Institute Name

Human Subject Protocol Application

Submission Date:
Beginning Date:
Type of Project: Survey
Type of Funding Support:
Investigator information:

1. Background and Purpose:

Research on Asian Psychotropic prescription study (REAP) is an organization formed by psychiatrists, pharmacologists, epidemiologists, and researchers in Asia. Since 2001, REAP has completed four prescription patterns of antipsychotics (schizophrenia), two surveys of antidepressants (major depression), and one prescription pattern analysis of mood stabilizers (affective disorders). The cumulative research has involved more than 600 psychiatrists, more than 100 psychiatric medical units, and 13,500 patients in the data analysis of REAP; so far, more than 90 research reports have been published in international journals. Major depressive disorder is a common mental health disorder that affects approximately 280 million people worldwide. World Health Organization research data shows that the number of major depressive illnesses worldwide increased from 172 million in 1990 to 258 million in 2017, an increase of nearly 50%. Given the rising incidence of major depression, it's no surprise that the consumption of antidepressants is increasing every year. With the development of some new antidepressants with different pharmacological mechanisms, clinical prescriptions and treatment models are gradually applied to other mental disorders besides major depression. At present, many western countries have conducted relevant research on this issue. In Asia, we hope to use this survey to understand changes in antidepressant prescribing patterns in these regions. In addition, since the COVID-19 pandemic has been an important social issue in every country in recent years, regardless of whether it is infected or not, it will affect the physical and mental health and quality of life of individuals, and a pathological social withdrawal (Hikikomori), so this study will also collect information on related issues. The results of this study can provide clinicians with information on antidepressant prescription patterns in various countries, analyze the impact of COVID-19 on patients, and provide reference for competent authorities to formulate policies.

2. Design, Procedures and Methods:

This is an international, multiple sites, cross-sectional survey of antidepressant prescriptions of patients, with around half will be recruited from outpatient clinics and the other half from inpatient wards. Overall, the aim is to recruit at least 2000 subjects from the 16 countries for this study.   Followings are the participating countries:

1. China   2. Hong Kong   3. Japan   4. Korea   5. Singapore   6. Taiwan   7. India   8. Malaysia   9. Thailand   10. Indonesia   11. Bangladesh   12. Myanmar   13. Pakistan   14. Sri Lanka   15. Vietnam   16. Iran.

Convenience sampling method will be used to enroll the study subjects. Each country will decide which center (Research institutes and hospitals) will participate in the survey. From each country and area, the maximum number of centers will be six. In total, it is expected that there will be 60-80 centers to participate in the study from Asia. The minimum number of cases to be collected will be 30 and the maximum 60 from each site. The total patient number is expected to be around 3000 in this surveys (100-300 cases from 16 countries).

Data including diagnosis, demographics, daily medications regimen, laboratory checks, side effects, comorbidities, and self-rated questionnaires will be collected using internet web-based data key-in system to analysis the prescription patterns. The self-rated questionnaires include: 1. Nine questions of the Patient Health Questionnaire-9 (PHQ-9); 2. Seven questions of the Generalized Anxiety Disorder 7 (GAD-7); Seven questions of the Fear of COVID-19 Scale and experiences of COVID-19; and Twenty-five questions of the One month version of Hikikomori Questionnaire (HQ-25M) according to your current situation (Appendix).

The total time spent by one patient will be about 30 to 40 minutes.

3. Timeline:

This study will enroll patients taking antidepressants. The study timeline is from 1 March to 30June.

4. Measures and Data to be Collected:

Data including diagnosis, demographics, daily medications regimen, laboratory checks, side effects, comorbidities, and self-rated questionnaires will be collected using internet web-based data key-in system to analysis the prescription patterns. The self-rated questionnaires include: 1. Nine questions of the Patient Health Questionnaire-9 (PHQ-9); 2. Seven questions of the Generalized Anxiety Disorder 7 (GAD-7); Seven questions of the Fear of COVID-19 Scale and experiences of COVID-19; and Twenty-five questions of the One month version of Hikikomori Questionnaire (HQ-25M) according to your current situation. The total time spent by

one patient will be about 30 to 40 minutes.

