



## Letter to the Editor

### Psychiatrists' perceptions of medication adherence among patients with schizophrenia: An international survey



## Keywords:

Adherence  
Antipsychotics  
Long-acting injectable antipsychotics  
Schizophrenia  
Perception

## To the Editors

It is well known that at least 40–50% of patients with schizophrenia fail to take their medications as prescribed (Kane et al., 2013; Valenstein et al., 2006). Previous studies have focused mainly on patient factors related to non-adherence, such as insight into illness and perception of their physicians (DiMatteo, 2004; Velligan et al., 2017). However, there is growing evidence that physicians tend to overestimate their patients' adherence and provide inadequate interventions to promote adherence (Clyne et al., 2016; Remington et al., 2007). Misjudging actual medication adherence may lead to mistaken treatment selection, such as inappropriate dosage increases, unnecessary medication switches, and underutilization of long-acting injectable antipsychotics (LAIs), consequently leading to negative outcomes. Therefore, in order to: 1) investigate perceptions about medication adherence among numerous psychiatrists treating schizophrenia across a broad range of countries; and 2) identify the factors that influence physicians' perceptions of their own patients' adherence, we conducted an international survey. This study was exempted from review by the Institutional Review Board of the Northwell Health System, New York.

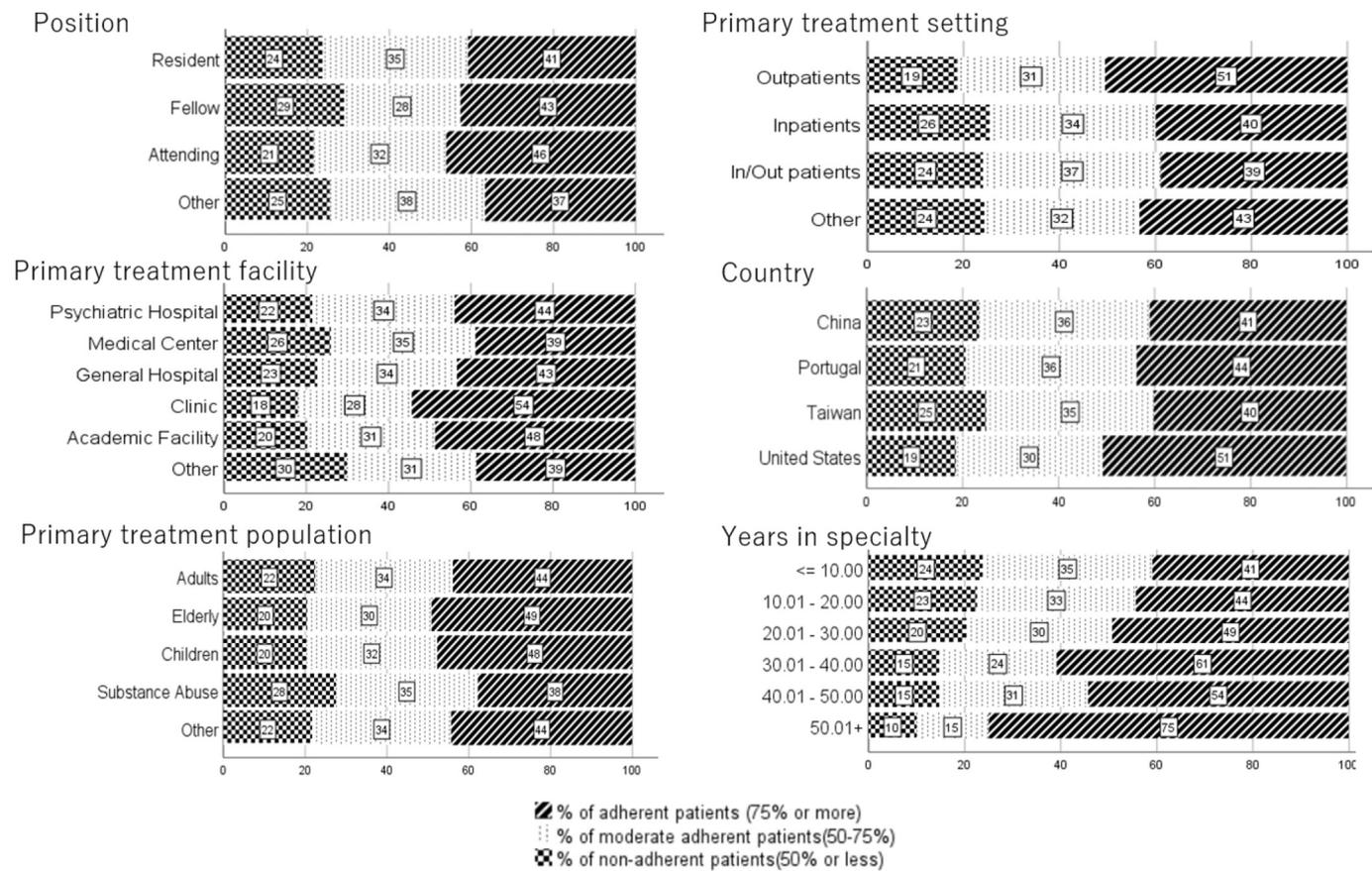
The survey was conducted between March 2012 and June 2015, targeting psychiatrists and nurse practitioners who had prescribed antipsychotics. The survey is available upon request to the corresponding author. It consisted of 55 questions targeting various decision-making aspects specific to treating patients with schizophrenia and related disorders, including the medical professionals' perceptions of their patients' adherence, and utilization of LAIs, clozapine, and other approaches. We here report a portion of the results, focusing on questions about psychiatrists' perceptions of medication adherence among their patients with schizophrenia, and how to confirm and improve adherence. Recruitment was done at the facilities via paper brochures, or online by distributing a URL link to members of scientific societies, attendees at scientific meetings, or various individuals/facilities. Adherence perceptions across different participant groups were compared using the Kruskal–Wallis one-way analysis of variance (ANOVAs) test. Chi-squared tests were conducted to compare the frequencies of different methods to confirm and improve adherence between groups. Bonferroni correction was applied to avoid type I

