

# Non-adherence with Antipsychotics - How Do We Assess and Assist These Patients with Schizophrenia?

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## Background

The long-term goal of the treatment of schizophrenia is the prevention of recurrence. To achieve this goal, the continuation of medication is important.

Lack of adherence to medication regimens is a critical issue in the treatment of schizophrenia and has serious impacts on the course of the illness, including **worsening of symptoms, relapse, suicidal attempts, repeated emergency room visits or re-hospitalization, and poor functional outcomes** (Ascher-Svanum et al., 2006).

Factors inhibiting medication adherence have been suggested to be associated with **1) Patients' poor understanding of their diseases, 2) unfavorable relationship between patients and healthcare workers and 3) Side effects of drugs.**

In this session, I would like to suggest how we can assess the adherence and how we can improve adherence in patients with schizophrenia, by indicating our research.

## Study 1

### Association between the psychiatric symptoms and illness insight / medication adherence in patients with schizophrenia

#### Objects

The long-term goal of the treatment of schizophrenia is the prevention of recurrence. To achieve this goal, the continuation of medication is important. We considered that the continuation of medication may require improvement in insight / medication adherence, not improvement in symptoms by involuntary Medication. We then evaluated the association between the severity of symptoms and insight / medication adherence.

#### Methods

The subjects were comprised of 101 outpatients with schizophrenia. Psychiatric symptoms were evaluated using BPRS and CGI, illness insight using SAI, and drug adherence using DAI-10.

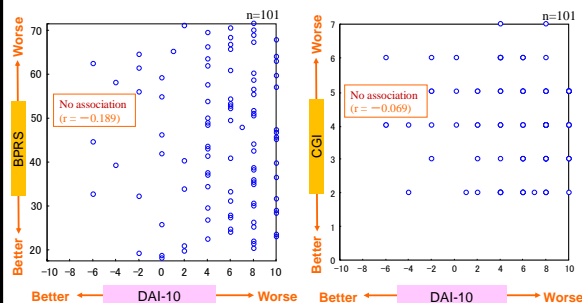
BPRS: Brief Psychiatric Rating Scale  
CGI: Clinical Global Impression Scale  
SAI: Schedule for Assessment of Insight  
DAI-10: Drug Attitude Inventory-10 Questionnaire

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## Evaluation of medication adherence

DAI-10 (Drug Attitude Inventory-10 Questionnaire)	Yes	No	Score
1. For me, the good things about medication outweigh the bad	Yes	No	1
2. I feel weird, like a "zombie", on medication	Yes	No	1
3. I take medication of my own free choice	Yes	No	1
4. Medication makes me feel more relaxed	Yes	No	1
5. Medication makes feel tired and sluggish	Yes	No	1
6. I take medication only when I am sick	Yes	No	1
7. I feel more normal on medication	Yes	No	1
8. It is unnatural for my mind and body to be controlled by medication	Yes	No	1
9. My thoughts are clearer on medication	Yes	No	1
10. By staying on medication I can prevent getting sick	Yes	No	1
Total			10

## Association between BPRS and CGI or DAI-10

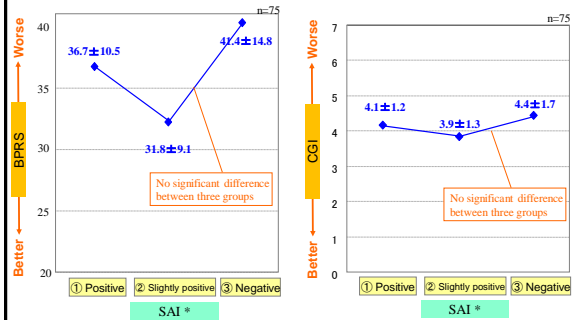


BPRS: Brief Psychiatric Rating Scale  
CGI: Clinical Global Impression Scale  
DAI-10: Drug Attitude Inventory-10 Questionnaire

