

# Suicidal thoughts/acts and clinical correlates in patients with depressive disorders in Asians: results from the REAP-AD study

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**Objective:** Using data from the Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) study, we aimed to present the rates and clinical correlates of suicidal thoughts/acts in patients recruited from a total of 40 centres in 10 Asian countries/areas: China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Singapore, Taiwan, and Thailand.

**Methods:** Data from 1122 patients with depressive disorders in the REAP-AD study were used. The ICD-10 was employed to diagnose depressive episodes and recurrent depressive disorder. The presence or absence of suicidal thoughts/acts and profile of other depressive symptoms was established using the National Institute for Health and Clinical Excellence guidelines for depression. Country/area differences in rates of suicidal thoughts/acts were evaluated with the  $\chi^2$  test. In addition, depressive symptom profiles, other clinical characteristics, and patterns of psychotropic drug prescription in depressed patients with and without suicidal thoughts/acts were compared using analysis of covariance for continuous variables and logistic regression analysis for discrete variables to adjust the effects of covariates.

**Results:** The rates of suicidal thoughts/acts in 10 countries/areas varied from 12.8% in Japan to 36.3% in China. Patients with suicidal thoughts/acts presented more persistent sadness (adjusted odds ratio [aOR] = 2.64,  $p < 0.001$ ), loss of interest (aOR = 2.33,  $p < 0.001$ ), fatigue (aOR = 1.58,  $p < 0.001$ ), insomnia (aOR = 1.74,  $p < 0.001$ ), poor concentration (aOR = 1.88,  $p < 0.001$ ), low self-confidence (aOR = 1.78,  $p < 0.001$ ), poor appetite (aOR = 2.27,  $p < 0.001$ ), guilt/self-blame (aOR = 3.03,  $p < 0.001$ ), and use of mood stabilisers (aOR = 1.79,  $p < 0.001$ ) than those without suicidal thoughts/acts.

**Conclusion:** Suicidal thoughts/acts can indicate greater severity of depression, and are associated with a poorer response to antidepressants and increased burden of illness. Hence, suicidal thoughts/acts can provide a clinical index reflecting the clinical status of depressive disorders in Asians.

Keywords: Asians; depressive disorders; mood stabilisers; suicidal thoughts/acts

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### Significant outcomes

- Analysis of the data from 1122 patients with depressive disorders in the Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) study, showed that the rates of suicidal thoughts/acts of patients with depressive disorders in 10 Asian countries/areas varied from 12.8% in Japan to 36.3% in China.
- Patients with suicidal thoughts/acts presented more persistent loss of interest, fatigue, insomnia, poor concentration, low self-confidence, poor appetite, guilt/self-blame, and use of mood stabilisers than those without suicidal thoughts/acts.
- In Asian patients with depressive disorders, suicidal thoughts/acts can indicate greater severity of depression, and are associated with a poorer response to antidepressants and an increased burden of illness

### Limitations

- Generalisation and extrapolation of our findings should be limited since the REAP-AD study was not designed as an epidemiological study.
- We did not distinguish between suicidal thoughts and acts.
- Comorbid personality problems and emotional disorders can contribute to the use of mood stabilisers by depressed patients with suicidal thoughts/acts but these conditions were not evaluated in our study.

### Introduction

Major depressive disorder (MDD) is closely associated with suicide and/or suicide attempts (1). Several factors, such as type-D personality and alcoholism, have been proposed as intervening variables linking suicidality and MDD (2,3). The Suicide Prevention Resource Guide of the Massachusetts Government has described the evidence for a close relationship between suicide and depression as follows: (i) an increased risk of suicide has been reported in 50% of patients with depressive disorders; (ii) about 60% of patients who commit suicide suffer previously from depressive disorders; (iii) the risk of suicide in patients with depressive disorders is about 20-fold greater than in the general population; and (iv) patients with multiple episodes of depressive disorder are at greater risk of suicide than those with one episode (4). In addition, in the Australian National Survey of Mental Health and Wellbeing, death and suicidal thoughts, among depressive symptom profiles, were regarded as reflecting the severe end of the depression continuum (5). In a comparison of symptom profiles between Korean and American outpatients with MDD, it was found that suicidal ideation/gesture and hypochondriasis were more common in Koreans than in Americans, whereas depressive mood and feelings of guilt were more common in Americans (6). Suicide deaths in most countries were found to be more frequent in men than women, whereas those in China were found to be more frequent in women rather than men since suicidal behaviours of women in China were associated with low status and negative life-events (7,8).

