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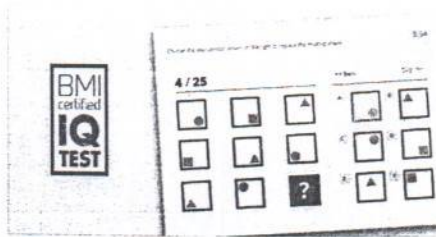
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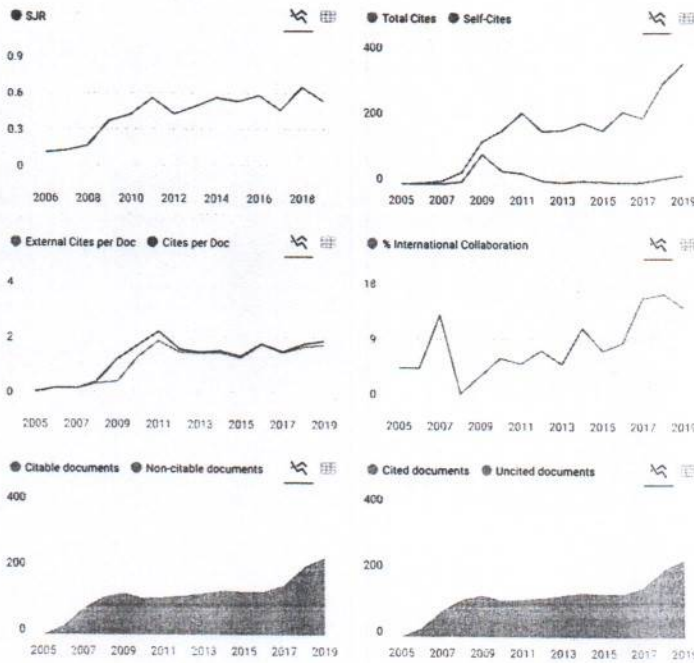
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ORIGINAL ARTICLES

Admission of people with dementia to psychiatric hospitals in Japan: factors that can shorten their hospitalizations

Takako Morikawa, Kiyoshi Maeda, Tohmi Osaki, Hiroyuki Kajita, Kayano Yotsumoto, Toshio Kawamata

Pages: 341-347 | First Published: 10 February 2017

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A comparison of clinical characteristics of older adults treated with antidepressants in general and psychiatric hospitals in Asia

Yuan-Yuan Wang, Yu-Tao Xiang, Gabor S. Ungvari, Chee H. Ng, Helen F.K. Chiu, Larina C.L. Yim, Tian-Mei Si, Kok-Yoon Chee, Ajit Avasthi, Sandeep Grover, Mian-Yoon Chong, Kang Sim, Shigenobu Kanba, Yan-Ling He, Min-Soo Lee, Shu-Yu Yang, Pichet Udomratn, Roy A. Kallivayalil, Andi J. Tanra, Margarita M. Maramis, Winston W. Shen, Norman Sartorius, Rathi Mahendran, Jia-Ying Teng, Chay-Hoon Tan, Naotaka Shinfuku

Pages: 348-355 | First Published: 21 April 2017

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Cardiac function and cognition in older community-dwelling cardiac patients

Laura H.P. Eggermont, Mohamed F.A. Aly, Pieter J. Vuijk, Karin de Boer, Otto Kamp, Albert C. van Rossum, Erik J.A. Scherder

Pages: 356-363 | First Published: 17 April 2017

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Cognitive decline and slower reaction time in elderly individuals with mild cognitive impairment

Ko-Chia Chen, Chia-Ying Weng, Sigmund Hsiao, Wen-Long Tsao, Malcolm Koo

Pages: 364-370 | First Published: 06 March 2017

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Detailed analysis of the Japanese version of the Rapid Dementia Screening Test, revised version

Yasushi Moriyama, Aihide Yoshino, Taro Muramatsu, Masaru Mimura

Pages: 371-376 | First Published: 06 June 2017

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Why do people with dementia pretend to know the correct answer? A qualitative study on the behaviour of *toritsukuroi* to keep up appearances

Masateru Matsushita, Yusuke Yatabe, Asuka Koyama, Yukiko Ueno, Daisuke Ijichi,

Shiroto Ikezaki, Mamoru Hashimoto, Noboru Furukawa, Manabu Ikeda

Pages: 377-381 | First Published: 04 April 2017

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Earlier and greater hand pre-shaping in the elderly: a study based on kinematic analysis of reaching movements to grasp objects