Spearman rank correlation

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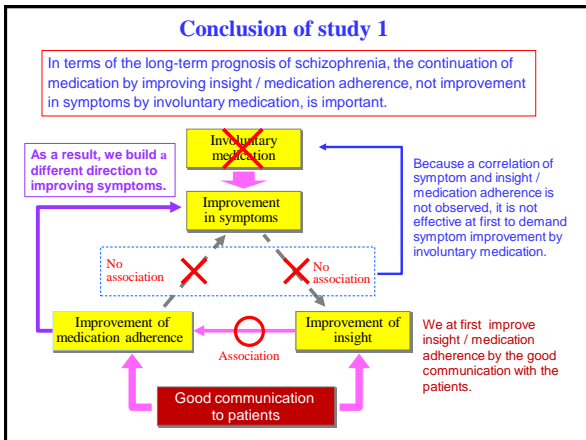
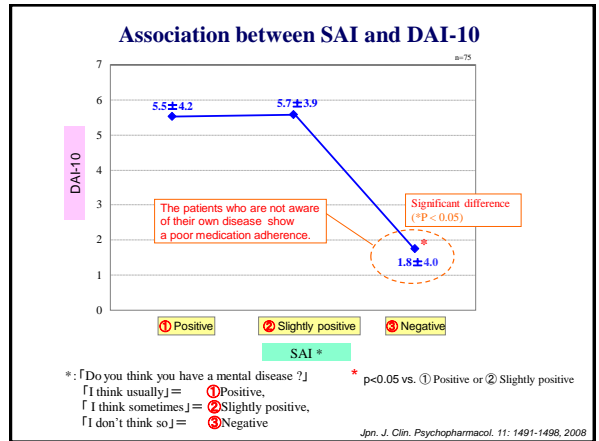
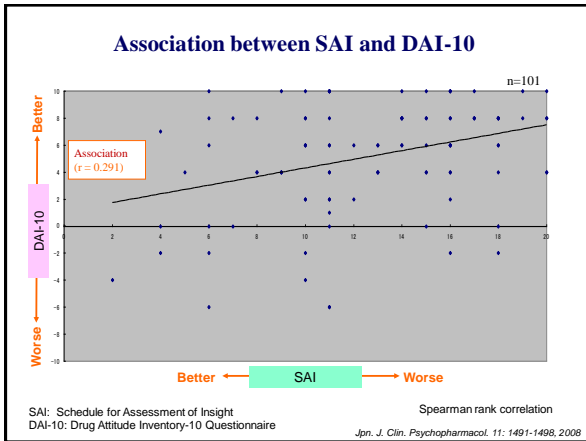
## Association between BPRS and CGI or SAI



\*: 「Do you think you have a mental disease?」  
「I think usually」= Positive,  
「I think sometimes」= Little positive,  
「I don't think so」= Negative

BPRS: Brief Psychiatric Rating Scale  
CGI: Clinical Global Impression Scale  
SAI: Schedule for Assessment of Insight

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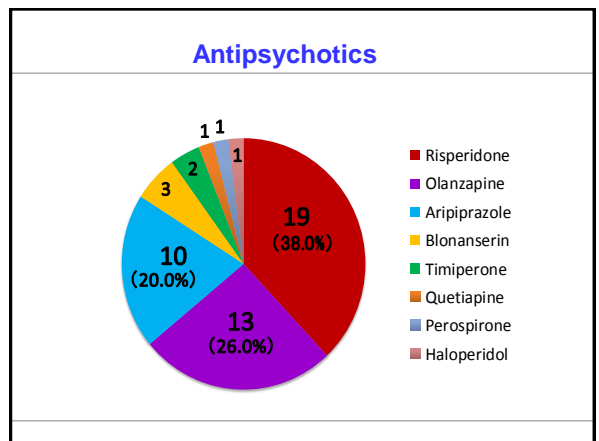
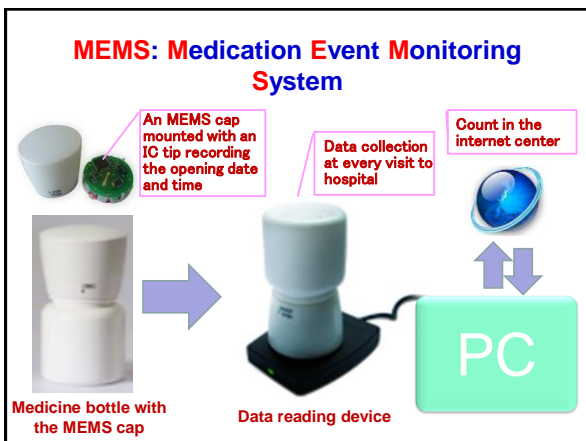


