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Prescription of antipsychotic and concomitant medications for adult Asian schizophrenia patients: Findings of the 2016 Research on Asian Psychotropic Prescription Patterns (REAP) survey

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ABSTRACT

Objective: Regular surveys are important to monitor the use of psychotropic medications in clinical practice. This study examined the psychotropic prescription patterns in adult Asian schizophrenia patients based on the data of

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Schizophrenia
Prescription patterns

the Research on Asian Psychotropic Prescription (REAP) 2016 survey.
Methods: : This cross-sectional survey across 15 Asian countries/territories collected socio-demographic and clinical data with standardized procedures between March and May 2016. The socio-demographic and clinical characteristics of the patients were recorded with a standardized questionnaire.
Results: Altogether 3,537 adult patients with schizophrenia were consecutively screened and enrolled in the survey. The mean age was 38.66 ± 11.55 years and 59.7% of the sample were male. The mean dose of antipsychotics in chlorpromazine equivalents (CPZeq) was 424 ± 376 mg/day; 31.3% and 80.8% received first- and second- generation antipsychotics, respectively and 42.6% had antipsychotic polypharmacy, 11.7% had antidepressants, 13.7% had mood stabilizers, 27.8% had benzodiazepines, and 45.6% had anticholinergics.
Conclusions: Psychotropic prescription patterns in Asian adult patients with schizophrenia varied across countries. Regular surveys on psychotropic medications for schizophrenia are important to monitor pharmacotherapy practice in Asia.

1. Introduction

Schizophrenia is a disabling and mainly chronic psychiatric disorder, characterized by hallucinations, delusions and impairment of cognitive and social functioning (APA, 1994). According to a recent review the age-standardized point prevalence of schizophrenia globally is 0.28% (Charlson et al., 2018). The WHO estimated that more than 21 million individuals are affected by schizophrenia worldwide (WHO, 2014). Schizophrenia is associated with increased risk of major medical conditions, such as cardiovascular diseases, hepatitis, and HIV infection (Leucht et al., 2007), all of which significantly reduce life expectancy (Laursen et al., 2014). Schizophrenia ranked 12th out of 310 diseases and injuries causing disability worldwide in 2016 (Vos et al., 2017), which is partly due to the early onset and low remission rate of schizophrenia. The suicide risk is 13-fold higher in schizophrenia compared to the general population (Saha et al., 2007). Furthermore, schizophrenia is associated with significant treatment burden, especially in Asia (Holla and Thirthalli, 2015). Last but not least, schizophrenia causes immeasurable suffering for patients and families alike.

Antipsychotic medications, broadly classified as first (FGAs) and second generation antipsychotics (SGAs), are the mainstay treatment for schizophrenia, although they differ in efficacy and adverse effects (Leucht et al., 2013). SGAs are associated with high risk of metabolic side-effects, such as obesity and diabetes mellitus, while FGAs are more likely to cause extrapyramidal symptoms (EPS) and rarely neuroleptic malignant syndrome (NMS) (Orsolini et al., 2016). As for efficacy, clozapine is the most efficacious of all antipsychotics and the best option for treatment-resistant schizophrenia (De Berardis et al., 2018). Prescription patterns of antipsychotic medications are greatly influenced by socio-demographic and economic factors, such as delivery of health care, treatment guidelines, clinicians' training in psychopharmacology, and local prescription practices. Many treatment guidelines for antipsychotic prescription (2005; Canadian Psychiatric Association, 2005; Galletly et al., 2016; Lehman et al., 2004) are based on the robust scientific evidence of randomized controlled trials but they do not entirely reflect routine clinical practice (Harrington et al., 2002). For instance, hospitalized patients frequently received depot antipsychotics in Singapore because of their low price and availability (Sim et al., 2004b), while antipsychotic polypharmacy (APP) was common in Japan due to prescribers' positive attitudes towards APP (Chong et al., 2010; Kishimoto et al., 2013); in addition, young psychiatrists usually follow and are less likely to amend or challenge traditional prescribing traditions introduced by senior clinicians in Japan. For the aforementioned reasons, regular surveys are important to monitor prescription patterns of psychotropic medications in clinical settings (Hu et al., 2016; Sim et al., 2011; Xiang et al., 2017).

