Patients' awareness of recovery mediates the link between clinical and level of functional remission in schizophrenia to a larger extent in those treated with long-acting antipsychotics

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Abstract

Background: Clinical remission is a step towards functional remission for subjects with schizophrenia. While recovery is both a subjective personal journey and a clinical outcome to be targeted, data on patient self-rated outcomes are scarce.

Objectives: (i) To determine the extent to which the association between clinical and functional remission is mediated by the subjective experience of recovery as reported by patients *versus* their relatives or their psychiatrist and (ii) to assess differences according to treatment, specifically with oral antipsychotics only *versus* long-acting injectable antipsychotics (LAIs).

Design: Clinical observational study.

Methods: Community-dwelling participants with schizophrenia enrolled in the EGOFORS cohort ($N=198$) were included. Clinical symptoms and remission were assessed using the Positive and Negative Syndrome Scale. Functional remission was assessed with the Functional Remission of General Schizophrenia Scale. Awareness of recovery was assessed with one question 'What percentage of recovery do you think you have now (from 0% – no recovery – to 100% – full recovery)?', asked of the patient, also of the patient's close relative, and the psychiatrist. We used mediation analyses, taking into account the type of pharmacological treatment.

Results: Remission criteria and perceived remission measures were significantly correlated, both within and between groups ($r > 0.330$). The patient's awareness of recovery mediated the relationship between clinical remission and level of functional remission, while the level of recovery according to psychiatrists or close relatives did not. The direct effect of clinical remission on the level of functional remission became non-significant when taking into account the mediator (patients' awareness of recovery) in the group of patients with LAI ($t=1.5$, $p=0.150$) but not in the group of patients with other treatments ($t=3.1$, $p=0.003$).

Conclusion: Patients with LAIs may be more efficient in reporting their level of functional remission. Higher patient awareness could be an interesting candidate to explain this. However, as the study was cross-sectional, such a proposal should be tested with a more specifically designed protocol, such as a long-term cohort.

Keywords: antipsychotics, functional outcome, long-acting antipsychotics, patient-reported outcome measures, recovery, remission, schizophrenia

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Introduction

For many years, schizophrenia was considered a chronic and devastating illness with little or no chance of recovery.[1] Since the discovery of the psychoactive properties of chlorpromazine in the 1950s, the treatment of schizophrenia has undergone a major transformation, offering new perspectives to psychiatrists, patients and families. Psychiatric treatment has largely been driven by minimizing agitation and aggression and controlling positive symptoms (delusions, hallucinations). Indeed, the primary effect of antipsychotic drugs has been to reduce symptoms, which has not necessarily correlated with an improvement in social functioning.[2–4] However, the development of long-acting atypical antipsychotics, alongside the growth of psychosocial interventions, has demonstrated benefits for functional outcomes.[5] We assisted in a shift of treatment objectives from pharmacological containment to remission and, lately to recovery.[6] Although rarely measured in clinical trials, subjective functionality, quality of life, empowerment and the removal of internalized stigma are more important to patients and their families than clinical remission when considering recovery as a goal.[7]

Clinical (clinician) recovery is not patient recovery.[8,9] Patients report experiencing personal recovery despite persistent symptoms of psychosis.[10] Thus, recovery can occur even when psychotic symptoms persist.[11] Recovery can be considered both an outcome and a process. The combination of these two concepts provides the most comprehensive framework,[8] underscoring the need for more subjective measures that can reflect an awareness of recovery rather than 'insight' *per se*. For example, many consumer-based groups view recovery as a personal journey (i.e. a subjectively evaluated process of coping with symptoms over time) rather than a defined outcome (complete recovery *versus* persistent illness).[12,13] Increased patients' awareness of how close they are to functional remission may be an important factor in medication adherence (understanding of benefits) and related to the process of recovery (as both an outcome and a process). Alternatively, it is also possible that increased functional remission may lead to an increased subjective experience of recovery.