errors due to multiple comparisons. All analyses were two-sided with alpha set at 0.05, using SPSS 25.0 software (SPSS Inc., Chicago).

We collected 1316 survey responses representing 11 countries (Australia, Brazil, Canada, China, Denmark, Greece, New Zealand, Portugal, Taiwan, United States, United Kingdom). The average years of experience in specialty among the participants were  $12.9 \pm 11.0$ . In regards to position, most were attending psychiatrists (qualified specialists) (65.2%), followed by residents (27.4%) (see Supplementary Table). Fig. 1 shows estimations of patients' adherence arranged by psychiatrist characteristics. Participants were asked to estimate the percentage of patients they see who are “adherent” (take >75% of the prescribed medication), “partially adherent” (take 50–75%), or “poor/non-adherent” (take <50%). Overall,  $45.4\% \pm 23.4$  of the patients were estimated to be adherent. Attending physicians were more likely to consider patients to be adherent compared to residents ( $p = 0.011$ ). Psychiatrists who work mainly in clinics were more likely to consider patients to be adherent compared to those in medical centers, general hospitals, or psychiatric hospitals ( $p < 0.001$ ,  $p = 0.005$ ,  $p = 0.003$ , respectively). Also, psychiatrists who mainly see outpatients were more likely to consider patients to be adherent compared to those who see mainly inpatients, both in/outpatients, and others ( $p < 0.001$ ,  $p < 0.001$ ,  $p = 0.002$ , respectively). Years of experience in one's specialty was positively correlated with good adherence estimation ( $r = 0.205$ ,  $p < 0.001$ ). Multiple regression analysis using stepwise selection showed that, after controlling for physicians' demographics, the estimated proportion of “adherent” patients was related to “years of experience” ( $\beta = 0.151$ ,  $p = 0.001$ ) and “primary setting = outpatient” ( $\beta = 0.104$ ,  $p = 0.017$ ).