Prescription patterns of antipsychotic medications and other psychotropic drugs for schizophrenia in Asia have been reported (Chong et al., 2004). The objective of this study was to revisit the prescription patterns of psychotropic medications in adult patients with schizophrenia across 15 Asian countries/territories analyzing the data of the 2016 survey conducted by Research on Asian Psychotropic Prescription (REAP) scientific consortium.

2. Methods

2.1. Participants

The REAP project is a series of cross-sectional psychopharmacoepidemiological investigation on the prescription pattern of psychotropic medications in schizophrenia and mood disorder across Asia. The first REAP survey on antipsychotic (AP) treatment (REAP-AP1) was conducted in 2001, followed by REAP-AP2 in 2004, and REAP-AP3 in 2008-2009. The findings of the first three REAP surveys have been published (Chong et al., 2010; Xiang et al., 2016).

The REAP-AP4 survey was conducted in March–May 2016. Patients were consecutively screened and recruited from 71 hospitals across 15 Asian countries/territories, including Bangladesh, China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Myanmar, Pakistan, Singapore, Sri Lanka, Taiwan, Thailand and VietNam.

Patients entered the survey if they fulfilled the following criteria: (1) diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) or the International Classification of Disease, 10th Revision (ICD-10); (2) treated either as inpatient or outpatient at the hospital or clinic; and (3) age between 18 and 64 years. Patients with major medical diseases were excluded because severe medical comorbidity influences psychotropic prescriptions and medically compromised psychiatric patients are not usually treated in psychiatric settings in many countries/territories in Asia.

2.2. Data collection

Following previous REAP surveys (Chong et al., 2010; Xiang et al., 2012b), the relevant demographic and clinical information (age, gender, the presence or absence of significant positive and negative symptoms in the past month, length of illness, type and doses of psychotropic medications and adverse effects) was collected on a standard data collection form from either a review of medical records or a clinical interview supplemented by a review of medical records by research psychiatrists involved in the REAP project. The doses of antipsychotics were expressed in chlorpromazine equivalents (CPZeq) (Leucht et al., 2015; Woods, 2003) to facilitate comparison of doses between participating centers.

The study protocol was approved by the Institutional Review Boards of the respective hospitals. Consistent with the local ethical standards (Shinfuku and Tan, 2008), informed consent was waived at some study sites when only the medical records were reviewed to collect data. All patients who were interviewed provided written informed consent.

2.3. Statistical analysis

The computation of continuous variables is reported as mean and standard deviation (SD), while categorical variables are reported as frequencies and percentage. The dose distribution expressed in CPZeq is depicted by countries/territories. Independent demographic and clinical correlates of high antipsychotic dose (> 1000 mg/day in CPZequ) (Sim et al., 2009) were explored with binary logistic regression analysis with the "enter" method. The level of significance was set at 0.05, with two sided test.

3. Results

Altogether, 3,537 patients were included in this study (Table 1). The mean age of patients was 38.66 ± 11.55 years, the proportion of male patients was 59.7%; 51.4% of the sample were inpatient, and 65.9% had an illness duration of > / = five years. Nearly one-third (31.3%) received FGAs and 80.8% received SGAs. The prescription rate of FGAs ranged from 3.3% in Hong Kong to 60.1% in Thailand, while the rate of SGAs ranged from 54.9% in Thailand to 100.0% in Hong Kong. In total, 42.6% of patients received antipsychotic polypharmacy (APP), with Vietnam (59.2%) and Japan (57.4%) having the highest rates. With respect to APP, 6.3% of patients received combination of FGAs + FGAs, 15.7% received FGAs + SGAs, and 20.5% received SGAs + SGAs. Thailand had the highest rate of FGAs + FGAs (22.7%), while Vietnam had the highest rate of FGAs + SGAs (32.5%) and Singapore had the highest rate of SGAs + SGAs (43.0%). Antidepressants (AD) were prescribed to 11.7% of the sample, 13.7% received mood stabilizers (MS), 27.8% received benzodiazepines (BDZ), and 45.6% received anticholinergic medications (ACM).