When evaluating the efficacy of pharmacological (and psychosocial) interventions in clinical trials, functional remission is a more realistic measure than recovery. More precisely, functional remission affects only one-third of treated patients who achieve symptomatic remission.[14–16] Some authors have suggested that '*When meeting criteria for clinical remission, symptoms can be present but must be mild in nature. Following this logic, complete achievement of wide-ranging normality in everyday functioning or "full recovery" should not be required to consider a person to be in functional remission, but the standards for what defines "minimal impairment" requires some thought and some research*'. By contrast, the ultimate goal of recovery in schizophrenia includes sustained resolution of symptoms and a return to full functioning.[17]

The inconsistencies in this area of research call for more investigations into the crucial indicators for predicting functional remission.[18] Treatment of schizophrenia is complicated by a number of challenges, including inconsistently defined clinical outcomes, failure to consider patients' perspectives, and adverse events that contribute to medication non-adherence (which increases the likelihood of relapse).[19] Other important factors that may associated with remission (clinical and functional) are the type of antipsychotic medication used and the route of administration. French guidelines recommend the use of LAIs in all patients for whom maintenance antipsychotic treatment is indicated, starting from the first psychotic episode[20] but LAIs remain underprescribed. LAIs have historically been used in subjects who have shown non-adherence, whereas they are potentially beneficial for all patients with schizophrenia, as they improve treatment adherence, reduce treatment discontinuation, and may potentially reduce the risk of relapse and rehospitalization.[21–23] This last point is still controversial,[24] with some arguing that all trials were clinician centred and mostly based on clinical remission.[25] However, recent studies converge on evidence that functional outcomes are particularly improved with LAIs, especially when offered early rather than late in the illness.[21,26,27]

Different types of instruments are used to assess functional remission. These instruments include the Global Assessment of Functioning Scale (GAF) and the Functional Remission of General Schizophrenia Scale (FROGS), the latter being a tool specifically designed to assess qualitative and quantitative functional remission in schizophrenia, with good reliability.[28,29] Recent years have also highlighted the importance of patient-reported outcome measures (PROMs) and information on how patients feel, their preferences and

what types of care make them feel authentically better.[25] PROMs are self-rated scales or indices designed to better capture the subjective experience of patients,[30] and are not interpreted by the clinician. To determine whether LAIs are more effective than oral versions in achieving recovery (presumably through medication adherence), more emphasis needs to be placed on patient-centered outcomes, for example using patient-centred outcomes; for example, using patient-reported remission/recovery, rather than clinician-based remission criteria. Family-reported outcomes may also be of great value in understanding the concept of functional remission and recovery.[31]

Clinicians generally agree that symptom reduction is an essential component of recovery. We showed that in a sample of patients with schizophrenia, experiencing clinical remission at 6 months increased the odds of achieving functional remission 6 months later by a factor of 15 (odds ratio = 14.74)[18] Recovery involves both a subjective personal journey (for patients) and a clinical outcome to be achieved (for clinicians). However, it remains unclear how the subjective experience of recovery by patients (i.e. their awareness of recovery), by their relatives or by their psychiatrist mediates the association between clinical and functional remission, especially when distinguishing between patients with and without LAI.

In this European observational multicentre study, our aims were (i) to determine whether the association between clinical remission and level of functional remission is mediated by the subjective experience (awareness) of recovery reported by patients, their relatives or their psychiatrist and (ii) to assess whether this association is equivalent in patients treated with oral antipsychotics *versus* those treated with long-acting injectable antipsychotics (LAI).

Methods

Design
The EGOFORS initiative is based on the European scientific collaboration of 11 centres across Europe. The centres are located in France, Belgium, Germany, Israel, Italy, Spain, Sweden, Turkey and the United Kingdom. The criteria of patient selection, the methods of data collection and socio-demographic/clinical characteristics of participants have been previously detailed.[32] Patients included in the present analyses were recruited from eight centres of the EGOFORS project (two centres from France and one from Germany, Sweden, Belgium, Spain, England and Turkey).

Participants
Each member of the research team conducted a cross-sectional evaluation of community-dwelling adult subjects with a DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) diagnosis of schizophrenia. Socio-demographic, clinical characteristics and medication status were assessed. Several clinical parameters were assessed in subjects, including global severity of psychotic symptoms, remission of psychosis [measured by the Positive and Negative Syndrome Scale (PANSS)][32] and overall functioning (measured by the FROGS).[33] Treatments were recorded, and we divided our subjects into subgroups according to the antipsychotic route (oral *versus* long-acting injectable).

