# Determination of Adherence Profiles in Schizophrenia Using Self-Reported Adherence:
## Results From the FACE-SZ Dataset

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**ABSTRACT**

***Objective:*** Medication nonadherence is one of the most important, and potentially modifiable, prognostic factors in the outcome of patients with schizophrenia. The aim of this article is to propose a new classification of adherence profiles according to the Medication Adherence Rating Scale (MARS) in a large community-dwelling sample of French patients with schizophrenia to provide a new tool to help clinicians in daily practice.

***Methods:*** 319 community-dwelling patients from a national network of 10 Schizophrenia Expert Centers were interviewed between January 2009 and January 2014. Assessments were conducted with a dedicated electronic medical record including the Structured Clinical Interview for *DSM-IV* Disorders. A cluster analysis was performed to explore clinical variables associated with poor adherence.

***Results:*** Two distinct groups of patients were identified relative to their main adherence style. Items about medications' subjective negative effects constituted the greatest discriminating factor between the 2 clusters. Patients with poor adherence (n = 117) were significantly younger (adjusted OR [aOR] = 1.036; 95% CI, 1.004–1.069) and had higher levels of current depression (aOR = 0.894; 95% CI, 0.829–0.964) and lower insight (aOR = 0.820; 95% CI, 0.693–0.970).

***Conclusions:*** The MARS provides a useful tool for clinicians and can also aid in the evaluation of adherence styles and their determinants in patients with schizophrenia. The element providing the greatest discriminative power between the 2 clusters was a subjective negative attitude toward medication. The findings also suggest that depression is more frequent in schizophrenia patients with poor adherence and that improving insight into illness might be suggested as a first-line intervention to improve adherence in this population.

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Medication nonadherence among patients with schizophrenia has often been estimated at greater than 50%,[1–3] leading to higher rates of relapse and hospitalization as well as to worsening cognitive and functional prognosis.[4–7] While the reasons for nonadherence can be categorized by patient characteristics, interpersonal relationship factors (including therapeutic alliance), and issues related to the service delivery system,[3,8] the identification of patients with poor adherence remains an important challenge for clinicians. Three strategies have nonetheless been suggested to reliably assess adherence, of which none can be considered to date as a "gold standard."[9] First, measures such as electronic pillbox monitoring devices provide an objective measure of medication manipulation by the patient, but this strategy cannot confirm drug intake. As these measures are also expensive, their use is limited in current practice and in large cohorts studied in clinical settings. Second, while plasma levels are more direct measures of medication absorption, assessing plasma levels remains costly and its use is limited both by pharmacokinetic discrepancies between subjects and by a phenomenon known as "white-coat adherence," in which patients improve their medication-taking behavior in the 5 days before and after an appointment with the health care provider.[10] As a result, the third method, self-report questionnaires, is generally considered as the most cost-effective and time-efficient way to assess medication adherence, although it has also been reported to potentially overestimate adherence.[9]

The Medication Adherence Rating Scale (MARS)[11] is a 10-item self-report questionnaire resulting from the combination of the Medication Adherence Questionnaire[12] and the Drug Attitude Inventory,[13] which were validated in patients with psychosis. Although initial results suggested that the scale had good reliability and

**Clinical Points**

- Medication nonadherence in schizophrenia is a crucial topic because it concerns 50% of patients and leads to higher rates of relapse and hospitalization as well as to reduced cognitive and functional prognosis.
- The Medication Adherence Rating Scale (MARS) questionnaire is a reliable and useful tool in clinical practice to assess therapeutic adherence in schizophrenia. The information provided by cluster analysis underscores important issues for clinicians to better understand the complexity of adherence behaviors in their patients.
- Exploring objective side effects of medication is essential, but in clinical practice asking patients about their subjective feelings concerning antipsychotics appears to be very relevant to understanding adherence.

