

Original Research

Psychological effects on self-medication during the pandemic COVID-19 in WP Labuan: A development of questionnaire and pilot-testing

Michelle L Tan , Shamsur Rahman , Freddie Robinson , Mohd Hijaz Mohd Sani 

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Abstract

Introduction: Self-Medication, which is a practice to self-treat using medicine without consulting a medical practitioner or a doctor, is a common practice and the Pandemic Covid-19 may have caused people to resort to self-medication in order to reduce the infectivity of the Covid-19. **Objective:** To validate and develop an instrument in Bahasa Melayu to assess the psychological distress and self-medication during pandemic Covid-19 in WP Labuan. **Methods:** A pilot study was conducted among 160 participants in WP Labuan. Reliability testing on internal consistency and content validity was performed on the adapted Covid-19 Peritraumatic Distress Index (CPDI) as well as domain on knowledge, practice and attitude of self-medication. **Result:** A panel of seven experts evaluated the research instrument for content validity and it was found to have good content item validity. The CPDI domain showed good internal consistency of Cronbach's Alpha of 0.919. The mean (SD) CPDI score of the respondents in WP Labuan was 32.55 (15.98). 64.2% of the respondents experienced psychological distress. The variable for Area (town/countryside) was found to be statistically significant ($p < 0.05$) to be associated with self-medication during the pandemic. **Conclusion:** The instrument established sound reliability and validity and therefore, can be an effective tool for assessing psychological distress and self-medication in the Malaysian population.

Keywords: self-medication; questionnaire; CPDI; Covid-19

INTRODUCTION

Covid-19, also initially known as the novel coronavirus, is a disease that is very infectious and can spread among humans. Covid-19 was initially detected in Wuhan China in December 2019. This outbreak has spread to over 200 countries that caused tremendous concerns on public health worldwide in a short span of time.¹ In March 2020, WHO declared a global pandemic as many countries were affected by the disease. This pandemic caused a serious socio economic crisis due to many people losing their source of income, as well as high mortality and morbidity rates.²

During the pandemic Covid-19 in Malaysia, almost all daily routine has been screeched to a halt especially people who are in non-essential services. Countless services and jobs have been shut down due to the Movement Control Order (MCO). Furthermore, daily statistics and case reports from the Health Ministry as well as healthcare practitioners through social media and electronic media may have an effect on people's awareness about the dire situation of the pandemic and the disease.

According to daily statistics in Malaysia dated in June 2021, WP Labuan has the most incidence and death rate compared to other states due to the rampant spread of the Delta variant, which was approximately 60 per cent more transmissible compared to the Alpha variant and has a higher risk of hospitalization.³ This situation generally may trigger anxiety and stress towards mental health on those who were affected.^{4,5} Many people who are affected resorted to self-care and self-medication in order to reduce the infectivity of the Covid-19.⁶

In addition, the public started to take the matter into their own hands by getting information on Covid-19. The Google Trends search has become a valuable source of information especially on public health topics. The words such as 'self-medication', 'self-care', and 'self-administration' were studied and it was found out that there was a relative increase in the number of searches worldwide since the 2019 coronavirus pandemic was declared. This indicated that there has been an increased interest in the number of public searching for information about self-medication of various ailments during the pandemic.⁷

Self-Medication, which is a practice to self-treat using medicine without consulting a medical practitioner or a doctor, is an ongoing issue globally that affects most countries including developing countries. It is estimated that prevalence of self-medication is 32.5 - 81.5% globally, which indicates it is a very common practice.⁸ The World Health Organization (WHO) emphasized that with proper self-medication, this can help to prevent and manage illness or symptoms that may not require consultation with a doctor. A systematic review in concluded that with proper knowledge and responsibility on self-medication, it can be a crucial alternative to the current healthcare system.⁹ With easy access to medication, this can

Michelle L TAN*. Pharmacy Services Division, Ministry of Health Malaysia, Malaysia. mtan121286@gmail.com

Dr Md Shamsur RAHMAN*. Faculty of Medicine and Health Science, Universiti Malaysia Sabah, Malaysia. shamsur@ums.edu.my

Dr Freddie ROBINSON. Faculty of Medicine and Health Science, Universiti Malaysia Sabah, Malaysia.