Interventions
In the APAP group, 54% of participants received risperidone, 20% haloperidol, 20% flupentixol and 6% clopentixol. Thirty-four percent of participants in this group received a combination of antipsychotics, whereas only 20% in the oral treatment group received two antipsychotics. More information on combinations or types of antipsychotics is provided in Supplemental Table 1.

Measurements
Psychotic symptomatology was assessed with the PANSS.[33] The standardized remission criteria were assessed using the binary cross-sectional criteria established by the Remission in Schizophrenia Working Group [each of these eight PANSS items ⩽3: delusions (P1), hallucinatory behaviour (P3), conceptual disorganization (P2), mannerisms (G5), unusual thought content (G9), blunted affect (N1), social withdrawal (N4) and lack of spontaneity (N6)].[34] Clinical remission was thus defined according to The Remission in Schizophrenia Working Group (Andreasen's criteria),[1] with systematic operational criteria. Patients must score less than or equal to 3 (mild) on these eight items and this must be maintained for at least 6 months.

Perceived recovery was assessed using the following simple question: '*What is for you the percentage of recovery you/your relative/your patient have/has*

now (with 0% = no recovery and 100% = complete recovery)', asked to the patient (patient-perceived recovery), a patient's close relative (relative-perceived recovery) and the psychiatrist in charge of care (psychiatrist-perceived recovery).

The level of functional remission was assessed using the FROGS total scores. Functional improvement was assessed using FROGS total scores. The FROGS is a semi-structured interview with a questionnaire using 5-point Likert ratings. It has good psychometric properties.[28,35,36] No cut-off value was used in this study; functional remission was only measured quantitatively. The FROGS was developed by expert consensus and consists of 19 items, as previously described.[37] The scale has good internal consistency/reliability (Cronbach's $\alpha = 0.919$) and significant correlations with other indices of functioning, including the GAF ($r = 0.58$; $p < 0.001$).[38] Five domains are assessed (daily life, social activities, social functioning, quality of rehabilitation and general health and treatment) and three factors were observed (social functioning, daily life and treatment). The FROGS measures the core aspects of functional remission in schizophrenia. Items are rated on a Likert-type scale ranging from 'does not' (1) to 'does completely' (5).[37]

Analyses

All statistical analyses were carried out using SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY, USA). For all tests, significance was set at $p < 0.05$. Socio-demographic and clinical characteristics between groups were compared using independent-sample two-sided Student's *t*-tests for continuous values, exact Fisher's *F* for categorical values and chi-square for binary.

To inform the mediation analyses, the relationships between the three main outcomes (clinical remission rate, perceived remission and level of functional remission) were determined by Pearson correlations. We employed the PROCESS.sps file in SPSS by Andrew F. Hayes to conduct the mediation analysis using a path diagram.[39] Mediation analysis allows considering an additional type of variable, called a mediator, which can help determine how an independent variable influences a dependent variable. In turn, this analysis tests for a hypothesized causal relationship between at least three separate measurements that follow a chronologically ordered sequence.[40,41] We used a multiple mediators model to test whether the continuous mediator variables (here, patient-perceived, relative-perceived and psychiatrist-perceived recovery) fully mediate a relationship between the continuous dependent (functional outcome) and the binary independent variable (standardized clinical remission) in the schizophrenia groups by evaluating the impact of the dependent variable on the independent variable controlling for the mediation variables.[42] Effects between variables were calculated as path diagram coefficients, which are viewed as regression coefficients that assess a relationship between two variables.[43] In the path analysis model, a direct effect is a direct relationship between the dependent variable and the independent variable in the presence of the Mediator (c'). An indirect effect is the relationship that flows from the independent variable to a mediator and then to the dependent variable ($a*b$). The term total effect is the combined influence of the direct effect and the indirect effect flowing through the mediator ($c = c' + a*b$).[44] A significant effect without direct effect indicates a full mediation of the total effect by the mediator, while both indirect and direct significant effects indicate partial mediation which points to the possible existence of some omitted other mediator.[45]

As these variables may differ according to the route of pharmacological treatment (LAI *versus* not), we decided to conduct these mediation analyses in these two groups of subjects.

