him on everyday activities. He is prescribed an antipsychotic by a clinic twice a month. When his condition worsens, he receives almost daily visits by the nurse, and at times he also sees the clinic's psychiatrist. Prior to receiving visiting care, he was hospitalised about three times a year, but in the last five years he has only had two short stays in hospital.

Amendments to the Mental Hygiene Act in 1965 required the establishment of publicly run community mental health centres, and public health centres were positioned as the first line of community mental health services. Home visit services were increased until the early 1990s. Due to financial difficulties faced by local government, provision of these public services has been scaled down since the late 1990s.

Home visit services are limited in public health centres and mental health and welfare centres. Since the late 1990s, care has primarily taken the form of visiting care for persons with mental illness who live in the community. Visiting care originally began as a service with reimbursed medical fees that involved home visits to the elderly, but this service is now provided by community service departments of psychiatric hospitals and persons with mental illness are now visited by nurses from independent visiting nurse stations. As of 2008, 47.7 per cent of visiting nurse stations conduct visits to persons with mental illness.

In recent years, clinics and outpatient departments of hospitals have combined home visits by nurses and visiting care by physicians to begin offering services that provide assertive community treatment (ACT).[5] ACT provides assertive and comprehensive community-based services by a multidisciplinary team to persons with severe and persistent mental disorders. The government recommends these services and in 2011 began creating model communities through financial assistance to communities and hospitals to enhance outreach services.

Outpatient clinics

Case D: a 35-year-old male working at a large firm felt depressed by his mistakes at work and was diagnosed with major depression by a psychiatric clinic. He took sick leave for three months. Initially, he visited the clinic, but at the recommendation of his primary physician he was admitted for a month to a stress care unit at a psychiatric hospital. When his condition stabilised, he was discharged. He participated in the clinic's return-to-work programme after discharge. He began with simple tasks two days a week in the day care office, which resembled the office setting where he worked. He gradually began participating more often and had the same starting and finishing times as he did at work. He became accustomed to the programme, so talks were held with a company physician and a psychologist involved in the return-to-work programme. He subsequently returned to work at his old company. He continues to visit the hospital twice a month.

Socioeconomic factors are impacting the mental health of employees. In the current economic downturn, more and more employees have mental problems, and

workplace mental health is a vital issue in Japan. Prevention, treatment and rehabilitation programmes can be provided in and out of the workplace. The employees can return to work in most of the large corporations and public organisations, however, those who work for medium-sized corporations often lose their jobs. Support services for such people are needed.

Dementia care

Case E: accompanied by family, a 75-year-old male was seen by the Centre for Dementia Care. Tests, including brain imaging, led to a diagnosis of dementia of the Alzheimer type. A year later, his spouse passed away; he became restless and began wandering. He began accusing his family of hiding his belongings and would forget to put out his cigarettes, so he was admitted to a dementia unit in a psychiatric hospital. His family was told by hospital staff that he would be hospitalised for a maximum of three months, so they began looking for discharge destinations immediately after his admission. However, many facilities for the elderly had a waiting list of over 100 people and he was turned away by numerous residential facilities and group homes since they could not accept patients with dementia and problem behaviour. Two months later, the family finally found a facility that would accept him.

The proportion of older people is increasing at a rapid pace in Japan. The number of patients who have dementia but no facility to accept them is rapidly increasing and facilities will have to fill their empty beds with patients with dementia. This trend is already becoming apparent: inpatients age 65 and over accounted for 47 per cent of inpatients in 2008, and this number is predicted to increase further in the future. If this situation continues, medical expenses for persons with mental illness will turn into medical expenses for the elderly. This presents a major policy dilemma that is being debated even now.

Mental health system

Legislation

Mental health policies in Japan have been stipulated by general laws such as the Medical Care Act, Health Insurance Act and Mental Health and Welfare Act, which regulates psychiatric care such as involuntary admission, seclusion and restraint. Also, a forensic mental health law was enacted after the school massacre in 2001 in which many school children were killed and injured by a man with a long history of mental illness.

The government plays a key role in setting overall policy, implementing health services based on the legislation, and standardising health care fees in co-ordination with providers, consumers and payers.[6] Medical fees were revised every two years whilst the Mental Health and Welfare Act was amended every five years. Importantly, a roadmap for mental health reform, 'A Vision for Reform of the

Mental Health Care System', was released by the Minister of Health, Labour and Welfare in September 2004, addressing the direction of mental health and welfare policies up to 2014.[7] It has two aims that it hopes to achieve over the coming decade. First, at least 90 per cent of citizens will recognise that mental illness is a common disease that can affect anyone, similar to lifestyle-related diseases. Second, the focus of services will shift from hospitals to the community by shortening the length of stay, discharging long-stay patients and developing community services. This roadmap is a basis of the government's policy. Since 2004, revisions have been made in medical fees and the Mental Health and Welfare Act according to this roadmap.

Psychiatric beds

It was stated for the first time in 1950 in the Mental Hygiene Act that persons with mental illness have a right to medical care. Until that time, under the Mentally Disordered Persons Supervision and Protection Act, legislation provided protection more to society than to the persons with mental illness themselves. The Mental Hygiene Act was renamed through a series of amendments and is presently the Mental Health and Welfare Act. Because the establishment of public psychiatric hospitals in every prefecture did not move quickly, despite the recommendations for such institutions in the Mental Hygiene Act, the Medical Care Act was revised in 1958 to set a staff-to-beds ratio for psychiatric care units to half that for other clinical departments. The amendment enabled many private psychiatric clinics to upgrade their beds, which led in turn to an increase in the total number of psychiatric beds available. Today, Japan is unique in that 83 per cent (as of 2009) of existing psychiatric beds are provided by private hospitals. Private hospitals in Japan are non-profit organisations and are disallowed from distributing any profits. However, this policy resulted in an increase in the number of beds without a concurrent increase in the number of personnel, and this small staff-to-patient ratio put a halt to subsequent quality improvement of inpatient psychiatric care.

As a result of these policies, Japan is characterised by a large number of psychiatric beds per capita, compared not only to Asia but also the world. As Table 2.1 shows, there were 27 beds per 10,000 population in 2010. It should be noted, however, that the number of registered psychiatric beds has been gradually decreasing because of an upper limit put in place by the 1985 revision of the Medical Service Act.

Although not much has changed with regard to inpatient numbers, there have been changes in inpatient characteristics and bed utilisation. The number of acute care psychiatric beds is on the rise because the majority of inpatients in recent years are discharged within approximately two months, as described in Case B. However, patients who have been hospitalised for more than one year generally have long-term mental illness and are mostly elderly. As far as the number of acute care beds is concerned, the number per capita is close to that of South Korea.

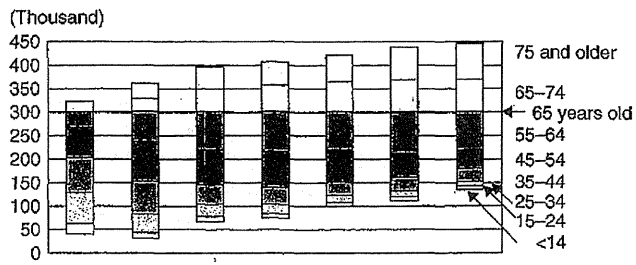
Changes in the numbers of psychiatric inpatients in different age groups are shown in Figure 2.2. Although the total number of inpatients showed no change,

Table 2.1 Psychiatric beds in Asia

	Total number of psychiatric beds (per 10,000 population)
Brunei	1.2
Cambodia	0
China	1.06
Indonesia	0.4
Japan	28.4 (9.8*)
Laos	0.07
Malaysia	2.7
Mongolia	2.4
Myanmar	0.55
Philippines	0.9
Singapore	6.1
South Korea	13.8 (6.2*)
Thailand	1.4
Vietnam	0.63

Note: * Number of inpatients staying less than one year.

the number of inpatients older than 65 years increased, while those younger than 65 years decreased. This suggests that psychiatric care has been functionally divided into long-term care units for elderly persons with mental illness and acute care units for young adults with mental illness. Rather than focusing on the number of psychiatric beds available in Japan, current issues are emphasising the need to establish measures to treat long-stay patients.



	1977	1987	1996	1999	2002	2005	2008
Total	282	327	326	329	321	324	307
≥ 65	24	62	96	109	123	139	145
(%)	8.4	19.0	29.5	33.1	38.3	42.8	47.4

Figure 2.2 Number of inpatients by age group.

Source: Patient Survey.

Human rights

Table 2.2 lists changes made to the law concerning the protection of human rights of persons with mental illness under inpatient care. It was only after 1950 that involuntary admission was limited to psychiatric hospitals. Although individual medical facilities were in charge of human rights protection in inpatient care, an incident at one hospital led to an amendment in 1987 to establish Psychiatric Review Boards in all prefectures. Under the law, psychiatric care units are required to install public telephones with the office phone number of the Review Board so that patients can freely make a phone call at any time. When a patient requests discharge or improved treatment, the Review Board responds by assigning third parties, including a lawyer, to investigate the case, makes a decision based on the findings and then reports the decision to the patient and hospital.

Monitoring of seclusion and restraint was mandated in 1998, and psychiatric care units are required to prepare monthly summary tables showing how seclusion and restraint procedures are being carried out. They are also required to hold monthly meetings of the committee for minimising seclusion and restraint to discuss the appropriateness of seclusion and restraint. The National Centre of Neurology and Psychiatry provides training programmes to minimise seclusion and restraint in an effort to improve the techniques used.

User involvement

Former patients called 'survivors' are speaking publicly at symposia, conferences and government panels on mental health policies.[8] In 2004, for the first time, as an official constituent member of the government committee, a user who had previously been involuntary admitted to a psychiatric hospital joined a meeting held by the Ministry of Health, Labour and Welfare. This was an unprecedented development in the history of Japan's health and welfare policy. This arrangement allows the opinions of third parties to be reflected in government committee's discussions. The Cabinet Office and other governmental offices plan to adopt a similar system whereby the users become constituent members.

Table 2.2 Changes to the law on protection of human rights of persons with mental illness

1900:	Mentally Disordered Persons Supervision and Protection Act
1919:	Mental Hospital Act
1950:	Mental Hygiene Act
1965:	amendment to the Mental Hygiene Act (establishment of community mental health centres)
1987:	Mental Health Act (establishment of Psychiatric Review Boards)
1993:	Disabled Persons' Fundamental Act
1998:	Enhanced monitoring of seclusion and restraint
2003:	Medical Observation Act
2009:	amendment to the Mental Health and Welfare Act (concerning psychiatric emergency care)

It is also important to assist interested parties in organising themselves into groups. In Japan, a family advocacy group for persons with mental illness was founded after holding a workshop on this issue. The National Federation of Families for the Mentally Ill in Japan was also formed, but it was closed in 2007 due to financial problems. Now a newly formed similar organisation is working to reflect the voices of users and families in policy making.

Anti-stigma campaign

Educational programmes on depression have been available for over 30 years. In 1975, at the conclusion of one of their studies, the World Health Organization (WHO) established the International Committee for Prevention and Treatment of Depression (ICPTD) to educate general practitioners and health care professionals on the prevention and treatment of depression. Four years later, Japan launched the Japan Committee of Prevention and Treatment of Depression (JCPTD). JCPTD was later taken over by the World Psychiatric Association (WPA), and, as WPA/PTD (Prevention and Treatment of Depression), has been offering educational programmes – beyond the scope of depression – on the prevention and treatment of common mental illnesses.

Despite such educational activities, awareness of depression is not high in Japan. When a comparative study on the stigma of mental illness was conducted in Japan and Australia, 20–30 per cent of Japanese were aware of depression and schizophrenia to a similar extent, while 60–70 per cent of Australians were aware of depression.[9] In Australia, Beyondblue, a national organisation that addresses issues associated with depression, proactively performs educational activities on depression, and the success of its operations is thought to reflect the difference in awareness of depression between the two countries.[10]

Japan's Ministry of Health, Labour and Welfare, as the public administration body responsible for health care, finally began to address the issue of anti-stigma after announcing its intention to reform mental health and welfare policies in 2004.

An interesting attempt was observed in that the Japanese term 'schizophrenia' was renamed. Traditionally, psychiatrists were reluctant to inform their patients of a diagnosis of schizophrenia because the Japanese term *Seishin Bunretsu Byo* (disease of split and disorganised mind) had negative connotations.[11,12] The WPA initiated the 'Worldwide Programme to Fight Stigma and Discrimination Because of Schizophrenia' in 1996. As part of this activity and also in response to the request from the National Federation of Families for the Mentally Ill in Japan, in 2002 the Japanese Society of Psychiatry and Neurology decided to change the Japanese term schizophrenia to *Togo Shicchou Sho* (dysfunction of integration) to reduce stigmatisation against people with schizophrenia.[13,14] Renaming schizophrenia has been well accepted in Japan and Hong Kong.[15,16] Similar movements are seen in other East Asian countries where Chinese characters are used.

Policy outcomes and payment system

Policy and outcomes

The fact that private, not public, hospitals are the major suppliers of psychiatric beds available in Japan, has its roots in the nation's unique mental health care policies. Because private hospitals are operated independently, even when an amendment is introduced to mental health and welfare policy at national level, it is up to individual hospitals to decide whether they adopt the amendment. In other words, central and local governments have limited control over private hospitals (Figure 2.3). As it is difficult to bring about drastic changes, a trial-and-error approach has been used to determine which policies effect favourable changes in psychiatric care. Let us review the positive and negative effects of past policies:

- In the 1950s to 1960s, because the development of prefectural hospitals did not progress as anticipated, the government allowed and provided financial aid for private hospitals with a reduced number of staff to be established and granted them the role of public hospitals. As a result, a large proportion of existing inpatient psychiatric beds in Japan has been owned by private psychiatric hospitals. When the staffing requirements for psychiatric care units were down-regulated, it soon became clear that it would be difficult to upgrade the new standard. Moreover, because of the policy – which focused on the improvement of private psychiatric hospitals – the increase in the number of psychiatric beds in general hospitals has either been halted or shows a decreasing trend due to low health insurance reimbursements.
- The increase in the number of psychiatric beds came to an end in 1985 when the Mental Hygiene Act was revised to limit the number of psychiatric beds available in each prefecture and to prevent a prefecture with an excess of beds from owning even more. The policy effectively stopped the number of beds from increasing, but did not reduce the number of existing beds. This is because, to a hospital, the number of beds it owns directly translates into the amount of profit it generates.
- In the 1990s, a health insurance reimbursement system for community care was developed by increasing the reimbursements for outpatient treatment and establishing a reimbursement system for day care. This policy also led to the establishment of psychiatric clinics and thus dramatically increased the number of outpatients. This policy contributed little to reducing the number of psychiatric beds, because psychiatric hospitals responded to the policy by only enhancing outpatient capabilities without downsizing the number of beds.
- In general, the government initiates a pilot project that reflects a prospective mental health policy for a limited period of time and provides financial incentives before officially implementing the entire policy. If the pilot project is successfully completed within a few years, it is converted into policy by standardising and scaling up the reimbursement system to meet the national level. Then, private hospitals begin a new insurance reimbursement service with the hope that the reform will have a successful outcome.

