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Exploring cross-sectional and longitudinal symptomatic remission and subjective quality of life in schizophrenia

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ABSTRACT

Achieving symptomatic remission, as defined by the Remission in Schizophrenia Working Group, is intended to be a meaningful outcome for individuals with schizophrenia, resulting in enhanced well-being. Cross-sectional studies have reported an association between symptomatic remission and subjective quality of life (QoL). Longitudinal studies aimed at examining this association have showed mixed results. The aim of this study was to explore the relationship between symptomatic remission and subjective QoL, both cross-sectionally and longitudinally.

The study comprised data from what were at most 386 patients with schizophrenia, of whom 122–140 were followed over a period of four years. Based on cross-sectional remission status and longitudinal remission pattern, differences in subjective QoL were explored. Remission status was assessed using the Positive and Negative Syndrome Scale (PANSS), and subjective QoL using the Short Form-36 Health Survey (SF-36).

Both the cross-sectional and the longitudinal approach showed that patients in symptomatic remission had significantly higher subjective QoL. Patients who were in non-remission at baseline, but who achieved remission at follow-up, also had significantly higher subjective QoL at follow-up compared with baseline.

The results from the study show a clear association between symptomatic remission and subjective QoL. However, achieving symptomatic remission does not appear to be a guarantee of sustained subjective QoL, and only continued stable remission appears to result in such an outcome.

1. Introduction

In 2005, the Remission in Schizophrenia Working Group (RSWG) formulated criteria for remission in schizophrenia (Andreasen et al., 2005). The emphasis was on the importance of measuring clinical factors linked to the patients' well-being that were of benefit not only to the patients and those close to them, but also to clinicians. Symptomatic remission in schizophrenia is defined as core symptoms improving to such an extent that any remaining symptoms are of such low intensity that they do not restrict an individual's ability to manage activities of daily living (ADLs) for a period of at least six months (Andreasen et al., 2005; van Os et al., 2006). Recovery is a multidimensional concept (Vita and Barlati, 2018). Most studies on recovery include at least clinical and social improvement, over a persistent period of at least two years (Jääskeläinen et al., 2013). Symptomatic remission is not equivalent to recovery, but is described as a necessary step toward recovery (Andreasen et al., 2005). Unless stated otherwise, from this point forward the meaning of the term *remission* is as defined in Andreasen's criteria for symptomatic remission.

The aim of remission is that it should be meaningful for the patient, which is in line with the World Health Organization's (WHO) definition of health as a fundamental human right. In the WHO definition the emphasis is on both physical and mental health, together with social well-being (Health 2013, 2020). The Quality of Life (QoL) concept was developed to assess subjective, experience-based well-being (Lehman et al., 1982; Awad et al., 1997), which must be the aim in the treatment of every disease (Health 2013, 2020), including schizophrenia (Haro et al., 2014). It has been noted in a number of scientific articles, including a meta-review by Dong et al. (2019), that individuals with schizophrenia typically have lower subjective QoL compared with a healthy population. From this point forward in the paper, the term SQoL refers to *subjective* QoL, if not stated otherwise.

Being in remission, as opposed to not being in remission, has been shown to be associated with improved functional status (Karow et al.,

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2012), improved social functioning (Lasser et al., 2007), improved cognitive functioning (Helldin et al., 2006; Holthausen et al., 2007; Johansson et al., 2020) and reduced burden on relatives (Hjärthag et al., 2008). Cross-sectional studies have also shown remission to be associated with higher SQoL (Helldin et al., 2008; Karow et al., 2012). However, longitudinal studies examining associations between remission and SQoL have produced mixed results. This could be attributed to the use of different measurement methods, mainly when measuring SQoL, but also to some extent when measuring remission. Some studies that failed to find associations between remission and SQoL, viewed general symptoms, such as depression and anxiety, as potential contributing factors. Despite remission status, they argue, these factors could be present and have a negative impact on SQoL (e.g. Karow et al., 2012).