Results

Group comparisons

A sample of 198 schizophrenia subjects enrolled in the EGOFORS cohort was included in the study. The majority of the subjects were male (58.6%) and the mean age was 40.3 ± 12.4 years. The mean age at first schizophrenia episode was 23.4 ± 7.9 years and the mean duration of illness was 16.8 ± 11.2 years. The mean PANSS total score was 72.6 ± 25.5, the mean FROGS total score was 60.1 ± 15.2. The standardized remission criteria by Andreasen *et al.* were fulfilled by 66/198 (33.3%) subjects. Overall, 30 subjects were treated with LAI (19.1%) and 160 with oral antipsychotics (80.9%). No socio-demographic or clinical characteristics significantly differed between groups (all *p* values > 0.05, Supplemental Material). There were no group differences in remission, FROGS score and perceived recovery

Table 1. Socio-demographic and clinical characteristics of 198 patients with schizophrenia treated by LAI or other treatments.

Patient's characteristics	LAI group, *N* = 30 (15.2%)	Non-LAI group, *N* = 168 (82.3%)	*p**
Demographic characteristics			
Gender			
Male	18 (60%)	98 (58.3%)	
Female	12 (40%)	70 (41.7%)	0.864[a]
Age (years), mean (SD)	42.6 (10.9)	39.8 (12.6)	0.236
Years of education, mean (SD)	14.8 (37.1)	15.0 (44.7)	0.856
Disease characteristics			
Duration of illness (years), mean (SD)	18.9 (12.0)	16.3 (11.0)	0.216
Age of first treatment, mean (SD)	24.9 (6.7)	25.2 (8.0)	0.852
Age of schizophrenia onset (years), mean (SD)	23.1 (6.0)	23.5 (6.5)	0.784
Duration of untreated psychosis, (years), mean (SD)	1.2 (2.7)	1.7 (3.5)	0.401
Number of hospitalizations, mean (SD)	5.4 (4.3)	4.3 (5.4)	0.257
Psychotic symptomatology (PANSS total score), mean (SD)	78.1 (25.7)	71.4 (25.4)	0.163
Remission and recovery			
Functional score (FROGS score), mean (SD)	56.7 (14.3)	60.9 (15.2)	0.132
Clinical remission	8 (26.7%)	58 (34.5%)	0.400[b]
Patient subjective recovery (%), mean (SD)	61.1 (20.6)	60.2 (22.5)	0.833
Clinician subjective recovery (%), mean (SD)	69.1 (24.5)	64.5 (23.6)	0.320
Relative subjective recovery (%), mean (SD)	63.3 (20.6)	57.4 (23.2)	0.266

*Chi-square test for categorical variables and Student's *t*-test or Wilcox test for continuous variables.
[a]χ^2 = 0.003.
[b]χ^2 = 0.710.
LAI, long-acting injectable antipsychotics; PANSS, Positive and Negative Syndrome Scale; SD, standard deviation.

measures. The socio-demographic and clinical characteristics of the two samples are described in Table 1.

Relationships among measures
The standardized remission criteria and perceived recovery measures (patient-perceived, relative-perceived and psychiatrist-perceived) were significantly correlated with each other both within and across groups (all partial $r > 0.330$ and p values < 0.001). Both within and across groups, the FROGS total score correlated significantly with standardized remission criteria and perceived recovery measures, except for the correlation between FROGS and psychiatrist-perceived recovery that was not significant within the LAI group ($r = 0.34$, $p = 0.570$).