Yoshiki Tamaru, Yasuo Naito, Takashi Nishikawa

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The association between objective income and subjective financial need and depressive symptoms in South Koreans aged 60 and older

Woorim Kim, Tae Hyun Kim, Tae-Hoon Lee, Yeong Jun Ju, Eun-Cheol Park

Pages: 389-396 | First Published: 04 April 2017

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Antipsychotic prescription and mortality in hospitalized older persons

Deborah Chiesa, Alessandra Marengoni, Alessandro Nobili, Mauro Tettamanti, Luca Pasina, Carlotta Franchi, Codjo D. Djade, Salvatore Corrao, Francesco Salerno, Maura Marcucci, Giuseppe Romanelli, Pier Mannuccio Mannucci, REPOSI Investigators

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Evaluation of nursing interventions using minimally invasive assessments methods for patients in a persistent vegetative state

Mitsue Sato, Masahiro Sugimoto, Kazuo Yamaguchi, Takeshi Kawaguchi

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The factors related to early-onset depression after first stroke

Kadir Karakus, Refik Kunt, Cagdas O. Memis, Duygu A. Kunt, Bilge Dogan, Filiz Ozdemiroglu, Levent Sevincok

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ORIGINAL ARTICLE

A comparison of clinical characteristics of older adults treated with antidepressants in general and psychiatric hospitals in Asia

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Key words: antidepressants, Asia, prescription patterns.

Abstract

Aim: This study compared the demographics, clinical characteristics, and antidepressant prescription patterns between Asian patients aged 50 years and older attending psychiatric hospitals and those attending general hospitals.

Methods: In total, 955 patients (604 in general hospitals, 351 in psychiatric hospitals) aged 50 years or older treated with antidepressants in 10 Asian countries and territories were examined. Patients' demographics, clinical features, and prescriptions of psychotropic drugs were recorded using a standardized protocol and data collection procedure.

Results: Binary logistic regression revealed that high income and diagnosis of schizophrenia were independently associated with psychiatric hospital treatment, whereas outpatient care, diagnosis of anxiety disorders, and multiple major medical conditions were independently associated with general hospital treatment. In addition, tetracyclic and noradrenergic and specific serotonergic antidepressants were more likely to be prescribed in general hospitals.

Conclusion: Older adults treated with antidepressants showed different demographic and clinical features between general hospitals and psychiatric hospitals in Asia.

INTRODUCTION

Due to the low birth rate and increased life expectancy, the proportion of the ageing population in many Asian countries has been rapidly increasing.¹ As a consequence, health issues in this population have attracted much attention.² Depressive disorders, such as major depression and dysthymia, are common in the elderly and have negative outcomes including functional disability, increased mortality, high utilization of health-care services, and high health-care costs.^{3,4}

In recent decades, antidepressants have been among the most widely prescribed medications in many countries.^{5–8} The reasons for increased antidepressant use include the introduction of many new and safe antidepressants and a broad range of indications for their use.^{9,10} For example, apart from depression, selective serotonin reuptake inhibitors (SSRI) have also been used for alcoholism, eating disorders, and anxiety disorders.^{11,12}

In Asian countries, stand-alone psychiatric hospitals and general hospitals are the two major mental health service providers. Patients treated in different clinical settings usually have different demographic and clinical features, including prescription patterns of psychotropic medications. For example, in China, psychiatric hospitals are mainly located in suburban areas and provide intensive services for severe psychiatric disorders, whereas general hospitals are located in cities.¹³ In China, it has been reported that 73% of antidepressants are prescribed in general hospital settings.¹⁴ To date, no study has examined the demographic and clinical features of older Asian adults attending psychiatric and general hospitals.

Regular surveys on prescription patterns in psychiatry are an efficient way of identifying the use and trend of specific treatments over time in a given clinical setting.^{15,16} A large-scale longitudinal, observational project—the Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD)—was initiated in 2003. The first and second REAP-AD surveys were conducted in November 2003 and between March and June 2013, respectively, and they employed the same research design and protocol.^{17,18}

To provide a better understanding and improve the rationale of antidepressant use in older Asian adults, we conducted a secondary analysis of the

data in the 2013 REAP-AD survey that sought to do the following: (i) compare the demographic and clinical features of Asian patients aged 50 years and older treated with antidepressants at both general and psychiatric hospitals; and (ii) identify the independent correlates of antidepressant treatment between these two treatment settings. Considering that antidepressants are psychiatric medications, we hypothesized that there would be more patients receiving antidepressants in psychiatric hospitals than in general hospitals.

