

Study of Medication Adherence in Patients with Schizophrenia

Yassamine Bensalah^{1*}, Nihad AitBensaid¹, Amal Zaki¹, Abderrazzak Ouanass¹

¹Ar-razi Psychiatric University Hospital, Salé, Morocco, Faculty of Medicine and Pharmacy of Rabat, Mohamed V University, Morocco

DOI: <https://doi.org/10.36347/sasjm.2024.v10i09.030>

| Received: 05.08.2024 | Accepted: 13.09.2024 | Published: 25.09.2024

*Corresponding author: Yassamine Bensalah

Ar-razi Psychiatric University Hospital, Salé, Morocco, Faculty of Medicine and Pharmacy of Rabat, Mohamed V University, Morocco

Abstract

Original Research Article

Introduction: Non-adherence to treatment is a major issue in the management of schizophrenia. **Objectives:** To evaluate medication adherence among patients with schizophrenia and to identify predictive factors of poor therapeutic adherence. **Methods:** This is a cross-sectional study conducted among patients with schizophrenia at Ar-Razi Hospital in Salé, Morocco, from January 1 to March 31, 2024. Data collection (sociodemographic, clinical, and therapeutic) was carried out using a specifically designed questionnaire. Medication adherence was assessed using the Medication Adherence Rating Scale (MARS), and insight was evaluated using the Q8 scale. **Results:** In our study, 44.4% of the included schizophrenia patients were non-adherent. Poor therapeutic adherence was associated with lower socioeconomic status, lack of employment, lack of family support, substance use, negative insight, and a higher number of medication doses. **Conclusion:** The implementation of therapeutic and preventive strategies to address substance use, structured psychoeducational strategies to improve insight, and training for therapists to enhance the therapeutic alliance should be established to improve medication adherence among patients with schizophrenia.

Keywords: Schizophrenia, medication adherence, relapse, risk Factor, antipsychotics.

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

I. INTRODUCTION

Schizophrenia is a chronic psychiatric disorder that affects approximately 1 in 100 individuals and is the eighth leading cause of disability among people aged 15 to 44 worldwide [1]. Although antipsychotic treatments can improve patient outcomes, their effectiveness is often limited by issues related to medication adherence [2].

The study of medication adherence in psychiatry is complicated by the lack of uniform definitions and measurement methods [3]. Adherence encompasses not only medication intake but also therapeutic follow-up, socio-occupational measures, psychotherapeutic interventions, and various factors influencing morbidity and mortality [4].

The rate of non-adherence among patients with schizophrenia is estimated to range from 20% to 72% [5]. According to Kampman *et al.*, [6], the prevalence of non-adherence among patients with a first episode of psychosis is approximately 50%. It can reach up to 75% after discharge from the hospital [7].

Suboptimal medication adherence has substantial effects on the clinical condition, quality of life, and psychosocial functioning of patients [8-11].

Inadequate medication adherence is associated with increased clinical costs due to relapses and exacerbates the overall prognosis of the disorder, particularly concerning cognitive outcomes [12].

Our study aims to evaluate medication adherence among patients with schizophrenia and identify predictive factors for poor therapeutic adherence.

II. MATERIALS AND METHODS

1) Study Type and Population:

This is a descriptive and analytical cross-sectional study conducted over a three-month period from January 1 to March 31, 2024, involving patients with schizophrenia followed at Ar-Razi Hospital in Salé, Morocco.

2) Eligibility Criteria:

✚ Inclusion Criteria

- Diagnosis of schizophrenia according to DSM-5-TR criteria
- Age \geq 18 years
- Adherence to anonymity and data confidentiality

Citation: Yassamine Bensalah, Nihad AitBensaid, Amal Zaki, Abderrazzak Ouanass. Study of Medication Adherence in Patients with Schizophrenia. SAS J Med, 2024 Sep 10(9): 966-972.

Exclusion criteria

- Patients with an intellectual developmental disorder
- Individuals with severe cognitive impairments

3) Data Collection and Measuring Instrument:

To this end, we used a data collection form to gather the following characteristics:

- Socio-demographic characteristics: age, gender, educational level, socio-economic status, professional activity
- Clinical characteristics: age of onset of the illness, duration of illness ...
- Therapeutic characteristics: class of medication, number of medications taken per day, side effects ...