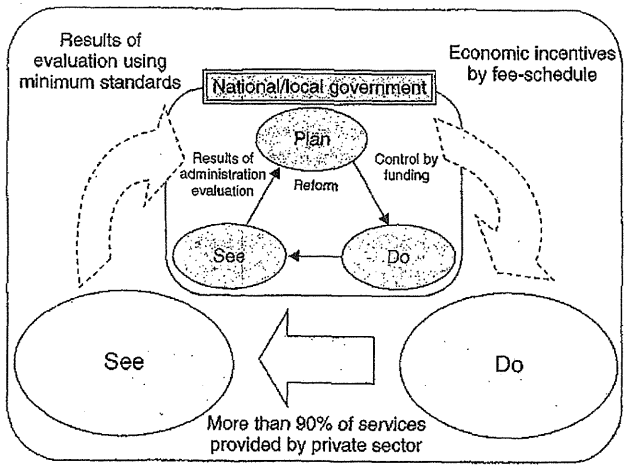


Figure 2.3 Mental health services in Japan.

- Interestingly, insurance reimbursement for psychiatric care at national/public and private hospitals is handled under the same system, and consequently similar behaviours are observed in these hospitals. Actually, the roles of national/public and private hospitals are not very different.

Insurance system

Japan has a universal health care insurance system, and residents are required to enrol in some kind of insurance plan. Health care insurances are classified as three types: employers' insurance including government-managed societies and mutual-aid associations for employees; national health insurance for the self-employed and unemployed; and insurance for the elderly. The cost of health insurance differs depending on the income of the insured. Although an individual needs to pay 10–30 per cent of the medical expenses incurred, there is a monthly upper limit to co-payment, and any payment above the limit will be taken from public funds. Public funds also cover all medical expenses incurred by a family receiving public assistance. Although the medical expenses of persons with intractable illness are covered entirely through the publicly insured programme, mental illness is not included under intractable diseases.

Even though several insurance providers are available, when health insurance is used to receive medical care, the service fee is reimbursed based on the price authorised for the service under the Health Insurance Act. In the case of hospitalisation, basic inpatient charges per diem are set at certain values and include essential hospital fees. The total cost for a single admission is calculated by multiplying the basic inpatient charge by the total number of hospital days and then adding treatment costs that are not included in the basic inpatient charge (e.g. costs for

prescription drugs and specialised psychiatric treatment). Outpatient services are covered on a fee-for-service basis. Authorised fees for health care services are revised every two years.

In 2003, the Diagnosis Procedure Combination/Per-Diem Payment System (DPC/PDPS) was introduced as a payment plan for acute inpatient care.[17] This system sets official per-diem payments for a combination of diagnosis and treatment and covers part of the treatment provided to inpatients at general hospitals. However, the system does not cover most psychiatric care. The reimbursements for the treatment of persons with mental illness are mainly covered by the following two methods.

Per-diem payment system for psychiatric inpatient care

Basic per-diem payments for psychiatric inpatient care differ depending on the type of unit they enter. Although a fee-for-services may be added to the basic payment, the basic inpatient charge accounts for most of inpatient medical expenses paid for by health insurance. The basic inpatient charge is relatively high for the use of an acute care unit or a unit specialising in complications, but small for a chronic care unit. Although dementia patients are admitted to special units, this is not the case with other kinds of mental illness. If persons with mental illness – whether that be schizophrenia or depression – are admitted to the same unit, they are charged the same inpatient fee.

Institutional standards are determined by the types of units operated. In 1994, long-term care units were established to improve inpatient care for patients with long-term mental illness. The establishment of acute care units in 1996 is particularly noteworthy. To be authorised as an acute unit, 40 per cent or more of inpatients must have stayed in the community for more than three months before admission, and another 40 per cent or more of the inpatients must have stayed in the community for more than three months after discharge. This requirement became a huge incentive to promote acute psychiatric care and shorter hospitalisations, and changed the insurance reimbursement evaluation system for psychiatric inpatient care into an evaluation system based on comprehensive units. In addition, emergency care units were established in 2002 with even higher insurance reimbursements and with the specific requirement that they cover more than 25 per cent of compulsory admitted persons with mental illness who are at a high risk of harming themselves or others in each medical district. In 2008, emergency care units for patients with comorbidity were newly established to treat the physical complications of psychiatric patients.

Fee-for-service system for psychiatric outpatient care

Outpatient care is basically provided on the basis of fee-for-services and is not classified by psychiatric diagnosis. From the standpoint of promoting community-oriented care rather than inpatient care, the reimbursements for outpatient care have been prioritised over those for long-term care. In addition to outpatient services,

psychiatric day care services aimed to improve social functioning were introduced into the system in 1974. A combination of outpatient care and day care services sometimes costs more than comprehensive long-term inpatient care. Given the evidence that acute day care treatment is effective,[18] the reimbursements for day care treatment within one year of discharge were increased in 2010. For a facility to receive insurance reimbursements for day care services, it is necessary for it to fulfil the personnel requirements stipulated for such facilities. However, it is up to individual facilities to decide the specifics of the programmes and services they provide. Day care service reimbursement covers return-to-work programmes for individuals with depression and early intervention for individuals with schizophrenia. In addition, the visiting nurse service has been operating since 1986, and a special programme was introduced in 2008 to prevent medication interruptions and minimise readmissions by examining patients' adherence to treatment and the presence of medication side-effects. Although medical reimbursement for psychotherapy has been available for some time, the reimbursement for cognitive behavioural therapy was introduced into the system only recently, in 2010.

Strategic directions for mental health

Liaison consultation psychiatry

Integrating the mental health system into the general health system is a challenge for Japan. Until now, psychiatric care has been regulated under the Disability Policy. This is because mental health and welfare is managed by the Department of Health and Welfare in the Ministry of Health, Labour and Welfare, which also functions as a branch for the Department of Health and Welfare for Persons with Disabilities. Following physical and intellectual disabilities, mental disabilities were first introduced into law in 1993 with the promulgation of the Disabled Persons' Fundamental Act.

The development of 'psychiatric care' has been historically independent from that of general health care, and consequently psychiatric hospitals outnumber general hospital psychiatric departments. Because psychiatry does not have a strong voice in the general health care system, the number of general hospital psychiatric departments, which generally have low revenues, is continuing to decrease. Integrating the mental health system into the general health system is therefore a major challenge, and the position of psychiatric care in the field of general medical care needs to be strengthened.

Since most psychiatric beds were historically provided by individual psychiatric hospitals, only a small proportion of psychiatric beds are owned by general hospital psychiatric departments. In addition, compared with other clinical departments, the medical reimbursements for psychiatric care are relatively low, which has led to the closure of some psychiatric departments in general hospitals.

Several attempts have been made to improve the medical reimbursement status for psychiatric care. The involvement of psychiatrists in palliative care was mandated in 2002, while additional fees were provided to the reimbursement for

treatment provided by designated psychiatrists to persons who attempt suicide transported to general emergency departments in 2008. Also in the same year, additional fees were provided to the reimbursement for referrals by primary care physicians to psychiatrists of patients with depression.

From the standpoint of positioning in a general care system, it is a huge step forward to have mental illness ranked as a high-priority disease in prefectural medical care plans. Starting in April 2013, each prefecture will plan future health care for mental illness as a high priority in addition to cancer, acute myocardial infarction, stroke and diabetes.

Identification of those who need care

According to a study conducted in the United States, 28.5 per cent of the total population has been diagnosed with some type of mental illness.[19] As it is impractical to publicly support mental health services for nearly 30 per cent of the population, it is inevitable that the need for public support must be prioritised. For example, groups of individuals who require more intensive care packages, such as outreach services or home visits, need to be recognised. If this does not happen, intensive services might go to individuals who do not actually need them, rather than to those who do. Thornicroft and Tansella also pointed out and explained this issue using a clear model.[20]

As shown in Figure 2.1, the prevalence of mental illness has been increasing since 1999 and has now surpassed that of diabetes. With no change in the number of inpatient psychiatric beds, this rise is attributable to increases in the number of outpatients. Some of the related developments are as follows:

- The proportion of outpatient psychiatric care costs among all outpatient medical expenses has increased for all age groups. In particular, the increase was pronounced in the 15–44 age group, accounting for 10 per cent of all outpatient medical expenses.
- A home-visit care service is an essential community care service for the prevention of medication interruptions and to enable readmissions for persons with mental illness. Because Japan has long been promoting home-visit nursing services, the number of home visits to persons with mental illness has been climbing, from 4,427 visits in 2000 to 12,777 visits in 2007. In contrast, the number of home visits made by public health centres decreased from 405,966 visits made by 594 public health centres in 2000 to 332,810 visits made by 518 public health centres in 2007.[21]
- Among the different types of clinics operating, the number of outpatient psychiatric clinics without inpatient beds has increased substantially since the 1990s, from 4.3 per cent in 1987 to 8.2 per cent in 2005. Along with this change, the number of outpatients has shown a steady increase. Day care and night care services developed for persons with mental illness in the community have also increased.

The question is whether such increases in mental health services and clinics have actually brought uninterrupted care to persons with mental illness in need of continuous care. To answer this, a detailed analysis needs to be conducted because an adequate national database to analyse the characteristics and patterns of outpatients is currently not available. To improve services, it is necessary to clarify whether limited resources are being utilised for mentally ill persons in the order of highest to lowest priority.

Because of Japan's free-access health care system, which allows people to use health insurance at any medical facility, it is difficult to adjust medical reimbursements based on the severity of illness or to establish the role of medical facilities according to the needs of the community or the priority of target diseases. In that sense, it is particularly noteworthy that the health reimbursement policy was revised in 2010 to include severity of the illness in the reimbursement requirements for inpatient care. To move towards strengthening support for community life, a system is needed that can respond to an exacerbation in patients' conditions and provide the intensive mental health care they need. At the same time, a systematic framework for evaluating the system and facilities from a third party's perspective should be developed to certify the facilities. We should also consider developing outpatient policies.

A flexible catchment system

Japan's health care system has two characteristics: it is a universal national health insurance system as well as a free practice system. There is no general practitioner system in Japan. As a result, people in Japan are able to receive any type of health care service from any provider with minimal co-payment. Although this is an advantage, it also poses a problem: awareness of catchment areas is weak. Psychiatrists and mental health care professionals are simply required to treat patients who visit their clinics and hospitals, and under the current system, it is difficult to assess whether all residents in need of care in the community are accessing health care services. In addition, the policy does not offer strong incentives for preventing treatment interruptions. It is necessary, therefore, to strengthen support for groups with severe and persistent mental illness.

How to set up catchment areas is a major issue to be faced when developing a system to promote community care. Essentially, it falls to the public organisations responsible for the particular catchment area – the public health department, municipal government, mental health and welfare centres and so forth – to strengthen support for community life support and provide outreach services. In Japan, a catchment area system should be functioning under the initiative of the public health department, however, local governments face the financial difficulties to provide community health services. As the number of home-visit nurses and mental health counsellors continues to fall at public health centres, the concept of the catchment area is diminishing in local government.

Consequently, currently available private services should be used to supplement publicly provided care in the community. In the case of outpatient services, which

are provided on a fee-for-services basis, it is simpler, highly efficient and more profitable to provide services to a large number of visiting patients than to prevent some persons with severe mental illness in the community from discontinuing treatment. It is certainly not profitable – and therefore is rarely done – to visit and provide services to patients who refuse treatment.

At the same time, the free access to health care guaranteed by Japan's health care system does not make it easy for medical facilities to foster responsibility towards the community in which they operate. The following characterises the health care services of countries that implement a catchment system:

- Residents visit their primary care physician.
- Patients are referred by their primary care physician to a specialist as necessary.
- Primary care physicians are aware of residents who are in need of medical care.
- Primary care physicians are responsible for following their patients after discharge.

None of the above currently applies in Japan's system, where it is possible to visit any medical facility or specialised hospital using national health insurance. This, unfortunately, makes it difficult to develop a continuous care system and this is a major issue associated with a free-access system. Therefore, a flexible catchment area system needs to be established in Japan that ensures patients with severe and persistent mental disorders are treated.

Long-term inpatients

Psychiatric beds in Japan fall mainly into two distinct categories: beds in acute inpatient care units that meet international standards, and beds in chronic care units for patients with long-term or severe mental disorders. The challenge that Japan faces today is the future of chronic inpatient care units for long-stay patients and those with severe mental disorders.

As one of the visions of the Ministry of Health, Labour and Welfare in 2004, to shift from hospital-based care to community care, it was deemed necessary to transfer current expenditure for inpatient care to community services. This means that existing resources must be re-allocated as it is difficult to increase the national budget drastically. It is unlikely that private medical facilities will willingly reduce their profits or welcome radical change because they are generally conservative in nature. Therefore, it will be necessary to develop economic incentives that bring maximum profits to private psychiatric hospitals if they have to re-allocate some existing inpatient care staff to cover community care services.

The Ministry of Health, Labour and Welfare announced in 2009 that the number of patients with schizophrenia in inpatient care would be likely to decrease. The number of inpatients with schizophrenia was 215,000 in 1996 and 196,000 in 2005. According to the estimate, the number will decrease to 172,000 in 2014, 149,000 in 2020 and 124,000 in 2026. It is not difficult to see that the money generated

from eliminating excessive beds due to a decrease in the number of inpatients with schizophrenia could be used for community care.

Monitoring quality

Although the Japanese insurance reimbursement system predetermines health care prices, it is up to health care providers to decide (1) the types of patients they treat and (2) the types of treatments they provide, as long as they fulfil institutional requirements. The health insurance payments are not directly linked with the types of patients they treat, for example, the patient with a severe and persistent disorder, which is an upcoming challenge for Japan. Patient characteristics and treatment types need to be incorporated with the health insurance payment system.