METHOD

Study sample and sites

The second REAP-AD survey was conducted in 40 psychiatric hospitals/units in mainland China (China), Hong Kong, Taiwan, India, Indonesia, Japan, Korea, Malaysia, Singapore, and Thailand. A consensus meeting was held to determine the procedures for case selection, data collection, and data entry. The same standardized protocol and data collection procedure were used at all the participating centres. Patients were included if they met the following criteria: (i) were either inpatients or outpatients; (ii) were aged 50 years or older; (iii) received antidepressants on the day of the survey; and (iv) were able to comprehend the aims of the study and provide informed consent if interviewed. The age cut-off for older adults varied from 50 to 65 years across the participating institutions according to local cultural and professional traditions. To make the population homogeneous, those aged 50 years and older in the dataset of the REAP-AD project were defined as ‘older adults’ in this study. The same age cut-off was also used in World Health Organization reports and other recent studies.^{19–22} There were no exclusion criteria.

Procedures

All eligible patients were recruited consecutively at each site. Basic demographic and clinical characteristics, including the type of clinical setting; age; gender; financial category; principal International Classification of Diseases, 10th revision; psychiatric diagnosis; depressive symptoms; and medical treatment, were collected using a data collection form designed for the study. Because of logistical limitations, no standardized instruments on the presence and severity of depressive symptoms were used. Instead, the

presence of 10 core depressive symptoms selected from the National Institute for Health and Care Excellence guidelines, International Classification of Diseases, 10th revision,²³ and *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, were used;²⁴ symptoms included insomnia, appetite change, agitation, fatigue, suicidal ideation, guilt/self-blame, lack of confidence, low concentration, sadness, and loss of interest.²⁵ In addition, all the participating countries and territories were divided into high-income (Hong Kong, Singapore, Japan, Korea, and Taiwan), upper-middle-income (China, Malaysia, and Thailand), and lower-middle-income sites (India and Indonesia) according to the The World Bank, 2016 criteria.²⁶ The data were collected either by a review of medical records only or by a medical review supplemented with a clinical interview. Data were collected by the patients' attending psychiatrists or by members of the research team with the agreement of the psychiatrists in charge of the patients.

Classification of prescribed medications

The prescribed medications were classified as antidepressants, first-generation antipsychotics, second-generation antipsychotics, mood stabilizers, or benzodiazepines according to the Anatomical Therapeutic Chemical classification.²⁷ In this survey, second-generation antipsychotics included aripiprazole, amisulpride, blonanserin, clozapine, olanzapine, paliperidone, perospirone, quetiapine, risperidone, ziprasidone, and zotepine. Antidepressants included escitalopram, mirtazapine, sertraline, trazodone, paroxetine, fluoxetine, duloxetine, fluvoxamine, venlafaxine, amitriptyline, citalopram, imipramine, bupropion, clomipramine, mianserin, agomelatine, dosulepin, doxepin, milnacipran, maprotiline, nortriptyline, and tandospirone. Antidepressants were classified into seven classes: (i) tricyclic antidepressants; (ii) tetracyclic antidepressants; (iii) monoamine oxidase inhibitors; (iv) SSRI; (v) serotonin norepinephrine reuptake inhibitors; (vi) noradrenergic and specific serotonergic antidepressant (NaSSA); and (vii) other antidepressants.

The study was approved by the clinical research ethics committees of the respective institutions. Given the anonymous nature of the retrospective chart review for the purpose of a clinical audit, informed consent was not required at some study sites, which was consistent with local ethical standards, provided that only the medical records were

reviewed. All patients who were interviewed gave written consent according to the requirements of the respective clinical research ethics committees.

Data analysis

All analyses were performed using the SPSS version 20.0 (IBM, Armonk, NY, USA). Comparisons of the sociodemographic and clinical characteristics of patients treated in general and psychiatric hospitals were performed by independent sample *t*-test, Mann-Whitney *U*-test, and χ^2 test, as appropriate. Binary logistic regression analyses with the 'enter' method were used to identify independent demographic and clinical correlates of the two treatment settings. The variables that were statistically significant in the univariate analysis were entered as independent variables, while the treatment setting was the dependent variable. The significance level was set at 0.05 (two-tailed).