For the assessment of medication adherence and insight, we utilized two scales:

The Medication Adherence Rating Scale (MARS) [13]:

This is a self-report questionnaire designed to measure adherence, consisting of 10 items to which respondents answer either "yes" or "no." The questions address both the patient's behavior regarding their treatment and their subjective perceptions of the treatment.

The three main components of the items in this scale are:

- The behavioral component of adherence (items 1, 2, 3, 4)
- The subject's attitude towards medication intake (items 5, 6, 7, 8)
- The side effects associated with the patient's attitude towards psychotropic medications (items 9 and 10).

The items are scored as 0 for a "no" response and 1 for a "yes" response, except for items 7 and 8, which are scored as 1 for a "no" response and 0 for a "yes" response. The result is expressed as a total score ranging from 0 to 10, with a threshold score set at 7.

The Q8 Scale [14]:

This is a hetero-questionnaire consisting of eight questions posed to the patient by the investigator, serving as a guide to explore various dimensions of insight into the disorder. These are open-ended questions designed to guide the assessment of insight. For each question, the examiner assigns a score: either 0 indicating a lack of discernment, or 1 indicating at least a partial awareness of the psychopathological issue and its consequences. The maximum score is 8, indicating complete awareness of the disorder, good understanding of the illness, the maladaptation, psychological suffering, the desire, and belief concerning recovery and specialized help.

The overall score allows for categorization of insight into three levels:

- Score < 2: Absence of insight into the disorder

- Score 3–5: Poor or intermediate insight into the disorder
- Score 6–8: Good insight into the disorder

4) Statistical Analysis:

Qualitative variables were expressed in numbers and percentages, and quantitative variables were expressed as mean +or- standard deviation because the variable distribution was symmetrical.

Univariate analysis was performed using the chi-square test or Fisher's exact test, depending on the test conditions.

Data analysis was performed using jamovi 2.3.19 statistical software.

III. RESULTS**1) Socio-Demographic and Clinical Characteristics of Our Patients (Table I)**

Our study included 180 patients with schizophrenia. The mean age of our patients was 37.6 ± 10.9 years, with an age range from 18 to 60 years. The majority of our patients were male (75.6%) and single (69.4%). Regarding educational level, 80.5% had not progressed beyond secondary education, 79.4% were unemployed, and 90.6% lived within a family setting.

A history of medical and surgical conditions was noted in 27 patients: diabetes (10 cases), hypertension (6 cases), dyslipidemia (3 cases), asthma (3 cases), epilepsy (3 cases), peptic ulcer disease (1 case), and acute rheumatic fever (1 case).

A history of suicide attempts was noted in 18.9% of the cases. However, more than half of our patients had been previously hospitalized for psychiatric reasons, and 28.3% had a family history of psychiatric disorders.

The use of psychoactive substances was reported in 61.1% of our patients. Tobacco was the most commonly used substance (60%), followed by cannabis (36.1%) and benzodiazepines.

The mean age of patients at the onset of schizophrenia was 23.15 ± 5.6 years, while the mean duration of the illness was 14.46 ± 9.5 years.

Regarding therapeutic characteristics, 88.3% of patients were on oral medication. Second-generation antipsychotics were the most commonly prescribed (43.3%). Additionally, 28.8% of patients took more than two doses of neuroleptics per day.

Side effects of neuroleptics were reported in 52.2% of patients: extrapyramidal symptoms (16.7%), sexual disturbances (16.1%), sedation (10.5%), and metabolic and endocrine side effects (8.9%).

Most of our patients had a good level of insight (45%), 23.9% had an intermediate level of insight, and 31.1% had poor insight according to the Q8 scale.