### Aims of the study

The Research on Asian Psychotropic Prescription Patterns for Antidepressants (REAP-AD) study has provided data on the general and clinical characteristics and patterns of psychotropic drug use in patients with depressive disorders in 10 Asian countries/areas: China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Singapore, Taiwan, and Thailand. The study is the largest international survey of antidepressant use in Asian regions and partially reflects the overall trend of depressive symptom profiles and patterns of psychotropic drug use, although it was limited to the aspects covered by an epidemiological study (9–14). Using data from the REAP-AD study, we aimed to (i) present international differences in rates of suicidal thoughts/acts, and (ii) identify the clinical correlates of suicidal thoughts (including other depressive symptom profiles and patterns of psychotropic drug use).

### Materials and methods

#### Study overview

In the REAP-AD study (9–14), 2470 patients who had used antidepressants were enrolled in 40 psychiatric centres in 10 Asian countries/areas during the period March–June 2013; patients in departments of medicine or surgery were excluded. The 2470 patients comprised 350 Chinese, 81 Hong Kongers, 309 Indians, 269 Indonesians, 246 Japanese, 259 Koreans, 311 Malaysians, 135 Singaporeans, 199 Taiwanese, and 311 Thais. The 40 survey centres

consisted of four in China, one in Hong Kong, five in India, four in Indonesia, five in Japan, four in Korea, six in Malaysia, two in Singapore, four in Taiwan, and five in Thailand. The institutional review boards of the survey centres approved the study procedures and the informed consent forms. A consensus conference was held before the start of the study to guarantee consistency of data collection and diagnosis between centres. All demographic and clinical variables of the patients were collected by research coordinators or clinical psychiatrists at the survey centres.

### Study subjects

A sub-sample of patients in the REAP-AD study served as the subjects of our study. Inclusion criteria were as follows: (i) diagnosis of depressive episode (F32) or recurrent depressive episode (F33), made by clinical psychiatrists and based on the International Classification of Diseases and Related Health Problems, 10th revision (ICD-10) (15) and (ii) age  $\geq 18$  and  $\leq 80$  years. Exclusion criteria were: (i) comorbid diagnosis of organic mental disorders, schizophrenia, bipolar disorders, or intellectual developmental disorders and (ii) comorbid seizure disorders and other neurological diseases. Finally, a total of 1122 patients with depressive disorders were enrolled.

### Baseline characteristics

The 10 Asian countries/areas were grouped on the basis of geographic region and income level. Using the United Nations classification, China, Hong Kong, Japan, Korea, and Taiwan were defined as East Asia; Indonesia, Malaysia, Singapore, and Thailand as South-East Asia; and India as South Asia (10,11). Using the World Bank income designation, Hong Kong, Japan, Korea, Singapore, and Taiwan were defined as high-income countries/areas; China, Malaysia, and Thailand as upper-middle income countries/areas; and India and Indonesia as lower-middle income countries/areas (10,11). These groups were transformed to dummy variables as follows: geographic region grouping (East Asia and South/South-East Asia) and income level grouping (high-income countries and upper- and lower-middle income countries/areas).

