-Specific Quality-of-life Scale	52	12	Yes	Franz 2012, 2013 [21,22]

patients with schizophrenia in general, although including patients with SNS. Five instruments (SWN-38, SWN-20, QoLI, Q-LES-Q-18, and S-QoL-18) were negatively correlated with the negative factor of PANSS. The correlation between HRQoL instrument and instruments assessing SNS was not assessed in 3 validation studies (TOOL, S-QUA-LA, and QLIS). PANSS negative scores were not assessed in the SWN-20 and the Q-LES-Q-18 validation studies. In all these studies, no data on the percentage of patients with SNS, and items expressing SNS were available (Table 5).

Discussion

We failed to identify any HRQoL instrument validated in patients with SNS; however, we found 19 instruments validated in patients with schizophrenia, potentially including those with SNS. Nevertheless, the lack of information related to the proportion of patients with SNS in the study populations and the negative correlation between instruments assessing SNS and HRQoL instruments suggest that they were not intended for patients with SNS. Our findings confirm that today, HRQoL instruments lack sufficient validity to assess condition and treatment effects in patients with schizophrenia.

Instruments that measure HRQoL in mental health, especially in schizophrenia, have been increasingly introduced to clinical practice as a good method to monitor treatment results, functioning, and quality of life [18,25]. No HRQoL questionnaire specific to patients

with SNS was identified in this review; however, we identified 6 non-specific mental health instruments and 3 schizophrenia-specific instruments that included patients with SNS in their validation studies, but did not present any psychometric properties for this specific population. Additional 10 instruments were validated in patients with schizophrenia in general without any information about patients with SNS. Among schizophrenia-specific instruments, PANSS was used to assess SNS; however, specific data on those patients was unavailable. The lack of information on SNS population and items that capture quality of life in patients with SNS make HRQoL instruments unable to assess the entire range of SNS and the level of their expression. Thus, those results question the level of measurement of these instruments specific to schizophrenia in SNS population.

Baumstarck et al. [26,27] demonstrated that cognitive dysfunction (including in SNS symptoms) did not compromise the reliability or validity of HRQoL questionnaire and highlighted the relevance of using HRQoL assessments in clinical practice. In addition, Savill et al. [28] showed recently that subjective quality of life is associated with anhedonia, amotivation (avolution), and asociality but not with blunted affect and alogia. The authors conclude that an improvement in these symptoms can translate into the improvement in subjective quality of life. Those recent studies raise awareness around the need of a better understanding of the SNS

Table 4. Psychometric validation of schizophrenia-specific HRQoL instruments.

Acronyms	validity						Studies	
	Face validity/Content validity	Construct validity (internal validity)	Construct validity (external validity)	Cross-cultural validity	Reliability internal consistency	Reliability reproducibility (test-retest)		
S-QoL-18	Face validity <ul style="list-style-type: none">• Floor effects from 10.2% to 28.8%• Ceiling effects from 12.7% to 35.1%• Missing data 2–10%	Discriminant validity <ul style="list-style-type: none">• Items internal consistency >0.4• Satisfactory internal consistency (from 0.80 to 0.93)• NA	<ul style="list-style-type: none">• High correlation between S-QoL-18 and S-QoL 41 >0.80• Negative correlation between S-QoL 18 dimension scores, CGI and CDSS scores (except CGI-RFa and CDSS-RFa)	• NA	• Cronbach's alpha: from 0.72 to 0.84	• Satisfactory test–retest reliability for 72 stable patients	• Study on 28 patients: Improved health status (reduced total PANSS≥ 20%) after 6 months	Boyer 2010 [19]
SLDS	Face validity <ul style="list-style-type: none">• Filling time: 10 min Content validity <ul style="list-style-type: none">• Pilot study to check comprehensibility of the instrument	<ul style="list-style-type: none">• NA	Divergent validity <ul style="list-style-type: none">• No correlations between SLDS and other instruments that evaluated different constructs.• Correlation between SLDS and PANSS, general subscale and with the score in the Strauss and carpenter ($r = 0.2$)• Positive correlation between QLIS and WHOQOL-BREF dimensions Variance for non-QLIS QoL instruments was >20% after controlling for global life satisfaction	• Translation and back-translation of SLDS by 2 natives Discrepancies: approved by consensus	• Cronbach's alpha: 0.84	• High intraclass correlation coefficient for all domains except for 3 (<0.60).	• NA	Carlson 2009 [20]
QLIS	Content validity <ul style="list-style-type: none">• FStructured open-ended interview• Literature review	• NA		• NA	• Cronbach's alpha: >0.70 with the exception of 1 subscale	• Reproducibility assessed between (D1 and D7 or D14) Positive correlation between PANSS scores and the GAF global score	• NA	Franz 2012, 2013