Table I: Sociodemographic and clinical characteristics of our patients

Characteristics		N (%)
Sex	Male	136 (75.6)
	Female	44 (24.4)
Marital status	Single	125 (69.4)
	Married	35 (19.4)
	Divorced	20 (11.1)
Socio-economic status	Low	83 (46.1)
	Average	97 (53.9)
Educational level	Never attended school	8 (4.4)
	Primary school level	49 (27.2)
	Secondary school level	88 (48.9)
	Academic level	35 (19.4)
Professional activity	Yes	30 (20.6)
	No	143 (79.4)
Lifestyle	Solitary	17 (9.4)
	With family	163 (90.6)
Use of psychoactive substances	Yes	110 (61.1)
	No	70 (38.9)
Previous hospitalizations	Yes	104 (57.8)
	No	76 (42.2)
Insight	Good	81 (45)
	Intermediate	43 (23.9)
	Absent	56 (31.1)
Prescribed treatments (therapeutic classes)	First-generation	71 (39.4)
	Second-generation	78 (43.3)
	1 + 2 generation	31 (17.2)
Administration route	Oral	159 (88.3)
	Long-acting antipsychotic (LAI)	8 (4.4)
	LAI + Oral	13 (7.2)
Number of antipsychotics per day	1	125 (69.4)
	≥ 2	55 (30.6)
Presence of side effects		(52.2)

2) Therapeutic Adherence and Associated Factors

According to the MARS scale, 100 patients (55.6%) were classified as good adherers, while 80 patients (44.4%) were identified as having poor therapeutic adherence.

Poor therapeutic adherence was associated with low socioeconomic status, lack of employment, absence

of family support, use of psychoactive substances, poor insight, and a high number of medication doses.

The various sociodemographic and clinical factors associated with therapeutic adherence are presented in Table II.

Table II: Comparative table of sociodemographic and clinical characteristics of adherent and Non-adherent Patients

Characteristics	Adherent patients N (%)	Non-adherent patients N (%)	P
Sex			
Male	76 (55.9)	60 (44.1)	NS
Female	24 (54.4)	20 (45.5)	
Marital status			
Single	65 (52)	60 (48)	NS
Married	24 (68.6)	11 (31.4)	
Divorced	11 (55)	9 (45)	
Socio-economic status			

Low	36 (43.4)	47 (56.6)	0.002
Average	64 (66)	33 (34)	
Educational level			
Never attended school	6 (75)	2 (25)	NS
Primary school level	35 (71.4)	14 (28.6)	
Secondary school level	45 (51.1)	43 (48.9)	
Academic level	14 (40)	21 (60)	
Professional activity			
Yes	31 (83.8)	6 (16.2)	< 0.05
No	69 (48.3)	74 (51.7)	
Lifestyle			
Solitary	4 (23.5)	13 (76.5)	0.005
With family	96 (58.9)	67 (41.1)	
Use of psychoactive substances			
Yes	53 (48.2)	57 (51.8)	0.01
No	47 (67.1)	23 (32.9)	
Previous hospitalizations			
Yes	32 (30.8)	72 (69.2)	NS
No	70 (92.1)	6 (7.9)	
Insight			
Good	81 (100)	0	< 0.05
Intermediate	19 (44.2)	24 (55.8)	
Absent	0	56 (100)	
Prescribed treatments (therapeutic classes)			
First-generation	15 (48.4)	16 (51.6)	NS
Second-generation	47 (60.3)	31 (39.7)	
1 + 2 generation	15 (48.4)	16 (51.6)	
Administration route			
Oral	90 (56.6)	69 (43.4)	NS
Long-acting antipsychotic (LAI)	5 (62.5)	3 (37.5)	
LAI + Oral	5 (38.5)	8 (61.5)	
Number of antipsychotics per day			
1	78 (62.4)	47 (37.6)	< 0.05
≥ 2	22 (40)	33 (60)	
Presence of side effects	55 (58.5)	39 (41.5)	NS

NS: not statistically significant

IV. DISCUSSION

Our study revealed that 44.4% of patients with schizophrenia were non-adherent to their antipsychotic treatment. Lacro *et al.* [5] estimated the rate of non-adherence among patients with schizophrenia at 41.2% in their literature review, and at 49.5% in studies with more rigorous methodologies. The CATIE study [15], conducted across 57 North American sites with 1493 patients, demonstrated that even patients who voluntarily participated in the study on medication treatments discontinued their medication at very high rates. Studies show variable prevalence rates of therapeutic adherence due to several factors [8]. On one hand, there is no consensus on the definition and methods for assessing adherence, which may include indirect techniques (questionnaires, clinical observation) or direct methods (plasma level measurements, electronic pill dispensers) [16]. These methods can yield divergent results [3]. On the other hand, evaluation periods vary between 6 months and 2 years, whereas adherence, being dynamic, tends to decrease over time [17]. It is therefore

recommended to use multiple methods to obtain a more accurate assessment.