validity, its psychometric properties were examined in a sample of moderate size (n = 66) and included patients with both bipolar disorder and schizophrenia.[11] More recently, Fialko et al[14] explored the psychometric properties of the MARS in a larger sample of 277 patients with schizophrenia, schizoaffective disorder, or delusional disorder who took part in the Psychological Prevention of Relapse in Psychosis Trial (PRP), a multicenter randomized controlled trial of cognitive-behavioral therapy and family intervention for psychosis. These authors replicated the 3 factors reported by previous research but also found the internal consistency of the MARS to be lower than what was found in the original observations. However, this latter study included inpatients as well as outpatients, with potential memory biases concerning adherence-preceding hospitalization. To date, it is therefore unclear how this scale may help clinicians to identify subgroups of schizophrenic patients regarding their adherence to antipsychotic medication.

Using a large sample of French outpatients with schizophrenia, this investigation therefore aims to propose a new classification of adherence profiles using the MARS in order to provide a practical tool to help clinicians in daily practice.

## METHODS

### Recruitment and Population

The FACE-SZ (FondaMental Academic Centers of Expertise for Schizophrenia) cohort is issued from a French national network of 10 Schizophrenia Expert Centers established by a French foundation for scientific cooperation (www.fondation-fondamental.org). Stable patients aged 16 years or older with schizophrenia or schizoaffective disorder according to the Structured Clinical Interview for *DSM-IV* Mental Disorders (SCID)[15] were enrolled in the FACE-SZ cohort. The assessment protocol was approved by the relevant ethical review board (CPP-Ile de France IX; January 18, 2010). All subjects enrolled in that cohort provided written informed consent. The details of the study design and rationale have been presented in a previous publication.[16]

### Data Collection

Clinical and sociodemographic factors were collected with a dedicated electronic medical record during in-person evaluations between January 2009 and January 2014. Standardized assessments were used to assess positive and negative psychotic symptoms and general psychopathology with the Positive and Negative Syndrome Scale (PANSS).[17] Insight was evaluated with the Insight-Scale of Unawareness of Mental Disorder (SUMD)[18] and item G12 from the PANSS. Depressive symptoms were assessed with the Calgary Depression Scale for Schizophrenia (CDSS).[19] Illness severity was measured using the Clinical Global Impression-Schizophrenia scale (CGI),[20] and overall functioning was estimated by the Global Assessment of Functioning scale (GAF).[15] Antipsychotic extrapyramidal side effects and akathisia were also assessed, respectively, by the Simpson-Angus Rating Scale (SARS)[21] and the Barnes Akathisia Scale (BAS).[22]

Self-reported adherence to pharmacologic treatment was evaluated by the French translation of the MARS.[23] The sum of items yields a final score ranking from 0 (poor adherence to treatment) to 10 (good adherence to treatment). In our sample, the internal consistency of the overall scale was 0.66. Cronbach α levels were reduced or remained unchanged if any items were deleted from the scale, suggesting that there were no redundant items. A principal component analysis produced a 3-factor solution. After varimax rotation, factor 1, "medication adherence," accounted for 18.9% of the variance; factor 2, "attitudes to taking medication," for 16.8%; and factor 3, "negative side effects," for 15.5%. The 3 factors accounted for 51.2% of the total variance.

### Statistical Methods

In order to identify different groups of patients showing similar response patterns, a 2-step cluster analysis based on hierarchical clustering was conducted. The optimal number of clusters given the input variables was automatically selected according to the Akaike information criterion (AIC), which was used to identify latent types of attitude structures and to report behaviors in the individual patterns of responses to the 10 dichotomous items of the MARS. To examine associations between class membership and covariates as indicators of validity, membership probabilities were calculated from the estimated conditional response probabilities of the MARS items. In order to evaluate whether the identified subgroups differed in external variables that were not included in the clustering process, and consequently to validate the observed attitudinal profiles, we conducted nonparametric analyses ($\chi^2$, Mann-Whitney *U*). We used multivariate logistic regression to estimate odds ratios to ascertain the effects of significant variables identified by univariate analyses between the 2 clusters, adjusting for the potential confounders listed previously (see Table 1 for details on covariates). To evaluate the MARS factor structure, we conducted a principal component factor analysis with varimax rotation, retaining factors with an eigenvalue greater than 1. Internal consistency was assessed using the Cronbach

α. All analyses were performed with the Statistical Package for the Social Sciences (SPSS) Version 20 computer software for Windows (SPSS Inc, an IBM Company, Chicago, Illinois).