Dr Mohd Hijaz Mohd SANI. Faculty of Medicine and Health Science, Universiti Malaysia Sabah, Malaysia.



result in more profits to the pharmaceutical industry as well as reducing consultation time for minor symptoms, especially in a crowded government healthcare where Medical officers tend emergency cases and normal cases simultaneously. Moreover, this also helps in reducing the burden of healthcare expenditure linked to treatment on minor illnesses. With all the benefits mentioned above, Self-medication may have a few downfalls. Self-medication is associated with negative outcomes such as wastage of medications or resources, increased resistance of pathogens, serious adverse drug reactions, prolonged sickness or admission and drug dependence.

Another systematic review concluded that there was a heterogeneous prevalence of self-medications that have not proven to benefit in the prevention or management of Covid-19.¹⁰ These medications such as Antibiotics, Hydroxychloroquine, vitamins or supplements, Ivermectin and antiasthmatics, as stated by the current Covid-19 guidelines by WHO.¹¹

According to the review, the practice of self-medication during the pandemic was assessed and it was found out there were a variety of reasons. One study showed that self-medication was mainly due to experiencing symptoms that related to Covid-19. Other reasons have been noted such as fear of stigmatization, fear of quarantine, affordability, the convenience of self-medication, and patients' belief on the symptoms being mild only. The Common source of self-medication were from pharmacy and patent medicine vendors.

Till date there is a limited amount of evidence on psychological distress that is associated with self-medication during an outbreak in Malaysia. A recent study on mental health, focusing on depression and anxiety was carried out in Malaysia showed that a significant proportion of the public experienced mental health issues during the pandemic.² Most research mainly focused on the prevalence, an individual's knowledge, attitude and practices on self-medication as general, but limited data on the effect of mental health that induce self-medication to prevent or manage Covid-19 during the pandemic.

In order to fill the research gap, the main objective of this study is to validate and develop an instrument in Bahasa Melayu to assess the psychological distress and self-medication during pandemic Covid-19 in WP Labuan. The secondary objectives are to determine if there is an association between psychological distress and self-medication during pandemic Covid-19 and to investigate other factors contributing to self-medication during the pandemic according to different socio demographics, occurrence and potential side effects.

This study can assist future health policy makers crucially on regulatory and control media on drugs which are still in clinical trials. Better health education and counseling can be focused on particular demographics based on the outcome of the study. Proper facts on self-medication can be used during health education. This study can also assist in developing and implementing mental health intervention policies to cope with challenges during a pandemic in the future.

METHODS

This study was a cross-sectional study using a structural

questionnaire among the population in WP Labuan. In Questionnaire development, Covid-19 Peritraumatic Distress Index (CPDI) was chosen as this measurement was an effective instrument for detecting stress during the Covid-19 Pandemic with acceptable validation scores.^{12,13} The questionnaire design consisted of three parts: 1) Socio Demographic data; 2) CPDI, which consists of 24 questions based on a Likert scale on four (4) domains: Negative mood, Change in behavior and cognitive skills, Tired and hyperactivated and Somatization. The total score ranges from 0 to 100 with the indication of mild to moderate distress with the score of 28 - 51 and severe distress with score more than 52. The third part consisted of a set of questions on Knowledge, behavioral and Practice and Attitude of Self Medication.

After extensive literature review, the content domains for the questionnaire were structured. The initial questionnaire was in English language. To target the general population in WP Labuan, CPDI was translated into *Bahasa Malaysia* by an expert whose native language is *Bahasa Malaysia* and English as the second language. The *Bahasa Malaysia* version was back-translated into English by an expert whose native language is English and who is fluent in *Bahasa Malaysia*. The consistency between the original scale items and the items obtained by back translation were checked by an expert whose native language is English. The Bahasa Malaysia version was applied into pilot study which was able to study the comprehensibility, perception and the rationality of the questions.

For the instrument questionnaire to be valid and reliable, it is important for the expert panel to evaluate the items in the questionnaire. A panel of 7 experts, who are senior pharmacists, psychologist and epidemiologist, appraised content validity for the final version of the questionnaire. The content validity index (CVI) and Kappa-based for questions had been calculated and modified as required. For reliability testing, Cronbach's Alpha, which is used to determine inter-item correlations, was analyzed during the pilot study.