Nevertheless, adherence is a complex phenomenon in which multiple factors interact to determine it. These factors have been extensively studied and schematically categorized into factors related to the individual, factors related to the treatment and therapeutic relationship, and factors related to the environment [1,17,18,19].

In our study, poor therapeutic adherence was associated with low socioeconomic status, lack of employment, and absence of family support, which aligns with existing literature [20, 21, 22].

However Young *et al.* [23] highlight the importance of family support in improving adherence; conversely, family hostility towards the patient would contribute to non-adherence.

In our study, a statistically significant difference was observed between poor therapeutic adherence and the use of psychoactive substances. The direct role of psychoactive substance use in poor adherence is widely accepted [17, 24, 25]. Indeed, the use of psychoactive substances impairs adherence by disrupting dopaminergic systems at the mesolimbic level, which may reduce patients' responsiveness to the effective action of antipsychotics [26]. This partial therapeutic inefficacy, combined with the persistence of disease symptoms, constitutes an indirect predictive factor for poor treatment adherence [3].

Insight, like treatment adherence, is a non-dichotomous, complex, and multidimensional phenomenon. In our study, a low level of insight was associated with poor medication adherence. A study by Droulout *et al.* [27] conducted in a hospital setting with patients with schizophrenia, which assessed patients' attitudes towards their treatments, confirmed that higher levels of insight corresponded to better perception of treatment. Consequently, improving insight is likely to have a dual beneficial effect: directly through enhanced adherence by increasing awareness of the illness and the importance of treatment, and indirectly through fostering positive attitudes towards antipsychotic treatment [8].

We did not find a statistically significant relationship between the type of antipsychotic and therapeutic adherence. However, researchers have anticipated that second-generation antipsychotics might improve adherence because patients experience fewer side effects with these medications and generally have a better quality of life [28, 29]. To enhance adherence, there are arguments in favor of using long-acting antipsychotics [30]. Simplifying the treatment regimen and requiring regular visits to local medical facilities can improve adherence and facilitate comprehensive patient care.

In our study, monotherapy was associated with better therapeutic adherence. Among the factors identified as detrimental to adherence, the number of daily doses and the complexity of the medication regimen are most frequently cited by various studies [31, 32].

However, we did not find a relationship between adherence and side effects of antipsychotics, contrary to the results of several studies that suggest side effects play a decisive role in adherence [8, 33, 34]. Indeed, the presence of side effects leads to negative attitudes toward both the treatment [35] and its prescriber. This, in turn, undermines the quality of the therapeutic alliance, which is an important factor in determining the level of adherence [8, 36].

This underscores the importance of early and personalized psychoeducational and psychotherapeutic

interventions in managing side effects of antipsychotic treatments and preventing non-adherence [8].

Similarly, implementing therapeutic and preventive strategies for psychoactive substance use, structured psychoeducational strategies to improve insight, and training for therapists to enhance the therapeutic alliance should be established to improve therapeutic adherence among patients with schizophrenia [8].

Study limitations

- The evaluation conducted within a single hospital setting limits the ability to generalize the findings.
- The assessment of adherence using an indirect measurement scale has the disadvantage of potentially overestimating therapeutic adherence.
- The cross-sectional nature of the study does not allow for the determination of the direction of the significant associations found.

V. CONCLUSION

Non-adherence to treatment is a major issue in the management of schizophrenia.

Our study revealed that 44.4% of patients with schizophrenia were non-adherent to their antipsychotic treatment. Poor therapeutic adherence was associated with low socioeconomic status, lack of employment, absence of family support, use of psychoactive substances, poor insight, and a high number of medication doses.

Its multifactorial and complex nature underscores the need for a multidisciplinary, personalized approach integrated into a comprehensive bio-psychosocial therapeutic strategy.