Next we compared the strategies employed by “optimistic” psychiatrists ( $n = 263$ ), and “pessimistic” psychiatrists ( $n = 310$ ) in how they measure and promote patients' adherence. This grouping was based on the participants' responses to estimating the percentage of patients they see who are “adherent” (take >75% of the prescribed medication), by selecting the top and bottom groups from a quartile split. The “optimistic” psychiatrists were less likely to confirm adherence by “asking the caregivers” ( $p < 0.001$ ) and were more likely to confirm adherence by “asking the patient” and utilizing “self-report” ( $p < 0.001$ ,  $p < 0.001$ , respectively) (Supplementary Figure). The pessimistic psychiatrists were less likely to promote adherence by “motivational interviewing” ( $p = 0.004$ ).

As a whole, the results from this study suggest that psychiatrists across different countries are relatively realistic in their awareness of adherence rates. It may sound counterintuitive that the longer one's experience in psychiatry, the higher one estimates their patients' adherence. But experienced psychiatrists may be better at building rapport with patients and therefore tend to think they are adherent. Psychiatrists in inpatient settings see many patients admitted due to non-adherence, which could lead to a negative view of overall adherence rates among inpatients. Previous studies have shown that estimation error and optimistic bias are seen consistently in clinics and university hospitals (Acosta et al., 2009; Brain et al., 2014; Byerly et al., 2005),



**Fig. 1.** Subgroup analysis of participants' estimates of patient adherence. For the comparison between countries, countries with >100 participants were included in order to avoid potential sampling bias.

both of which have used MEMS caps, currently considered one of the gold standards for objective adherence assessment.

In regards to the actions taken to confirm and to promote adherence, these results may reflect that the optimistic psychiatrists trust patients more than the pessimistic psychiatrists, who are more likely to seek information from patients' caregivers instead. The objective tools currently available for measuring medication adherence such as MEMS, pill count, electronic refill records, and digital ingestion tracking systems are not easy to access in daily practice, and the most commonly-used modalities are subjective approaches relying on patient self-reporting or caregiver assessment (Velligan et al., 2006). In such cases, one of the treatment approaches would be the utilization of LAIs, which will be the focus of our next paper from this survey.

The largest limitation in this study is that this survey was not designed to measure actual patient adherence. Also, selection bias and recall bias may exist. Considering the results from this study, which show that the perceptions of psychiatrists influence their actions in the medical decision-making process when treating schizophrenia, development of a feasible method to accurately and objectively capture patient adherence is warranted.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2019.07.028>.

#### Contributors

TK and JK designed the study and created the survey. All the authors contributed to translating the survey into the respective languages, distributing it, and collecting the data. TK and SK analyzed the data. All authors contributed to drafting and critically revising the paper and have approved the manuscript for publication.

#### Declaration of Competing Interest

Dr. Kishimoto has received consultant fees from Otsuka, Pfizer, and Daiinippon Sumitomo, and speaker's honoraria from Banyu, Eli Lilly, Daiinippon Sumitomo, Janssen, Novartis, Otsuka, and Pfizer. He has received grant support from the Byoutaitaishakenkyukai Fellowship (Fellowship of Astellas Foundation of Research on Metabolic Disorders) and Eli Lilly Fellowship for Clinical Psychopharmacology.

Drs. J. Chang, H. Chang, and Su are supported by the following grants: MOST 106-2314-B-039-027-MY3, 106-2314-B-038-049, 106-2314-B-039-031, 106-2314-B-039-035, and 105-2918-I-039-001 from the Ministry of Science and Technology, Taiwan; NHRI-EX106-10528NI from the National Health Research Institutes, Taiwan; and CMU106-S-33, CRS-106-063, DMR-107-202, DMR-107-204, DMR-107-091, DRM-107-097, DRM-108-091, CRS-108-048 and the Chinese Medicine Research Center from the China Medical University, Taiwan.