Academics, including professors in psychiatry and professional groups, have developed guidelines and algorithms for schizophrenia and mood disorders. The Japanese versions of major guidelines for diagnosis and treatment, such as those of the American Psychiatric Association and Maudsley Hospital in London, are also available. Accurate diagnosis and appropriate practice guidelines are important for delivering high-quality care. For diagnosis, both the International Classification of Diseases 10 (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) are used in clinical practice.

The quality of medical care is evaluated based on a system in which standard medical care is (1) developed by health care providers; (2) assessed by a third party; and (3) selected by patients.[22] Hospital care has been evaluated by a third party since 1997,[23] with the results being made public since 2007. This system of third-party evaluation and release of the results is rather novel even by international standards.[24] Some hospitals have been participating in the development of an international framework for evaluating psychiatric care performance and outcomes.[25] Starting in 2013 in Japan, prefectures will evaluate their own psychiatric care system as well as develop and implement health care plans. The evaluation of health care services by the individual prefecture responsible for the community will be an important initiative for Japan. If information on the aspects of health care evaluated by each prefecture is made publicly available, people will be able to obtain better treatment as they are free to visit hospitals of their choice.

The schematic diagram in Figure 2.4 showing the direction for optimal services was generated based on a model figure recommended by WHO.[26] While specialised care might not be needed often, the demand for psychiatric care provided by a primary care system might be high. Moreover, it is essential that social services such as those promoting and implementing suicide prevention measures are enhanced in order to improve public mental health. When developing user-centred services, it is important to include self-care tips for patients at every level.

Recommendations and conclusions

Japan has continuously changed psychiatric care services in decades. The Japanese psychiatric care system reflects both the strengths and weaknesses of Japan's health

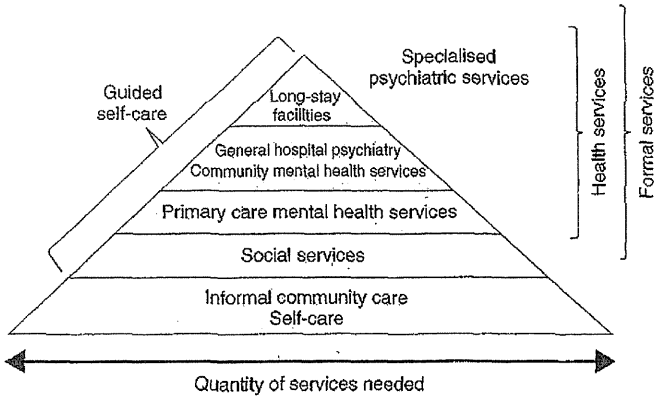


Figure 2.4 Direction for optimal services.
Source: Modified from the WHO Service Organisation Pyramid.

care system, and the country has made various attempts to address the weaknesses while maintaining the strengths. Below, some helpful points are summarised, derived from Japan's own experiences.

Legislation

- Institutional requirements, such as patient and staff ratio, should not be downgraded at any time in order to ensure the quality of care.
- It is effective to develop acute care units with a provision that limits length of stay.
- A regulation (ceiling) on the total number of beds per prefecture effectively prevents psychiatric beds from increasing.

Integration with the general health system

- Psychiatric care should be placed within general medical care.

Support for those who are most in need

- With a highly accessible health care system, it is necessary to establish a system to identify and support persons with severe mental illness.

Policy making

- It is necessary to incorporate the viewpoint of users in every aspect of policy making and daily clinical practice.
- It is necessary to reduce the burden of family responsibility, especially in regard to the treatment of mental illness.

- As policy, the issues of 'illness that can affect anyone (anti-stigma)' and 'measures for severe mental illness' need to be addressed.
- In countries with an ageing society, to prevent the current psychiatric care costs from being converted into medical care expenses for the elderly, general mental health care needs to be separated from the care provided to the elderly with mental illness or dementia.
- In a country with a highly accessible health care system, a flexible catchment area system should be developed.

Funding and economic incentives

- Deciding what types of financial assistance and incentives should supplement the services provided is a major challenge. Financial incentives should be developed to improve the quality of care (creating academic guidelines, a third-party evaluation system and patient selection of medical facilities through disclosure of information).

Notes

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JAPAN SERIES

MENTAL HEALTH CARE IN JAPAN

Mental health, including widespread depression, a high suicide rate and institutionalisation, is a major problem in Japan. At the same time, the mental health care system in Japan has historically been more restrictive than elsewhere in the world. This book looks at the challenges of mental health care in Japan, including problems such as the institutionalisation of long-term patients in mental hospitals. The book discusses the latest legislation to deal with mental health care, and explores the various ideas and practices concerning rehabilitation into the workforce, the community and service user groups that empower the mentally ill. It goes on to look at the social stigma attached to the mentally ill in Japan and Britain, which touches upon the issue of counselling those with post traumatic stress after the recent earthquake.

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International variation in antipsychotic prescribing for schizophrenia: Pooled results from the research on East Asia psychotropic prescription (reap) studies

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ABSTRACT

Objective: To identify updated trends in antipsychotic prescribing patterns in patients with schizophrenia in East Asia. Methods: Using the data from the 2001, 2004, and 2008 Research on East Asia Psychotropic Prescription (REAP) studies, we compared the proportions of acute inpatients (stay <6 months), new long-stay patients (6 months to 3 years), and old long-stay patients (≥3 years), the rates of excessive dosing (more than chlorpromazine 1,000 mg equivalent) and polypharmacy (the coprescription of more than 1 antipsychotic). Findings: While the proportion of long-term inpatients increased over time in Chinese mainland and Taiwan, it decreased in Japan, Singapore and Hong Kong. The proportion of acute inpatients receiving more than one drug was highest in Singapore, followed by Japan, Korea and Chinese Mainland. Two-drug combination therapy was especially high in Singapore. Korea had the highest rate of excessive dosing followed by Japan and Hong Kong. While the rates of both polypharmacy and excessive dosing decreased significantly over time in Japan, polypharmacy increased significantly in Chinese Mainland and Taiwan and excessive dosing increased significantly in Korea and Hong Kong. Conclusion: Our results suggest that the change in antipsychotic prescribing patterns, including excessive dosing and polypharmacy, varied among the participating East Asian countries/areas.

Keywords: Antipsychotic; East Asia; Polypharmacy; Schizophrenia

1. INTRODUCTION

Antipsychotic polypharmacy, the prescribing of more than one antipsychotic drug concurrently, is a common prescription pattern in clinical practice [1]. Although the prevalence of anitipsychotic polypharmacy varies, the results from most studies ranged between 10% and 30% [2]. Polypharmacy may result exceed the total dose of antipsychotics [3], and may cause increases in admissions to hospital [4] and mortality [5].

Polypharmacy was frequently observed in patients with severe conditions [4,6]. Long-stay patients are likely to be severe and treatment-resistant; therefore, they are at risk of polypharmacy. Recent studies showed that the length of stay of patients receiving antipsychotic polypharmacy was longer than that of patients receiving monotherapy [7,8]. The prescription of high-dose antipsychotics is also of concern because of the lack of evidence to support its effectiveness and because of its association with greater adverse effects [9]. The probability of the prescription of high-dose antipsychotics is increased by polypharmacy [1].

Compared with the West, hospital care for patients with schizophrenia is still prevalent in many East Asian countries/areas. The treatment pattern of inpatients, however, is changing in East Asia [10]. Of newly admitted patients, most are discharged earlier, but some stay longer due to treatment-resistant and severe diseases [11]. Those who are newly admitted and stay longer in hospitals are referred to as "new long-stay" patients in addition to "old long-stay" patients who are older and resistant to discharge.

The objective of this study was to identify updated trends in the prescription patterns of antipsychotics in patients with schizophrenia in East Asia. We compared the proportions of acute, new long-stay, and old long-stay inpatients and the rates of excessive dosing and polypharmacy in 2001, 2004 and 2008 using the data from the Research on East Asia Psychotropic Prescrip- tion (REAP) studies.

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2. METHODS

2.1. Study Design

The Research on East Asia Psychotropic Prescription (REAP) studies were designed as hospital-based cross-sectional surveys to examine the prescription patterns of psychotropic drugs (antipsychotics, mood stabilizers and antidepressants) among inpatients in East Asia. The details of the REAP studies have been described elsewhere [12-15]. The studies were conducted in 2001, 2004 and 2008 in six Asian countries/areas (Chinese mainland, Hong Kong, Japan, Korea, Singapore and Taiwan) using a standardized protocol and data collection procedure.

The REAP studies were approved by the Institutional Review Boards of all the participating centers in each country. The Institutional Review Board of the National Center of Neurology and Psychiatry, Japan, also approved the analysis of data for this study.

2.2. Participants

The participants were patients with schizophrenia who were consecutively admitted to each site. We identified inpatients using the diagnostic criteria for schizophrenia according to the International Classification of Disease, 10th edition (ICD-10) [16] or the 4th version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [17]. The REAP study coordinators collected data from the medical charts of inpatients at each site, transcribed them into a uniform data entry sheet, and forwarded the sheet to the national coordinating centers of each country. Each national coordinating center compiled data from the participating centers and sent them on to the overall coordinator in Kobe, Japan, for compilation and analysis. Patients with clinically significant medical conditions or active psychotic symptoms related to comorbid substance use disorders were excluded.

2.3. Patient Groups by Length of Stay

We divided the patients into three groups based on length of stay: acute (stay <6 months), new long-stay (6 months to 3 years), and old long-stay inpatients (≥3 years). New long-stay patients were defined as those who occupied psychiatric beds for a prolonged period among individuals receiving services oriented towards community living [11].

2.4. Variables

The primary psychiatrist completed uniform questionnaires about the participating patient at each site. Alternatively the questionnaire was completed by a member of the research team with the agreement of the primary psychiatrist [15]. The questionnaire included sociodemographic information and clinical characteristics including psychopathology and all psychotropic drugs prescribed. Depot antipsychotics given within 30 days of admission were also documented. Daily doses of antipsychotics, including depot preparations, were converted to approximate daily mean chlorpromazine mg equivalents (CPZeq) using standard guidelines [18-21].

2.5. Indicators of Antipsychotic Prescription

In this analysis, we assessed the excessive dosing of antipsychotics and antipsychotic polypharmacy during inpatient care. In terms of excessive dosing, we divided the prescribing patterns of the total daily doses of antipsychotic medications into two categories: 1) those patients receiving ≤1000 CPZeq mg per day (appropriate dosing group) and 2) those receiving >1000 CPZeq mg (excessive dosing group). The second indicator, antipsychotic polypharmacy, was defined as the concurrent use of more than one antipsychotic drug.

2.6. Analysis

Data were analyzed using SPSS 13.0 for Windows. We performed t-tests, Mann-Whitney U tests and chi-square tests. The one-sample Kolmogorov-Smirnov test was used to assess the normality of distribution of continuous variables. The level of significance was set at 0.05 (two-tailed).

3. RESULTS

3.1. Participants

The 2001, 2004, and 2008 studies included 2399, 2136, and 1906 participants with schizophrenia admitted to psychiatric hospitals at the study sites, respectively.

3.2. Changes in Patient Groups

In 2008, the proportion of patients in acute care was 57.7% in Chinese mainland, 68.9% in Hong Kong, 33.0% in Japan, 63.9% in Korea, 100% in Singapore, and 43.2% in Taiwan (**Table 1**), and was significantly higher in Hong Kong, Japan and Singapore and lower in Chinese mainland than in 2001.

3.3. Prescription of Antipsychotics for Acute patients

The trend in the prescription of antipsychotics in acute patients is shown in **Table 2**. Excessive dosing was seen in 18.8% of cases in Korea, 15.3% in Japan and 13.7% in Hong Kong in 2008. In Korea, the rate of excessive dosing in 2008 was significantly higher than that in 2004 (7.0%). The rates in 2004 in Japan and Hong Kong were significantly lower than those in 2001.

The rate of polypharmacy in 2008 was 74.0% in Sin-

Table 1. Changes in patient groups.

	2001		2004		2008			Multiple comparison		
Patients by region	n	%	n	%	n	%	p	a	b	c
Chinese mainland										
Acute	421	69.9	388	78.5	209	57.7	0.00*	0.00*	0.00*	0.00*
New long stay	110	18.3	70	14.2	99	27.3				
Old long stay	71	11.8	36	7.3	54	14.9				
Hong Kong										
Acute	51	49.5	41	41.8	51	68.9	0.00*	0.35	0.02*	0.00*
New long stay	38	36.9	46	46.9	21	28.4				
Old long stay	14	13.6	11	11.2	2	2.7				
Japan										
Acute	94	15.2	172	30.1	150	33.0	0.00*	0.00*	0.00*	0.61
New long stay	119	19.3	111	19.4	85	18.7				
Old long stay	405	65.5	289	50.5	220	48.4				
Korea										
Acute	254	58.4	228	57.4	69	63.9	0.08	-	-	-
New long stay	124	28.5	102	25.7	32	29.6				
Old long stay	57	13.1	67	16.9	7	6.5				
Singapore										
Acute	149	51.2	90	100.0	96	100.0	0.00*	0.00*	0.00*	1.00
New long stay	71	24.4	0	0.0	0	0.0				
Old long stay	71	24.4	0	0.0	0	0.0				
Taiwan										
Acute	182	59.1	262	60.4	212	43.2	0.00*	0.91	0.00*	0.00*
New long stay	73	23.7	102	23.5	172	35.0				
Old long stay	53	17.2	70	16.1	107	21.8				

p, p values derived by chi-squared test or Fisher's exact test; a, p values derived by multiple comparisons for proportional differences between 2001 and 2004; b, p values derived by multiple comparisons for proportional differences between 2001 and 2008; c, p values derived by multiple comparisons for proportional differences between 2004 and 2008. *$p < 0.05$.

gapore, 51.3% in Japan, 40.6% in Korea, 36.8% in Chinese mainland, 29.4% in Hong Kong and 25.0% in Taiwan in 2008. In Japan, the rate in 2008 was significantly lower than that in 2001 (73.4%). In contrast, the rate in 2008 was significantly higher than that in 2001 (25.2%) in Chinese mainland, that in 2004 in Chinese mainland (22.7%) and that in Taiwan (14.1%). The most frequent patterns of polypharmacy in Singapore in 2008 were risperidone and zuclopenthixol decanoate (n = 8), followed by risperidone and flupentixol decanoate (n = 7), and trifluoperazine and fluphenazine decanoate (n = 5).

The proportion of inpatients receiving three or more antipsychotics in 2008 was 23.3% in Japan, 12.5% in Singapore, 5.9% in Hong Kong, 4.3% in Chinese mainland, 2.9% in Korea and 0.9% in Taiwan.