Haro et al. (2014) followed more than 6000 patients over a three-year period and found that SQoL in all groups increased over the three years, irrespective of the remission pattern (stable remission, intermittent remission, and never in remission). The group in stable remission was the one whose SQoL increased the most. Significant differences between the groups' SQoL emerged during each measurement, even after controlling for confounding factors. In this study, Andreasen's criteria for remission were not used and a Visual Analogue Scale (VAS) was applied to measure SQoL. Bodén et al. (2009) found that patients in remission five years after the first episode had a significantly higher SQoL compared with patients who were in non-remission. However, in this study there was no baseline score that allowed a comparison to be made with the follow-up. Jaracz et al. (2015) also found that remission status over time was associated with improved SQoL as patients in stable remission had a higher SQoL than patients in stable non-remission. Wunderink et al. (2007) found a moderate improvement in SQoL from baseline to follow-up regardless of remission status, although no difference was found in SQoL based on remission status at follow-up. However, as this study did not use Andreasen's criteria for remission and only included patients in remission based on positive symptoms at baseline, comparison with other studies is difficult. Emsley et al. (2007) found a higher SQoL after two to four years compared with baseline, along with a concurrent decrease in core symptoms. In their longitudinal follow-up study, van Os et al. (2006) found that SQoL was not affected by remission status to the same extent as other clinical and outcome variables. In a 10-year follow-up study, Gardsjord et al. (2018) found that individuals in remission at the 10-year follow-up had a higher SQoL compared with those in non-remission (this finding could also be traced back a few years) whereas there was no significant difference in the baseline measurement. Individuals in full recovery reported a higher SQoL compared with individuals in remission.

However, to our knowledge, no previous study has examined longitudinal remission pattern (stable remission, stable non-remission, unstable: remission - non-remission, unstable: non-remission - remission) based on the remission criteria defined by Andreasen et al. (2005) and at the same time examined potential differences in SQoL. In previous studies we showed that patients in remission with lower symptom intensity (minimal), compared to those in remission with mild symptom intensity, had longer sustainability of remission (Johansson et al., 2018) and improved cognitive functioning (Johansson et al., 2020). This warrants the examination in this study of symptom intensity over time and its possible association with SQoL.

1.1. Purpose and questions

The overall purpose of this study is to investigate whether being in remission can be perceived as meaningful for patients with schizophrenia. Adopting an explorative approach, the relationship between remission and SQoL is examined, using both cross-sectional and longitudinal methods.

The following questions were examined:

Q1: Are there differences in the two composite summary scores of SQoL between patients in remission and patients in non-remission? Furthermore, are there differences in SQoL within the group in remission, between patients with a minimal degree of symptom intensity and patients with a mild degree of symptom intensity? This is studied cross-sectionally at baseline and at four-year follow-up, respectively.

Q2: Are there differences in the eight domains of SQoL between patients in remission and patients in non-remission? This is studied cross-sectionally at baseline and at four-year follow-up, respectively.

Q3: Are there differences in the two composite summary scores of SQoL at baseline and four-year follow-up between patients who exhibit different remission patterns (stable remission, stable non-remission, unstable: remission - non-remission, unstable: non-remission - remission) over a four-year period from baseline to four-year follow-up?

Q4: Within each group of remission pattern (stable remission, stable non-remission, unstable: remission - non-remission, unstable: non-remission - remission), are there differences in the two composite summary scores of SQoL over time between baseline and four-year follow-up?

2. Methods

2.1. Procedure

This study is part of the Clinical Long-term Investigation of Psychosis in Sweden (CLIPS) project, which is a naturalistic follow-up study of individuals diagnosed with schizophrenia spectrum disorders. Since the project began in the year 2000, more than 500 individuals have taken part in the study. Assessments in the current study were made by case managers in the psychiatric outpatient care, all of whom had undergone training and completed joint rating exercises for the instruments used. Participants in the study were baseline rated at some point between the year 2000 and 2015.

The primary inclusion criteria for the study were that the participants met the DSM-IV criteria for one of the sub-types within schizophrenia spectrum disorders (American Psychiatric Association, 2000, 2014). Further inclusion criteria in the study were that each participant should have data on both remission status and SQOL. The exclusion criteria were comorbidity in ongoing substance abuse, autism, dementia, or intellectual development disorder.

2.2. Measurements

In order to define remission status according to the Andreasen criteria (Andreasen et al., 2005), eight core symptoms from Positive And Negative Syndrome Scale (PANSS) (Kay et al., 1987) were used. In this study, the Swedish translation of the instrument was used (Structured Clinical Interview – Positive and Negative Syndrome Scale (SCI-PANSS)) (Lindström et al., 1994).