The most commonly prescribed antipsychotics are shown in Table 2. Haloperidol (14.1%) was the most frequently prescribed FGA, followed by chlorpromazine (8.6%), fluphenazine decanoate (7.4%), trifluoperazine (4.0%) and flupentixol decanoate (3.3%). The most commonly prescribed SGAs was risperidone (36.0%), followed by olanzapine (20.1%), clozapine (18.9%), quetiapine (7.7%) and aripiprazole (5.5%). The mean dose of all antipsychotics was 424 ± 376 CPZeq mg/day. Around half of patients received low dose antipsychotics (defined as < 300 CPZeq mg/day), one third received medium doses (300–599 CPZeq mg/day) and 4.7% received high doses (> 1200 CPZeq mg/day) (Table 3).

Men, more severe positive and negative symptoms, inpatient treatment, and more frequent prescriptions of FGA, SGA, APP and anticholinergics were significantly associated with high-dose antipsychotics (> 1000 mg/day in CPZequ) (Table 4).

4. Discussion

The main finding of the study is that compared to previous REAP surveys, antipsychotic prescription patterns have changed significantly over a period of 15 years. The prescription of FGAs in consecutive REAP surveys has decreased over time, from 67.8% in 2001, to 51.9% in 2004, 41.7% in 2009 (Xiang et al., 2016), and 31.3% in this 2016 survey. FGAs were most commonly prescribed in Thailand (60.1%), but rarely used in Hong Kong (3.3%).

Possible reasons for the discrepancy between Asian countries/territories with respect to prescription patterns include different prescribing traditions, treatment guidelines and economic factors, such as cost of psychotropic drugs, access to health care services and availability of psychotropic medications (Xiang et al., 2016). In many Asian countries/territories, FGAs are mainly used for aggressive behavior (Chong et al., 2004). More recently, SGAs are preferred in treating schizophrenia due to their affordable costs, widespread availability, satisfactory efficacy and less severe EPS (Zhang et al., 2013). In Thailand, both FGAs and SGAs are recommended for the treatment of schizophrenia (The Royal College of Psychiatrists of Thailand, 2013),

Table 1
Socio-demographic and clinical characteristics and prescription of psychotropic medications in participating countries and territories in 2016.