3.4. Prescription of Antipsychotics for New Long-Stay Patients

As shown in **Table 3**, excessive dosing was seen in 34.4% of cases in Korea, 17.6% in Japan and 17.2% in Chinese mainland in 2008. In Chinese mainland, the rate of excessive dosing in 2008 was significantly higher than those in 2001 (0.9%) and 2004 (2.9%).

The rate of polypharmacy in 2008 was 65.9% in Japan, 50.5% in Chinese mainland, 46.9 in Korea, 33.3% in Hong Kong and 26.2% in Taiwan. The rate in 2008 in Chinese mainland was significantly higher than that

Table 2. Excessive dosing and polypharmacy in acute patients by region.

	2001			2004			2008					Multiple comparison		
Region	n	%	N	n	%	N	n	%	N	ES	p	2001 vs 2004	2001 vs 2008	2004 vs 2008
							Polypharmacy							
Chinese mainland	106	25.2	421	88	22.7	388	77	36.8	209	0.25	0.00*	0.45	0.01*	0.00*
Hong Kong	19	37.3	51	6	14.6	41	15	29.4	51	0.17	0.05	-	-	-
Japan	69	73.4	94	106	61.6	172	77	51.3	150	0.46	0.00*	0.14	0.00*	0.14
Korea	86	33.9	254	67	29.4	228	28	40.6	69	0.14	0.20	-	-	-
Singapore	102	68.5	149	69	76.7	90	71	74.0	96	0.12	0.35	-	-	-
Taiwan	36	19.8	182	37	14.1	262	53	25.0	212	0.13	0.01*	0.29	0.29	0.01*
							Excessive dosing							
Chinese mainland	27	6.4	421	26	6.7	388	17	8.1	209	0.07	0.71	-	-	-
Hong Kong	11	21.6	51	1	2.4	41	7	13.7	51	0.21	0.02*	0.03*	0.44	0.14
Japan	25	26.6	94	22	12.8	172	23	15.3	150	0.28	0.01*	0.02*	0.09	0.62
Korea	33	13.0	254	16	7.0	228	13	18.8	69	0.16	0.01*	0.09	0.30	0.02*
Singapore	18	12.1	149	11	12.2	90	7	7.3	96	0.16	0.43	-	-	-
Taiwan	8	4.4	182	16	6.1	262	21	9.9	212	0.22	0.08	-	-	-

n, number of patients receiving two or more antipsychotics (polypharmacy) or greater than 1,000 CPZeq mg antipsychotics (excessive dosing); ES, Cohen's effect size index for differences in proportions between 2001 and 2008; p, p values derived by chi-squared test or Fisher's exact test for proportional differences among three years. *$p < 0.05$.

Table 3. Excessive dosing and polypharmacy in care for new long stay patients by region.

	2001			2004			2008					Multiple comparison		
Region	n	%	N	n	%	N	n	%	N	ES	p	2001 vs 2004	2001 vs 2008	2004 vs 2008
							Polypharmacy							
Chinese mainland	32	29.1	110	26	37.1	70	50	50.5	99	0.44	0.01*	0.34	0.01*	0.24
Hong Kong	12	31.6	38	15	32.6	46	7	33.3	21	0.04	0.99	-	-	-
Japan	92	77.3	119	72	64.9	111	56	65.9	85	0.26	0.08	-	-	-
Korea	47	37.9	124	52	51.0	102	15	46.9	32	0.18	0.14	-	-	-
Singapore	52	73.2	71	0	-	0	0	-	0	-	-	-	-	-
Taiwan	20	27.4	73	15	14.7	102	45	26.2	172	0.03	0.06	-	-	-
							Excessive dosing							
Chinese mainland	1	0.9	110	2	2.9	70	17	17.2	99	0.66	0.00*	0.56	0.00*	0.01*
Hong Kong	5	13.2	38	1	2.2	46	3	14.3	21	0.03	0.07	-	-	-
Japan	28	23.5	119	19	17.1	111	15	17.6	85	0.15	0.41	-	-	-
Korea	29	23.4	124	31	30.4	102	11	34.4	32	0.24	0.33	-	-	-
Singapore	13	18.3	71	0	-	0	0	-	0	-	-	-	-	-
Taiwan	5	6.8	73	5	4.9	102	10	5.8	172	0.04	0.91	-	-	-

n, number of patients receiving two or more antipsychotics (polypharmacy) or greater than 1,000 CPZeq mg antipsychotics (excessive dosing); ES, Cohen's effect size index for differences in proportions between 2001 and 2008; p, p values derived by chi-squared test or Fisher's exact test for proportional differences among three years. *$p < 0.05$.

in 2001 (29.1%).

3.5. Prescription of Antipsychotics for Old Long-Stay Patients

In the prescription of antipsychotics for old long-stay patients in 2008, excessive dosing was seen in 18.6% of cases in Japan and 14.3% in Korea (**Table 4**). In Japan, the rates in 2008 (14.3%) and 2004 (23.5%) were significantly lower than that in 2001 (35.3%).

The rate of polypharmacy in 2008 was 63.6% in Japan and 33.6% in Taiwan. The rate in Japan in 2008 was significantly lower than those in 2001 (81.5%) and 2004 (73.7%). In Taiwan, the rate in 2008 was significantly higher than that in 2004 (10.0%).

4. DISCUSSION

The trends in the number of inpatients and in excessive dosing and polypharmacy varied across East Asia. While the proportion of long-term inpatients increased over time in Chinese mainland and Taiwan, it decreased in Japan, Singapore and Hong Kong. In Singapore and Hong Kong, inpatient care is now focused on acute care. Japan and Korea, where the numbers of beds per capita and long-stay inpatients are high, seem to be in a process of deinstitutionalization. In contrast, inpatient-care facilities are still lacking and the number of beds is increasing in Chinese mainland [22], thus, long-stay inpatients linger.

Japan has been often criticized for the use of polypharmacy [13-14,23]. There are multiple factor involved in the use of polypharmacy, such as physician distrust of the practice guidelines, requests to increase the number of nursing staff members, and patient characteristics [24]. The change in reimbursement which encourages the use of less than three antipsychotics over the use of more than three antipsychotics and third-party evaluation might have facilitated the changes in antipsychotic prescription patterns. Japan had the highest rate of the prescription of three or more drugs, but the percentage of patients treated with polypharmacy in acute care has been decreasing over time.

The rate at which acute care inpatients were prescribed two or more drugs was highest in Singapore, followed by Japan, Korea and Chinese mainland; however, the prescripion pattern in Singapore is different from those in the other countries/areas. A high rate of polypharmacy in Singapore has been demonstrated by previous studies [12,13]. However, the prescription of two drugs only was most prevalent, and most of these prescriptions are co-prescription with depot. Chinese mainland, Korea, and Taiwan show opposite trends of increased polypharmacy.

Although polypharmacy has long been discouraged due to issues of limited efficacy, long-term safety, mortality and higher cost [2], an increase in antipsychotic prescriptions has been prevalent [25-26]. According to a meta-analysis of randomized controlled trials comparing single-drug and multiple-drug regimens in schizophrenia, polypharmacy was demonstrated to be superior in terms of efficacy and the discontinuation of medicine [2], which suggests that polypharmacy may not necessarily always be contraindicated. However, it remains controversial [2,9].

Regarding excessive dosing, Korea had the highest rate of patients who received excessive dosing, followed by Japan and Hong Kong, while this rate was relatively low in Singapore. Interestingly, while the rates of excessive dosing were declining significantly in Japan, the rate of excessive dosing was increasing in Korea. This study demonstrated the characteristic prescribing trends in Chinese mainland and Korea. Previous studies reported that the antipsychotic dosage prescribed in Chinese mainland was lower than that prescribed in Japan [23]. However, the results of the present study demonstrated that the dosage was increasing among long-stay inpatients in Chinese mainland. China is currently undertaking a policy of expanding mental hospitals and psychiatric departments in general hospitals [22], which is leading to an increase in the number of patients who become resistant to treatment, resulting in higher rates of excessive dosing. Higher antipsychotic doses may be needed in cases with more severe illness [27], but the efficacy of higher doses (sometimes with polypharmacy) should be employed only as a strategy for dealing with treatment-resistant schizophrenia [28,29].

A further question to be considered is whether the prescription styles used in the treatment of long-stay inpatients influence the prescription practice for acute care patients. Implementing changes in care styles, such as improving polypharmacy and excessive dosing, takes a long time; for example, Japan needed at least 20 years to improve the prescription patterns and nearly 50 years to achieve deinstitutionalization in psychiatric inpatient care because of the predominance of private hospitals.

There are several limitations to this study. First, due to its cross-sectional research design, this study does not investigate the efficacy of different prescription regimens. Second, we examined the antipsychotic prescription patterns at a single or several sites within each country. Although we could examine the chronological changes that occurred in each country, it is difficult to determine across-country differences because the population samples used are non-representative.

Despite these limitations, this cross-sectional study provides insights into the antipsychotic prescription patterns for inpatients with schizophrenia in East Asian countries. The West and the East have pursued different paths in the field of mental health care. Western countries started to reduce the number of psychiatric beds in the middle of the 20th century and shifted from traditional hospital care to community care [30,31]. In contrast, institutionalized care has remained a mainstream practice in many Asian countries [10]. Although a recent global trend involves a shift in care from hospitals to communities, the role of inpatient care is different among individual East Asian countries, and the development of community services is at different stages in each of these countries. At any stage, the recommendations for the prescription of antipsychotics should be followed in practice.

Table 4. Excessive dosing and polypharmacy in care for old long stay patients by region.

	2001			2004			2008					Multiple comparison		
Region	n	%	N	n	%	N	N	%	N	ES	p	2001 vs 2004	2001 vs 2008	2004 vs 2008
Polypharmacy														
Chinese mainland	15	21.1	71	6	16.7	36	10	18.5	54	0.07	0.90	-	-	-
Hong Kong	7	50.0	14	3	27.3	11	1	50.0	2	0.00	0.60	-	-	-
Japan	330	81.5	405	213	73.7	289	140	63.6	220	0.41	0.00*	0.04*	0.00*	0.04*
Korea	23	40.4	57	36	53.7	67	2	28.6	7	0.25	0.21	-	-	-
Singapore	55	77.5	71	0	-	0	0	-	0	-	-	-	-	-
Taiwan	13	24.5	53	7	10.0	70	36	33.6	107	0.20	0.00*	0.11	0.32	0.00*
Excessive dosing														
Chinese mainland	4	5.6	71	1	2.8	36	4	7.4	54	0.07	0.69	-	-	-
Hong Kong	2	14.3	14	0	0.0	11	0	0.0	2	0.78	0.56	-	-	-
Japan	143	35.3	405	68	23.5	289	41	18.6	220	0.38	0.00*	0.00*	0.00*	0.22
Korea	19	33.3	57	24	35.8	67	1	14.3	7	0.46	0.62	-	-	-
Singapore	20	28.2	71	0	-	0	0	-	0	-	-	-	-	-
Taiwan	8	15.1	53	10	14.3	70	7	6.5	107	0.28	0.14	-	-	-

n, number of patients receiving two or more antipsychotics (polypharmacy) or greater than 1,000 CPZeq mg antipsychotics (excessive dosing); ES, Cohen's effect size index for differences in proportions between 2001 and 2008; p, p values derived by chi-squared test or Fisher's exact test for proportional differences among three years. *$p < 0.05$.

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A comparison between augmentation with olanzapine and increased risperidone dose in acute schizophrenia patients showing early non-response to risperidone

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ABSTRACT

We examined whether augmentation with olanzapine would be superior to increased risperidone dose among acute schizophrenia patients showing early non-response to risperidone. We performed a rater-blinded, randomized controlled trial at psychiatric emergency sites. Eligible patients were newly admitted patients with acute schizophrenia. Early response was defined as Clinical Global Impressions-Improvement Scale score ≤3 following 2 weeks of treatment. Early non-responders were allocated to receive either augmentation with olanzapine (*RIS+OLZ* group) or increased risperidone dose (*RIS+RIS* group). The 78 patients who completed 2 weeks of treatment were divided into 52 early responders to risperidone and 26 early non-responders to risperidone (RIS+OLZ group, $n=13$; RIS+RIS group, $n=13$). No difference in the achievement of ≥50% improvement in Positive and Negative Syndrome Scale total score was observed between RIS+OLZ and RIS+RIS groups. Although time to treatment discontinuation for any cause was significantly shorter in the RIS+RIS group (6.8 weeks [95% confidence interval, 5.2–8.4]) than in early responders to risperidone (8.6 weeks [7.9–9.3]; $P=0.018$), there was no significant difference between the *RIS+OLZ* group (7.9 weeks [6.3–9.5]) and early responders to risperidone. Secondary outcomes justify the inclusion of augmentation arms in additional, larger studies comparing strategies for early non-responders.

1. Introduction

As a strategy for antipsychotic treatment of schizophrenia, monotherapy is clearly optimal when both effective and tolerated. When a patient fails to respond to an adequate dose of an antipsychotic, the alternatives include switching, administering a higher dose (above the licensed dose), polypharmacy, or clozapine. Clozapine is the only option with established efficacy. However, clozapine is less manageable than other antipsychotics, because the frequency of clozapine-induced agranulocytosis is relatively high. Other options therefore need to be comprehensively evaluated.

A substantial proportion of schizophrenia patients receive more than one antipsychotic (Edlinger et al., 2005; Correll, 2008). The problem currently is that the degree of polypharmacy being practiced seems far in excess of the supporting data (Kane and Leucht, 2008). In a systematic review of 19 randomized studies, the pooled odds ratio suggested a small effect favoring combination treatment, and positive effects appear to have been associated with studies using clozapine combinations (Correll et al., 2009). However, clozapine is not tolerated by some patients. Studies combining non-clozapine second-generation antipsychotics with each other and with the first-generation antipsychotics utilized most in clinical practice are thus required (Correll et al., 2009). Kotler et al. (2004) indicated no significant differences in changes to positive or negative symptomatology between patients receiving a combined regimen of olanzapine with sulpiride augmentation and patients receiving olanzapine monotherapy among chronic schizophrenia patients unresponsive to olanzapine. Kane et al. (2009) reported that addition of aripiprazole to either risperidone or quetiapine in 323 patients showed no efficacy over placebo added to either risperidone or quetiapine. In contrast, Essock et al. (2011) reported that patients assigned to a switch to monotherapy displayed shorter times to all-cause treatment discontinuation than those assigned to remain on polypharmacy. These studies were indicators of what could happen with antipsychotic combinations in chronic-phase patients. In acute-phase patients, however, randomized controlled trials of second-generation antipsychotic combinations have not yet been reported.