The Medical Outcomes Study Short Form-36 Health Survey (SF-36) were used to assess SQOL. SF-36 is a self-administered questionnaire measuring eight of the most important health domains: *Physical functioning* (PF), *Social role functioning* (SF), *Physical role functioning* (RP), *Emotional role functioning* (RE), *Mental health* (MH), *Vitality* (VT), *Bodily Pain* (BP), and *General health perceptions* (GH) (Ware et al., 1993). Based on the eight health domains, two composite summary scores can be calculated to facilitate analysis and comparison – a mental composite summary (MCS) score for mental health and a physical composite summary (PCS) score for physical health. In the calculation from raw scores to index scores, each dimension has been recoded and assigned a score ranging from 0 (lowest SQoL) to 100 (highest SQoL). The RAND (Research and Development Corporation) instructions were used to compute the results, where the domain points represent the mean of the recoded answers within each domain (Hays et al., 1998). The Swedish

translation of SF-36 version 1 was used in this study (Sullivan et al., 1995, 2002).

2.3. Participants and design

The mean age at baseline was 47 years (SD = 12.5), and the participants consisted of 170 women and 216 men. There were no significant differences regarding age or gender between the patients included and excluded in the study. After checking the baseline group ($n = 386$) for age and gender, no significant differences emerged between the groups in remission and non-remission. Characteristics for the participants is presented in Table 1.

Two questions in the study were analysed cross-sectionally (Q1-Q2), and two longitudinally (Q3-Q4). For Q1-Q2, patients needed data on remission and SQoL for baseline ($n = 386$) and four-year follow-up ($n = 240$), respectively. For Q3-Q4 patients needed data on remission for five consecutive years (ratings), from baseline to four-year follow-up. In addition to that they also needed data on SQoL for both baseline and four-year follow-up. 140 patients met these inclusion criteria for MCS, and 122 for PCS, creating two groups for answering Q3-Q4.

The patients were further divided into groups based on remission status. For Q1-Q2, one group of patients was in remission, the other one not in remission at the two assessments, respectively. The remission groups were further split into two groups based on symptom intensity (only minimal symptoms versus mild symptoms). For Q3-Q4, patients were divided into four groups, based on longitudinal remission data: Stable remission at all assessments; Stable non-remission at all assessments; Unstable with remission at baseline and non-remission at four-year follow-up; and Unstable with non-remission at baseline and remission at four-year follow-up.

2.4. Data analysis

Descriptive statistics – mean value, standard deviation, and percentage – summarised the participants' data on remission and SQoL. Mann-Whitney U test and Chi-Square test were conducted to determine whether age and gender (dependent variables) differed based on remission status or study inclusion/exclusion (independent variables).

Differences in SQoL based on remission status at baseline and four-year follow-up, were investigated using Mann-Whitney U test (two groups: remission and non-remission), and Kruskal-Wallis H test was used to include symptom intensity (three groups: remission - minimal symptoms, remission - mild symptoms, and non-remission). The Mann-Whitney U test was used to examine whether the eight health domains had any association with remission status at baseline and four-year follow-up.

The Kruskal-Wallis H test was used to examine the differences in SQoL based on the longitudinal remission pattern with a subsequent Mann-Whitney U test. The Wilcoxon signed-ranks test was used to examine differences in SQoL between baseline and four-year follow-up for each group of remission pattern.

SQoL (MCS and PCS) was a consistently dependent variable throughout the analyses. The independent variable was remission status, except for the Wilcoxon signed ranks test where the independent variable was the measurement point (baseline and four-year follow-up). Non-parametric analysis methods were used due to non-normally distributed data and at times small groups ($n < 30$).

All statistical data analyses were carried out using the IBM SPSS Statistics version 28.0.0.0 software.

Table 1
Clinical and demographic characteristics at baseline
Presentation of age of onset, age at baseline, level of education, gender and marital status in the three remission-groups minimal symptoms, mild symptoms and non-remission, respectively.

	Remission minimal symptoms	Remission mild symptoms	Non-remission
Age of onset m (sd)	29.5 (13.2)	26.3 (10.1)	25.8 (9.6)
Age m (sd)	47.4 (12.7)	46.0 (12.3)	46.7 (12.6)
Number of psychiatric hospitalizations m (sd)	5.2 (5.0)	7.0 (8.1)	7.4 (10.1)
Level of education%			
Primary	39.3	40.4	48.4
Secondary	41.0	41.4	39.4
Tertiary	19.7	18.2	11.8
Gender%			
Female	47.7	43.4	43.2
Male	52.3	56.6	56.8
Marital status%			
Married/cohabiting	40.0	25.3	13.6
Divorced/widowed/ separated	18.5	23.2	22.6
Single	41.5	51.5	63.8

2.5. Ethics

The study was approved by the Ethics Committee in Gothenburg and complied with the ethical principles set out in the Helsinki Declaration. All the patients provided informed written consent before inclusion in the study.