### Suicidal thoughts/acts and other depressive symptom profiles

Suicidal thoughts/acts and other depressive symptom profiles (persistent sadness, loss of interest, fatigue, insomnia, poor concentration, low self-confidence, poor appetite, agitation/retardation, and guilt/self-blame) were evaluated using the 10 depressive symptoms listed in the National Institute for Health and Clinical Excellence

guidelines for depressive disorders (16). The degree of depression was defined by the number of symptoms:  $<4$  indicated subthreshold depression, 4 indicated mild depression, 5 or 6 indicated moderate depression, and  $>6$  indicated severe depression.

Anxiety and somatic, psychotic, and other mental symptoms were evaluated. Comorbid psychiatric disorders, including mental and behavioural disorders caused by psychoactive substance abuse (F1) and neurotic, stress-related, and somatoform disorders (F4), were also assessed. Comorbid physical diseases, including chronic obstructive pulmonary disease, rheumatic disease, peptic ulcer disease, mild liver disease, diabetes mellitus, renal disease, moderate to severe liver disease, malignancy, AIDS/HIV, and other medical illnesses were also evaluated.

### Patterns of psychotropic drug use

Based on the Anatomical Therapeutic Chemical Classification index of the World Health Organization Collaborating Center for Drug Statistics Methodology, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, norepinephrine and dopamine reuptake inhibitors, mixed noradrenergic-serotonergic antidepressants, selective norepinephrine reuptake inhibitors and serotonin receptor antagonists were considered newer antidepressants; tricyclic antidepressants and monoamine oxidase inhibitors (both irreversible and reversible) were considered older antidepressants (10,11). In relation to the introduction of clozapine, antipsychotics were divided into first- and second-generation (17).

### Statistical analysis

International differences in rates of suicidal thoughts/acts among the patients were evaluated using the  $\chi^2$  test. General and clinical characteristics and patterns of psychotropic drug use were compared in patients with and without suicidal thoughts/acts using independent *t*-tests for continuous variables and  $\chi^2$  tests for discrete variables. Logistic regression analysis for discrete variables controlled for the potential effects of covariates. To reduce the family wise error rate in multiple comparisons, statistical significance was set at  $p < 0.01$  (two-tailed) for all tests. SPSS 21 for Windows (SPSS Inc., Chicago, IL, USA) was used for all the statistical analyses.

## Results

### Country/area differences in rates of suicidal thoughts/acts

The overall rate of suicidal thoughts/acts in the 1122 patients was 23.1%. The rates for individual

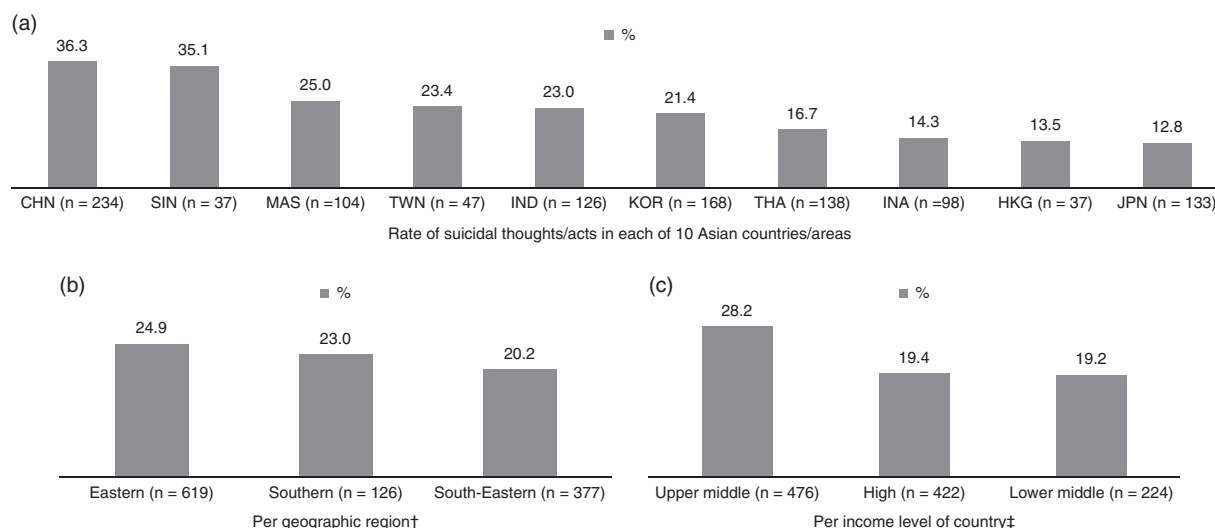


Fig. 1. Rates of suicidal thoughts/acts among 1122 depressed patients in 10 Asian countries/areas.