	Bangladesh	China	Hong Kong	India	Indonesia	Japan	Korea	Malaysia	Myanmar	Pakistan	Singapore	Sri Lanka	Taiwan	Thailand	Vietnam	Total
Patients (n)	95	144	30	467	539	197	126	295	163	288	151	93	376	308	265	3537
Age, years																
Mean	32.60	39.13	37.86	35.29	35.90	43.13	39.34	38.32	37.68	36.08	45.52	39.67	45.96	38.09	38.46	38.66
SD	10.67	14.74	12.99	10.71	9.97	11.96	11.28	11.19	11.15	10.45	11.65	12.14	10.27	10.68	10.89	11.55
CPZeq (mg/d)																
Mean	577	555	478	388	294	689	595	306	280	528	420	438	433	327	550	424.94
SD	368	342	284	333	220	604	595	289	124	449	356	429	381	244	338	376.08
Men (%)	57.9	65.3	60.0	67.2	63.5	63.5	46.0	51.9	65.6	56.6	39.1	60.2	46.8	68.2	68.3	59.7
Inpatient	47.4	90.3	100	31.0	50.8	52.8	4.8	33.9	55.2	48.3	72.8	50.5	53.5	43.2	100.0	51.4
FGAs (%)	30.5	29.2	3.3	18.6	38.0	33.0	18.3	20.3	17.2	33.0	19.2	19.4	25.0	60.1	54.7	31.3
SGAs (%)	83.2	96.5	100.0	83.7	78.7	90.9	90.5	75.3	90.8	81.6	85.4	82.8	83.8	54.9	77.7	80.8
APP (%)	45.3	52.1	30.0	25.7	41.4	57.4	46.0	43.7	22.1	52.1	53.6	41.9	27.4	54.9	59.2	42.6
FGA + FGA (%)	5.3	0	0	1.5	6.5	2.5	0.8	10.8	0	3.8	5.3	7.5	2.7	22.7	11.7	6.3
FGA + SGA (%)	15.8	26.4	3.3	8.8	19.7	27.9	14.3	2.7	8.0	19.1	5.3	7.5	13.8	17.5	32.5	15.7
SGA + SGA (%)	24.2	25.7	26.7	15.4	15.2	26.9	31.0	30.2	14.1	28.8	43.0	26.9	10.9	14.6	15.1	20.5
Antidepressant (%)	0.0	18.1	26.7	15.6	4.3	2.5	36.5	6.4	3.1	13.5	24.5	14.0	13.3	19.5	4.2	11.7
Mood stabilizer (%)	1.1	34.7	16.7	7.3	6.1	33.0	8.7	6.1	9.8	25.3	17.9	7.5	13.3	19.5	13.6	13.7
Benzodiazepines (%)	40.0	13.9	16.7	32.1	16.1	33.5	54.8	15.6	8.6	51.7	30.5	9.7	40.7	30.2	15.1	27.8
Anticholinergic (%)	88.4	29.9	40.0	37.5	39.0	41.6	50.8	37.3	60.1	69.1	43.7	34.4	38.8	85.7	10.9	45.6

APP, antipsychotic polypharmacy (two or more antipsychotic medication); CPZeq, chlorpromazine equivalents; FGA, first-generation antipsychotic; SGA, second-generation antipsychotic.

Table 2
The most commonly prescribed antipsychotic medications.

	n	%
FGAs		
Haloperidol	497	14.1
Chlorpromazine	305	8.6
Fluphenazine decanoate	261	7.4
Trifluoperazine	143	4.0
Flupentixol decanoate	118	3.3
SGAs		
Risperidone	1272	36.0
Olanzapine	710	20.1
Clozapine	668	18.9
Quetiapine	272	7.7
Aripiprazole	196	5.5

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

although local studies have found that switching patients from SGAs to FGAs increased the hospitalization rate and health care costs (Boonlue et al., 2016). Haloperidol and chlorpromazine were the most commonly prescribed FGAs in Asia, despite having more frequent EPS than most other antipscchotics (Leucht et al., 2013). Depot FGAs were commonly prescribed, which is due to their low cost, availability and local clinical traditions and training. Depot antipsychotics were commonly used in Singapore but were rarely used in China due to lack of availability; in addition, patients recruited from the participating hospitals in China mostly had acute schizophrenia, thus patients are less likely prescribed depot antipsychotics (Xiang et al., 2016).