3. Results

3.1. Symptomatic remission status and remission pattern of the study participants

In the cross-sectional analyzes 42.4 percent of the participants were in remission at baseline, and another 16 percent at the four-year follow-up. In the longitudinal analyzes there were about 22 percent in the stable remission group, and between about 17 and 19 percent in the stable non-remission group. In the unstable group, about 42 percent moved from non-remission at baseline to remission at follow-up, whereas between 16 and 17 percent moved from remission to non-remission (Table 2).

Regarding type of antipsychotic medication there were no significant differences between the group in remission and in non-remission at baseline, analyzed with the Chi square test ($x^2 = 6.263$, $p = .099$). In the remission group, 66.3 percent had second generation antipsychotics, versus 71.8 percent in the non-remission group. The percentage of first generation antipsychotics were 22.3 in the remission group, versus 16.8 in the non-remission group. In the remission group, 2.4 percent had a combination of both second and first generation antipsychotics, versus 5.9 in the non-remission group. No antipsychotic medication was prescribed to 9 percent in the remission group, versus 5.5 percent in the non-remission group. Further analysis on the remission group divided into mild and minimal symptoms showed similar results ($x^2 = 6.300$, $p = .390$).

3.2. Q1 & Q2: cross-sectional analyses (baseline and four-year follow-up)

In total, cross-sectional analyses revealed significant differences in SQoL between patients in remission and in non-remission. Patients in remission achieved significantly higher MCS- and PCS scores at baseline and four-year follow-up. After the patients in remission were divided based on symptom intensity (mild and minimal), no significant difference emerged between these two groups, regarding either MCS or PCS. However, both patients with minimal and mild symptom intensity differed significantly in comparison with those not in remission (Table 3).

Regarding the eight health domains of SQoL (*PF, SF, RP, RE, MH, VT, BP,* and *GH*), there were significant differences at baseline between patients in remission and patients in non-remission ($p < 0.001$ for all

Table 2
Participants' symptomatic remission status and remission pattern
Symptomatic remission status and remission pattern of the study participants, related to the four research questions (Q1-Q4) and their research designs (cross-sectional and longitudinal, respectively).

Cross-sectional	Remission status total	*Remission*	*Remission mild symptoms*	*Remission minimal symptoms*	*Non-remission*
Baseline (Q1) N (%)	386 (100)	164 (42.4)	99 (25.6)	65 (16.8)	222 (57.6)
4-year follow-up (Q2) N (%)	240 (100)	140 (58.4)	81 (33.8)	59 (24.6)	100 (41.6)
Longitudinal	Remission pattern total	*Stable remission*	*Stable non-remission*	*Unstable: remission-nonremission*	*Unstable: nonremission-remission*
SQoL MCS (Q3 & Q4) N (%)	140 (100)	32 (22.9)	24 (17.1)	24 (17.1)	60 (42.9)
SQoL PCS (Q3 & Q4) N (%)	122 (100)	27 (22.1)	23 (18.9)	20 (16.4)	52 (42.6)

Table 3
Subjective Quality of Life for Mental and Physical Composite Scores
Differences in Subjective Quality o Life (Mental Composite Score and Physical Composite Score) according to cross-sectional remission status (without and with symptom intensity levels – mild/minimal). The superscripts signify the Kruskal-Wallis H-value between the different remission groups.

Remission & non-remission	*SQoL MCS baseline*	*SQoL MCS 4-year follow-up*	*SQoL PCS baseline*	*SQoL PCS 4-year follow-up*
Remission mean rank (M/SD)	229.85 (73.7/19.1)	140.26 (74.9/18.1)	221.86 (74.4/18.6)	136.60 (74.6/20.1)
Non-remission mean rank (M/SD)	166.08 (61.2/22.7)	92.84 (60.3/21.8)	172.10 (64.8/21.5)	97.97 (63.3/21.2)
Mann-Whitney U (p-value)	12,226.5 (<0.001)	4233.5 (<0.001)	13,552.5 (<0.001)	4746.5 (<0.001)
Remission minimal & remission mild & non-remission				
Remission minimal mean rank (M/SD)	247.67[a] (77.7/14.1)	146.43[c] (76.9/16.0)	231.58[e] (76.3/17.5)	141.25[g] (76.0/19.2)
Remission mild mean rank (M/SD)	217.76[b] (71.0/21.6)	135.77[d] (73.4/19.5)	216.10[f] (73.2/19.4)	133.21[h] (73.5/20.7)
Non-remission mean rank (M/SD)	166.08[a,b] (61.2/22.7)	92.84[c,d] (60.3/21.8)	172.10[e,f] (64.8/21.5)	97.97[g,h] (63.3/21.2)
Kruskal-Wallis H (p-value)	32.694 (<0.001)	28.028 (<0.001)	19.679 (<0.001)	18.526 (<0.001)