## RESULTS

### Population Description

Three hundred nineteen participants with a *DSM-IV-TR* diagnosis of schizophrenia (81.5%) or schizoaffective disorder (18.5%) were included in the present study. Sociodemographic and clinical characteristics of the sample are summarized in Table 1. The mean age was 34.7 (SD = 10.3) years, and 240 patients (75.2%) were men. Overall, 127 patients (39.8%) had a low education level (primary or lower), and 209 patients (85.7%) were treated with a second-generation antipsychotic (SGA).

### Cluster Analysis

The cluster analysis provided a model of 2 classes according to the AIC. The MARS response profile of the 2 clusters and the predictive values of each item are presented in Table 2. Items 9 and 10 concern negative perceived side effects of treatments and were found to be the most robustly discriminant between the 2 clusters, whereas the remaining items were less discriminant.

Cluster 1 had a low mean MARS total score (4.38). One hundred four patients (88.9%) in this cluster reported that they "feel weird" on medication treatment (item 9), and 74 (63.2%) felt fatigue or other side effects (item 10). At least two-thirds of the patients in this cluster forgot their medication (item 1), were careless at times about taking medication (item 2), and stated that it was unnatural for their mind and body to be controlled by medication (item 6).

Cluster 2 had a high mean MARS total score (7.92). One hundred forty-seven (72.8%) of the patients in this cluster did not feel weird on medication treatment (item 9), and 197 (97.5%) did not feel any fatigue or other side effects (item 10). One hundred fifty-nine (78.7%) considered to have never forgotten to take their medication (item 1), 135 (66.8%) were careful at times about taking medication (item 2), and 145 (71.8%) understood the importance of drug medication to their mental balance (item 6).

### Associations Between Clinical Variables and Clusters

The results of univariate and multivariate analyses of clinical correlates of the 2 clusters are presented in Table 1. Compared to patients with a higher total MARS score (cluster 2), patients in cluster 1 (lower total MARS score) were significantly younger ($P = .01$); were more frequently administered a first-generation antipsychotic ($P = .037$) or anxiolytics ($P = .015$); received a higher total number of psychotropic drugs ($P = .034$); had higher current substance use or abuse ($P = .023$); had higher levels of general psychopathology ($P = .022$), disease severity ($P = .049$), depression ($P < .001$), suicidal ideation ($P = .02$), and akathisia ($P = .045$); and had lower functioning ($P = .024$) and insight ($P = .01$). No significant association was found with sex, body mass index, extrapyramidal side effects, and PANSS subscores for both positive and negative symptoms. After adjustment for confounding factors, the cluster with the better adherence score was significantly older (adjusted odd ratio [aOR] = 1.036; 95% CI, 1.004–1.069; $P = .026$) while the group with the worse adherence score had higher depression score (CDSS score) (aOR = 0.894;, 95% CI, 0.829–0.964; $P = .003$) and poorer insight into illness (SUMD score) (aOR = 0.820; 95% CI, 0.693–0.970; $P = .021$). The model explained 16.2% (Nagelkerke $R^2$) of the variance in adherence behavior and correctly classified 65.4% of cases.