† Defined by United Nations classification: Eastern Asia (China, Hong Kong, Japan, Korea and Taiwan), Southern Asia (India) and South-Eastern Asia (Indonesia, Malaysia, Singapore and Thailand).

‡ Defined by World Bank designation: High income countries/areas (Hong Kong, Japan, Korea, Singapore and Taiwan), upper middle income countries/areas (China, Malaysia and Thailand) and lower middle income countries/areas (India and Indonesia).

countries/areas varied from 12.8% in Japan to 36.3% in China (Fig. 1a). The geographic regions are ranked in order of the rate of suicidal thoughts/acts in Fig. 1b: Eastern Asia, 24.9%; Southern Asia, 23.0%; and South-Eastern Asia, 20.2%. Country/area income levels are ranked in order of rate of suicidal thoughts/acts in Fig. 1c: upper-middle income countries/areas, 28.2%; high-income countries/areas, 19.4%; and lower-middle income countries/areas, 19.2%.

Baseline characteristics of patients with and without suicidal thoughts/acts

Patients with suicidal thoughts/acts were more often treated in public settings ( $\chi^2 = 14.97, p < 0.001$ ) and enrolled as inpatients ( $\chi^2 = 83.62, p < 0.001$ ) than those without suicidal thoughts/acts (Table 1). Although the differences were not significant, those with suicidal thoughts/acts tended to be younger ( $t = -2.05, p = 0.04$ ) and from high-income countries ( $\chi^2 = 5.08, p = 0.02$ ). There were no significant differences by sex ( $\chi^2 = 2.95, p = 0.09$ ), geographic region ( $\chi^2 = 2.51, p = 0.11$ ) or diagnosis ( $\chi^2 = 0.16, p = 0.69$ ) between patients with and without suicidal thoughts/acts, although previous studies have reported that sex and geographic region were potential contributors to suicidal behaviours in depressive disorders (3,7, 18–20). Thus, using a conservative method, age, sex, treatment setting, and enrolment setting were defined as the covariates in the following statistical analyses.

Other depressive symptom profiles of patients with and without suicidal thoughts/acts

After adjusting the effects of the covariates, patients with suicidal thoughts/acts presented significantly more persistent sadness (adjusted odds ratio [aOR] = 2.64,  $p < 0.001$ ), loss of interest (aOR = 2.33,  $p < 0.001$ ), fatigue (aOR = 1.58,  $p < 0.001$ ), insomnia (aOR = 1.74,  $p < 0.001$ ), poor concentration (aOR = 1.88,  $p < 0.001$ ), low self-confidence (aOR = 1.78,  $p < 0.001$ ), poor appetite (aOR = 2.27,  $p < 0.001$ ) and guilt/self-blame (aOR = 3.03,  $p < 0.001$ ) than those without suicidal thoughts/acts; the exception was agitation/retardation (aOR = 1.18,  $p = 0.36$ ) (Table 2). In terms of degree of depression, taking subthreshold depression as the reference category, patients with suicidal thoughts/acts were characterised by higher rates of moderate (aOR = 6.34,  $p < 0.001$ ) and severe (aOR = 16.60,  $p < 0.001$ ) depression and by a low rate of mild depression (aOR = 0.60,  $p < 0.001$ ).