[a] $=H = 31.803$, $p<.001$.
[b] $=H = 13.537$, $p<.001$.
[c] $=H = 23.353$, $p<.001$.
[d] $= H = 16.310$, $p=.001$.
[e] $= H = 14.939$, $p<.001$.
[f] $= H = 10.609$, $p<.001$.
[g] $= H = 13.752$, $p<.001$.
[h] $= H = 11.329$, $p=.001$.

domains apart from *BP* ($p = .005$) and *GH* ($p = .012$)). However, at the four-year follow-up there was no significant difference between patients in remission and patients in non-remission for the *BP* domain ($p = .259$). Also, the *GH* domain had a higher significance level ($p < .001$) at four-year follow-up compared with baseline ($p = .012$). In other respects, the results at follow-up remained unchanged compared with baseline (Table 4).

3.3. Q3 & Q4: longitudinal analyses

The analyses related to symptomatic remission pattern over time showed significant variations in SQoL between different remission patterns. Variations were obtained for both MCS and PCS at both baseline and four-year follow-up (Tables 2 and 5; Figs. 1 and 2).

Patients in stable remission had a significantly higher MCS-score at baseline compared with patients in stable non-remission, and with

Table 4
Comparison of SQoL during Remission and Non-Remission
Differences on the eight health domains of SQoL between remission and non-remission, analyzed with Mann-Whitney *U* test, at baseline and 4-year follow up, respectively.

Remission vs. non-remission	*Baseline*	*4-year follow-up*
Mental health	13,171.0/	4597.0/
U/p-value	<0.001	<0.001
Emotional role functioning	14,039.5/	4956.5/
U/p-value	<0.001	<0.001
Social role functioning	13,880.0/	4646.5/
U/p-value	<0.001	<0.001
Vitality	13,488.0/	4877.5/
U/p-value	<0.001	<0.001
Physical functioning	14,521.5/	4956.0/
U/p-value	.001	<0.001
Physical role functioning	14,144.0/	5387.5/
U/p-value	<0.001	.001
Bodily pain	15,357.5/	6426.0/
U/p-value	.005	.259
General health perceptions	15,532.5/	4352.0/
U/p-value	.012	<0.001

patients who began in non-remission but ended in remission. However, the patients who began in remission but ended in non-remission had a significantly higher MCS-score at baseline than those in stable non-remission. At baseline, the two unstable groups differed regarding MCS. The unstable group in remission at baseline had a significantly higher MCS-score than the unstable group that was in non-remission at the same point. At the four-year follow-up, patients in stable remission had a significantly higher MCS-score than the patients who switched from remission at baseline to non-remission at follow-up. A significantly higher MCS-score at follow-up was also achieved by those patients who switched from non-remission to remission, compared with those in stable non-remission. Even at the four-year follow-up, the unstable group differed regarding MCS. The group in remission at follow-up achieved a significantly higher MCS-score than the group in non-remission at follow-up.

Regarding PCS at baseline, the score was significantly higher for the patients in stable remission compared with those in stable non-remission and the unstable group that began in non-remission. Compared with the patients in stable non-remission, a significantly higher PCS-score was achieved at baseline for the unstable group that began in remission. At the four-year follow-up, patients in stable remission continued to achieve a significantly higher PCS-score compared with those in stable non-remission. A significantly higher PCS-score was also noted for patients who switched from non-remission to remission at follow-up compared with those in stable non-remission. Parallel, the group that started in remission and ended in non-remission lost the significant higher PCS-score compared to the group that never reached remission.

Finally, a Wilcoxon signed ranks test indicated that the group who went from not being in remission at baseline to being in remission at the

Table 5
Subjective Quality of Life for Mental and Physical Composite Scores and Longitudinal remission pattern
Differences in Subjective Quality of Life (Mental Composite Score and Physical Composite Score) according to longitudinal remission status. The superscripts signify the Kruskal-Wallis H-value between the different longitudinal remission groups.