RESULTS

Altogether 955 patients from the REAP-AD database fulfilled the study criteria; 604 (63.2%) received treatment in general hospitals and 351 (36.8%) in psychiatric hospitals. Table 1 presents the sociodemographic and clinical characteristics of patients by study site. Table 2 shows the sociodemographic and clinical characteristics of the whole sample and separately by treatment setting. Compared to patients treated at general hospitals, patients treated at psychiatric hospital were younger; were more likely to be men, inpatients, and diagnosed with schizophrenia; had lower income; had fewer major medical conditions; and were less likely to receive tetracyclic and NaSSA antidepressants, but more likely to receive antipsychotics.

Table 3 shows that being an outpatient, having anxiety disorders, and having more major medical conditions were independently associated with less frequent treatment in psychiatric hospitals; in contrast, falling into the upper-middle financial category and having schizophrenia were associated with more frequent treatment in psychiatric hospitals. In addition, tetracyclic antidepressants and NaSSA were more likely to be prescribed in general hospitals.

Table 1 Sociodemographic and clinical characteristics of the sample

	China (n = 158)		Hong Kong (n = 39)		Japan (n = 119)		Korea (n = 150)		Singapore (n = 48)		Taiwan (n = 109)		India (n = 63)		Malaysia (n = 67)		Thailand (n = 128)		Indonesia (n = 74)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age (year)	61.89	8.37	57.9	7.46	65.71	9.4	64.61	9.37	61.00	9.46	63.45	11.18	60.73	8.66	61.87	9.72	63.21	10.26	58.43	7.19	
Depressive symptoms (n)	4.10	2.29	2.15	1.50	3.70	1.88	3.88	1.85	3.63	2.48	3.36	1.61	3.63	2.52	4.49	2.17	2.59	1.57	2.01	1.29	
Major medical conditions (n)	0.32	0.62	0.49	0.60	1.06	1.20	0.56	0.70	0.75	0.81	0.70	0.81	0.49	0.64	0.87	0.94	0.41	0.62	0.49	0.69	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Male gender	54	34.2	10	25.6	25.6	52	43.7	42	28.0	24	50.0	55	50.5	34	54.0	25	37.3	52	40.6	27	36.5
Outpatient care	84	53.2	28	71.8	76	63.9	135	90.0	35	72.9	75	68.8	60	95.2	61	91.0	109	85.2	59	79.7	
Financial category																					
High	0	0	39	100	119	100	150	100	48	100	109	100	0	0	0	0	0	0	0	0	0
Upper-middle	158	100	0	0	0	0	0	0	0	0	0	0	0	0	67	100	128	100	0	0	
Lower-middle	0	0	0	0	0	0	0	0	0	0	0	0	0	63	100	0	0	0	74	100	
Principal psychiatric diagnosis																					
Mood disorders	137	86.7	23	59.0	93	78.2	117	78.0	24	50.0	67	61.5	44	69.8	50	74.6	81	63.3	35	47.3	
Anxiety	17	10.8	8	20.5	14	11.8	11	7.3	11	22.9	4	3.7	17	27.0	6	9.0	19	14.8	23	31.1	
Schizophrenia	0	0	6	15.4	2	1.7	7	4.7	11	22.9	28	25.7	1	1.6	7	10.4	7	5.5	10	13.5	
Other	4	2.5	2	5.1	10	8.4	15	10.0	2	4.2	10	9.2	1	1.6	4	6.0	21	16.4	6	8.1	
SGA	48	30.4	11	28.2	31	26.1	28	18.7	14	29.2	41	37.6	12	19.0	14	20.9	19	14.8	20	27.0	
FGA	5	5.3	6	15.4	11	9.2	8	5.3	4	8.3	10	9.2	6	9.5	6	9	12	9.4	15	20.3	
Mood stabilizers	44	27.8	4	10.3	20	16.8	12	8.0	6	12.5	31	28.4	29	46.0	12	17.9	42	32.8	4	5.4	
Benzodiazepines	30	19.0	14	35.9	35	29.4	40	26.7	20	41.7	38	34.9	7	11.1	24	35.8	45	35.2	56	75.7	
Major medical conditions	41	25.9	17	43.6	73	61.3	68	45.3	26	54.2	56	51.4	26	41.3	41	61.2	44	34.4	29	39.2	

FGA, first-generation antipsychotics; SGA, second-generation antipsychotics.