In addition, those with suicidal thoughts/acts tended to show a higher rate of comorbid physical disease (aOR = 1.47,  $p = 0.02$ ), although the difference was not significant. There were no significant differences between patients with and without suicidal thoughts/acts in relation to other symptom profiles (aOR = 0.95,  $p = 0.99$ ), including anxiety symptoms (aOR = 0.49,  $p = 0.21$ ), somatic symptoms (aOR = 1.39,  $p = 0.56$ ), and psychotic symptoms (aOR = 1.61,  $p = 0.40$ ), no differences in comorbid psychiatric disorders including substance abuse (aOR = 0.74,  $p = 0.60$ ), and anxiety and somatoform disorders (aOR = 1.67,  $p = 0.07$ ).

## Suicidal thoughts/acts in depressive disorders in Asians

Table 1. General characteristics of depressed patients with and without suicidal thoughts/acts in 10 Asian countries/areas

	Total sample ( <i>n</i> = 1122)	Suicidal thoughts/acts		Statistical coefficients	Unadjusted <i>p</i> value	Adjusted <i>p</i> value*
		Presence ( <i>n</i> = 259)	Absence ( <i>n</i> = 863)			
Age, mean (SD) years	48.1 (15.6)	46.3 (15.4)	48.6 (15.6)	<i>t</i> = -2.05	0.04	–
High-income level country [ <i>n</i> (%)] <sup>§</sup>	422 (37.6)	82 (31.7)	340 (39.4)	$\chi^2$ = 5.08	0.02	–
Treatment setting [ <i>n</i> (%)]				$\chi^2$ = 14.97	<0.001	–
Public	842 (75.0)	218 (84.2)	624 (72.3)			
Private	280 (25.0)	41 (15.8)	239 (27.7)			
Hospital setting [ <i>n</i> (%)]				$\chi^2$ = 2.45	0.48	–
Psychiatric	419 (37.3)	92 (35.5)	327 (27.9)			
General	119 (10.6)	29 (11.2)	90 (10.4)			
University-affiliated psychiatric	77 (6.9)	23 (8.9)	54 (6.3)			
University-affiliated general	507 (45.2)	115 (44.4)	392 (45.4)			
Outpatient enrolment [ <i>n</i> (%)]	806 (71.8)	128 (49.4)	678 (78.6)	$\chi^2$ = 83.62	<0.001	–
Diagnosis (ICD-10)				$\chi^2$ = 0.16	0.69	0.62
Depressive episode (F32) [ <i>n</i> (%)]	843 (75.1)	197 (76.1)	646 (74.9)			
Recurrent depressive disorder (F33) [ <i>n</i> (%)]	279 (24.9)	62 (22.2)	217 (25.1)			

\* Adjusted for the effects of age, sex, treatment setting, and enrolment setting.

<sup>§</sup> Defined by World Bank designation: High income countries/areas (Hong Kong, Japan, Korea, Singapore and Taiwan), upper middle income countries/areas (China, Malaysia and Thailand) and lower middle income countries/areas (India and Indonesia).

Table 2. Depressive symptom profiles and clinical characteristics of depressed patients with and without suicidal thoughts/acts in 10 Asian countries/areas