### Study 2

#### Medication event monitoring system (MEMS) trial to evaluate the adherence of patients with schizophrenia in Japan

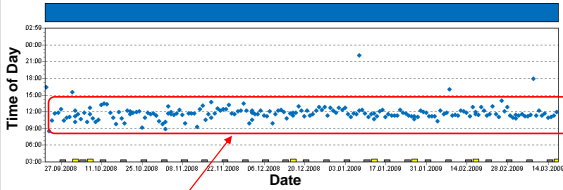
**Objects**  
In order to accurately detect the medication adherence of patients with schizophrenia, for the first time in Japan a study that examines the consistency of medication adherence when using MEMS was conducted as a multicenter study, in which one university hospital and six mental hospitals participated.

**Methods**  
The subjects were comprised of 50 outpatients with schizophrenia. Medication adherence and its tendencies were continuously monitored for up to a period of 6 months after discharge from hospital by using MEMS. The endpoint was the continuing treatment.



### Patients medication pattern - Case ①

**Kept taking the medicine at almost the same time**

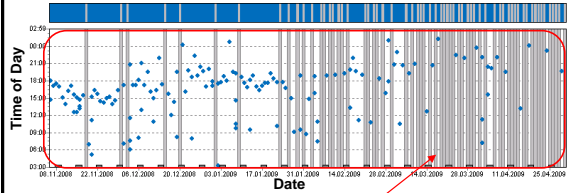


Medication compliance is high, and time of taking medicine is constant

Final status: Good compliance in taking medication  
 Patient background : Male, 38 years old / schizophrenia paranoid type  
 Average of medication compliance : 98 %  
 The time of taking medicine range : 46.9 min

### Patients medication pattern – Case ②

**The days of not taking medicine gradually increase**

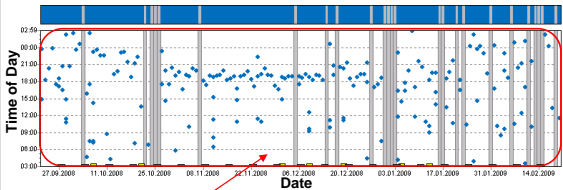


The days when medicine is not taken at all, in the latter half, in particular increases

Final status: Poor medication  
 Patient background : Female, 36 years old / schizophrenia paranoid type  
 Average of medication compliance : 55 %  
 The time of taking medicine range : 212.9 min

### Patients medication pattern – Case ③

**Taking medication is not constant, and there are the days when medicine was not taken**

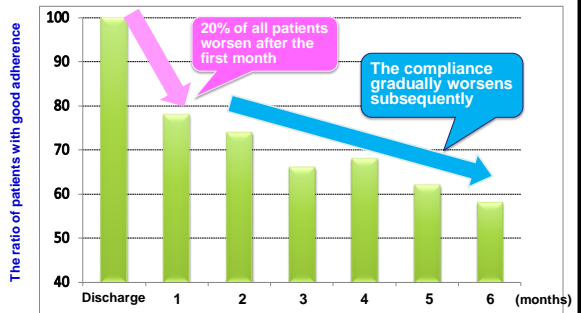


The days when medicine was not taken increase, and the time of taking medicine is not constant

Final status: Dropout (re-hospitalization)  
 Patient background : Male, 41 years old / schizophrenia paranoid type  
 Average of medication compliance : 66 %  
 The time of taking medicine range : 253.4 min

### Time course in the ratio of the patients with good adherence

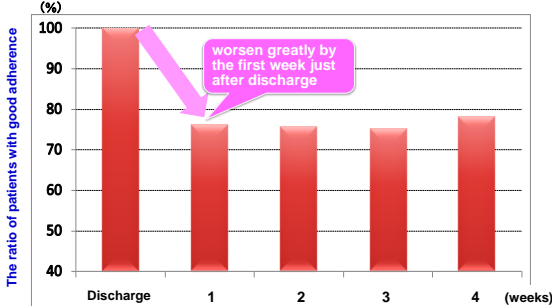
**The medicine compliance worsens with time**