Differences in levels of insight between patients treated with LAI *versus* oral antipsychotics might affect patients' perceived level of recovery. There

(a) SZ non-LAI group

(b) SZ LAI group
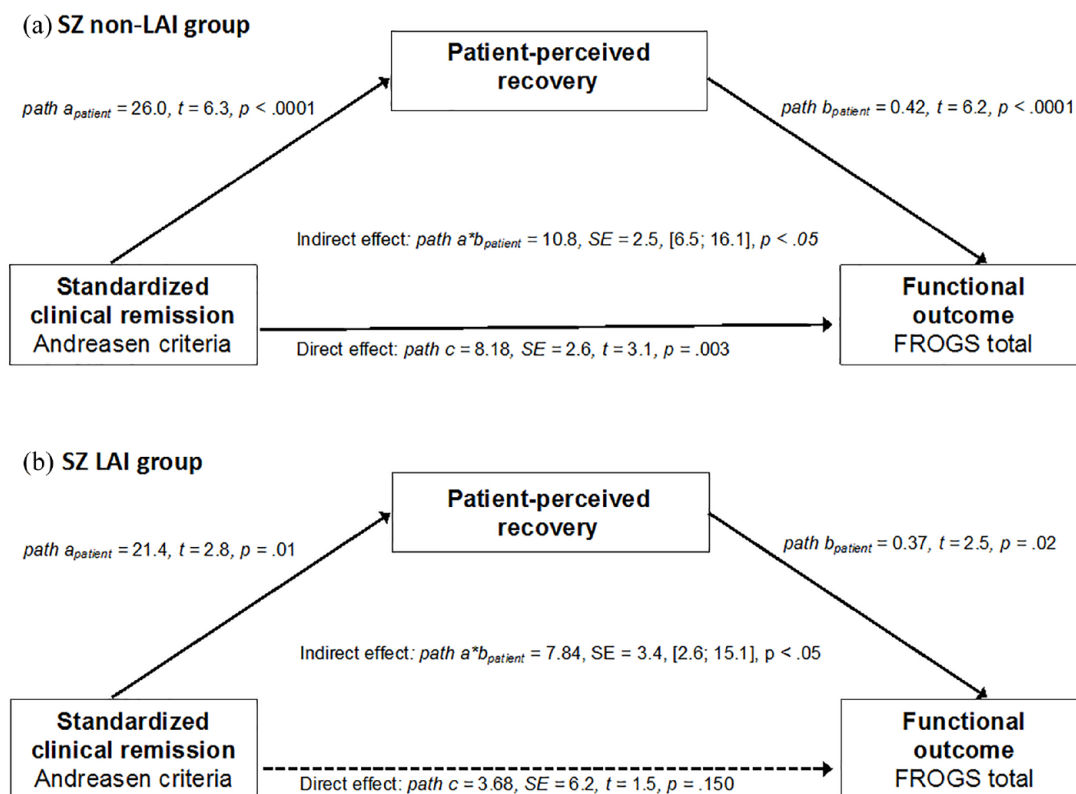
Figure 1. Path analysis between the direct effect of clinical remission on the level of functional remission in 198 patients with schizophrenia, and the indirect effect through the patient-perceived level of recovery, in patients treated by LAI (b) or other treatments (non-LAI, a).
LAI, long-acting injectable antipsychotics.

is indeed a significant correlation between insight (lack of judgement G12 item) and patient-rated recovery in all groups ($r=-0.44$, $p<0.001$), showing that insight might have an impact on a patient's perceived level of recovery. However, such an effect is observed equally in both groups, treated with LAI ($r=-0.54$, $p=0.001$) and with oral ($r=-0.34$, $p<0.001$) antipsychotics. Furthermore, the level of insight according to the G12 item was not significantly different in patients with LAI (mean = 3.294, SD = 1.661) compared to patients with oral treatment (mean = 2.929, SD = 1.607) (Student's $t=1.190$, df = 198, $p=0.240$). A different level of insight has therefore limited the risk of confounding the link between perceived recovery and functional remission differently in the two groups.

Mediation analysis
Mediation analysis evaluated the relationship between standardized clinical remission, perceived recovery and functional outcome in each group. For this analysis, the Andreasen criteria

score was entered as the independent variable and the percent of perceived recovery (psychiatrist-perceived, patient-perceived and relative-perceived) as the mediator variable. Functional outcome measure (FROGS total score) was entered as the dependent variable.