	Total sample ( <i>n</i> = 1122)	Suicidal thoughts/acts		Statistical coefficients ( $\chi^2$ )	Unadjusted <i>p</i> value	Adjusted <i>p</i> value*
		Presence ( <i>n</i> = 259)	Absence ( <i>n</i> = 863)			
Depressive symptom profiles						
Persistent sadness [ <i>n</i> (%)]	822 (73.3)	222 (85.7)	600 (69.5)	26.65	<0.001	<0.001
Loss of interest [ <i>n</i> (%)]	600 (53.5)	176 (68.0)	424 (49.1)	28.37	<0.001	<0.001
Fatigue [ <i>n</i> (%)]	514 (45.8)	138 (53.3)	376 (43.6)	7.57	<0.001	<0.001
Insomnia [ <i>n</i> (%)]	725 (64.6)	190 (73.4)	535 (62.0)	11.26	<0.001	<0.001
Poor concentration [ <i>n</i> (%)]	336 (29.9)	99 (38.2)	237 (27.5)	11.00	<0.001	<0.001
Low self-confidence [ <i>n</i> (%)]	263 (23.4)	83 (2.0)	180 (20.9)	13.90	<0.001	<0.001
Poor appetite [ <i>n</i> (%)]	370 (33.0)	127 (49.0)	243 (28.2)	39.29	<0.001	<0.001
Agitation/retardation [ <i>n</i> (%)]	257 (22.9)	61 (23.6)	196 (22.7)	0.08	0.78	0.36
Guilt/self-blame [ <i>n</i> (%)]	179 (16.0)	79 (30.5)	100 (11.6)	53.15	<0.001	<0.001
Degree of depression				177.61	<0.001	–
Subthreshold depression [ <i>n</i> (%)]	504 (44.9)	42 (16.2)	462 (53.5)			–
Mild depression [ <i>n</i> (%)]	197 (17.6)	41 (15.8)	156 (18.1)			<0.001 <sup>†</sup>
Moderate depression [ <i>n</i> (%)]	291 (25.9)	99 (38.2)	192 (22.2)			<0.001 <sup>†</sup>
Severe depression [ <i>n</i> (%)]	130 (11.6)	77 (6.9)	53 (6.1)			<0.001 <sup>†</sup>
Other symptom profiles [ <i>n</i> (%)]	174 (15.5)	50 (19.3)	124 (14.4)	3.71	0.05	0.27
Anxiety symptoms [ <i>n</i> (%)]	20 (1.8)	3 (1.2)	17 (2.0)	0.75	0.39	0.56
Somatic symptoms [ <i>n</i> (%)]	15 (1.3)	6 (2.3)	9 (1.0)	2.45	0.12	0.62
Psychotic symptoms [ <i>n</i> (%)]	15 (1.3)	6 (2.3)	9 (1.0)	2.45	0.12	0.40
Comorbid mental disorder						
Substance abuse (F1) [ <i>n</i> (%)]	20 (1.8)	4 (1.5)	16 (1.9)	0.11	0.74	0.60
Anxiety and somatoform disorders (F4) [ <i>n</i> (%)]	85 (7.6)	21 (8.1)	64 (7.4)	0.14	0.71	0.07
Comorbid physical disease [ <i>n</i> (%)]	327 (29.1)	86 (33.2)	241 (27.9)	2.69	0.10	0.02

\* Adjusted for the effects of age, sex, treatment setting, and enrolment setting.

<sup>†</sup> Multinomial logistic regression analysis with subthreshold depression as reference category.

Patterns of psychotropic drug use in patients with and without suicidal thoughts/acts

After adjusting the effects of the covariates, it was found that patients with suicidal thoughts/acts were

more frequently prescribed mood stabilisers than those without suicidal thoughts/acts (aOR = 1.78, *p* < 0.001). In addition, those with suicidal thoughts/acts tended to be prescribed more combination antidepressant treatments (aOR = 1.44, *p* = 0.03)



Table 3. Patterns of psychotropic drug use of depressed patients with and without suicidal thoughts/acts in 10 Asian countries/areas