## DISCUSSION

The main findings in this sample of 319 community-dwelling patients with schizophrenia or schizoaffective disorder may be summarized as follows: (1) Using cluster analysis, 2 groups were identified on the basis of responses to items on the MARS, providing more insight into the main adherence styles in patients with schizophrenia. Items about the subjective negative effects of medication were the most discriminating between the 2 clusters. The patients in cluster 1, who had a low mean total MARS score (< 5), more frequently perceived negative side effects and had negative thoughts about the medication. They were more careless at times about taking their medication or forgot to take it. Conversely, patients in cluster 2, who had a high mean total MARS score (> 7), included individuals who perceived having fewer side effects and had a better understanding of the importance of drug medication. (2) Lower age, high depressive symptomatology, and low insight were significantly associated with poor medication adherence independent of sex, substance abuse, psychotic symptomatology, objective side effects, and antipsychotic class.

The cluster analysis helped identifying 2 distinct groups of adherence styles. The last 2 items of the MARS are related to patients' experiencing subjective negative side effects (feeling weird, tired, and sluggish) and were found to be the most discriminating of the scale relative to the 2 clusters. The MARS explores the complexity of adherence in a continuous manner rather than using a more simplistic dichotomous approach. A cutoff score is therefore not provided for this scale, but the mean MARS total scores of 4.38 and 7.92 in clusters 1 and 2, respectively, might help clinicians to better explore therapeutic adherence. A score of approximately 7–8 or higher can be considered as indicating good adherence. A score around 4–5 or lower may be considered as indicating poor adherence according to our cluster analysis. A score of 6 may be considered as intermediate. In any case, the clinician should examine the responses to the last 2 questions of the MARS, which have particular importance. If the patient reported having subjective negative feelings during treatment, the clinician should further investigate treatment adherence, whatever the MARS total score. The treatment may subsequently be modified during a clinical consultation in order to precisely evaluate and improve subjective feelings

**Table 1. Population Characteristics and Factors Associated With the 2 Clusters Defined by the Medication Adherence Rating Scale (MARS)[a]**