Table 2 Comparison of basic demographic and clinical characteristics of patients aged 50 years and older treated with antidepressants in general and psychiatric hospitals

	Total sample		General hospital sample		Psychiatric hospital sample		Statistics		
	<i>(n = 955)</i>		<i>(n = 604)</i>		<i>(n = 351)</i>		χ^2	d.f.	P-value
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%			
Male gender	375	39.3	222	36.8	153	43.6	4.3	1	0.03*
Outpatient care	722	75.6	508	84.1	214	61.0	64.4	1	<0.001*
Financial category							21.3	2	<0.001*
High	465	48.7	326	54.0	139	39.6			
Upper middle	353	37.0	192	31.8	161	45.9			
Lower middle	137	14.3	86	14.2	51	14.5			
Principal psychiatric diagnosis							41.7	2	<0.001*
Mood disorders	671	70.3	427	70.7	244	69.5			
Anxiety	130	13.6	102	16.9	28	8.0			
Schizophrenia	79	8.3	27	4.5	52	14.8			
Other	75	7.9	48	7.9	27	7.7			
Use of antidepressants									
TCA	99	10.4	70	11.6	29	8.3	2.6	1	0.10
Tetracyclic	27	2.8	23	3.8	4	1.1	5.7	1	0.01*
SSRI	593	62.1	370	61.3	223	63.5	0.5	1	0.48
SNRI	155	16.2	92	15.2	63	17.9	1.2	1	0.27
NaSSA	163	17.1	119	19.7	44	12.5	8.0	1	0.005*
Other	127	13.3	78	12.9	49	14.0	0.2	1	0.64
SGA	238	24.9	120	19.9	118	33.6	22.4	1	<0.001*
FGA	83	8.7	43	7.1	40	11.4	5.1	1	0.02*
Mood stabilizers	204	21.4	125	20.7	79	22.5	0.4	1	0.51
Benzodiazepines	309	32.4	189	31.3	120	34.2	0.8	1	0.35
Major medical conditions	421	44.1	304	50.3	117	33.3	26.0	1	<0.001*
	Mean	SD	Mean	SD	Mean	SD	T/Z	d.f.	P-value
Age (years)	62.6	9.5	63.3	9.4	61.3	9.6	3.0	953	0.003*
Depressive symptoms (<i>n</i>)	3.4	2.0	3.5	2.0	3.3	2.0	-1.0	— [†]	0.3
Major medical conditions (<i>n</i>)	0.5	0.8	0.7	0.9	0.3	0.5	-5.6	— [†]	<0.001*

P < 0.05.

[†] Mann-Whitney *U*-test.

d.f., degrees of freedom; FGA, first-generation antipsychotics; NaSSA, noradrenergic and specific serotonergic antidepressant; SGA, second-generation antipsychotics; SNRI, serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors; TCA, tricyclic antidepressants.

DISCUSSION

This was the first large-scale, multicentre survey comparing the clinical characteristics of older adults treated with antidepressants in general hospitals and those treated in psychiatric hospitals in Asia. Around two-thirds of the whole sample received antidepressants in general hospitals, consistent with a previous finding (73%) in adult patients with mood disorders in China.¹⁴ The results did not support our hypothesis that there would be more patients receiving antidepressants in psychiatric hospitals than in general hospitals. Before SSRI were introduced, traditional antidepressants, particularly tricyclic antidepressants and monoamine oxidase inhibitors, had been prescribed cautiously because of their cardiotoxicity and high lethality in overdose. In recent decades, however, the use of antidepressants has increased rapidly in all

age groups in psychiatric and other clinical settings because SSRI and other novel antidepressants are more tolerable and safe. Apart from the broad range of indications for novel antidepressants,^{9,10} off-label use and overuse of antidepressants could contribute to their increasing use.²⁸ Off-label use and overuse of antidepressants are associated with a number of negative outcomes, such as increased treatment costs and risk of adverse events, withdrawal reactions, and even suicide.^{29,30}

There were significant demographic and clinical differences between the two treatment settings across Asia. Surprisingly, on average, around three depressive symptoms were reported by the members of the sample receiving antidepressants, which possibly may be because of the wide indications for antidepressants. For example, patients with anxiety or

Table 3 Basic demographic and clinical data independently associated with older patients receiving antidepressant treatment in Asian psychiatric hospitals