REFERENCES

1. Charrier, N., Chevreur, K., & Durand-Zaleski, I. (2013). Le coût de la schizophrénie: revue de la littérature internationale. *L'encéphale*, 39, S49-S56.
2. Leijala, J., Kampman, O., Suvisaari, J., & Eskelinen, S. (2021). Daily functioning and symptom factors contributing to attitudes toward antipsychotic treatment and treatment adherence in outpatients with schizophrenia spectrum disorders. *BMC psychiatry*, 21, 1-11.
3. Weiden, P. J., Sajatovic, M., Scott, J., Carpenter, D., Ross, R., & Docherty, J. P. (2009). The expert consensus guideline series: adherence problems in patients with serious and persistent mental illness.
4. Gourevitch, R. (2006). Comment améliorer l'observance chez le patient souffrant de schizophrénie?. *L'Encéphale (Paris)*, 32(5).
5. Lacro, J. P., Dunn, L. B., Dolder, C. R., & Jeste, D. V. (2002). Prevalence of and risk factors for

- medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. *The Journal of clinical psychiatry*, 63(10), 15489.
6. Kampman, O., Laippala, P., Väänänen, J., Koivisto, E., Kiviniemi, P., Kilkku, N., & Lehtinen, K. (2002). Indicators of medication compliance in first-episode psychosis. *Psychiatry research*, 110(1), 39-48.
 7. Weiden, P. J., & Olfson, M. (1995). Cost of relapse in schizophrenia. *Schizophrenia bulletin*, 21(3), 419-429.
 8. El Ammouri, A., & Kisra, H. (2017). Étude de l'observance thérapeutique chez une population de patients atteints de schizophrénie au Maroc. *L'Encéphale*, 43(6), 522-527.
 9. Kokurcan, A., Karadağ, H., Doğu, S. E., Funda, E. R. D. İ., & Örsel, S. (2020). Clinical correlates of treatment adherence and insight in patients with schizophrenia. *Archives of Clinical and Experimental Medicine*, 5(3), 95-99.
 10. Gorwood, P., Burns, T., Juckel, G., Rossi, A., San, L., Hargarter, L., & Schreiner, A. (2013). Psychiatrists' perceptions of the clinical importance, assessment and management of patient functioning in schizophrenia in Europe, the Middle East and Africa. *Annals of General Psychiatry*, 12, 1-8.
 11. Kennedy, J. L., Altar, C. A., Taylor, D. L., Degtiar, I., & Hornberger, J. C. (2014). The social and economic burden of treatment-resistant schizophrenia: a systematic literature review. *International clinical psychopharmacology*, 29(2), 63-76.
 12. Lafeuille, M. H., Gravel, J., Lefebvre, P., Fastenau, J., Muser, E., Doshi, D., & Duh, M. S. (2013). Patterns of relapse and associated cost burden in schizophrenia patients receiving atypical antipsychotics. *Journal of medical economics*, 16(11), 1290-1299.
 13. Thompson, K., Kulkarni, J., & Sergejew, A. A. (2000). Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. *Schizophrenia research*, 42(3), 241-247.
 14. Bourgeois, M. L., Koleck, M., & Jais, E. (2002, September). Validation de l'échelle d'insight Q8 et évaluation de la conscience de la maladie chez 121 patients hospitalisés en psychiatrie. In *Annales Médico-psychologiques, revue psychiatrique* (Vol. 160, No. 7, pp. 512-517). Elsevier Masson.
 15. Lieberman, J. A. (2005). Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med*, 353(12), 1209-23.
 16. Benoit, M., Pon, J., & Zimmermann, M. A. (2009). Expert opinion on APAP (prolonged action atypical antipsychotic agents). How to evaluate the quality of observations. *L'encephale*, S87-90.
 17. Quach, P. L., Mors, O., Christensen, T. Ø., Krarup, G., Jørgensen, P., Bertelsen, M., ... & Nordentoft, M. (2009). Predictors of poor adherence to medication among patients with first-episode schizophrenia-spectrum disorder. *Early intervention in psychiatry*, 3(1), 66-74.
 18. San, L., Bernardo, M., Gómez, A., Martínez, P., González, B., & Peña, M. (2013). Socio-demographic, clinical and treatment characteristics of relapsing schizophrenic patients. *Nordic journal of psychiatry*, 67(1), 22-29.
 19. Misdrahi, D., Llorca, P. M., Lançon, C., & Bayle, F. J. (2002). L'observance dans la schizophrénie: Facteurs prédictifs, voies de recherches, implications thérapeutiques. *L'Encéphale: Revue de psychiatrie clinique biologique et thérapeutique*.
 20. Gilmer, T. P., Ojeda, V. D., Barrio, C., Fuentes, D., Garcia, P., Lanouette, N. M., & Lee, K. C. (2009). Adherence to antipsychotics among Latinos and Asians with schizophrenia and limited English proficiency. *Psychiatric Services*, 60(2), 175-182.
 21. Gilmer, T. P., Dolder, C. R., Lacro, J. P., Folsom, D. P., Lindamer, L., Garcia, P., & Jeste, D. V. (2004). Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *American Journal of Psychiatry*, 161(4), 692-699.
 22. Feki, I., Medhaffar, K., Sallemi, R., Baati, I., Trigui, D., & Masmoudi, J. (2018). Compliance and adverse effects of neuroleptics in a population of elderly patients with schizophrenia. *NPG Neurologie-Psychiatrie-Gériatrie*, 18 (104), 102-108.
 23. Young, J. L., Zonana, H. V., & Shepler, L. (1986). Medication noncompliance in schizophrenia: codification and update. *Journal of the American Academy of Psychiatry and the Law Online*, 14(2), 105-122.
 24. Ameller, A., & Gorwood, P. (2015). Weight of addictive comorbidity in the risk of partial adherence to drug treatment and relapse in schizophrenia. *L'Encéphale*, 41 (2), 174-183.
 25. Jónsdóttir, H., Opjordsmoen, S., Birkenaes, A. B., Simonsen, C., Engh, J. A., Ringen, P. A., ... & Andreassen, O. A. (2013). Predictors of medication adherence in patients with schizophrenia and bipolar disorder. *Acta Psychiatrica Scandinavica*, 127(1), 23-33.
 26. Buckley, P. F. (1998). Substance abuse in schizophrenia: a review. *Journal of Clinical Psychiatry*, 59(3), 26-30.
 27. Droulout, T., Liraud, F., & Verdoux, H. (2003). Influence of awareness of the disorder and subjective perception of treatment on medication compliance in psychotic disorders. *Encéphale*, 29 (5), 430-7.
 28. Awad, A. G., & Voruganti, L. N. (2004). New antipsychotics, compliance, quality of life, and subjective tolerability—are patients better off?. *The Canadian Journal of Psychiatry*, 49(5), 297-302.
 29. Love, R. C. (2002). Strategies for increasing treatment compliance: the role of long-acting antipsychotics. *American Journal of Health-System Pharmacy*, 59(suppl_8), S10-S15.