In emergency and acute-phase wards, not all patients respond to antipsychotic monotherapy, and we are often faced with difficulties in managing psychotic and aggressive patients. As early non-response to a standard dose of risperidone (≤6 mg) can predict subsequent response (Kinon et al., 2010; Hatta et al., 2011), taking measures to improve outcomes among early non-responders to risperidone is reasonable. We therefore prospectively examined whether augmentation with olanzapine would be superior to increasing the risperidone dose in acute schizophrenia patients showing early non-response to risperidone. The present study was performed with emergency-based, newly admitted patients without support from pharmaceutical companies, reflecting real-world practice.

2. Methods

2.1. Setting and participants

Of the 63 psychiatric emergency wards authorized by the Japanese government, 18 (29%) participated in the present study. These wards were located all over Japan, and were responsible for local emergency cases. Most admissions to these hospitals represented behavioral emergencies and approximately 60% were brought in by the police. All were involuntary admissions as an immediate danger to themselves or others, according to the 1995 Law Concerning Mental Health and Welfare for the Mentally Disabled. Details of the clinical setting are described elsewhere (Hatta et al., 1998). According to government policies, psychiatric emergency services have been expanded in both metropolitan and local areas over the last 16 years. The quality of sites and patients in the present study was therefore homogenous. This activity was conducted by the Japan Acute-phase Schizophrenia Trial (JAST) study group (Hatta et al., 2009, 2011).

During the study period, between July 1 and October 31, 2010, a total of 786 patients were admitted and assessed for eligibility. Eligible patients were 18–64 years old, newly admitted as emergency cases, and meeting the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) for schizophrenia, schizophreniform disorder, or schizoaffective disorder. Patients with obvious complications such as liver dysfunction, renal dysfunction, heart failure, respiratory failure, or diabetes mellitus were excluded, as were patients who were pregnant or who wanted to become pregnant.

2.2. Study design

All study protocols were approved by the institutional review board at each site, and written informed consent was obtained from patients or their legally authorized representatives. Patients who refused oral medication were initially treated with injections. After resolution of agitation, the investigators informed patients orally and in writing about the trial, and invited them to participate.

Patients were treated with flexible-dose oral risperidone for 2 weeks, then divided according to the Clinical Global Impressions-Improvement Scale (CGI-I) (Guy, 1976) into early responders (CGI-I score ≤3) and early non-responders (CGI-I score ≥4). Early responders to risperidone continued with risperidone therapy, whereas early non-responders to risperidone were randomized using the sealed envelope method in a rater-blind manner to either continue on risperidone at an increased dose (RIS+RIS) or to receive risperidone with addition of olanzapine (RIS+OLZ) for the next 8 weeks. For randomization, we referred to a random number table, with sequentially numbered, opaque, sealed envelopes used to conceal the allocation sequence.

The initial dose of risperidone was 3 mg/day. Doses were subsequently increased or decreased at the discretion of the treating psychiatrist. During the first 2 weeks, the maximum dose of risperidone was 6 mg/day. During the next 8 weeks, the dose of risperidone was allowed to reach 12 mg/day for the RIS+RIS group, while the maximum doses of risperidone and olanzapine were 6 mg/day and 20 mg/day, respectively, for the RIS+OLZ group, considering dose equivalency (Kane et al., 2003). Use of benzodiazepines was allowed and documented. Use of valproate as a mood stabilizer was also allowed and documented. However, use of other mood stabilizers and antidepressants was not permitted. Use of anticholinergic drugs was also not allowed unless acute extrapyramidal side effects appeared.

2.3. Procedures

Before starting the trial, site-coordinators were trained to assess outcomes as raters. All site-coordinators were experienced psychiatrists. A training video was used to train raters in assessment of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1991). The primary outcome measure was ≥50% improvement in PANSS total score by 10 weeks.

Efficacy outcomes consisted of PANSS, CGI-I (1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; and 7, very much worse), and the Global Assessment of Functioning (GAF) (Jones et al., 1995). Safety and tolerability outcomes were determined based on vital signs, weight, laboratory data, electrocardiography (ECG), and the Drug-induced Extrapyramidal Symptom Scale (DIEPSS), which includes parkinsonism, akathisia, dystonia, and dyskinesia (Inada, 1996). Data including PANSS, CGI, GAF, vital signs, weight, laboratory data, ECG, and DIEPSS were collected on admission and every 2 weeks thereafter. Data were also collected at the time of discontinuation of the allocated treatment. Sexual side effects were recorded when reported by patients, and sedation was recorded when described by patients as an aversive subjective experience or when observed. Raters did not work on the wards involved in the study, were not involved with treatment, and were blinded to the drug assignments of early non-responders to risperidone. The tested drug was discontinued when the treating psychiatrist judged the efficacy of the drug to be insufficient, when the treating psychiatrist judged side-effects of the drug to be intolerable, or when the patient reported non-adherence. Before a judgment of insufficient efficacy could be made, the drug dosage was increased to the maximum. Another outcome measure was treatment discontinuation for any cause.

2.4. Statistical analysis

Differences between categorical variables in patient demographics and clinical characteristics were calculated using Fisher's exact test. Differences between sequential variables were calculated using the unpaired *t* test (with Welch correction if applicable). If data were not sampled from Gaussian distributions, a non-parametric test (Mann–Whitney test) was used. Mean improvement in the PANSS total score was calculated as 100×(baseline score − week×score)/(baseline score − 30) (Leucht et al., 2009). Kaplan–Meier curves were used to estimate the probability of treatment discontinuation at 10 weeks. Statistical analyses were performed using SPSS version 17.0 J software (SPSS, Tokyo, Japan). All statistical tests were two-tailed. Values of $P<0.05$ were regarded as statistically significant.

In our previous randomized clinical study, 9% of early non-responders to risperidone staying on risperidone subsequently achieved ≥50% response (Hatta et al., 2011). No previous data are available regarding the rate of response to adding olanzapine among early non-responders to risperidone. Suzuki et al. (2008) reported that 17 patients with treatment-refractory schizophrenia who failed to respond to sequential monotherapy with olanzapine, quetiapine and risperidone were subsequently treated using combination therapy with olanzapine plus risperidone for ≥8 weeks. Of these, seven responded according to the primary endpoint, four showed sufficient improvement to be discharged from hospital, and six patients showed no response. That open-label study thus found that 11 of 17 patients (65%) with treatment-refractory schizophrenia were full or partial responders to combination therapy comprising olanzapine plus risperidone. Accordingly, we assumed that subsequent response among early non-responders to risperidone by increasing the dose (RIS+RIS group) would be 9%, and that subsequent response among early non-responders to risperidone by addition of olanzapine to risperidone (RIS+OLZ group) would be 60%. The statistical power was set as power $=1-\beta=80\%$, and sensitivity as $\alpha=5\%$ to enable detection of differences in the effects of the augmentation strategy. Power analysis consequently set the required number of patients at 13 patients per group.

This study is registered in the UMIN Clinical Trials Registry (number: UMIN000003531; http://www.umin.ac.jp/ctr).

3. Results

The trial profile is shown in Fig. 1. Eighty-eight patients were enrolled and started on risperidone treatment. The rate of study participation among eligible patients was 23% (88/389). Two patients

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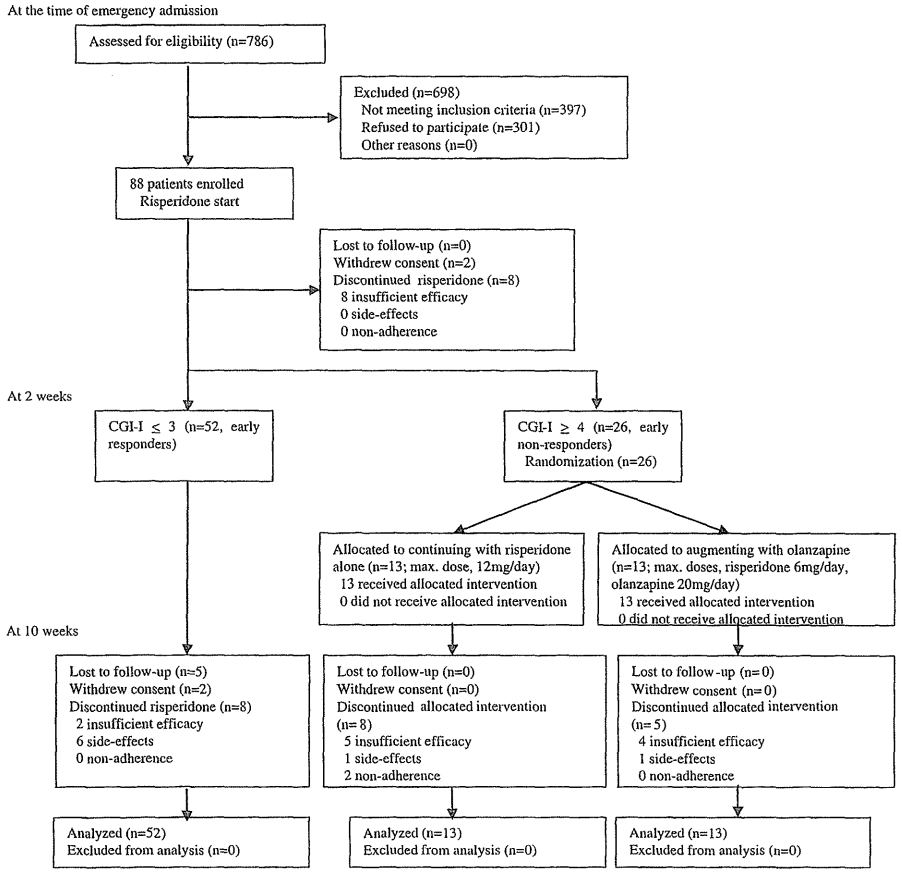

Fig. 1. Trial profile.

withdrew consent, and eight patients discontinued risperidone treatment due to a lack of efficacy before the end of the first 2 weeks. Data from these patients were not included in the final analysis. A total of 78 patients thus completed 2 weeks of treatment. Mean age was 39.5 years (standard deviation (S.D.), 11.9 years), and 49% (38/78) were men. Sixty of the 78 patients were enrolled at the time of emergency admission. The remaining 18 patients were enrolled within 3 days after admission, during which time only haloperidol injections were given. The median interval before enrolment was 0 day. Diagnoses were as follows: schizophrenia/schizophreniform disorder, 94% (73/78); and schizoaffective disorder, 6% (5/78). Six patients (7%) showed comorbidities of substance dependence, involving alcohol in all cases. Antipsychotic-naïve patients comprised 40% (35/78), while haloperidol injection had been received prior to enrolment in 20% (18/78). Mean CGI-S score was 5.6 (S.D., 0.8), and mean PANSS total score was 106.2 (S.D., 24.3). Mean PANSS subscale scores were as follows: positive scale, 29.5 (S.D., 7.3); negative scale, 23.9 (S.D., 9.1); general psychopathology scale, 52.8 (S.D., 13.0); and PANSS-excitement component (PANSS-EC), 18.0 (S.D., 6.1). Mean GAF score was 20.6 (S.D., 7.9). Mean body mass index was 22.5 (S.D., 3.9).

The 78 patients were first divided into early responders to risperidone ($n=52$, 67%), and early non-responders to risperidone ($n=26$, 33%), according to the CGI-I score at 2 weeks, as mentioned in the Study design section. Baseline characteristics of early responders to risperidone and early non-responders are listed in Table 1. No significant differences in each item were found between groups, although the proportion of antipsychotic-naïve patients tended to be higher among early responders to risperidone than among early non-responders.

Mean CGI-I scores at 2 weeks in early responders and early non-responders to risperidone were 2.3 (S.D., 0.6) and 4.5 (S.D., 0.7), respectively. Mean improvements in PANSS total score between baseline and at 2 weeks in early responders and early non-responders to risperidone were 52.2% (S.D., 18.7) and −11.7% (S.D., 26.9), respectively.

Table 1
Baseline characteristics of early responders to risperidone and early non-responders.

	Early responders to risperidone ($n=52$)	Early non-respondersto risperidone ($n=26$)	*P*
Age (years)	39.6 (12.0)	39.4 (12.0)	0.94
Men	25/52 (48%)	13/26 (50%)	0.81
Asian	52/52 (100%)	26/26 (100%)	
Diagnosis			
Schizophrenia/ schizophreniform	49/52 (94%)	24/26 (92%)	1.00
Schizoaffective	3/52 (6%)	2/26 (8%)	
Substance dependence	3/52 (6%)	3/26 (12%)	0.39
Antipsychotic-naïve	27/52 (52%)	8/26 (31%)	0.09
Haloperidol injection received before enrolment	14/52 (27%)	4/26 (15%)	0.39
CGI-S	5.5 (0.9)	5.8 (0.8)	0.26
PANSS			
Total	106.2 (24.2)	106.1 (24.9)	0.98
Positive scale	29.7 (6.8)	29.1 (8.3)	0.76
Negative scale	23.1 (9.1)	25.2 (9.0)	0.35
General psychopathology scale	53.5 (13.1)	51.8 (12.9)	0.61
PANSS-EC	17.6 (6.5)	18.6 (7.3)	0.58
GAF	20.0 (8.3)	21.6 (7.2)	0.41
BMI (kg/m^2)	22.5 (3.5)	22.3 (4.5)	0.84
Overweight (BMI ≥25)	13/52 (25%)	6/26 (23%)	1.00
Hyperglycemia	0/52 (0%)	0/26 (0%)	
Hypercholesterolemia	7/52 (13%)	4/26 (15%)	1.00
Hypertriglyceridemia	3/52 (6%)	5/26 (19%)	0.11
Median dose of risperidone at 2 weeks (mg/day)	5.5	6.0	0.17

Data represent mean (S.D.) or *n/N* (%), unless otherwise indicated. Diagnosis was made at discharge according to DSM-IV-TR. All substance dependence was alcohol dependence. 'Haloperidol injection received before enrolment': the maximal duration until enrolment was 3 days. CGI-S, Clinical Global Impression Severity rating scale; PANSS, Positive and Negative Syndrome Scale; PANSS-EC, excitement (item number P4), hostility (P7), tension (G4), uncooperativeness (G8), poor impulse control (G14); GAF, Global Assessment of Functioning; BMI, body mass index. Hyperglycemia: ≥200 mg/dL or fasting glucose ≥126 mg/dL. Hypercholesterolemia: cholesterol concentration ≥220 mg/dL. Hypertriglyceridemia: triglyceride level ≥150 mg/dL. Differences in age, CGI-S, PANSS, GAF, and BMI were calculated using the unpaired *t*-test. Differences in sex, diagnosis, and frequencies of substance dependence, haloperidol injection received before enrolment, and hypertriglyceridemia were calculated using Fisher's exact test.