Longitudinal remission pattern	*SQoL MCS baseline*	*SQoL MCS 4-year follow-up*	*SQoL PCS baseline*	*SQoL PCS 4-year follow-up*
Stable remission mean rank (M/SD)	94.94[a,b] (78.7/ 17.1)	77.5[e] (72.9/ 17.3)	81.87[g,h] (81.0/ 16.8)	75.59[j] (81.1/ 15.7)
Stable non-remission mean rank (M/SD)	56.13[a,c] (56.3/ 24.0)	58.38 (62.4/ 23.0)	41.67[g,i] (56.3/ 21.9)	44.02[j,k] (64.5/ 19.9)
Unstable: remission-nonremission mean rank (M/SD)	80.1[c,d] (70.2/ 21.1)	55.5[e,f] (58.9/ 24.9)	72.33[i] (76.09/ 18.7)	58.18 (71.3/ 21.2)
Unstable: nonremission-remission mean rank (M/SD)	59.38[b,d] (57.8/ 25.0)	77.62[f] (72.4/ 19.5)	55.53[h] (66.0/ 20.1)	63.19[k] (74.7/ 19.0)
Kruskal-Wallis H (p-value)	20.493 (<0.001)	8.229 (0.042)	19.556 (<0.001)	10.209 (0.017)

[a] $=H = 171.000$, $p<.001$.
[b] $=H = 480.500$, $p<.001$.
[c] $=H = 183.000$, $p=.030$.
[d] $= H = 505.000$, $p=.033$.
[e] $= H = 254.000$, $p=.031$.
[f] $= H = 504.500$, $p=.033$.
[g] $= H = 123.500$, $p<.001$.
[h] $= H = 386.000$, $p=.001$.
[i] $= H = 117.600$, $p=.006$.
[j] $= H = 147.500$, $p=.001$.
[k] $= H = 4.522$, $p=.033$.

four-year follow-up significantly improved their MCS- and PCS scores between the two assessments. The same test also showed that the group that was in stable non-remission had a significantly higher PCS-score at follow-up compared with baseline. None of the other remission groups differed significantly between the two assessments regarding MCS or PCS (Figs. 1 & 2).

4. Discussion

The results of the study show a clear association between SQoL and remission status. Patients who were in remission had a significantly higher SQoL in both the cross-sectional and longitudinal analyses. Patients who were in non-remission at baseline but who achieved remission at follow-up, also achieved a significantly higher SQoL at follow-up compared with baseline. The results from the cross-sectional analyses are in line with previous research, which showed a similar association between remission and SQoL (e.g. Karow et al., 2012). When making a comparison with similar previous research that used a longitudinal approach, the association between remission and SQoL appears to be more distinct in this study. This difference could be attributed to previous research using other instruments, other remission criteria, and other ways of measuring longitudinal remission status (e.g. Haro et al., 2014).

A previous study in the CLIPS project, showed that we should preferably strive for minimal rather than mild symptoms to increase the probability of sustained remission (Johansson et al., 2018). However, in the current study no significant differences emerged between patients with mild and minimal remission symptoms regarding SQoL. For SQoL to be improved, it thus appears to be sufficient that remission is achieved, and that the symptoms are defined based on the premise that they no longer constitute an obstacle to an individual's ability to live a normal daily life (Andreasen et al., 2005). Reducing the symptoms to an even lower intensity does not appear to result in any significant increase in SQoL. All eight health domains for SQoL differed significantly at baseline between patients in remission and those in non-remission, where the remission group achieved higher scores than the non-remission group. At the four-year follow-up, the results were the same with the exception of the bodily pain health domain, which no longer differed between the remission groups. The bodily pain health domain is included in physical composite score, as it proved to be valid for measuring physical health (Ware, 2000). Physical health does not appear to be as clearly affected by schizophrenia, which is the case with mental health. According to one study, physical health did not differ significantly between a healthy control group and a group with schizophrenia (Strassnig et al., 2003). Bodily pain is not a traditional symptom associated with schizophrenia even if mental disorders can