| Variable | Whole Sample (N = 319), n (%) | Univariate Model: Cluster 1 (n = 117), n (%) | Univariate Model: Cluster 2 (n = 202), n (%) | Univariate Model: *P* Value | Multivariate Model: aOR | Multivariate Model: 95% CI | Multivariate Model: *P* Value |
|---|---|---|---|---|---|---|---|
| Sex, male | 240 (75.2) | 90 (76.9) | 150 (74.3) | .595 | 1.344 | 0.630–2.869 | .445 |
| Marital status, married | 32 (10.0) | 12 (10.3) | 20 (9.9) | .919 | | | |
| Educational level, primary or lower | 127 (39.8) | 44 (37.6) | 83 (41.1) | .540 | | | |
| Diagnosis, schizophrenia (vs schizoaffective disorder) | 260 (81.5) | 91 (77.8) | 169 (83.7) | .191 | | | |
| Current substance, use or abuse | **98 (30.7)** | **45 (38.5)** | **53 (26.2)** | **.023** | 0.723 | 0.385–1.357 | .313 |
| Second-generation antipsychotic (vs first-generation)[b] | **209 (85.7)** | **64 (79.0)** | **145 (89.0)** | **.037** | 1.574 | 0.653–3.793 | .312 |
| Other psychotropic drugs, yes | | | | | | | |
| Any | **141 (44.2)** | **54 (65.1)[c]** | **89 (50.9)[d]** | **.032** | | | |
| Antidepressants | 52 (16.3) | 18 (21.7) | 34 (19.4) | .673 | | | |
| Mood stabilizers | 47 (14.7) | 17 (20.5) | 30 (17.1) | .517 | | | |
| Anxiolytics | **71 (22.3)** | **31 (37.3)** | **40 (22.9)** | **.015** | | | |
| Hypnotics | 29 (9.1) | 13 (15.7) | 16 (9.1) | .121 | | | |
| Others | 46 (14.4) | 18 (21.7) | 28 (16.0) | .265 | | | |
| | Mean (SD) | Mean (SD) | Mean (SD) | *P* Value | aOR | 95% CI | *P* Value |
| Age, y | **34.7 (10.3)** | **32.56 (9.8)** | **35.32 (10.5)** | **.010** | **1.036** | **1.004–1.069** | **.026[e]** |
| BMI, kg/m$^2$ | 26.7 (5.3) | 27.42 (5.6) | 26.35 (5.1) | .096 | | | |
| No. of psychotropic drugs | **2.1 (1.4)** | **2.32 (1.5)** | **1.95 (1.3)** | **.034** | 0.871 | 0.677–1.120 | .281 |
| PANSS score | | | | | | | |
| Total | 70.8 (19.2) | 73.49 (19.0) | 69.43 (19.2) | .121 | 1.005 | 0.989–1.021 | .557 |
| Positive | 14.6 (5.5) | 14.97 (5.2) | 14.48 (5.6) | .322 | | | |
| Negative | 21.2 (7.4) | 21.44 (7.4) | 21.00 (7.4) | .630 | | | |
| General | **35.0 (10.3)** | **37.08 (10.6)** | **33.98 (10.0)** | **.022** | | | |
| G6: depression | **2.3 (1.4)** | **2.72 (1.5)** | **2.09 (1.3)** | **<.001** | | | |
| G11: poor attention | **2.2 (1.2)** | **2.49 (1.3)** | **2.12 (1.2)** | **.014** | | | |
| G12: insight | **3.2 (1.6)** | **3.43 (1.6)** | **3.02 (1.6)** | **.020** | | | |
| SUMD score | **4.7 (1.9)** | **5.03 (2.0)** | **4.49 (1.8)** | **.010** | **0.820** | **0.693–0.970** | **.021[e]** |
| CDSS score | | | | | | | |
| Total | **3.6 (4.1)** | **4.85 (4.7)** | **3.06 (3.6)** | **<.001** | **0.894** | **0.829–0.964** | **.003[e]** |
| 8: suicide | **0.25 (0.6)** | **0.32 (0.6)** | **0.20 (0.6)** | **.020** | | | |
| MARS score | **6.7 (2.2)** | **4.38 (1.5)** | **7.92 (1.3)** | **<.001** | | | |
| BARS score | **86.9 (22.5)** | **80.32 (27.7)** | **89.65 (18.0)** | **.001** | | | |
| GAF score | **48.1 (14.8)** | **45.82 (12.4)** | **48.84 (15.8)** | **.024** | | | |
| CGI score | **4.5 (1.1)** | **4.62 (1.0)** | **4.40 (1.1)** | **.049** | | | |
| BAS score | **0.5 (1.0)** | **0.62 (1.0)** | **0.40 (0.8)** | **.045** | 0.856 | 0.616–1.190 | .355 |
| SARS total score | 0.3 (0.1) | 0.27 (0.4) | 0.28 (0.4) | .701 | | | |

[a]Significant associations are in bold.
[b]Data missing for 75 subjects.
[c]Data missing for 34 subjects.
[d]Data missing for 27 subjects.
[e]Adjusted for gender, current substance use or abuse, second versus first generation antipsychotic, the number of daily administered psychotropic drugs, PANSS total score, and BAS score.
Abbreviations: aOR = adjusted odds ratio, BARS = Brief Adherence Rating Scale, BAS = Barnes Akathisia Scale, BMI = body mass index, CDSS = Calgary Depression Scale for Schizophrenia, CGI = Clinical Global Impression-Schizophrenia scale, GAF = Global Assessment of Functioning, MARS = Medication Adherence Rating Scale, PANSS = Positive and Negative Syndrome Scale, SARS = Simpson-Angus Rating Scale, SUMD = Scale of Unawareness of Mental Disorder.