Among early non-responders to risperidone, 13 patients were allocated to continue receiving risperidone alone (RIS + RIS group), and the remaining 13 patients were allocated to receive risperidone augmented with olanzapine (RIS + OLZ group). Baseline characteristics of patients were much the same between the RIS + RIS and RIS + OLZ groups (Table 2). In the RIS + RIS group, previous antipsychotics taken by patients who were not on their first episode were as follows: risperidone, two patients; aripiprazole, two patients; haloperidol, two patients; fluphenazine, one patient; and unknown, two patients. Those taken by patients in the RIS + OLZ group were as follows: risperidone, two patients; aripiprazole, two patients; haloperidol, one patient; and unknown, four patients. Unfortunately, data on exact dosages were not available. No significant differences between groups were seen according to the kinds of previous antipsychotics taken.

Between 2 and 10 weeks, among the early responders to risperidone, five patients were lost to follow-up, and two patients withdrew consent. In addition, eight patients discontinued risperidone due to insufficient efficacy ($n=2$) and side-effects ($n=6$; extrapyramidal side effects, $n=4$; hyperprolactinemia, $n=2$). In the RIS + RIS group, eight patients discontinued the allocated intervention due to insufficient efficacy ($n=5$), extrapyramidal side effects ($n=1$), and non-adherence ($n=2$). In the RIS + OLZ group, five patients discontinued the allocated intervention due to insufficient efficacy ($n=4$) and side-effects ($n=1$, weight gain) (Fig. 1).

Scattergrams of changes in PANSS total score at 10 weeks from baseline are shown in Fig. 2. At 10 weeks, early responders to risperidone showed a significantly higher percentage of improvement in PANSS total score than the RIS + RIS group (66.3% [S.D., 23.9] vs. 26.6% [S.D., 31.7]; $t=4.89$, $P<0.0001$). Meanwhile, no significant difference was observed between the RIS + RIS and RIS + OLZ groups (26.6% [S.D., 31.7] vs. 35.7% [S.D., 26.4]; $t=0.80$, $P=0.43$). A

Table 2
Baseline characteristics of early non-responders to risperidone.

	RIS + RIS ($n=13$)	RIS + OLZ ($n=13$)	*P*
Age (years)	41.9 (10.6)	36.8 (13.1)	0.29
Men	9/13 (69%)	4/13 (31%)	0.12
Asian	13/13 (100%)	13/13 (100%)	
Diagnosis			
Schizophrenia/schizophreniform	13/13 (100%)	11/13 (85%)	0.48
Schizoaffective	0/13 (0%)	2/13 (15%)	
Substance dependence	2/13 (15%)	1/13 (8%)	1.00
Antipsychotic-naïve	4/13 (31%)	4/13 (31%)	
Haloperidol injection received before enrolment	3/13 (23%)	1/13 (8%)	0.59
CGI-S	6.0 (0.7)	5.5 (0.9)	0.15
PANSS			
Total	109.7 (26.8)	102.5 (23.4)	0.48
Positive scale	29.7 (9.5)	28.5 (7.2)	0.73
Negative scale	26.6 (9.8)	23.8 (8.3)	0.44
General psychopathology scale	53.4 (15.7)	50.2 (9.6)	0.53
PANSS-EC	19.4 (7.9)	17.8 (6.8)	0.58
GAF	21.9 (6.9)	21.4 (7.7)	0.86
BMI (kg/m^2)	22.4 (5.5)	22.2 (3.6)	0.92
Overweight (BMI ≥25)	3/13 (23%)	3/13 (23%)	
Hyperglycemia	0/13 (0%)	0/13 (0%)	
Hypercholesterolemia	2/13 (15%)	2/13 (15%)	
Hypertriglyceridemia	1/13 (8%)	4/13 (31%)	0.32

RIS + RIS, Allocated to continuing with risperidone alone (max. dose, 12 mg/day); RIS + OLZ, Allocated to augmenting with olanzapine (max. doses, risperidone 6 mg/day, olanzapine 20 mg/day).

Data represent mean (S.D.) or *n/N* (%). Diagnosis was made at discharge according to DSM-IV-TR. All substance dependence was alcohol dependence. 'Haloperidol injection received before enrolment': the maximal duration until enrolment was 3 days. CGI-S, Clinical Global Impression Severity rating scale; PANSS, Positive and Negative Syndrome Scale; PANSS-EC, excitement (item number P4), hostility (P7), tension (G4), uncooperativeness (G8), poor impulse control (G14); GAF, Global Assessment of Functioning; BMI, body mass index. Hyperglycemia: ≥200 mg/dL or fasting glucose ≥126 mg/dL. Hypercholesterolemia: cholesterol concentration ≥220 mg/dL. Hypertriglyceridemia: triglyceride level ≥150 mg/dL. Differences in age, CGI-S, PANSS, GAF, and BMI were calculated using the unpaired *t*-test. Differences in sex, diagnosis, and frequencies of substance dependence, haloperidol injection received before enrolment, and hypertriglyceridemia were calculated using Fisher's exact test.

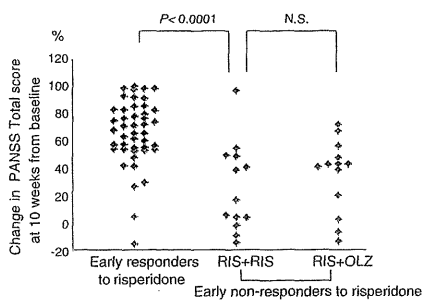

Fig. 2. Scatterplot of change in PANSS total score at 10 weeks from baseline. Early responders to risperidone showed significantly higher percentage of improvement in PANSS total score than the RIS + RIS group (66.3% [S.D., 23.9%] vs. 26.6% [S.D., 31.7%]; $t=4.89$, d.f. = 56, $P<0.0001$). No significant difference was observed between the RIS + RIS and RIS + OLZ groups (26.6% [S.D., 31.7%] vs. 35.7% [S.D., 26.4%]; $t=0.80$, d.f. = 24, $P=0.43$).

comparison of outcomes between the RIS + RIS and RIS + OLZ groups is shown in Table 3. Mean maximum dose of olanzapine in the RIS + OLZ group was 16.9 mg/day, equivalent to 5.1 mg/day of risperidone (Kane et al., 2003). The total dose of antipsychotics in the RIS + OLZ group was thus equivalent to 10.6 mg/day (5.5 + 5.1 mg) of risperidone, higher than that in the RIS + RIS group (8.5 mg/day). In the RIS + RIS group, adjunctive benzodiazepines were given to nine patients: lorazepam, three patients, 1 mg; nitrazepam, one patient, 10 mg; flunitrazepam, six patients, mean 1.8 mg (S.D., 0.4 mg). In the RIS + OLZ group, adjunctive benzodiazepines were given to 12 patients: lorazepam, nine patients, mean 1.5 mg (S.D., 0.9 mg); nitrazepam, four patients, mean 12.5 mg (S.D., 5.0 mg); flunitrazepam, one patient, 1 mg. In the RIS + RIS group, adjunctive valproate was given to four patients with the mean dose of 750 mg (S.D., 300 mg). In the RIS + OLZ group, adjunctive valproate was given to five patients, with a mean dose of 540 mg (S.D., 195 mg).

Achievement rates of ≥20%, ≥30%, ≥40%, and ≥50% improvement in PANSS total score in the RIS + OLZ group were 77%, 69%, 62% and 23%, respectively. Achievement rates of ≥20%, ≥30%, ≥40%, and ≥50% improvement in PANSS total score in the RIS + RIS group were 46%, 46%, 38% and 23%, respectively (Fig. 3). With respect to the primary outcome measure, no difference in the rate of achieving ≥50% improvement in PANSS total score was observed between groups (23% [n/N = 3/13] in each). There were no differences in the rate of achieving ≥20%, 30%, and 40% improvement in PANSS total score between the RIS + OLZ group and the RIS + RIS group (77% vs. 46%, $P = 0.23$, 69% vs. 46%, $P = 0.43$, 62% vs. 38%, $P = 0.43$). These are post hoc analyses, and no significant difference was found either with or without Bonferroni correction. Likewise, no significant differences in safety and tolerability outcomes were identified (Table 3). Among the six patients with akathisia in the RIS + RIS group, only two patients showed akathisia at the time of treatment discontinuation. Severity of akathisia in these two patients was just '1: minimal, questionable' (full score, 4), and the reasons for treatment discontinuation in both patients were insufficient efficacy. A trend-level difference in fasting glucose change from baseline was apparent between the RIS + RIS and RIS + OLZ groups.

Treatment discontinuation for any cause did not differ significantly between treatment groups ($P = 0.060$, Fig. 4). Comparisons by log-rank test showed that although time to treatment discontinuation was significantly shorter in the RIS + RIS group (6.8 weeks; 95%CI, 5.2–8.4 weeks) than in early responders to risperidone (8.6 weeks; 95%CI, 7.9–9.3; $P = 0.018$), it was not significantly shorter in the RIS + OLZ group (7.9 weeks; 95%CI, 6.3–9.5 weeks) than in early responders to risperidone (8.6 weeks; 95%CI, 7.9–9.3 weeks; $P = 0.37$).

Table 3
Comparison of outcomes between early non-responders to risperidone allocated to continuing with risperidone alone (RIS + RIS) and those allocated to augmenting with olanzapine (RIS + OLZ).

	RIS + RIS ($n = 13$)	RIS + OLZ ($n = 13$)	P
Dose of risperidone at 2 weeks (mg/day)	5.2 (0.9)	5.4 (1.2)	0.54
Max. dose of risperidone (mg/day)	8.5 (2.7)	5.5 (1.1)	
Max. dose of olanzapine (mg/day)	0	16.9 (6.0)	
Adjunctive benzodiazepines	9/13 (69%)	12/13 (92%)	0.32
Adjunctive valproate	4/13 (31%)	5/13 (38%)	1.00
Anticholinergic drug	6/13 (46%)	4/13 (31%)	0.69
PANSS (mean change from baseline)			
Total	−21.4 (22.8)	−25.9 (25.2)	0.63
Positive scale	−10.1 (9.0)	−10.1 (9.4)	1.00
Negative scale	−2.9 (6.1)	−4.2 (5.6)	0.60
General psychopathology scale	−8.4 (12.2)	−11.7 (11.7)	0.49
Percentage of improvement in PANSS total	26.6 (31.7)	35.7 (26.4)	0.43
≥50% improvement in PANSS total	3/13 (23%)	3/13 (23%)	
CGI-I	4.3 (1.9)	3.5 (1.3)	0.20
GAF	36.1 (12.6)	42.8 (19.4)	0.32
Any serious adverse event	0/13 (0%)	0/13 (0%)	
Extrapyramidal symptoms (DIEPSS)			
Any symptoms	9/13 (69%)	8/13 (62%)	1.00
Parkinsonism	6/13 (46%)	8/13 (62%)	0.70
Akathisia	6/13 (46%)	2/13 (15%)	0.20
Dystonia	1/13 (8%)	0/13 (0%)	1.00
Dyskinesia	0/13 (0%)	1/13 (8%)	1.00
Weight change from baseline (kg)	1.0 (2.8)	2.0 (3.2)	0.46
Fasting glucose change from baseline (mg/dL)	−2.0 (10.7)	7.8 (16.3)	0.081
Cholesterol change from baseline (mg/dL)	5.1 (37.3)	8.6 (38.6)	0.81
Triglycerides change from baseline (mg/dL)	24 (median)	27 (median)	0.80

Data represent mean (S.D.) or n/N (%), unless otherwise indicated. CGI-I, Clinical Global Impression Improvement rating scale; PANSS, Positive and Negative Syndrome Scale; GAF, Global Assessment of Functioning; DIEPSS, Drug-induced Extrapyramidal Symptom Scale.

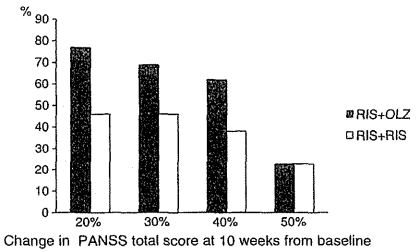

Fig. 3. Change in PANSS total score at 10 weeks from baseline among early non-responders to risperidone. Rates of achieving ≥20%, ≥30%, ≥40%, and ≥50% improvement in PANSS total score in the RIS + OLZ group were 77%, 69%, 62% and 23%, respectively. Rates of achieving ≥20%, ≥30%, ≥40%, and ≥50% improvement in PANSS total score in the RIS + RIS group were 46%, 46%, 38% and 23%, respectively.

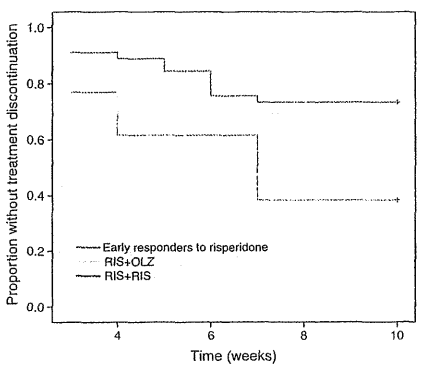

Fig. 4. Time to treatment discontinuation for any cause. Kaplan–Meier estimates of time to discontinuation were 8.6 weeks (95%CI, 7.9–9.3 weeks) for early responders to risperidone, 7.9 weeks (95%CI, 6.3–9.5 weeks) for the RIS + OLZ group, and 6.8 weeks (95%CI, 5.2–8.4 weeks) for the RIS + RIS group. Comparisons by log-rank test showed that time to treatment discontinuation was significantly shorter in the RIS + RIS group than in early responders to risperidone ($P = 0.018$), but was not significantly shorter in the RIS + OLZ group than in early responders to risperidone ($P = 0.37$).