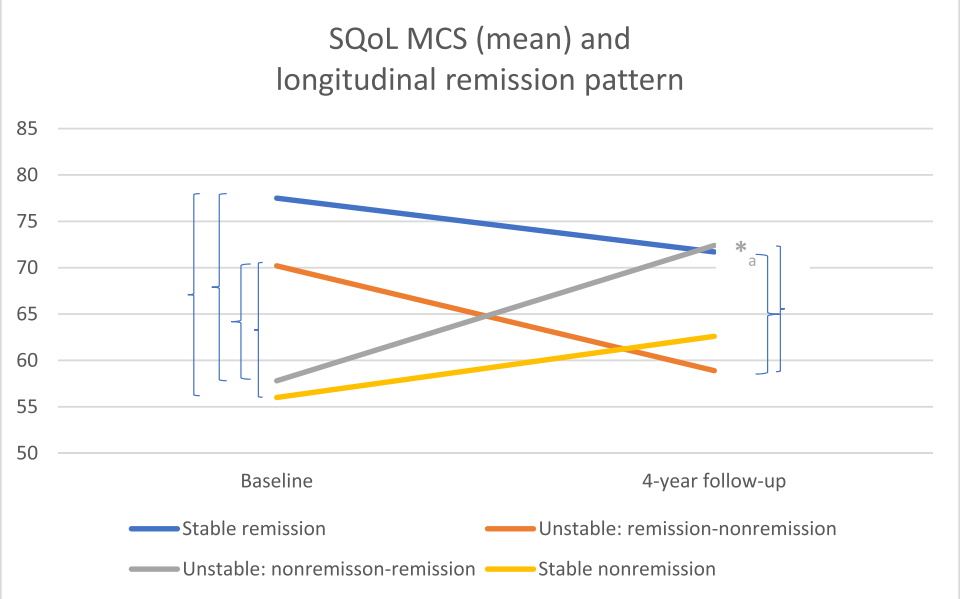

Fig. 1. Means of Subjective Quality of Life (Mental Composite Score) for different longitudinal remission patterns at baseline and 4-year follow-up. Significant differences between remission patterns at baseline and 4-year follow-up, respectively, are marked with brackets. Significant differences within each group of remission pattern, between baseline and 4-year follow-up, are marked with *.

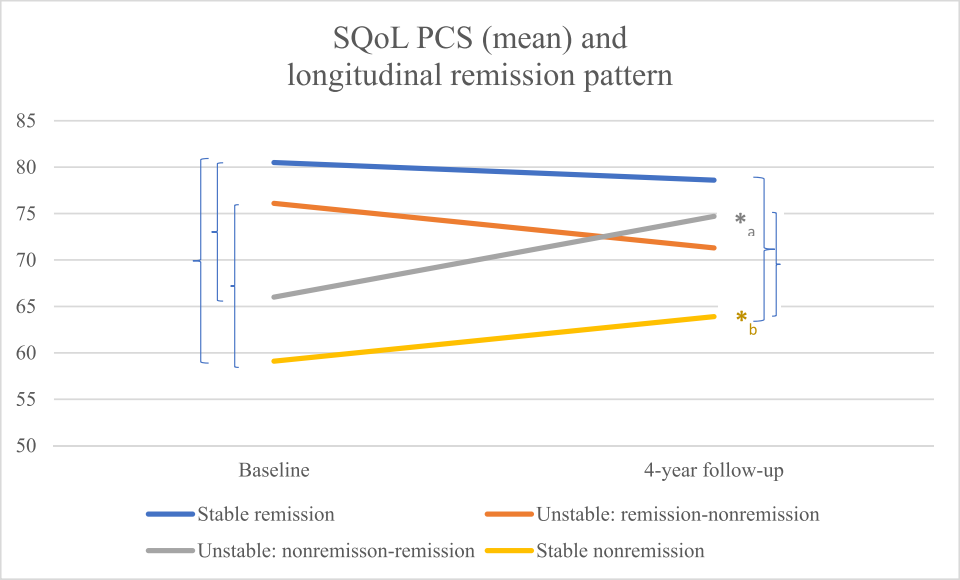

Fig. 2. Means of Subjective Quality of Life (Physical Composite Score) for different longitudinal remission patterns at baseline and 4-year follow-up. Significant differences between remission patterns at baseline and 4-year follow-up, respectively, are marked with brackets. Significant differences within each group of remission pattern, between baseline and 4-year follow-up, are marked with *.

involve elements of bodily pain (Bondesson et al., 2018). In our patient cohort the patients in non-remission at baseline had a lower physical composite score. Between the two cross-sectional analyses, 60 of the patients achieved remission, whilst 24 with a higher physical composite score experienced loss of remission. The change in group affiliation for the 84 patients could explain the disappearance of the difference between the groups as their bodily pain was probably not affected by the changes in remission status.

The study showed that the patients in stable remission over time had a significantly higher mental composite score at baseline compared with patients who began in non-remission but ended in remission. At the four-year follow-up, when both patient groups were in remission, there was no longer any difference in their mental composite scores, as the patients who had gone from non-remission to remission increased their mental composite scores.