	Total sample ( <i>n</i> = 1122)	Suicidal thoughts/acts		Statistical coefficients ( $\chi^2$ )	Unadjusted <i>p</i> value	Adjusted <i>p</i> value*
		Presence ( <i>n</i> = 259)	Absence ( <i>n</i> = 863)			
<b>Antidepressant</b>						
Combination treatment [ <i>n</i> (%)]	283 (25.2)	76 (29.3)	207 (24.0)	3.03	0.08	0.03
Newer antidepressant [ <i>n</i> (%)]	849 (75.7)	197 (76.1)	652 (75.6)	0.03	0.87	0.76
<b>Adjunctive medication</b>						
Any antipsychotic [ <i>n</i> (%)]	368 (32.8)	98 (37.8)	270 (31.3)	3.88	0.05	0.87
First-generation antipsychotic [ <i>n</i> (%)]	107 (9.5)	26 (10.0)	81 (9.4)	0.10	0.75	0.93
Second-generation antipsychotic [ <i>n</i> (%)]	290 (25.8)	79 (30.5)	211 (24.4)	3.81	0.05	0.93
Mood stabiliser [ <i>n</i> (%)]	229 (20.4)	78 (30.1)	151 (17.5)	19.53	<0.001	<0.001
Anxiolytic [ <i>n</i> (%)]	333 (29.7)	78 (23.4)	255 (29.5)	0.03	0.86	0.69
Hypnotic [ <i>n</i> (%)]	146 (13.0)	33 (12.7)	113 (13.1)	0.02	0.88	0.44
Antiparkinson medication [ <i>n</i> (%)]	58 (5.2)	11 (4.2)	47 (5.4)	0.58	0.45	0.05

\* Adjusted for the effects of age, sex, geographic region, income level of country/area, treatment setting, and enrolment setting.

and antiparkinson medication (aOR = 0.50,  $p = 0.05$ ), although the differences were not significant. There were no significant differences in use of newer antidepressants (aOR = 0.95,  $p = 0.76$ ), any antipsychotics (aOR = 0.99,  $p = 0.93$ ), first-generation antipsychotics (aOR = 0.82,  $p = 0.43$ ), second-generation antipsychotics (aOR = 0.99,  $p = 0.93$ ), anxiolytics (aOR = 0.94,  $p = 0.69$ ), and hypnotics (aOR = 0.84,  $p = 0.44$ ) (Table 3).

## Discussion

To our knowledge, variation in rates of suicidal behaviour among Asian countries/areas has rarely been reported in the past. In addition, depressed patients with suicidal thought/acts presented more additional depressive symptoms including persistent sadness, fatigue, insomnia, loss of interest, poor concentration, low self-confidence, poor appetite, and guilt/self-blame. They were also more often prescribed mood stabilisers than those without suicidal thoughts/acts.

A previous study found that unemployed status was associated with high suicidality in MDD patients in six Asian countries/areas (China, Korea, Malaysia, Singapore, Thailand, and Taiwan) (21). In addition, a community-based study showed that the subjective sense of economic status can be an important contributory factor for depression and psychosocial impairment in elderly people in three Asian countries/areas (Japan, Korea, and Taiwan) (22). A preponderance of women over men for suicides may be a phenomenon limited to China. Women in rural areas of China suffer greater suicidal risks than women in urban regions (23). In addition, the suicide rate among the Chinese elderly is the highest in the

world and, more specifically, their risk is higher in Northern China and in rural areas (24).

In our study, the relatively high rate of suicidal thoughts/acts in depressed patients in Malaysia is striking, because the prevalence of suicidal ideation in Malaysian people has previously been found to be relatively low and Malaysian law has defined attempted suicide as a crime (25,26). It can be speculated that, despite suppression by social regulation, suicidal ideation and/or intent may be overtly presented by depressed patients in Malaysia. Differences in suicidal behaviour in geographic regions can reflect variations in ethnic groups, cultures, and religions. In addition, colonialism, globalisation, industrialisation, and urbanisation have continuously affected religious affiliations and other cultural contexts in Asia (27). Among the geographic factors, religious affiliation has been proposed as the strongest cultural influence on suicidal behaviours (28). There have been many different religions in Asia: roughly speaking, Confucianism and Buddhism have been predominant in East Asia; Islam, Buddhism, and Hinduism in South-East Asia; and Hinduism and Islam in South Asia. More specifically in East Asia, Christianity (Protestantism and Catholicism) has been also predominant in Korea and Shintoism in Japan, and some religious activities have been prohibited under regulation of the communist government in mainland China. Paradoxically, Confucianism and Buddhism have reduced suicidal ideation but lead to a greater stigma for suicidal survivors (8). Religious affiliations were not addressed in our analysis, but heterogeneity of religious affiliations in the different geographic regions of Asia might have contributed to the observed lack of significant differences in the rates of suicidal thoughts/acts. Further study is needed on the association between religious

affiliations and suicidal thoughts/acts in depressed patients in the Asian region.