during treatment (eg, by avoiding anxiolytic, hypnotic, and antipsychotic polytherapy prescriptions). Nonmedication strategies focusing on increased energy and activities may also be suggested. To our knowledge, only 1 study had explored adherence profiles with the MARS by using a latent class analysis.[24] The authors of that study identified 5 different latent styles of adherence attitudes and behaviors. The largest group (53%) of so-called "good compliers" corresponded to our cluster 2, whereas the remaining 4 groups of poorly adherent patients corresponded to cluster 1. Clinical discrepancies between the last 4 groups were distinguished by the authors, but these differences are difficult to exploit in clinical practice because they represent a complex mix of behaviors and attitudes. Moreover, the small class sizes of 2 of the 5 clusters (ie, "critical discontinuers" and "careless and forgetful," respectively 6% and 4% of the sample) made it difficult to conclude for a comprehensive adherence pattern, whereas the 6-month follow-up design nonetheless provided relevant information. Participants showing a "good complier" response pattern had a significantly better prognosis in terms of rehospitalization rates and maintenance of the original medication than "critical discontinuers."

One notable finding of the present study was that depression, low insight, and lower age were associated with poor adherence. The association between depression and poor adherence is relevant for clinical practice but has not been extensively studied. As suggested in a population of bipolar patients, cognitive depressive symptoms such as attention or memory disturbance may also partially explain poor adherence by medication omission.[25] Consistent

**Table 2. Response Pattern of the 2 Latent Adherence Clusters**

| MARS Variable | Response Indicating Adherence | Predictor Importance | Cluster 1, n = 117 (36.7%)[a] | Cluster 2, n = 202 (63.3%)[a] |
|---|---|---|---|---|
| Item | | | | |
| 1. Do you ever forget to take your medication? | "No" | 0.51 | 39 (33.3) | 159 (78.7) |
| 2. Are you careless at times about taking medication? | "No" | 0.37 | 33 (28.2) | 135 (66.8) |
| 3. When you feel better do you sometimes stop taking your medication? | "No" | 0.23 | 9 (7.7) | 59 (29.2) |
| 4. Sometimes if you feel worse when you take the medicine do you stop taking it? | "No" | 0.36 | 15 (12.8) | 92 (45.5) |
| 5. I take my medication only when I am sick. | "No" | 0.12 | 6 (5.1) | 36 (17.8) |
| 6. It is unnatural for my mind and body to be controlled by medication. | "No" | 0.36 | 39 (33.3) | 145 (71.8) |
| 7. My thoughts are clearer on medication. | "Yes" | 0.22 | 34 (29.1) | 117 (57.9) |
| 8. By staying on medication, I can prevent getting sick. | "Yes" | 0.10 | 12 (10.3) | 48 (23.8) |
| 9. I feel weird like a zombie on medication. | "No" | 1.00 | 13 (11.1) | 147 (72.8) |
| 10. Medication makes me feel tired and sluggish. | "No" | 0.88 | 43 (36.8) | 197 (97.5) |
| Total score, mean (SD) | … | … | 4.38 (1.5) | 7.92 (1.3) |

[a]Values shown as n (%) unless otherwise noted.
Abbreviation: MARS = Medication Adherence Rating Scale.
Symbol: … = not applicable.

with previous studies,[26–29] patients with poor adherence were also found to have lower insight in the present study. It may be argued that, like poor adherence, lack of insight is a multidimensional factor and shares the perception of negative subjective side effects during treatment with antipsychotics. Inconsistent associations were also found between sociodemographic variables and adherence to medication; however, most of the previous studies found that lower age and male gender were both associated with adherence problems.[3,30,31] In our study, only lower age was found to be associated with poor adherence, possibly due to the small percentage of female participants. Unlike insight and depression items from the general PANSS subscore, positive and negative symptom subscores were not associated with poor adherence. Tattan and Creed[32] found that negative symptoms may reduce patients' motivation to adhere to a treatment regimen. The specificity of our sample composed of patients with rather low positive and negative PANSS subscores (the mean [SD] PANSS positive and negative subscores were 14.6 ([0.3]) and 21.2 ([0.5]), respectively) and may explain this discrepancy. Another explanation is the possibility that the cross-sectional design could not reveal dynamic variations in both symptomatology and adherence. In this regard, the use of mobile technologies can improve assessment sensitivity of dynamic fluctuations in medication use, symptoms, and other daily life variables and should be recommended.[33]