Good adherence : the average value from MEMS is over than 75 %

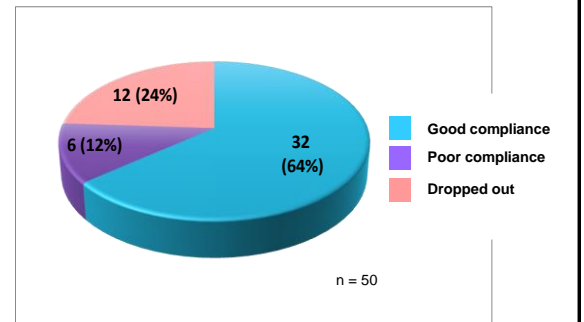
### Time course in the ratio of the patients with good adherence

**The medicine compliance worsens greatly just after discharge**



Good adherence : the average value from MEMS is over than 75 %

### MEMS study



Good adherence : the average value from MEMS is over than 75 %

## Study 3

### Investigation of the current state regarding side effects, which are less likely to be noted, in pharmacotherapy for schizophrenia

#### Objects

- It is essential to **improve adherence** for the continuous taking of medication, and the side effects of antipsychotics are partially responsible for poor adherence.
- Some of the side effects of antipsychotics are **not noted by healthcare workers or patients, and some are less likely to be identified for various reasons, such as patients being unwilling to tell.** There is a concern that such side effects may result in decreased adherence, and the taking of drugs may be discontinued.
- In this study, we investigated the current state regarding the side effects of antipsychotics, which are less likely to be noted, and the background causes.

## Method (1)

The subjects checked symptoms that had concerned them in the Self-Report Symptom Check Sheet. Pharmacists then conducted a questionnaire survey to evaluate the subjects' degree of recognition regarding side effects, and clarify whether or not a physician had been informed of their symptoms.

#### Body Check Sheet

Please check the presence or absence of the following symptoms in your recent daily life:

- I become sleepy during the daytime (I cannot think clearly).
- I have difficulties in getting up in the morning.
- I feel restless and uneasy.
- My appetite has grown.
- I have gained weight.
- I am lactating.
- I do not have sexual desires.

#### Females

- I have menstrual irregularities/amenorrhea.

#### Males

- I cannot ejaculate.
- I do not have erections.
- I have a feeling of fullness in my chest (I feel stiffness in my chest).

#### Others

Please write down what you would like to tell your physician

## Method (2)

### Details of the questionnaire for each symptom checked

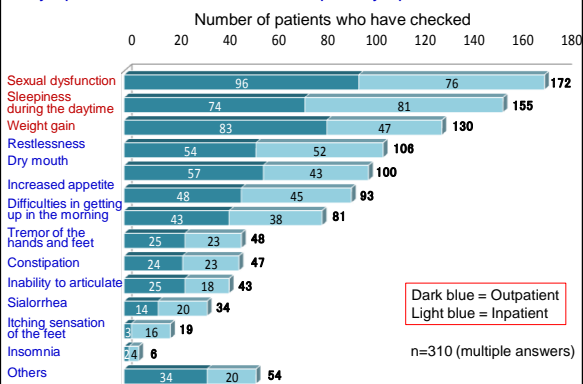
- Do you think the symptom is caused by the side effects of your medication?
  - Yes, I do.
  - The symptom may not be caused by the side effects of my medication.
  - I am not sure.
- Do you want to change your medication because of the symptom?
  - Yes, I do.
  - No, I don't.
- Has the symptom concerned you?
  - Yes, I have been concerned about the symptom, but it has remained untreated.
  - Yes, I have been concerned, and informed a physician of the symptom.
  - No, I have not really been concerned.