Similarly, although in reverse, the patients who had never been in remission had significantly lower mental composite scores at baseline compared with the group that began in remission but ended in non-remission. At follow-up, when none of the groups were in remission, there was no longer any significant difference in mental composite scores.

At baseline, mental composite scores were significantly higher for the two groups in remission compared with the two groups in non-remission. Even the two divisions in the unstable group (remission - non-remission and non-remission - remission) differed significantly, which could be an indication that it was current remission status rather than longitudinal remission status that actually had an impact on mental composite score. Based on this result, the mean score for mental composite score at baseline did not appear to provide any indication of how SQoL might be four years later.

The only group that achieved a significant change in mental composite score between the two assessments was the unstable group, which went from being in non-remission at baseline to being in remission at the four-year follow-up, and where mental composite score improved significantly over time. Taking the mean values in isolation, both the unstable groups increased and decreased respectively to a similar extent. However, there were fewer patients who went from remission to non-remission (24) compared with the group who went from non-remission to remission (60), which could have contributed to the difference not reaching statistical significance.

In the case of physical composite score, the results produced a picture similar to mental composite score. The largest difference could be attributed to patients who were never in remission achieving a significantly better physical composite score at the four-year follow-up compared with baseline, even if the physical composite scores for this group continued to be worse than for all the other remission groups. The improvement could be explained by the fact that despite the patients in the group not achieving remission they had regular contact with care staff, who worked with them systematically to improve their well-being. According to a study by Olsson-Tall et al. (2019), this probably also led to feedback and a greater understanding of the disease, enabling the patients to acquire a more realistic view of themselves, their illness, and their lives.

Previous studies have revealed a discrepancy between self-reported and clinically reported SQoL, where in many clinically reported instances functioning is measured rather than SQoL (Cummins, 2000; Jung et al., 2010). Nor is there any general consensus regarding either the definition or the measuring of SQoL (Eack and Newhill, 2007). Furthermore, there is a limitation within self-rating generally, and specifically for the investigated population. Despite this, there are studies that have demonstrated the validity and reliability of self-rating even in a population with schizophrenia and executive dysfunction (Baumstarck et al., 2013). Despite possible limitations with both self-rating in the patient group and measuring SQoL, it was the patients' subjective perception of their SQoL specifically that we wanted to know more about and with as little external influence as possible. Consequently, the authors of this article still view self-rating as the best available method for obtaining the information that was being sought.

4.1. *Strengths and limitations*

There are several limitations in this study that need to be highlighted.

One limitation in this study is related to the different group sizes, particularly in the longitudinal analysis, where some groups were small ($n < 30$). The analysis method was adapted accordingly and despite a number of small groups, significant differences emerged that could also be viewed as a strength in this study. However, the weakness lies in the possibility that results would have perhaps emerged more clearly or in a different way with a larger group.

A further limitation in this study is that treatment-related factors, which could potentially be confounding factors, are not included in the analysis (e.g. medication, therapeutic alliance, insight, treatment adherence). However, potential confounding factors relating to age and gender were checked for, with no significant differences regarding remission status.

The time criterion in the remission concept according to Andreasen et al. (2005) (six months with mild symptoms or lower) is a recurring challenge in remission studies. The participants in this study were rated once a year using PANSS along with case managers going through a patient's medical records for the preceding year to ensure the patient had not deteriorated, which would negate the assertion that they had been in remission. Continued research into schizophrenia and SQoL would probably benefit from a greater understanding of underlying factors for SQoL. Which factors, apart from remission, can be associated with SQoL, and what are the predictive factors?

4.2. Conclusion

The results from this study show a clear association between symptomatic remission and SQoL. Consequently, symptomatic remission not only means that the patient achieved a remission status where the symptoms are no longer an obstacle to functional ability, it also appears to imply improved SQoL, both mentally and physically. However, achieving symptomatic remission does not offer any guarantee of sustained SQoL, and only continued stable remission appears to entail such a sustainability. Ultimately, the study provides further support for the benefit that can be derived as a result of the patient, through treatment, achieving sustained symptomatic remission.

CRediT authorship contribution statement

Madeleine Johansson: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Fredrik Hjärthag:** Conceptualization, Methodology, Supervision, Formal analysis. **Lars Helldin:** Conceptualization, Methodology, Supervision, Project administration, Investigation.

Declaration of Competing Interest

Lars Helldin has participated as educational speaker in meetings organized by Otsuka Pharmaceutical (2016), Jansen (2018) and Sunovion (2021).

Madeleine Johansson and Fredrik Hjärthag report no conflicts of interest.

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