It is noteworthy that the most common side effects of antipsychotics, namely weight gain and extrapyramidal side effects, were not found to be associated with poor adherence. These results are consistent with those from Weiden et al,[34] which suggested that distress over weight gain was the primary mediator of poor adherence rather than the objective weight gain. Mutsatsa et al[35] also found that, unlike negative attitudes toward medication, extrapyramidal side effects were not associated with therapeutic adherence. This finding indicates that side effects may have less direct influence on adherence than is currently presumed.

Cluster 1 was found to be administered more psychotropic drugs than cluster 2. This finding may suggest that clinicians prescribed more psychotropic drugs to subjects with poor adherence, possibly due to more frequent symptoms in subjects with poor adherence. Our finding of higher depressive symptoms in subjects with poor adherence is also in favor of this hypothesis. These subjects are therefore more likely to be administered antidepressants, anxiolytics, and hypnotics. However, it cannot be excluded that the increase in prescribed medications may also be due to residual symptoms that clinicians may attempt to treat as resistant symptomatology, whereas the residual symptoms may be directly due to poor adherence. Taken together, these results highlight the need for clinicians to focus on 1 or 2 psychotropic medications, with a comprehensive assessment of adherence in treatment at baseline and over time.

## Limitations

Our assessment of adherence was restricted to a subjective self-rating scale, the MARS. This is a self-report scale and is therefore subject to bias that may overestimate adherence. Accurate and cost-effective measurements to address nonadherence, which is a complex and multidetermined, dynamic phenomenon, are particularly challenging to find. With no gold standard to date, the MARS was selected because it has been widely used and translated in multiple languages. It allows a continuous evaluation of adherence that could be considered as more relevant and less simplistic than a dichotomous approach. It should also be noted that our patients were all community-dwelling outpatients who agreed to a 2-day comprehensive clinical and neuropsychological assessment in the context of the clinical Expert Centers network. The prevalence of poor adherence may therefore be underestimated in our sample. However, our cluster analysis found that 37% of the patients were classified in the poor adherence profile group according to the MARS. In light of results from previous studies, this is a non-negligible rate. We therefore confirmed high rates of poor medication adherence in this large sample of subjects with schizophrenia independent of their adherence to the care system. This issue remains

a major topic for the development of future medications in the treatment of schizophrenia. Despite our potential underestimation, the rate of poor adherence enabled us to carry out a comparison between high and low adherence profiles. Due to the cross-sectional design of our study, it was not possible to prospectively determine the effect of each factor associated with poor adherence on clinical, neuropsychological, and functional outcomes. A follow-up study of our 2 clusters of adherence is warranted to address these issues. The choice of the segmentation method can also be considered as a limitation. The 2-step method yielded clusters with larger size ranges, and any missing values were excluded from the analysis. Two-step cluster analysis also automatically selects the number of clusters. Overall, it represents a mathematical improvement over factor segmentation and k-means clustering, as the importance of having a low number of groups in this analysis is essential to having a useful clinical interpretation and daily use of the MARS by practitioners. This method was chosen for these reasons, although it may not be the most efficient compared to more elaborate and specific approaches such as the Ward method or clustering using unsupervised binary trees (CUBT).[36]

The cluster analysis identified 2 main adherence styles mostly determined by the negative side effects of antipsychotics that are subjectively experienced by the patient. The findings suggest that depression is more frequent in patients with poor adherence and that improving insight into illness might be suggested as a first-line intervention to improve adherence in this population. The simplicity and brief administration time of the MARS questionnaire make it a particularly useful tool for the assessment of adherence in schizophrenia. The perspective of longitudinal analysis from this cohort will be of interest to confirm the 2 groups found and to explore prognostic factors associated with these adherence profiles.

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