## Method (3)

### Details of the questionnaire for each symptom checked

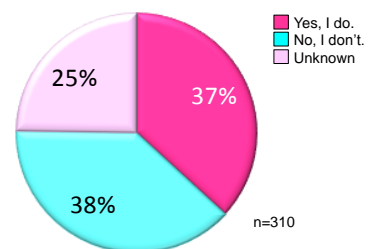
- To patients who answered "The symptom has remained untreated," why has it remained untreated? (multiple answers)
  - I'm unwilling to tell a physician/it is humiliating
  - Physicians have never asked me
  - There is no time to tell a physician
  - I want to avoid inconveniencing physicians
  - I am afraid to tell a physician (e.g., the physician may get angry)
  - I am satisfied with my medication at the moment
  - Side effects are inevitable to suppress the symptom
  - I thought that changing to other medication would make no difference
  - I do not want more types of medication
- To patients who answered "The symptom has remained untreated," do you think this kind of sheet would help you tell a physician about symptoms that concern you (remain untreated)?
  - Yes, I do.
  - No, I don't.

## Symptoms checked in the Self-Report Symptom Check Sheet

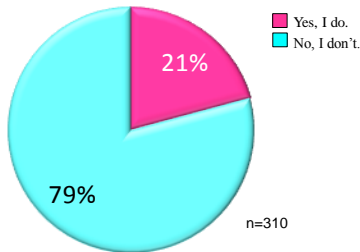


## Questionnaire survey after filling in the Self-Report Symptom Check Sheet

Q1. Do you think the symptom is due to the side effects of your medication?

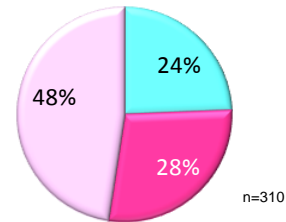


Q2. Do you want to change your medication because of the symptom?



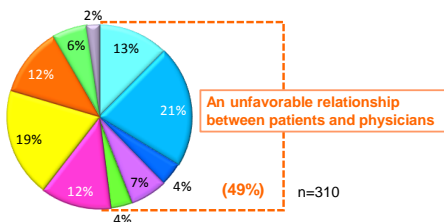
Q3. Has the symptom concerned you?

- Yes, I have been concerned about the symptom, but it has remained untreated.
- Yes, I have been concerned, and informed a physician of the symptom.
- No, I have not been concerned.

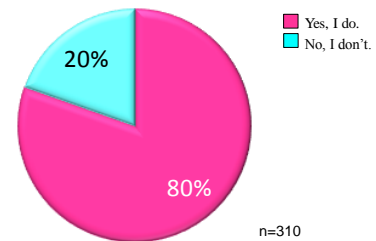


Q4. To patients who answered "The symptom has remained untreated," why has it remained untreated?

- I'm unwilling to tell a physician/it is humiliating
- Physicians have never asked me
- There is no time to tell a physician
- I want to avoid inconveniencing physicians
- I am afraid to tell a physician (e.g., the physician may get angry)
- I am satisfied with my medication at the moment
- Side effects are inevitable to suppress the symptom
- I thought that changing to other medication would make no difference
- I do not want more types of medication



Q5. To patients who answered "The symptom has remained untreated," does a check sheet help you tell your physician about the symptom?



## Discussion

- A large number of patients were not aware that symptoms concerning them were caused by the side effects of their medications. Also, some patients had not reported their symptoms to physicians for various reasons, such as they had been unwilling to tell, and they had not been asked by physicians. The undisclosed symptoms included: **weight gain, increased appetite, sexual dysfunction, inability to articulate, sialorrhea**, etc. These findings suggest that side effects that are less likely to be disclosed mainly because of an unfavorable relationship between patients and physicians, and improvement in such a relationship may lead to the disclosure of side effects.
- Using a number of methods, such as the Self-Report Symptom Check Sheet, pharmacists actively collect information on symptoms which patients are unwilling to disclose, and give physicians feedback, which is considered to help improve the medication adherence of each patient.

## Conclusion

- 1) Pharmacists sufficiently inform the patients with schizophrenia about their disease and have the patients understand the need for the medicine well.
- 2) Pharmacists suggest supporting the patients with schizophrenia by listening to and actively discerning their complaints about medication.
- 3) Pharmacists explain to patients that it is important to sufficiently understand the risks/benefits of treatment and early detection/treatment of side effects.
- 4) It is a great contribution to improving patients' daily life when the intervention of these pharmacists improve adherence in patients with schizophrenia.

**Thank you for your attention !**