As shown in Figure 1(a), path 'a' estimates the effect of standardized clinical remission on perceived recovery, path 'b' the effect of perceived recovery on functional outcome and path 'c' the effect of standardized clinical remission score on functional outcome. In the non-LAI group, the analysis showed that standardized clinical remission had a significant total effect on functional outcome measured by the FROGS total score (path 'c''' = 19.5, SE = 2.7, $t=7.1$, $p<0.001$), along with a significant indirect effect for patient-perceived recovery [path '$a*b_{patient}$' = 10.8, SE = 2.5 (6.5; 16.1), $p<0.05$], but not for relative-perceived and psychiatrist-perceived, on the FROGS (Figure 2). The direct effect of the three perceived remission scores on the FROGS did reach significance (path 'c'' = 8.18, SE = 2.6, $t=3.1$, $p=0.003$),
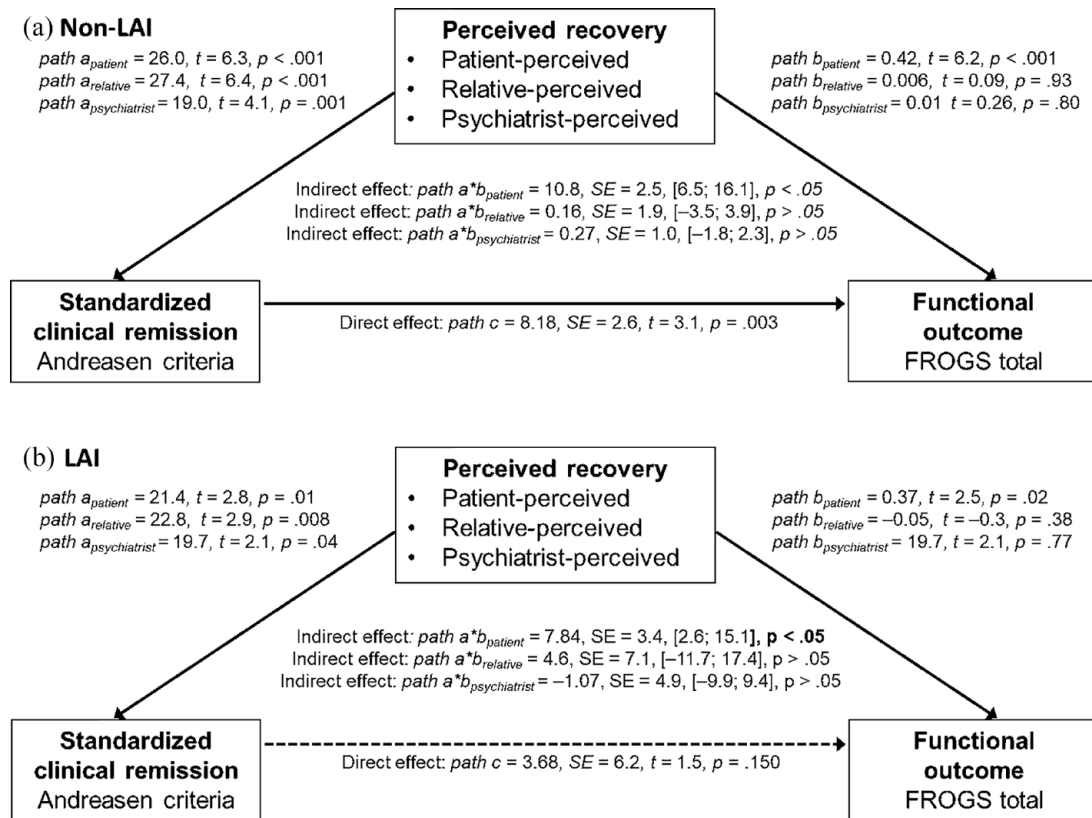
Figure 2. Path analysis between the direct effect of clinical remission on the level of functional remission in 198 patients with schizophrenia, and the indirect effect through the patient-perceived, relative-perceived and psychiatrist-perceived level of recovery, in patients treated by LAI (b) or other treatments (non-LAI, a). LAI, long-acting injectable antipsychotics.

suggesting that standardized remission criteria effect on FROGS is partially mediated by patient-perceived recovery, with standardized clinical remission also involved in functional outcome regardless of patient-perceived recovery.