[21,22]

Abbreviations: S-QoL-18 – Quality of Life Questionnaire in Schizophrenia – Short Form; RFa – Family relationships; PANSS – Positive and Negative Syndrome Scale; WHOQOL – The World Health Organisation Quality of Life Scale; CGI – Clinical Global Impressions Scale; SLDS – Satisfaction with Life Domains Scale; QLIS – Schizophrenia-specific Quality of Life Scale; GAF – Global Assessment of Functioning.

Table 5. Negative symptoms in HRQoL validation studies.

Acronyms	instrument assessing SNS	Correlation between 2 instruments	Score of patients with SNS in this instrument (mean \pm SD)	Studies
QoLI	PANSS	<ul style="list-style-type: none"> Significant correlation between PANSS Negative symptoms and 'satisfaction with leisure activities', 'satisfaction with life in general', 'friendships' and 'state of health' dimensions of the QoLI 	<ul style="list-style-type: none"> PANSS total score: 84.6 ± 20.8 Positive factor: 18.2 ± 7.0 Negative factor: 24.5 ± 6.9 General psychopathology: 41.7 ± 10.2 PANSS positive factor: 21.09 ± 5.84 PANSS negative factor: 23.69 ± 6.40 PANSS general psychopathology: 90.51 ± 18.72 NA 	Lançon 2000 [54]
SWN-38	PANSS	<ul style="list-style-type: none"> Negative correlations between SWN-38 domains and PANSS negative score 	<ul style="list-style-type: none"> PANSS positive factor: 21.09 ± 5.84 PANSS negative factor: 23.69 ± 6.40 PANSS general psychopathology: 90.51 ± 18.72 NA 	Naber 2001 [57]
SWN-38 and SWN-20	PANSS	<ul style="list-style-type: none"> Negative correlations between dimensions of SWN-38 and PANSS Negative score (-0.28) 	<ul style="list-style-type: none"> PANSS positive factor: 19.91 ± 7.94 PANSS negative factor: 19.91 ± 7.94 PANSS general psychopathology: 32.76 ± 12.09 PANSS total score: 43.74 ± 16.71 PANSS positive factor: 9.58 ± 4.38 PANSS negative factor: 15.25 ± 11.22 PANSS general psychopathology: 22.40 ± 7.94 NA 	De Hann 2002 [58]
TOOL	PANSS	<ul style="list-style-type: none"> Native correlation between dimensions of SWN-20 – PANSS negative score (-0.3) NA 	<ul style="list-style-type: none"> PANSS positive factor: 19.91 ± 7.94 PANSS negative factor: 19.91 ± 7.94 PANSS general psychopathology: 32.76 ± 12.09 PANSS total score: 43.74 ± 16.71 PANSS positive factor: 9.58 ± 4.38 PANSS negative factor: 15.25 ± 11.22 PANSS general psychopathology: 22.40 ± 7.94 NA 	Montejo 2011 [59]
SQUALA	PANSS	<ul style="list-style-type: none"> NA 	<ul style="list-style-type: none"> PANSS total score: 43.74 ± 16.71 PANSS positive factor: 9.58 ± 4.38 PANSS negative factor: 15.25 ± 11.22 PANSS general psychopathology: 22.40 ± 7.94 NA 	Nadalet 2005 [62]
Q-LES-Q-18	PANSS	<ul style="list-style-type: none"> Negative correlation between 'subjective feeling' and 'social relationship' and PANSS negative scores. 	<ul style="list-style-type: none"> PANSS total score: 69.6 ± 18.4 Positive factor: 15.7 ± 6.1 Negative factor: 19.2 ± 6.9 General psychopathology: 35.8 ± 9.6 NA 	Ritsner 2005 [64]
S-QoL-18	PANSS	<ul style="list-style-type: none"> Positive correlation between 'leisure activities', physical health and general index' Negative correlations between 5 dimensions of S-QoL-18 dimension scores PANSS- negative factor. Three significant correlations between 'relationships with friends', 'resilience and autonomy' dimensions of S-QoL-18 and PANSS- negative factor. 	<ul style="list-style-type: none"> PANSS total score: 69.6 ± 18.4 Positive factor: 15.7 ± 6.1 Negative factor: 19.2 ± 6.9 General psychopathology: 35.8 ± 9.6 NA 	Boyer 2010 [19]
SLDS	PANSS	<ul style="list-style-type: none"> Negative correlations between SLDS dimensions and PANSS negative factor. 	<ul style="list-style-type: none"> PANSS positive factor: 13.2 ± 5.5 PANSS negative factor: 15.0 ± 5.5 PANSS general psychopathology: 28.7 ± 7.3 	Carlson 2009 [20]
QLIS	PANSS	<ul style="list-style-type: none"> NA 	<ul style="list-style-type: none"> PANSS positive factor: 13.2 ± 5.5 PANSS negative factor: 15.0 ± 5.5 PANSS general psychopathology: 28.7 ± 7.3 	Franz 2012 [21]