Dr. Castle has received grant monies for research from Eli Lilly, Janssen Cilag, Roche, Allergan, Bristol-Myers Squibb, Pfizer, Lundbeck, Astra Zeneca, and Hospira. He has received travel support and honoraria for talks and consultancy from Eli Lilly, Bristol-Myers Squibb, Astra Zeneca, Lundbeck, Janssen Cilag, Pfizer, Organon, Sanofi-Aventis, Wyeth, Hospira, Servier, and Seqirus, and is a current Advisory Board Member for Lu AA21004: Lundbeck; Varenicline: Pfizer; Asenapine: Lundbeck; Aripiprazole LAI: Lundbeck; Lisdexamfetamine: Shire; Lurasidone: Servier; Brexpiprazole: Lundbeck; Treatment Resistant Depression: LivaNova. He is founder of the Optimal Health Program, currently operating as Optimal Wellness. He does not knowingly have stocks or shares in any pharmaceutical company.

Dr. Haddad has received honoraria for lecturing Lundbeck, NewBridge Pharmaceuticals, and Sunovion.

Dr. Petrides has received research support by the National Institute of Mental Health (NIMH), National Institute of Aging (NIA), and St. Jude Medical.

Dr. Agid has received speaker's honoraria from Janssen-Ortho (Johnson & Johnson), Lundbeck, Otsuka, Mylan Pharmaceuticals, HLS, and Novartis, and consultant fees from Janssen-Ortho (Johnson & Johnson), Lundbeck, Otsuka, Sumitomo Daiinippon Pharma, and Minerva. He has also received research support from Boehringer Ingelheim, Neurocrine Biosciences, Janssen-Ortho (Johnson & Johnson), Otsuka, Neurocrine Bioscience, Acadia, Syneurx, and diaMentis.

Dr. Kane has been a consultant to Alkermes, Janssen, Pfizer, Bristol-Myers Squibb, Daiinippon Sumitomo/Sunovion, Johnson & Johnson, Otsuka, Pierre Fabre, Takeda,

IntraCellular Therapies, Merck, Lundbeck, Neurocrine, Reviva, Roche, Teva, and he has received honoraria for lectures from Otsuka, Bristol-Myers Squibb, Janssen and Lundbeck. He is a shareholder LB Pharma and The Vanguard Research Group. He has received grant support from The Center for Medicare and Medicaid Innovation, National Institute of Mental Health, Otsuka, Lundbeck and Janssen.

#### Acknowledgements

The authors thank Stanley Ng for the data collection and entering.

#### References

- Acosta, F.J., Bosch, E., Sarmiento, G., Juanes, N., Caballero-Hidalgo, A., Mayans, T., 2009. Evaluation of noncompliance in schizophrenia patients using electronic monitoring (MEMS) and its relationship to sociodemographic, clinical and psychopathological variables. *Schizophr. Res.* 107, 213–217.
- Brain, C., Sameby, B., Allerby, K., Lindström, E., Eberhard, J., Burns, T., Waern, M., 2014. Twelve months of electronic monitoring (MEMS®) in the Swedish COAST-study: a comparison of methods for the measurement of adherence in schizophrenia. *Eur. Neuropsychopharmacol.* 24, 215–222.
- Byerly, M., Fisher, R., Whatley, K., Holland, R., Varghese, F., Carmody, T., Magouirk, B., Rush, A.J., 2005. A comparison of electronic monitoring vs. clinician rating of antipsychotic adherence in outpatients with schizophrenia. *Psychiatry Res.* 133, 129–133.
- Clyne, W., McLachlan, S., Mshelia, C., Jones, P., De Geest, S., Ruppert, T., Siebens, K., Dobbels, F., Kardas, P., 2016. "My patients are better than yours": optimistic bias about patients' medication adherence by European health care professionals. *Patient Prefer. Adherence.* 10, 1937–1944.
- DiMatteo, M.R., 2004. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med. Care* 42, 200–209.
- Kane, J.M., Kishimoto, T., Correll, C.U., 2013. Non-adherence to medication in patients with psychotic disorders: epidemiology, contributing factors and management strategies. *World Psychiatry* 12 (3), 216–226 Oct.
- Remington, G., Kwon, J., Collins, A., Laporte, D., Mann, S., Christensen, B., 2007. The use of electronic monitoring (MEMS®) to evaluate antipsychotic compliance in outpatients with schizophrenia. *Schizophr. Res.* 90, 229–237.
- Valenstein, M., Ganoczy, D., McCarthy, J.F., Myra Kim, H., Lee, T. a, Blow, F.C., 2006. Antipsychotic adherence over time among patients receiving treatment for schizophrenia: a retrospective review. *J. Clin. Psychiatry.* 67, 1542–1550.
- Velligan, D.I., Lam, Y.-W.F., Glahn, D.C., Barrett, J.A., Maples, N.J., Ereshefsky, L., Miller, A.L., 2006. Defining and assessing adherence to oral antipsychotics: a review of the literature. *Schizophr. Bull.* 32, 724–742.
- Velligan, D.I., Sajatovic, M., Hatch, A., Kramata, P., Docherty, J.P., 2017. Why do psychiatric patients stop antipsychotic medication? A systematic review of reasons for nonadherence to medication in patients with serious mental illness. *Patient Prefer. Adherence.* 11, 449–468.