Variables	P-value	OR	95% CI
Male gender	0.07	1.3	0.9–1.7
Outpatients	<0.001*	0.2	0.1–0.3
Financial category			
High	—	1.0	—
Upper-middle	<0.001*	1.9	1.4–2.7
Lower-middle	0.01	1.7	1.1–2.7
Principal psychiatric diagnosis			
Mood disorders	—	1.0	—
Anxiety disorders	0.003*	0.4	0.3–0.7
Schizophrenia	<0.001*	3.6	2.1–6.2
Other	0.60	1.1	0.6–2.0
Age (years)	0.83	0.9	0.9–1.0
Major medical conditions	<0.001*	0.5	0.4–0.6
On tetracyclic	0.02*	0.2	0.1–0.8
On NaSSA	0.008*	0.5	0.3–0.8
Use of SGA	0.09	1.3	0.9–1.9
Use of FGA	0.57	1.1	0.6–1.9

* $P < 0.05$. Binary logistic regression analysis with treatment in general hospitals as reference. Study sites have been controlled for. CI, confidence interval; FGA, first-generation antipsychotics; NaSSA, noradrenergic and specific serotonergic antidepressant; OR, odds ratio; SGA, second-generation antipsychotics.

eating disorders were usually prescribed antidepressants.^{11,12} The most frequent diagnosis in this survey was mood disorder (70.3%), followed by anxiety disorders (13.6%), schizophrenia (8.3%), and other psychiatric disorders (7.8%). The benefit and risk ratio associated with the common use of antidepressants still needs to be clarified. Although compelling evidence for the usefulness of antidepressants in schizophrenia is not available,^{31,32} a significant proportion of patients treated with antidepressants in this sample had a diagnosis of schizophrenia. Antidepressants are also not recommended for maintenance treatment of bipolar I disorder, as they may increase the risk of rapid cycling,³³ more severe symptoms, and impaired psychosocial functioning.³⁴ However, the subtypes of mood disorders, including bipolar I disorder, could not be identified in this sample because only the main International Classification of Diseases, 10th revision, codes were used in the REAP surveys.

Different health service models may help explain the relationship between patient characteristics and the type of hospitals found in this study. To explain the overall relationships between patients and providers, Penchansky and Thomas described the five As of access to health care: (i) affordability;

(ii) acceptability; (iii) accommodation; (iv) accessibility; and (v) availability.^{35,36} Another model concerning the use of mental health services has four interacting components: (i) patients' demographic and clinical features; (ii) patients' social support system; (iii) - illness-related factors such as sick role, recovery, compliance, and spacing of consultations; and (iv) the treatment system.^{13,37,38}

In this study, schizophrenia patients were more likely than other patients to be treated in psychiatric hospitals. This is consistent with a finding that the percentage of schizophrenia patients in psychiatric hospitals is higher than that in general hospitals.³⁹ Similar to another study,⁴⁰ financial factors may have played an important role in the selection of health service and treatment among patients in this study. Many Asian psychiatric hospitals largely treat patients with severe mental illness and are located in suburban areas, whereas general hospital psychiatric units are usually located in cities and provide outpatient services for patients with less severe mood and anxiety disorders.^{13,14} This likely explains the negative associations between psychiatric hospital treatment and care for outpatients with diagnosed anxiety and depressive disorders. Patients with both psychiatric and medical comorbidities need easy access to medical treatment and therefore are more likely to receive treatment in general hospitals as found in this study.

Psychiatric hospital patients received tetracyclic antidepressants and NaSSA less frequently than patients in general hospitals, and there is no clear explanation for this. A number of factors, including sociocultural and economic factors, clinical traditions, psychotropic drug availability, cost and insurance coverage, and health-care policy, may contribute to the variations in antidepressant-prescribing practice across Asian countries.

There were several limitations to this study. Firstly, several relevant variables, such as health-care policies, availability and cost of drugs, psychiatric training, treatment guidelines, prior treatment history, reasons for antidepressant prescriptions, and treatment responses, were not recorded in the REAP-AD survey. Secondly, because of the cross-sectional design, the causal relationships between variables could not be examined. Finally, for logistical reasons, the presence of depressive symptoms was not measured using standardized instruments. However, the

strengths of this study include the relatively large sample size, the diversity of the sample across 10 Asian countries, and the standardized nature of the data collection.

In conclusion, this REAP-AD survey found that majority of the whole sample received antidepressants in general hospitals. It also found considerable variation in demographic and clinical characteristics between older Asian adults receiving antidepressants in psychiatric hospitals and in general hospitals. The appropriateness of antidepressant prescriptions in general hospitals needs to be examined. Such findings would help clinicians to better understand and rationalize the prescription of antidepressants and the provision of different types of mental health services across Asia.

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