Analyses of data will be done using the Statistical Package for Social Sciences (SPSS). Normality of distributions of continuous measures will be checked using Kolmogorov-Smirnov one-sample test. Differences between groups will be tested by ANOVA (t-test) for normally distributed data, non-parametric Mann Whitney U tests for non-normally distributed continuous data and by contingency table for categorical variables. Averages will be reported as means ± standard deviation (SD) for continuous variables, risk estimates will be reported as odds ratios (OR) with their 95% confidence interval (CI). Multiple regression analyses are used to examine the association between the relevant variables.

5. Confidentiality of Records/Data and Privacy:

The data obtained from the research will be posted anonymously in the computer database. A total of 16 Asian countries participated in this study, and researchers from each country posted their research data in this database. Including 1. China 2. Hong Kong 3. Japan 4. Korea 5. Singapore 6. Taiwan 7. India 8. Malaysia 9. Thailand 10. Indonesia 11. Bangladesh 12. Myanmar 13. Pakistan 14. Sri Lanka 15. Vietnam 16. Iran . This database is established in Taiwan Ruifuyi Co., Ltd., and the person in charge of preservation is Dr. Shih-Ku Lin from Taipei Chang Gung Memorial Hospital. The preservation period is 5 years. This database is available to each Country Coordinator from all participating countries.
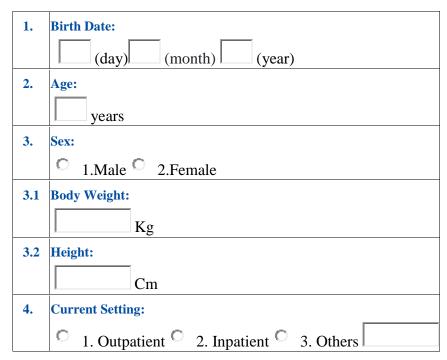
Appendix 1.

List of Antidepressants

code	generic name	code	generic name	code	generic name	code	generic name
101	agomelatine	116	doxepin	131	maprotiline	146	paroxetine
102	alaproclate	117	duloxetine	132	medifoxamine	147	phenelzine
103	amineptine	118	escitalopram	133	melitracen	148	pivagabine
104	amitriptyline	119	etoperidone	134	mianserin	149	protriptyline
105	amoxapine	120	fluoxetine	135	milnacipran	150	quinupramine
106	bifemelane	121	fluvoxamine	136	minaprine	151	reboxetine
107	bupropion	122	gepirone	137	mirtazapine	152	sertraline
108	butriptyline	123	Hyperici herba**	138	moclobemide	153	tianeptine
109	citalopram	124	imipramine oxide	139	nefazodone	154	toloxatone
110	clomipramine	125	imipramine	140	nialamide	155	tranylcypromine
111	desipramine	126	iprindole	141	nomifensine	156	trazodone
112	desvenlafaxine	127	iproclozide	142	nortriptyline	157	trimipramine
113	dibenzepin	128	iproniazide	143	opipramol	158	tryptophan
114	dimetacrine	129	isocarboxazid	144	oxaflozane	159	venlafaxine
115	dosulepin (dothiepin)	130	lofepramine	145	oxitriptan	160	vilazodone
						161	viloxazine
						162	zimeldine
						163	desvenlafaxine
						164	esketamine
						165	vortioxetine

Appendix 2. Rating Scales

1. Data form with socio-demographic, clinical and prescription details

Profile of this patient

1.	**Birth Date:**
	☐ (day) ☐ (month) ☐ (year)
2.	**Age:**
	☐ years
3.	**Sex:**
	◯ 1.Male ◯ 2.Female
3.1	**Body Weight:**
	☐ Kg
3.2	**Height:**
	☐ Cm
4.	**Current Setting:**
	◯ 1. Outpatient ◯ 2. Inpatient ◯ 3. Others ☐

2. Depressive Symptoms (NICE guideline)

Please check the targeted depressive symptoms to prescribe antidepressants for this patient (more than one).