Shunya Kurokawa<sup>1</sup>

Department of Psychiatry, Keio University School of Medicine, 35  
Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan

Taishiro Kishimoto\*,<sup>1</sup>

Department of Psychiatry, Keio University School of Medicine, 35  
Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan

Department of Psychiatry, The Donald and Barbara Zucker School of  
Medicine at Hofstra/Northwell, 75-59 263rd Street Glen Oaks, New York  
11004-1150, United States

\*Corresponding author at: Department of Psychiatry, Keio University  
School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582,  
Japan.

E-mail address: taishiro-k@mti.biglobe.ne.jp.

Kuan-Pin Su

Jane Pei-Chen Chang

Hui-Chih Chang

Department of Psychiatry & Mind-Body Interface Laboratory (MBI-Lab),  
China Medical University Hospital, No.91 Hsueh-Shih Road, Taichung,  
40402, Taiwan

Xin Yu

Peking University Sixth Hospital, No.51 Hua Yuan Bei Road, Haidian  
District, Beijing, 100191, China

Nuno Rodrigues-Silva

Department of Psychiatry and Mental Health, Cova da Beira University  
Healthcare Center, Quinta do Alvito, Covilhã, 6200-251, Portugal

Jimmi Nielsen

Mental health Centre Glostrup, Copenhagen University Hospital,  
Rigshospitalet, Blegdamsvej 9, Copenhagen, 2100, Denmark

Anish Unadkat

David Castle

The University of Melbourne and St Vincent's Hospital Melbourne, 41  
Victoria Parade, Fitzroy, Melbourne, 3065, Australia

Peter M. Haddad

Department of Psychiatry, University of Manchester, Oxford Rd,  
Manchester, M13 9PL, UK

Deyvis Rocha

Ary Gadelha

Departamento de Psiquiatria, Universidade Federal de São Paulo  
(UNIFESP), 650 - 3° andar, São Paulo 04039-032, Brazil

Styliani Kaliora

Georgios Petrides

Department of Psychiatry, The Donald and Barbara Zucker School of  
Medicine at Hofstra/Northwell, 75-59 263rd Street Glen Oaks, New York  
11004-1150, United States

Ofer Agid

Schizophrenia Program, Centre for Addiction and Mental Health (CAMH),  
Department of Psychiatry, Faculty of Medicine, University of Toronto, 250  
College Street, CS 732, Toronto, ON M5T 1R8, Canada

Yuki Tazawa

Akihiro Takamiya

Toshiro Horigome

Department of Psychiatry, Keio University School of Medicine, 35  
Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan

John M. Kane

Department of Psychiatry, The Donald and Barbara Zucker School of  
Medicine at Hofstra/Northwell, 75-59 263rd Street Glen Oaks, New York  
11004-1150, United States

13 June 2019

<sup>1</sup> Both authors contributed equally to this manuscript.