As expected, the proportion of SGAs prescription was higher than FGAs (80.8% vs 31.3%), which is similar to previous findings from Asia (Xiang et al., 2016). Although SGAs appear to be more effective for certain positive and negative symptoms compared to FGAs (Leucht et al., 2009), they significantly increase the risk of metabolic adverse effects (Rummel-Kluge et al., 2010). Risperidone, olanzapine and clozapine were the three most commonly prescribed SGAs in this survey. Risperidone causes hyper-prolactinaemia, and olanzapine causes significant weight gain (Leucht et al., 2013). Similarly, while clozapine is the best option for treatment-resistant schizophrenia and reduces the risk of suicidality (Chakos et al., 2004; Meltzer et al., 2003), it is highly sedative and increases the risk of myocarditis and agranulocytosis (Leucht et al., 2013). It has been reported that clozapine was underprescribed in Arabian Gulf region partly due to prescriber-related barriers and lack of nationwide hematological monitoring program (Ismail et al., 2019). In contrast, prescription of clozapine was common in this study, but varied greatly across countries and territories. Clozapine was not available in Japan until 2009, while it is one of the most widely used antipsychotics in China, and even prescribed for first episode psychosis (Xiang et al., 2016, 2011a). The common use of clozapine in China could be due to the following factors. Unlike in most Western countries, clozapine has been widely used in China since 1970s, even as the first-line treatment in some areas as an off-label prescription (Liu and Li, 2003), yielding extensive clinical and research experience (Xiang et al., 2007b). Further, clozapine is one of the cheapest antipsychotics in China, costing around US$0.08 for a dose of 300 mg. Recently, clozapine prescription has been decreased in China (Xiang et al., 2011a) because of the release of strict treatment guidelines and widespread availability of other SGAs (Xiang et al., 2013a).

The doses of antipsychotics for schizophrenia in Asian countries are generally lower compared to Western countries (Bowers et al., 2004). In this survey, antipsychotic doses were highest in Japan and lowest in Myanmar. The proportion of high antipsychotic doses has decreased over time in Asian countries (Sim et al., 2009). High antipsychotic doses in Japan (Xiang et al., 2016) is probably due to the frequent APP (Sim et al., 2004a). Administration of high-dose antipsychotics was independently associated with male sex, more severe positive and negative symptoms, inpatient treatment, and more frequent prescriptions of FGA, SGA, APP and anticholinergics. Male patients and inpatients

Table 4
Factors associated with high-dose antipsychotics (n = 247).

Variables	P value	Odds Ratio	95% CI
Age	0.82	0.998	0.984-1.013
Male	**0.001**	1.672	1.224-2.238
Outpatients	**< 0.001**	0.454	0.314-0.656
ID	0.48	1.143	0.784-1.666
PS	**0.04**	1.484	1.019-2.160
NS	**0.004**	1.611	1.166-2.225
Acute EPS	0.18	1.235	0.902-1.690
FGA	**< 0.001**	3.196	2.257-4.525
SGA	**0.002**	2.234	1.341-3.721
APP	**< 0.001**	5.453	3.523-8.440
AD	0.23	1.320	0.839-2.075
MS	0.37	1.188	0.811-1.739
BZD	0.31	1.181	0.855-1.631
ACM	**0.03**	1.403	1.019-1.931

Bolded values: < 0.05; participating country/territory has been controlled for as a covariate. ACM, anticholinergic medications; AD, antidepressant; APP, antipsychotic polypharmacy; BZD, benzodiazepine; EPS, extrapyramidal side-effects; FGA, first-generation antipsychotic; ID, illness duration; MS, mood stabilizer; NS, negative symptom; PS, positive symptom; SGA, second-generation antipsychotic.

Table 3
Comparison of antipsychotics doses (mg/day in CPZ eq).