30. Davis, J. M., Kane, J. M., Marder, S. R., Brauzer, B., Gierl, B., Schooler, N., ... & Hassan, M. O. H. A. M. M. E. D. (1993). Dose response of prophylactic antipsychotics. *The Journal of clinical psychiatry*, 54, 24-30.
31. Blackwell, B. (1976). Treatment adherence. *B J Psych*, 129, 513—31
32. Claxton, A. J., Cramer, J., & Pierce, C. (2001). A systematic review of the associations between dose regimens and medication compliance. *Clinical therapeutics*, 23(8), 1296-1310.
33. Fenton, W. S., Blyler, C. R., & Heinssen, R. K. (1997). Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophrenia bulletin*, 23(4), 637-651.
34. Lieslehto, J., Tiihonen, J., Lähteenvuo, M., Tanskanen, A., & Taipale, H. (2022). Primary nonadherence to antipsychotic treatment among persons with schizophrenia. *Schizophrenia bulletin*, 48(3), 655-663.
35. Hashimoto, Y., Uno, J., Miwa, T., Kurihara, M., Tanifuji, H., & Tensho, M. (2012). Effects of antipsychotic polypharmacy on side-effects and concurrent use of medications in schizophrenic outpatients. *Psychiatry and clinical neurosciences*, 66(5), 405-410.
36. McCabe, R., Bullenkamp, J., Hansson, L., Lauber, C., Martinez-Leal, R., Rössler, W., ... & Priebe, S. (2012). The therapeutic relationship and adherence to antipsychotic medication in schizophrenia. *PLoS One*, 7(4), e36080.