Similarly, in the LAI group [Figure 1(b)], the analysis showed that standardized clinical remission had a significant total effect on the FROGS (path 'c''' = 15.1, SE = 5.8, t = 2.7, p = 0.02), along with a significant indirect effect for patient-perceived recovery [path '$a*b_{patient}$' = 7.84, SE = 3.4 (2.6; 15.1), $p < 0.05$], but not for relative-perceived and psychiatrist-perceived, on the FROGS (Figure 2). By contrast, the direct effect of the three perceived recovery scores on the FROGS did not reach significance (path 'c' = 3.68, SE = 6.5, t = 0.6, p = 0.580), suggesting that the standardized remission criteria effect on FROGS is fully mediated by patient-perceived recovery. However, a larger effect size of total effect shows that standardized clinical remission is also involved in functional outcomes regardless of

patient-perceived recovery. The indirect effect for patient-perceived recovery lost statistical significance after correction for multiple tests.

As an exploratory analysis, we performed the mediation analysis with the Andreasen criteria score as the independent variable, with the FROGS total score as the mediator and the percentage of perceived recovery as the dependent variable. Significant overall effects of standardized remission criteria on perceived remission scores were observed in both groups. In the non-LAI group, we observed significant indirect effects for patient [path '$a*b_{patient}$' = 0.7, SE = 0.1 (0.5; 0.9), $p < 0.05$], relative [path '$a*b_{relative}$' = 0.5, SE = 0.1 (0.2; 0.7), $p < 0.05$] and clinician-perceived remission [path '$a*b_{clinician}$' = 0.5, SE = 0.1 (0.3; 0.7), $p < 0.05$], and a significant direct effect of relative and patient-perceived remission scores on FROGS. This suggests that the effect of standardized remission criteria on relative and patient-perceived remission is partially mediated by FROGS, whereas the effect of standardized

remission criteria on clinician-perceived remission is fully mediated by FROGS. In the LAI group, we found a significant indirect effect for patient-perceived remission [path '$a*b_{patient}$'= 0.6, SE = 0.3 (0.2; 1.5), $p < 0.05$], while the direct effect of perceived recovery scores on the FROGS reached significance, suggesting that the standardized remission criteria effect on patient-perceived remission is partially mediated by the total FROGS score.

Discussion

In this study, we focused on the concept of recovery, which is a common goal for psychiatrists, patients and their families and which is linked to function and empowerment. The main finding of this study is that the patient's awareness of recovery better captures the relationship between clinical remission and level of functional remission in patients treated with LAI than in patients treated with oral antipsychotics alone. Second, in both treatment groups, we observed that only their subjective experience of recovery, and not that of their psychiatrist or family career, had a mediating effect. A previous study based on the EGOFORS initiative had already shown that self-rated and expert-rated clinical outcomes differ markedly when considering symptomatic remission, with a preference for subjective outcomes on the part of the patient.[31] Our results are consistent with the concept that recovery is mainly a subjective process. There were no group differences in remission rate, FROGS score and perceived recovery measures.

Efforts to develop new clinical trials that provide more patient-centred outcome assessment should use patient-reported outcomes and participatory methods to capture and incorporate patient perspectives and values. In this study, we observed that participants with lower insight (as assessed by the clinician using the PANSS) had lower self-perceived recovery scores. Nevertheless, in the modern era, treatment of schizophrenia should continue to focus on patient-centred goals: remission and recovery, health-related quality of life and functioning.[19] To achieve these goals, it is important to achieve a clinical remission as soon as possible[18] and one way to avoid medication discontinuation is the use of LAIs. We have shown in this study that their use is associated with an increased awareness of clinical and functional remission, providing a better insight into how patients

experience recovery. This may partly explain the improved adherence to treatments observed in schizophrenia patients treated with LAI.[46]