	< 300 mg n (%)	300–599 mg n (%)	600–899 mg n (%)	900–1199 mg n (%)	> 1200 mg n (%)	Mean (SD)
Bangladesh (n = 95)	11 (11.6)	53 (55.8)	14 (14.7)	10 (10.5)	7 (7.4)	577 (368)
China (n = 144)	31 (21.5)	58 (40.3)	28 (19.4)	21 (14.6)	6 (4.2)	555 (342)
Hong Kong (n = 30)	7 (23.3)	13 (43.3)	8 (26.7)	1 (3.3)	1 (3.3)	478 (284)
India (n = 467)	197 (42.2)	182 (39.0)	47 (10.1)	21 (4.5)	20 (4.3)	388 (333)
Indonesia (n = 539)	352 (65.3)	135 (25.0)	38 (7.1)	10 (1.9)	4 (0.7)	294 (220)
Japan (n = 197)	52 (26.4)	51 (25.9)	39 (19.8)	25 (12.7)	30 (15.2)	689 (604)
Korea (n = 126)	51 (40.5)	27 (21.4)	15 (11.9)	12 (9.5)	21 (16.7)	595 (595)
Malaysia (n = 295)	166 (56.3)	87 (29.5)	24 (8.1)	8 (2.7)	10 (3.4)	306 (289)
Myanmar (n = 163)	80 (49.1)	76 (46.6)	7 (4.3)	0 (0.0)	0 (0.0)	280 (124)
Pakistan (n = 288)	103 (35.8)	87 (30.2)	45 (15.6)	32 (11.1)	21 (7.3)	528 (449)
Singapore (n = 151)	72 (47.7)	42 (27.8)	13 (8.6)	15 (9.9)	9 (6.0)	420 (356)
Sri Lanka (n = 93)	40 (43.0)	31 (33.3)	9 (9.7)	5 (5.4)	8 (8.6)	438 (429)
Taiwan (n = 376)	145 (38.6)	127 (33.8)	70 (18.6)	16 (4.3)	18 (4.8)	433 (381)
Thailand (n = 308)	148 (48.1)	122 (39.6)	27 (8.8)	10 (3.2)	1 (0.3)	327 (244)
Vietnam (n = 265)	57 (21.5)	96 (36.2)	67 (25.3)	34 (12.8)	11 (4.2)	550 (338)
Total (n = 3537)	1512 (42.7)	1187 (33.6)	451 (12.8)	220 (6.2)	167 (4.7)	424 (376)

CPZeq, chlorpromazine equivalents.

usually present with more severe aggressive behaviour and psychotic symptoms, therefore they receive high antipsychotic doses and APP combining FGAs and SGAs that more likely to induce EPS. As a result, male patients, particularly inpatients, are more likely to need anticholinergics (Xiang et al., 2012a). High antipsychotic doses significantly increase the risk of side effects, mainly EPS, therefore is not recommended by most treatment guidelines (Gardner et al., 2010; Royal College of Psychiatrists, 2006; Thompson, 1994).

AP monotherapy has been recommended as first-line treatment in both acute and maintenance treatment of schizophrenia (Falkai et al., 2005; Hasan et al., 2012; National Collaborating Centre for Mental Health, 2009). However, many schizophrenia patients do not or only partially respond to AP monotherapy (Suzuki et al., 2011), hence, APP is often an appropriate augmentation strategy (Bruijnzeel and Tandon, 2018; Hatta et al., 2019; Pickar et al., 2008). Similar to findings in previous REAP surveys (46.8% in 2001, 38.3% in 2004, and 43.4% in 2009) (Xiang et al., 2012c), the proportion of APP was 42.6% in this 2016 study, with the most common type of APP was SGA + SGA (20.5%). The APP rate in Hong Kong (30.0%) was similar to the findings in a local study (26.0%) (Lung et al., 2018). The proportion of APP in this study was higher than in North America (16%) and Europe (23%) (Gallego et al., 2012a). APP was most widely practiced in Vietnam and Japan, which is probably due to local clinical traditions (Niemi et al., 2010). Previous studies found that risperidone was usually involved in APP prescription in Japan (Kishimoto et al., 2013), while quetiapine and clozapine were often involved in APP prescription in the USA (Correll et al., 2011). Different health care polices, drug availability and prices could partly account for the discrepancy in APP prescriptions across countries. Although APP may have superior efficacy to monotherapy (Barbui et al., 2009; Correll et al., 2009), it increases the risk of adverse events, discontinuation rate, treatment cost and hospitalization (Elie et al., 2010; Essock et al., 2011; Gallego et al., 2012b; Tiihonen et al., 2012). APP should be used conservatively; most APP could be switched to monotherapy successfully (Essock et al., 2011). Depressive symptoms are common in schizophrenia and associated with negative consequences (Conley, 2009). Antidepressants are primarily used for comorbid depressive and negative symptoms in schizophrenia (Galling et al., 2018; Helfer et al., 2016), and reduce the risk of suicide (Tiihonen et al., 2012). The proportion of antidepressant use in this study (11.7%) was higher compared to previous REAP surveys (5.3% in 2001, 6.5% in 2004 and 8.7% in 2009) (Xiang et al., 2016), but lower than the figure in the USA (38%) (Chakos et al., 2006). The possible reason for the increasing use of antidepressants may be related to the heightened awareness of comorbid depressive symptoms in schizophrenia in Asian countries (Xiang et al., 2013b). However, there is no compelling evidence for the efficacy of antidepressants in schizophrenia (Himelhoch et al., 2012).