4. Discussion

As the definitions of the outcomes adopted in a study represent a critical factor, the characteristics of the CGI classification to identify early non-response in this study require some discussion. Although we used CGI-I, another possibility may be to use a certain cutoff in the PANSS score to decide early non-response. However, such lengthy measures are not used in standard clinical practice. We have recently shown that early response/non-response to risperidone according to CGI-I at 2 weeks can predict subsequent clinical outcomes (Hatta et al., 2011). The negative likelihood ratio for the prediction of achieving ≥50% response at 4 weeks according to early response status to risperidone at 2 weeks was 0.057. This value was sufficiently small (<0.1), meaning that early non-response to risperidone at 2 weeks can predict <50% response at 4 weeks. The result was consistent with prospective findings by Kinon et al. (2010), in which the full 30-item PANSS had been used to assess early response and non-response. Furthermore, the present finding of a −11.7% mean improvement in PANSS total score between baseline and 2 weeks in early non-responders to risperidone is consistent with the linking of CGI-I to percentage PANSS reduction (Leucht et al., 2005). Using CGI-I (score ≥ 4 as a cutoff) to identify early non-response thus appears reliable.

In the present study, a predominance of early responders to early non-responders was observed, with 67% of patients identified as early responders to risperidone. This is consistent with the findings of our previous randomized clinical study on early prediction of antipsychotic response (Hatta et al., 2011), but inconsistent with the retrospective analysis and prospective studies by Kinon et al. (2008, 2010). The discrepancies can be explained by the following points. First, severity of symptoms differed between investigations. With respect to baseline PANSS, mean total scores were approximately 92 in the retrospective analysis (Kinon et al., 2008) and 99 in the prospective trial (Kinon et al., 2010), compared to 106.2 in the present investigation. Extremely high baseline PANSS scores were thus one characteristic of our study, as all patients required emergency admission. Agitation/excitement can be a particularly responsive domain during early treatment (Breier et al., 2002), and may be associated with the predominance of early responders to early non-responders in our emergency-based study. Another difference is that 40% of patients in the present study were drug-naïve, in contrast with the chronically ill patients investigated by Kinon et al. (2010). Since a substantial proportion of the patients in the present study were receiving treatment for the very first time, response times of such patients might have differed (Emsley et al., 2006). The tendency toward a higher rate of antipsychotic-naïve patients among early responders to risperidone compared to early non-responders (Table 1) may support this.

The objective of this study was to clarify whether augmentation with olanzapine would be superior to increased risperidone dose among acute schizophrenia patients showing early non-response to risperidone at 2 weeks in a real-world setting. The present finding that a ≥50% improvement in PANSS total score at 10 weeks among early non-responders allocated to augmentation with olanzapine (RIS + OLZ group) was achieved by 23% is new. In addition, the finding that a ≥50% improvement in PANSS total score at 10 weeks among early non-responders allocated to receive an increased risperidone dose (RIS + RIS group) was achieved by 23% is informative. Although we assumed that the subsequent response rate in the RIS + RIS group was 9%, and that the subsequent response rate in the RIS + OLZ group was 60% as described in the Statistical analysis section, we could not confirm our original hypothesis. This point requires further elaboration. A ≥50% improvement in PANSS total score was achieved by 23% in both groups. This rate was unexpectedly low for the RIS + OLZ group, and unexpectedly high for the RIS + RIS group. The assumption of 9% for the RIS + RIS group was based on our previous finding at 4 weeks, but the present study included a 10-week follow-up period. This prolonged follow-up period might have led to better outcomes than we had expected. Remarkably, rates of achieving a ≥40% improvement in PANSS total score in the RIS + OLZ and RIS + RIS groups were 62% and 38%, respectively (Fig. 3). If the primary outcome measure had been the achievement of ≥40% rather than ≥50%, yielding improvement in PANSS total score for a larger number of patients, a significant difference between groups might have been observed. Kinon et al. (2008) analyzed data from five randomized clinical trials in the treatment of chronically ill patients with schizophrenia, suggesting that the 40% cut-off may be a more appropriate criterion for subsequent improvement. Also, Kinon et al. (2010) reported that later response of ≥40% improvement in PANSS total score was associated with the greatest predictive accuracy. Stauffer et al. (2011) reported that at a threshold for later response of ≥50% improvement in PANSS total score, early non-response most strongly predicted later non-response in the treatment of patients with first-episode psychosis. Thus, what is the appropriate rate as a threshold for later response is still controversial.

Time to treatment discontinuation was significantly shorter in the RIS + RIS group than in early responders, but was not significantly shorter in the RIS + OLZ group than in early responders. In the case of increasing risperidone above a standard dose of 3–6 mg daily, many studies (in Caucasian populations) have shown this either has no benefit or may result in more extrapyramidal symptoms, less improvement in negative symtpoms, and longer hospital stays (Kopala et al., 1997; Emsley, 1999; Love et al., 1999; Lane et al., 2000; Volavka et al., 2002). However, only one treatment discontinuation due to side-effects was seen in the RIS + RIS group and in the RIS + OLZ group (Fig. 1). Among the six patients with akathisia in the RIS + RIS group (Table 3), only two patients showed akathisia at the time of treatment discontinuation. Furthermore, the severity of akathisia in these two patients was just '1: minimal, questionable' (full score, 4), and the reason for treatment discontinuation in both patients was insufficient efficacy. Flexible dose design and allowing use of anticholinergics and benzodiazepines as needed might have helped to prevent treatment discontinuations for side-effects. Toxicity from high-dose risperidone in the RIS + RIS group might not necessarily have been the primary cause for the disadvantage of the RIS + RIS group and the advantage of the RIS + OLZ group. In addition, the lack of significant difference in rates of discontinuation due to side-effects between groups suggests that the combination of risperidone and olanzapine is not necessarily risky.

Kinon et al. (2010) recently reported that switching risperidone to olanzapine at week 2 resulted in a small but significantly greater reduction in PANSS total score than continuing on risperidone among early non-responders. Tenacious monotherapy with risperidone without increasing the dose may thus be inferior to switching to olanzapine. However, the clinical significance of the switching strategy appears to be slight during acute-phase treatment, because the difference in mean PANSS total score between switching to olanzapine and staying on risperidone at 10 weeks was only 3 points. Unfortunately, the present study lacked a switching arm to another antipsychotic monotherapy. We therefore cannot claim that some benefit of augmentation therapy in the present study is superior to the small but significant effects of switching from risperidone to olanzapine reported by Kinon et al. (2010). Further studies comparing augmentation effects with switching effects seem justified.

To the best of our knowledge, this represents the first randomized clinical trial of olanzapine augmentation of risperidone in patients with acute-phase schizophrenia unresponsive to risperidone monotherapy. One strength of this study was that all participants were psychiatric emergency cases requiring admission, mirroring

real clinical practice. The absence of support from pharmaceutical companies was also a key characteristic of this study. One limitation was that the sample size was relatively small. Obtaining informed consent in emergency situations is often difficult. Accordingly, the rate of participation in the study among eligible patients was 23%. This rate is not particularly low for emergency situations (Hatta et al., 2008, 2009, 2011). Second, the study used a single-blind design. Both clinicians and patients may have had expectations about individual antipsychotics in terms of therapeutic potency for acute psychotic episodes, dosage requirements, side-effect profile, and likely need for as-needed medication. Such expectations could influence the dosage prescribed, decisions to prescribe as-needed medications, and decisions to discontinue the assigned drug. However, obtaining informed consent for a double-blind study of emergency situations may be extremely difficult, and the rate of participation in a double-blind study among eligible patients could well be much lower than that in a single-blind study. As excessively low participation rates cannot reflect real practice, this issue is of particular concern for research into emergency situations. Third, the time to all-cause discontinuation may be a more appropriate measure for double-blind trials in which both prescriber and patient expectations are controlled and both study conditions include newly started medications (Essock et al., 2011). In an open-label trial with blind raters, patients and prescribers in the switch condition may be more inclined to attribute alterations in feelings, symptoms, or side-effects to the change in medication compared to patients and prescribers in the stay condition, who may have experienced these same alterations as part of normal variations in illness and medication response. In the present study, neither randomized group represented a stay condition, using either augmentation or an increase in dose. As both groups were conditions with a change in medication, the comparisons may have been more appropriate than a comparison between stay and switch conditions, with respect to the time to all-cause discontinuation. Fourth, an interval of ≥1 week after increasing the doses of risperidone to 6 mg may be needed when determining early non-response. If such an interval is not applied, delayed effects could be seen after the decision to randomize, and thus affect the results. We should be wary of polypharmacy, as multiple agents are too often prescribed by clinicians when not warranted. However, when patients fail to respond to an adequate dose of antipsychotic, it is incumbent upon us to test other options. There was no RIS+OLZ advantage over RIS+RIS in the primary outcome of the present study. However, secondary outcomes justify the inclusion of augmentation arms in additional, much larger studies comparing strategies for early non-responders. More studies performed in real clinical practice with minimal bias are required to assist clinicians in making rational treatment decisions.

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Regular Article

Secluded/restrained patients' perceptions of their treatment: Validity and reliability of a new questionnaire

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Aim: To develop a standardized self-reporting questionnaire to evaluate patients' perceptions of their overall treatment in specific relation to the use of seclusion and/or restraint (SR) measures as part of the treatment program.

Methods: A 17-item self-rating questionnaire was given to 56 patients with experience of SR-related treatment to develop a new scale, the Secluded/Restrained Patients' Perceptions of their Treatment (SR-PPT). Concurrent validity was examined against the Client Satisfaction Questionnaire-8 Japanese Version (CSQ-8J). In addition, Patient burden induced by answering the SR-PPT was evaluated.

Results: On factor analysis, two factors named as Cooperation with Staff (nine items) and Perceptions of SR (two items) were derived. Cronbach's coefficient alphas were 0.928 and 0.887, and correlation coefficients against the CSQ-8J were 0.838 and 0.609, respectively. Answering the SR-PPT was found to induce little burden on the patients.

Conclusion: Adequate internal consistency and concurrent validity of the final version of the SR-PPT, which consists of 11 items, indicate that it is acceptable as a measurement scale. Use of this questionnaire will add the patient's view to the assessment of overall treatment involving SR.

Key words: coercion, inpatients, patient participation, patient satisfaction, profession–patient relations.

IN PSYCHIATRIC INPATIENT care, seclusion and/or restraint (SR) is often used to secure the safety of a patient whose disruptive behaviors due to mental disorder pose a potential danger to the patient him/herself and to others in the immediate vicinity, such as patients and care staff.[1] The aims of SR are to ensure a secure environment and to provide medication and care smoothly until SR is no longer considered necessary. It is also reported, however, that patients who have experienced SR felt fear, helplessness and distress. This suggests that they do not consider such intervention beneficial, but rather a form of punishment under the control of care staff.[2–5]

Through various discussions aimed at SR minimization and elimination,[6,7] it has been clarified that the amount of SR in Japan is high compared to other countries. The minimization of SR is an urgent task in Japan.[8] Finland, another country that recognizes itself as a heavy user of SR among European countries, has conducted substantial investigations and has been taking measures for SR minimization.[9,10] From this common awareness, Japan and Finland launched a bilateral project called SAKURA in 2007 to investigate the quality of care involving SR. The project follows the structure, process and outcome proposed by Donabedian[11] and as one of the outcomes, focuses on the evaluation of the patient's own perceptions of his/her treatment.

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Recent studies have found that patient perception of coercive interventions and/or a weak alliance with care staff lead to poorer adherence to treatment,[12] and that an involuntary admission without understanding the justification for treatment results in a higher rate of readmission.[13] It has been shown that in community mental health care, where patients generally receive treatment at will, closer agreement between the patient's needs and the physician's justification of treatment is associated with a higher level of patient satisfaction and consequently better adherence to the treatment.[14] In addition, the patient's involvement in making treatment decisions improves his/her quality of life (QOL) and satisfaction level.[15,16] Such findings can possibly be extrapolated to patients who have experienced SR, because their perceptions of such treatment and its justification as well as their perceptions of therapeutic collaboration with the staff might influence their prognosis. It is, therefore, necessary for staff providing SR treatment to make efforts to build a therapeutic relationship with the patients, identify their therapeutic needs, and involve them in establishing their own treatment goals. Such tasks are accomplished not only through close communication with SR patients but also by various types of quality care provided to them, such as offering medication, supporting nutrition and hydration, assisting in personal hygiene, and observing the somatic condition. Thus, any evaluation of how these tasks are accomplished must examine the patients' own rigorously measured perceptions of both the SR itself and the overall treatment related to SR.

Among the existing questionnaires examining how SR is perceived, some focus on negative emotions such as fear, hopelessness and punishment, or about positive experiences such as a calming effect or feeling of safety. Other questionnaires directly ask about the efficacy of SR.[2–5,17] The surveys of involuntarily admitted patients' perceptions of their treatment include questions referring to the involuntary admission itself such as perceived coercion, being respected and feeling safe, and those asking about the relationship with care staff, perceived improvement and satisfaction.[18–21] Most of those surveys explain the results by item individually, but do not provide a discussion using a composite score of each item, to grasp the overall aspects of patient perceptions.

In contrast, several questionnaires addressing patient satisfaction and collaboration between the patient and care staff were designed as a measurement using the total score, but did not include items specific to SR.[22–25] Moreover, some of them involve many questions, which imposes an excessive burden on a patient just after an SR event.

Accordingly, a questionnaire that measures all of the aforementioned aspects of patient perceptions in only a few items, to reduce patient burden, does not exist.

The aim of this study was to develop a self-reporting questionnaire as a tool for measuring patient perception in order to evaluate the quality of overall treatment related to SR – a questionnaire applicable even to emotionally labile patients right after an SR event.

METHODS

Scale development

To determine the items that would constitute the new questionnaire (hereafter referred to as the 'Secluded/Restrained Patients' Perceptions of their Treatment', SR-PPT), the items used in previous surveys and existing questionnaires were examined. These included surveys on perception of SR[2–5,17] and involuntarily admitted patients' perceptions of their treatment,[18–21] questionnaires on patient satisfaction,[22,23] and the Working Alliance Inventory (WAI).[24,25] The items identified from the existing questionnaires for development of the SR-PPT were reviewed by a professional group consisting of two psychiatrists, three psychiatric nurses and one psychiatric occupational therapist. In total, 17 items were selected and categorized into the following five domains: 'working alliance for treatment' (seven items) and 'respect and autonomy' (four items), which are considered to be the domains most influenced by the coercive manner of SR; and second, 'how patients felt about their SR' (three items), and then 'satisfaction' (two items) and 'perceived improvement' (one item) as general impressions. With regard to the number of items, careful consideration was given to minimize the survey-related burden on patients who might be distressed during or immediately after SR.