In our study, with the exception of agitation/retardation, other depressive symptom profiles were significantly more common in patients with suicidal thoughts/acts than those without. In terms of degree of depression, those with suicidal thoughts/acts had more moderate and severe depression and less mild depression than those without suicidal thoughts/acts. These findings are partly consistent with previous findings in Asian regions: for example, in Koreans, despite 12-week antidepressant treatment, suicidal ideation persisted significantly in patients with moderate to severe depression (29); in Han Chinese women, recurrent MDD patients with suicidality presented more MDD symptoms and more melancholia (30); and in Japanese patients, suicidal ideation was associated with moderate to severe depression (31). In addition, reduced projections to the orbitofrontal cortex and thalamus have been considered distinctive neural correlates of depressed patients with a history of suicidal attempts (32). On the basis of neurobiological underpinnings, suicidal thoughts/acts can reflect a greater severity of depressive disorder in Asians, despite the cultural variations in presenting depressive symptom profiles.

With regard to psychotropic medication, adjunctive use of mood stabilisers in our study was more common in patients with suicidal thoughts/acts than in those without. These findings can be partly explained by the anti-suicidal properties of lithium and other mood stabilisers (33). Hantouche et al. (34) have shown that, in terms of mood stabiliser augmentation in patients with unipolar MDD, poor responders present higher levels of suicidal thoughts than good responders. Adjunctive use of mood stabilisers has been associated with prolongation of length of hospital stay in patients with late-onset depression (35). Thus, it can be speculated that depressed patients with suicidal thoughts/acts are associated with poorer response to one or more antidepressants and poorer prognosis. There were no differences in the use of other psychotropic drugs between those with and without suicidal thoughts/acts in our findings. Nevertheless, a previous study showed that pharmacotherapy and interpersonal psychotherapy can reduce suicidal ideation in depressed patients (36). These subtle discrepancies cannot be simply explained and may be associated with the possibility that non-biological factors can shape patterns of psychotropic medication prescription.

There are several limitations to our study. First, generalisation or extrapolation of our findings must be limited, because the REAP-AD study was not designed as a form of epidemiological study. Second, data on religious affiliation and other sociodemographic

characteristics were not collected; therefore, the country-wise differences in rates of suicidal behaviour have limited value. Third, data on psychosocial approaches to suicidality and depression were not collected; thus, psychiatric treatments associated with suicidal thoughts/acts are only partly understood. Fourth, the design of the REAP-AD study was not longitudinal but cross-sectional. Fifth, we did not distinguish between suicidal thoughts and acts. Sixth, comorbid personality problems and emotional disorders can contribute to the use of mood stabilisers by depressed patients with suicidal thoughts/acts but these conditions were not evaluated in our study. Seventh, differences in cultural background, economic status, and other confounding factors may contribute to the relationships between depressive symptom profiles and suicidal thoughts/acts and between patterns of psychotropic drug use and suicidal thought/acts. In addition, genetic influences on the pharmacokinetics of psychopathology, and non-biological factors shaped mainly by culture, may contribute to patterns of psychotropic drug use (37).

Despite its limitations, our study has the strength of exploring the variation and clinical correlates of suicidal thoughts/acts in depressed patients in 10 Asian countries/areas. It can be concluded that, in Asian patients with depressive disorders, suicidal thoughts/acts can indicate greater severity of depression, and are associated with a poorer response to antidepressants and an increased burden of illness. Proactive screening and treatment for suicidal thoughts/acts is recommended in Asians with depressive disorders.

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None.

### Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.



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