- ☐ 1. Persistent sadness or low mood
- ☐ 2. Loss of interests or pleasure
- ☐ 3. Fatigue or low energy
- ☐ 4. Disturbed sleep
- ☐ 5. Poor concentration or indecisiveness
- ☐ 6. Low self-confidence
- ☐ 7. Poor or increased appetite
- ☐ 8. Suicidal thoughts or acts
- ☐ 9. Agitation or slowing of movements
- ☐ 10. Guilt or self-blame

3. Patient Health Questionnaire-9 (PHQ-9)

Over the last two weeks, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things?	0	1	2	3
2. Feeling down, depressed, or hopeless?	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much?	0	1	2	3
4. Feeling tired or having little energy?	0	1	2	3
5. Poor appetite or overeating?	0	1	2	3
6. Feeling bad about yourself - or that you are a failure or have let yourself or your family down?	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television?	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual?	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way?	0	1	2	3

4. Generalized Anxiety Disorder 7 (GAD-7)

Over the last 2 weeks, how often have you been bothered by the following problems?

	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

5. Fear of COVID-19 Scale (FCV-19S)

Please respond to each item by ticking (√) one of the five (5) responses that reflects how you feel, think, or act toward COVID-19

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1. I am most afraid of Corona	1	2	3	4	5
2. It makes me uncomfortable to think about Corona	1	2	3	4	5
3. My hands become clammy when I think about Corona	1	2	3	4	5
4. I am afraid of losing my life because of Corona	1	2	3	4	5
5. When I watch news and stories about Corona on social media, I become nervous or anxious	1	2	3	4	5
6. I cannot sleep because I'm worrying about getting Corona	1	2	3	4	5
7. My heart races or palpitates when I think about getting Corona	1	2	3	4	5

6. One Month Version of Hikikomori Questionnaire (HQ-25)

Over the <u>LAST MONTH</u>, how accurately do the following statements describe you?

		Strongly disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Strongly agree
1.	I stay away from other people.	0	1	2	3	4
2.	I spend most of my time at home.	0	1	2	3	4
3.	There really isn't anyone with whom I can discuss matters of importance.	0	1	2	3	4
4.	I love meeting new people.	0	1	2	3	4
5.	I shut myself in my room.	0	1	2	3	4
6.	People bother me.	0	1	2	3	4
7.	There are people in my life who try to understand me.	0	1	2	3	4
8.	I feel uncomfortable around other people.	0	1	2	3	4
9.	I spend most of my time alone.	0	1	2	3	4
10.	I can share my personal thoughts with several people.	0	1	2	3	4
11.	I don't like to be seen by others.	0	1	2	3	4
12.	I rarely meet people in-person.	0	1	2	3	4
13.	It is hard for me to join in on groups.	0	1	2	3	4
14.	There are few people I can discuss important issues with.	0	1	2	3	4
15.	I enjoy being in social situations.	0	1	2	3	4

		Strongly disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Strongly agree
16.	I do not live by society's rules and values.	0	1	2	3	4
17.	There really isn't anyone very significant in my life.	0	1	2	3	4
18.	I avoid talking with other people.	0	1	2	3	4
19.	I have little contact with other people talking, writing, and so on.	0	1	2	3	4
20.	I much prefer to be alone than with others.	0	1	2	3	4
21.	I have someone I can trust with my problems.	0	1	2	3	4
22.	I rarely spend time alone.	0	1	2	3	4
23.	I don't enjoy social interactions.	0	1	2	3	4
24.	I spend very little time interacting with other people.	0	1	2	3	4
25.	I strongly prefer to be around other people.	0	1	2	3	4