The SR-PPT consists of several existing items in English and new items originally drafted by the main author (T.N.) in Japanese. Both English and Japanese versions of the SR-PPT were prepared. Permission was obtained from all authors of the existing questionnaires in order to use the exact wording of the items. The existing items in English were translated into Japanese by the same author (T.N.) and back-

translated into English by two independent native speakers. The back-translation was checked against the original English sentences by another native English-speaking psychiatric care worker. The original items in Japanese were translated into English by two independent native English speakers and then back-translated into Japanese. The back-translation was then checked by the same author (T.N.).

A 100-mm visual analogue scale (VAS) was chosen as the measurement scale, allowing responses ranging from 'strongly disagree' to 'strongly agree' (scored correspondingly from 0 to 100 mm). Respondents were requested to answer based on their perceptions at the time of filling in the questionnaire and not to recall retrospectively the feelings experienced during SR.

The study was conducted between May and August 2008.

Setting

Two emergency wards and one acute ward in two psychiatric hospitals (N Hospital and K Hospital) in Japan participated in the study. 'Emergency ward' and 'acute ward' are ward categories stipulated by the national reimbursement system in Japan. The emergency and acute wards are those with ≥40% of patients newly admitted and with ≥40% of the newly admitted patients discharged to their home within 3 months. Emergency wards must also accept a required minimum number of compulsory involuntary admissions under orders from the hospital's catchment area. Accordingly, the average registered nurse allocation for an emergency ward is 10 patients per nurse per day (vs 13 patients per nurse per day for an acute ward).

The characteristics of the participating wards (emergency ward in N hospital, emergency ward in K hospital and acute ward in K hospital) are, respectively, as follows: number of beds, 60, 26 and 44; mean hospital stay days, 56.7, 25.0 and 37.7 days (in 2007); mean seclusion days per 1000 patient-days 176, 487 and 154 (in February 2008); and mean restraint days per 1000 patient-days 24, 32 and 5 (in February 2008). All three wards were mainly responsible for patients with schizophrenia or schizophrenia-related disorders (F 20-F29 category of the ICD-10).

Participants

The inclusion criteria were: age 18–65 years, an SR episode during current hospitalization, and written informed consent from the patient and his/her family (mandatory in Japan). Patients were excluded if they were receiving i.v. infusion due to a somatic disease, if their psychiatrist in charge did not agree to cooperate with the researchers, or if their clinical condition prevented their participation as judged by their psychiatrist.

Eligible candidates were selected by checking the patient records. At the same time, baseline variables (sex, age, diagnosis, number of admissions), duration of current hospitalization, interval from last SR treatment event until the date of survey and total duration of all SR treatment events were obtained for each of the eligible candidates.

Assessment

Prior to filling out the SR-PPT, the investigator showed the patient how to fill in the VAS and the patient practiced answering the questionnaire using an example. The patient then filled in each VAS of the 17 items of the SR-PPT.

Following the SR-PPT, the patient filled in another newly developed VAS form, enquiring how much difficulty, fatigue and strain they felt when answering the SR-PPT.

To evaluate the criterion-related validity of the SR-PPT, the Japanese version of the Client Satisfaction Questionnaire-8 (CSQ-8J) was filled out on the same occasion. The CSQ-8J is a measurement tool to rate the patients' satisfaction of a care service and contains eight items, all 4-point Likert scales. The overall score ranges from 8 to 32, and higher score indicates higher satisfaction.[22] It has been widely used with patients as part of the outcome assessments for health and welfare services.

There exists evidence of a correlation between the subjective outcome evaluation (completed by the patient him/herself) and the objective outcome evaluation (symptom assessment by a rater).[13,26] To assess such a kind of correlation between additional external criteria and the SR-PPT, the following assessments were performed by the psychiatrist in charge on the same day as the SR-PPT: the Brief Psychiatric Rating Scale (BPRS; 18 items, score range 1–7),[27] the Global Assessment of Functioning (GAF)[28] and GAF improvement (change from the admission date).

Ethics

The study was approved by the Ethics Review Board of the National Center of Neurology and Psychiatry.

In accordance with the national ethics requirement to first obtain proxy consent for research participation of an involuntarily admitted patient with limited comprehension, consent from the patients' relatives was obtained. Before completing the survey, all eligible patients for whom the informed consent by proxy was obtained were given a comprehensive description of the study and informed that their participation or refusal would not affect their care. Patients were informed that the ward staff would not see their SR-PPT responses, that the completed questionnaire would be sealed in an envelope directly in front of them and that the data would be treated anonymously. Thereafter their own written consent was obtained.

Taking into consideration the fact that some of the patients were currently under treatment programs that included SR, the main author (T.N., a psychiatrist) carefully observed the patient's level of fatigue or irritability and discontinued the procedure when necessary. In addition, after completing all of the questionnaires, the ward head nurse monitored the patients for any deleterious symptoms that might have been induced by the study procedure.

Statistical analysis

For the 86 participant candidates who met the inclusion criteria, the differences in patient characteristics between those who completed the SR-PPT and those who did not were analyzed using Student's *t*-test for continuous variables of normal distribution (Shapiro–Wilk test, $P \geq 0.1\%$) and the Mann–Whitney *U*-test for variables of non-normal distribution (Shapiro–Wilk test, $P < 0.1\%$). The χ^2 test was applied for categorical variables. The reliability was estimated by identifying factors using factor analysis (main factor method) and by examining the internal consistency of the subscales using Cronbach's alpha coefficient. The concurrent validity was estimated using Pearson's correlation coefficient between the SR-PPT score and the CSQ-8J score. To estimate the correlation of SR-PPT score with the external criteria, Pearson's correlation coefficient (for GAF and BPRS) and the partial correlation coefficient (for GAF improvement) were used. The relationship between patient characteristics and patient burden induced by answering the SR-PPT was tested using Pearson's correlation coefficient for continuous variables of normal distribution, and Spearman's rank correlation coefficient for variables of non-normal distribution. For categorical variables, one-way ANOVA was applied. The significance level was set according to two-tailed test. All statistical analyses were performed using SPSS version 15.0 (SPSS, Chicago, IL, USA).

RESULTS

Of 182 patients hospitalized on the study wards on the date of the survey, 110 patients were aged 18–65 years and had experienced SR. Of these, nine patients had been discharged prior to the survey date, five patients were treated by physicians who refused to cooperate in the study and 10 patients were, according to their attending psychiatrists, unable to tolerate the study procedure. Of the remaining 86 patients, two patients did not volunteer their consent. The families of 27 more patients could not be contacted by the staff and proxy consent was thus not obtained. One patient was excluded by the main author (T.N.) due to the patient's excessive fatigue while answering the questionnaire. Finally, the SR-PPT was completed fully by a total of 56 patients.

Patient characteristics are listed in Table 1 including the mean GAF and BPRS scores. There were no

Table 1. Patient characteristics ($n = 56$) and GAF/BPRS scores

	n, mean ± SD, or median (IQR 25%–75%)	%
Sex		
Male	31	55
Age (years)	42.4 ± 13.0	
Diagnosis[†]		
F20–F29	39	69
F30–F39	11	20
F10–F19	4	7
Others	2	4
No. admissions	1.5 (1.0–4.0)	
Days between last seclusion/restraint event and investigation	10.0 (3.5–38.5)	
Days between admission and investigation	36.0 (16.0–64.0)	
Days of seclusion	12.0 (6.0–21.0)	
Days of restraint[‡]	5.0 (2.0–8.0)	
GAF at admission	27.9 ± 11.4	
GAF at investigation	49.8 ± 16.3	
BPRS at investigation	40.1 ± 15.3	

[†]International Classification of Disease Tenth revision (ICD-10); [‡]20 patients experienced restraint.
BPRS, Brief Psychiatric Rating scale (18 items, score range 1–7); GAF, Global Assessment of Functioning.

significant differences in the patient characteristics between the 56 participants and the 30 excluded patients.

Factor analysis

Principal factor analysis on the 17 items selected as candidates was performed, because none of the 17 items exhibited ceiling or floor effects. The eigenvalue shifts were 9.80, 1.48, 1.1 and 0.85, assuming that the two-factor structure was valid. In addition, one item having low commonality of 0.224 following factor extraction was removed. At this point, a two-factor hypothesis emerged and factor analysis was performed using the principal factor method and varimax rotation. Next, the five items with a loading of ≥0.35 on both the primary and secondary factors were removed. The factor analysis was then repeated using the principal factor method and varimax rotation on the remaining 11 items. Table 2 lists the final factor pattern following varimax rotation. Incidentally, the ratio explaining the total variance of the 11 items for the two factors prior to rotation was 64.5%. In the nine primary factor items, those items that involved communication with staff toward mutual understanding of the treatment process and goals had a high loading and were therefore named 'Cooperation with Staff'. In the two secondary factors, those items involving perceptions of SR had a high loading and were thus named 'Perceptions of SR'.

Internal consistency of the SR-PPT

The subscale coefficient alpha was also calculated in order to evaluate internal consistency. Adequate alpha coefficients were obtained for Cooperation with Staff (0.928) and Perceptions of SR (0.887). The value for the 11 items of the SR-PPT was 0.916.

SR-PPT scores

The mean ± SD total score for all the final 11 items (ranging from 0 to 1100) was 658.7 ± 245.4, and the mean subscale scores for Cooperation with Staff (max. 900) and for Perceptions of SR (max. 200) were 559.3 ± 208.9 and 99.4 ± 65.9, respectively. Correlations between each subscale score and the total score were observed as shown (Table 3). No significant differences nor correlations between ST-PPT total scores and the patient characteristics (sex, age, diagnosis, number of admissions, days between last SR event or admission and investigation, and days of SR) existed.

Criterion-related validity

The mean ± SD CSQ-8J score was 21.7 ± 5.6. Significant correlations were observed between CSQ-8J

Table 2. Rotated factor matrix for 11 items of the SR-PPT

	Factor loading	
	1	2
Factor 1: Cooperation with staff		
Do you and the staff agree about the things you will need to do in treatment to help improve your situation?	0.838	0.204
Are you and the staff working towards mutually agreed upon goals?	0.832	0.323
Do you feel that the staff members understand your concerns?	0.825	0.251
Have you been respected on the ward as a person?	0.810	0.333
Is your opinion taken into account with regards to your treatment?	0.746	0.184
Are you being given enough time during your treatment or care?	0.737	0.216
Do you collaborate with the staff on setting goals for your treatment?	0.685	0.066
Can you voice your opinion?	0.667	0.130
Do you feel that staff members have ignored you in any way?	0.557	0.176
Factor 2: Perception of seclusion/restraint		
Was being restrained and/or secluded beneficial in treating your difficulties?	0.202	0.868
Was it necessary for you to be restrained and/or secluded?	0.228	0.860
Factor contribution	5.96	1.13
Contribution variance rate	54.2%	10.3%

SR-PPT, Secluded/Restrained Patients' Perception of their Treatment.

Table 3. SR-PPT subscale correlations with total score

	SR-PPT scale	SR-PPT Cooperation with Staff subscale	SR-PPT Perception of SR subscale
SR-PPT Cooperation with Staff subscale	0.971**		
SR-PPT Perception of SR subscale	0.648**	0.445*	
CSQ-8J	0.876**	0.838**	0.609**

*$P < 0.01$, **$P < 0.001$.
CSQ-8J, Client Satisfaction Questionnaire-8 Japanese version; SR-PPT, Secluded/Restrained Patients' Perception of their Treatment.

score, SR-PPT scale score, SR-PPT Cooperation with Staff subscale score and SR-PPT Perceptions of SR subscale score (Table 3).

A significant negative correlation was found between SR-PPT total score and BPRS total score ($r = -0.417$, $P < 0.01$), and a significant positive correlation was seen between SR-PPT total score and both the GAF ($r = 0.472$, $P < 0.001$) and the GAF improvement ($r = 0.406$, $P < 0.01$) scores.

Burden of answering the SR-PPT

The mean ± SD scores for difficulty, fatigue and strain experienced by the patients when answering the SR-PPT were 23.5 ± 26.7, 24.8 ± 29.2 and 30.2 ± 30.0, respectively (max. 100). The rate of the lowest burden scores for patients (<20) with regard to difficulty, fatigue and strain was 41.9%, 40.7% and 34.9% and that of the highest burden scores for patients (>80) was 3.5%, 5.8% and 5.8%, respectively. No correlation was observed between length of the interval from the last SR event to day of the survey and the burden of answering the SR-PPT. The BPRS and (inversely) the GAF correlated with fatigue ($r = 0.377$, $P < 0.01$ and $r = -0.296$, $P < 0.05$) and strain ($r = 0.519$, $P < 0.001$ and $r = -0.272$, $P < 0.05$), respectively. No cases of worsening of symptoms due to participation in the survey were observed.

DISCUSSION

To our knowledge, the SR-PPT is the first measurement developed for assessments by patients of their overall treatment in specific relation to the use of SR measures as part of the treatment program. It assesses not only the patients' perceptions of experienced SR itself but aspects such as respect, autonomy, and working alliance, which are often hindered by coercive interventions. Of 17 candidate questions, 11 were found to be relevant and sufficient. These questions constituted two factors, namely, Cooperation with Staff (nine items) and Perceptions of SR (two items). Both had sufficient internal consistency and concurrent validity. Furthermore, the SR-PPT total score had a significant inverse correlation with BPRS score, and direct correlations with GAF and GAF improvement on the day of the survey used as external criteria. The rater's assessment using GAF (assess impairment in social functioning) and/or BPRS (assess anxiety, hostility, suspiciousness) reflected on some level the patient's negative perception of cooperation with staff. These results suggest the validity of the SR-PPT.

In cases when SR is applied to secure patients against imminent danger caused by their disruptive behavior due to mental disorder, the patient's own view of such intervention is often left behind, yet the objective and subjective views may also diverge.[4] Indeed, although the correlations between the SR-PPT and, in contrast, the observer-rated assessment scales (GAF and BPRS) in the present study were statistically significant, the correlation coefficient of <0.7 was weak. This indicates that it is not sufficient to rely solely on the objective instruments, and that the staff assessment alone seems most likely to fail to identify adequately the dimension of patient perceptions. Because the patient's own perceptions of treatment considerably affect his/her prognosis, as mentioned in previous studies,[12–16] it is crucial to make these perceptions overt and measurable. It is especially true for such elements of treatment as respect for patient dignity and empowerment in shared decision making – even if the overall treatment includes coercive measures. Against such need for a standardized self-rating subjective measure that is easy to complete immediately after or even during SR, the SR-PPT appears to be a feasible, as well as a valid and reliable tool.