Mood stabilizers and benzodiazepines are frequent adjunctive medications in schizophrenia, especially for aggression and irritability (Citrome and Volavka, 1997). The proportion of mood stabilizers in this study (13.7%) was similar to the figures reported in Australia (10.6%) and Europe (7–19%) (Castle et al., 2002; Haro and Salvador-Carulla, 2006). The proportion of benzodiazepines was 27.8% in this study, which was lower than the figures in Western settings (e.g., 34.9% in Finland) (Tiihonen et al., 2012), as well as the finding of previous three REAP surveys (54%) (Tor et al., 2011). The different government enforcement of benzodiazepines could play an important role in the varied frequency of benzodiazepines across different regions in the world. Benzodiazepines are often used for treating insomnia, anxiety, acute agitation and short-term sedation in schizophrenia (Tor et al., 2011; Xiang et al., 2007a), but their long-term use increases the risk of mortality (Volz et al., 2007). Concurrent use of mood stabilizers and benzodiazepines is associated with increased adverse effects and treatment cost, and reduced treatment adherence (Parepally et al., 2002; Tiihonen et al., 2012).

The frequency of anticholinergic medications (45.6%) was high in this study, but was lower than in previous REAP surveys (66.3% in 2001, 52.8% in 2004 and 54.6% in 2009) (Xiang et al., 2011b) and in Western countries (e.g., 70.1% in Belgium) (De Hert et al., 2007). Frequent anticholinergic prescriptions could be explained by several reasons. First, Asian patients have a lower threshold for both therapeutic and adverse effects of antipsychotic medications than Caucasians (Frackiewicz et al., 1997; Lin and Finder, 1983), although more robust evidence is needed in this area (Zhang-Wong et al., 1998). Asian patients need more anticholinergics for treatment and prophylaxis of EPS. Another reason could be the concern about the worsening clinical condition following the cessation of anticholinergics once they were prescribed for short-term treatment of EPS (Gray and Gournay, 2000; Phillips et al., 1997). Anticholinergic medications increase the risk of sedation and cognitive impairment (D'Souza et al., 2018; San Ang et al., 2017), and should be prescribed with caution.

This study has several limitations. First, the survey did not cover all Asian countries, which could lead to certain selection. Second, due to logistical reasons, psychopathology was not measured using standardized rating scales and the study did not include all Asian countries, therefore the findings could not be generalized to schizophrenia patients in all Asian countries/territories. Nonetheless, the findings still represent a range of clinical settings in large parts of Asia. Third, sample sizes varied across the study sites. Fourth, important variables related to use of psychotropic medications, including the severity of psychotic symptom and characteristics of mental health services, were not recorded due to logistic reasons.

In conclusion, this latest REAP survey found that the psychotropic prescription patterns for adult patients with schizophrenia varied across Asian countries and over time. Regular surveys on psychotropic prescription practices for schizophrenia are crucial to monitor real world pharmacotherapy in Asia.

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Declaration of Competing Interest

The authors had no conflicts of interest related to the topic of the manuscript.

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