As the experience of recovery is partly subjective, it is not so surprising that there was no mediation effect by anyone other than the patient, namely the psychiatrists or relatives. Similarly, in the non-LAI group, partial mediation was observed with the patient-reported recovery but not with that of the relative or the psychiatrist. When we restricted the analyses to the LAI group, the patient's perceived recovery was of paramount importance between clinical and functional remission, as it more strongly mediated the link between these two clinical outcomes. No socio-demographic or clinical differences were found between the two groups, suggesting an intrinsic effect of LAI on the awareness of recovery in patients without major bias. These findings are consistent with a recent small observational study of clinically stable outpatients with schizophrenia treated with second-generation oral antipsychotics who were enrolled at the time of switching to the equivalent dose of LAI.[47] In this 2-year prospective study, the authors used psychometric scales and PROs (patients reported outcomes), and concluded that LAI antipsychotics may optimize the subjective experience of treatment, by reducing perceived disability. In a previous study, they showed that these improvements were seen in both remitters and non-remitters.[48] Psychiatrist-perceived recovery may not reflect the level of functional remission as perceived by the patient or as assessed by the FROGS. In this study, the FROGS total score correlated significantly with standardized remission criteria and perceived recovery measures, except in the LAI group for the correlation between FROGS and psychiatrist-perceived recovery. The functions measured by FROGS may be different from those perceived by the clinician as capturing the concept of recovery, but it is not clear how treatment type may affect this assessment, apart from statistical limitations. There were indeed five times more patients treated with oral antipsychotics alone than with LAI.

Finally, this study provides a better insight into how patients experience their recovery and supports the use of LAI treatments when maintenance treatment is required. It also highlights the need for a more patient-centred approach to treatment (subjective and phenomenological perspectives). This increased awareness may improve

adherence through various subjective experiences (including empowerment and 'reconstruction of the sense of personhood') that patients report as part of recovery.[49] These results also confirm the need to follow guidelines promoting the early use of LAIs, while psychiatrists, patients and relatives are still reluctant to prescribe LAIs.[20] Some guidelines recommend their use as soon as the first episodes of psychosis occur, not necessarily in patients with poor adherence, which is consistent with a recent systematic review.[50]

Strengths and limits

This study is an observational study conducted in different European sites, which has some important methodological limitations. Because the sample included only clinically stable subjects, it may not be representative of all patients with schizophrenia. In addition, only patients without guardianship or under curatorship were included in this study, excluding patients under tutorship, which may have influenced the patient profile of the study. Our sample also did not allow comparisons between antipsychotic dosages between subgroups. In addition, when assessing the ratio between direct and indirect paths, the effect size is moderate, and exposed to statistical power, which was not the same in the group of patients w/wo LAI. Furthermore, in patients treated with LAI, the direct path between clinical remission and level of functional remission represents 46.9% (3.68/7.84) of the indirect path (through patient-perceived recovery), while this percentage increases to 75.7% (8.18/10.8) in patients with other treatment, meaning that the smaller direct link between clinical remission and level of functional remission between the two groups is only 28.8%. Significant mediating effects of patient-perceived recovery did not survive correction for multiple analyses and thus should therefore be interpreted with caution. Finally, the authors cannot exclude that the lack of significance for the direct path in the LAI group is a power issue due to the small sample size.

Further studies with larger samples are needed to confirm the specific effect of LAI treatment on recovery perceptions. On the other hand, the strengths of this study are the naturalistic conditions, leading to a real-world assessment of recovery. The use of standardized measures contrasts with subjective measures but enriches our understanding of the framework of recovery according to patients, their relatives and their psychiatrists.

In conclusion, this study found that the awareness of their recovery in patients with schizophrenia captures part of the relationship between clinical remission and level of functional remission, as opposed to parent or clinician assessment of recovery, and that such a mediating effect of patients' sense of recovery was more statistically significant in those treated with LAI antipsychotics. A patient-centred approach to treatment evaluation is necessary for a thorough assessment of the effectiveness and impact of treatment in patients with schizophrenia.

Declarations

Ethics approval and consent to participate

The assessment protocol was approved by the relevant ethical review board for each country and all patients provided informed consent to participate.

Consent for publication

All participants gave written informed consent for the publication of their unidentifiable data.

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Supplemental material
Supplemental material for this article is available online.

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