Abbreviations: MANSA – Manchester Short Assessment of Quality of Life; PANSS – Positive and Negative Syndrome Scale; SWN – Subjective Well-being under Neuroleptics Scale; TOOL – The Tolerability and Quality of Life questionnaire; WQLI – Wisconsin Quality of Life Index; SQUALA – Subjective Quality of Life Analysis; Q-LES-Q-18 – Quality of Life Enjoyment and Satisfaction Questionnaire short form; S-QoL-18 – Quality of Life Questionnaire in Schizophrenia – Short Form; SLDS – Satisfaction with Life Domains Scale; QLIS – Schizophrenia-specific Quality of Life Scale; QoLI – The brief Quality of Life Interview.

population and may be very useful in the validation of HRQoL scales or for the development of a new HRQoL specific to this population.

Despite well assessed psychometric properties, the development and use of HRQoL scales require appropriate methodology and studies that justify the choice of an instrument [18,29]. In clinical practice, instruments that can show benefits are recommended, while in clinical research, those that respond to study objectives. Thus, using them in patients with SNS, these instruments should address specifics of this population. Furthermore, after the validation process and prior to the translation of an instrument that measures patient reported outcomes from its original language to others, we recommend a linguistic validation that adapts preliminary translation and reflects cultural and linguistic differences between diverse target populations [18,29]. We also recommend intercultural validation, which addresses cultural differences between the country where the instrument was validated and the country in which it was translated.

Currently, SNS represent an unmet therapeutic need as well as a highly personal and social burden for a large number of patients [4,30]. Patients with schizophrenia are unable to live independently and manage everyday social situations mainly due to SNS, especially since these symptoms are the most troubling [31]. Thus, targeting SNS in the treatment of schizophrenia may result in significant functional benefits [32]. Evaluation of SNS is still facing major limitations, such as heterogeneity of symptom definitions, even after the consensus statement from 2006 [3]. Furthermore, an assessment of a patient with SNS may be affected by co-occurrence of positive symptoms, such as hallucinations and difficulties in communication, like alogia and affective flattening [1]. Future studies should be performed with the aim to standardize definitions of SNS and to assess consequences of SNS on the patient's life.

Two limitations of this review should be noted. The first one was that the search was performed only in Medline and ISPOR databases. Secondly, included studies were in French and English only, thus questionnaires developed and validated in other languages were not analysed.

Conclusion

None of the HRQoL instruments has been validated in patients with SNS only; thus, it is unclear whether they can comprehensively evaluate their condition. A high prevalence of SNS in patients with schizophrenia highlights the need for the development of HRQoL

instruments that would allow clinicians to assess quality of life and monitor treatment results in patients with SNS.

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Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

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