A pilot testing is important to perform as this study can identify items that are lacking in clarity among respondents. For the pilot testing of the questionnaire, the recommended sample size was less than 100 subjects.¹⁴ Participants who were aged above 18 years old and resided in WP Labuan during the pandemic Covid-19 were included in the study. Any incomplete survey or criteria that does not meet the inclusion criteria will be excluded. The study site was in WP Labuan, using cluster random sampling by dividing the population in certain groups based on region. Questionnaire was distributed online through invitation, aiming at 200 respondents. The first page of the questionnaire contains information including CPDI as a screening tool and aims of study. Participants are assured that their participation is voluntary, their responses will be confidential, used for research purposes only and their identity will not be known to researchers.

The data was collected and analysed by using Statistical Package for Social Sciences (SPSS) version 26. The frequency and percentage of every demographic were evaluated as well as Mean and Standard deviation for Knowledge and Attitude of self-medication. Scoring of the questions on knowledge was



determined by giving one point (1) for each correct answer and zero (0) for incorrect answers or for no response. The level of significance was set at $p < 0.05$ throughout data analyses. Chi Square test will be used to determine the significance difference between variables and psychological distress and Self-medication.

All variables were entered into a logistic regression analysis to assess the association between the variables of interest and outcome. An odd ratio of more than 1 may indicate that the variables are associated.

RESULTS

From the 200 invitations, 162 respondents accepted and two (2) declined to participate. There were adults in the age range between 18 to 64 years with 68% were in the range 25 to 44 years old, with 75% were female and 25% were male. The half of respondents were Bumiputera Sabah (51.9%; $n=83$) and most respondents had a secondary school education (44.4%; $n=71$). Most respondents resided in rural areas/countryside (70.6%; $n=113$) compared to urban areas/towns. Among the respondents, 72.5% ($n=116$) were married and 40% ($n=64$) were in the government sector. Highest group was in the range RM 2,500 to RM 4,849 of household income (44.4%; $n=71$). From the data collection, 22.2% ($n=36$) were healthcare workers and 13.6% ($n=22$) were frontliners during the pandemic Covid-19. The sociodemographic characteristics are summarized in Table 1.

Demographic Variables	N	%
Gender		
Female	120	75.0
Male	40	25.0
Age		
18 - 24 years	5	3.1
25 - 34 years	56	35.0
35 - 44 years	54	33.8
45 - 54 years	33	20.6
55 - 64 years	12	7.5
More than 65 years	0	0.0
Area		
Urban area (town)	47	29.4
Rural area (countryside)	113	70.6
Education		

The results of internal consistency analysis for each domain are present in Table 2. Internal consistency was determined for Knowledge domain ($n=3$) has Cronbach alpha value of 0.555 while Attitude domain ($n=4$) has the value of 0.727. For the CPDI domain with 24 items, the Cronbach alpha was 0.919. A Cronbach's Alpha with the value equal or more than 0.5 for less

Primary school	1	0.6
Secondary school	71	44.4
Diploma	46	28.7
Bachelor Degree	29	18.1
Master Degree	13	8.1
Doctoral Degree	0	0.0
Race		
Bumiputra Sabah	83	51.9
Melayu	51	31.9
Cina	12	7.5
Bumiputra Sarawak	8	5.0
Brunei	4	2.5
Filipino	2	1.3
Marital Status		
Single	31	19.4
Married	116	72.5
Divorced/Widowed	13	8.1
Occupation		
Government sector	64	40.0
Private sector	42	26.3
Self employed	32	20.0
Unemployed	17	10.6
Retired	3	1.9
Student	2	1.3
Healthcare worker		
Yes	36	22.2
No	72	44.4
Frontliner		
Yes	22	13.6
No	86	53.1
Household Income		
Less than RM2,500	61	38.1
RM 2,500 - RM 4,849	71	44.4
RM 4,850 - RM 10,969	27	16.9
More than RM 10,970	1	0.6

than 10 items indicates that the consistency of the instrument is good. For items more than 10, a Cronbach's Alpha with value of equal or more than 0.7 is required.

The mean (SD) CPDI score of the respondents in WP Labuan was 32.55 (15.98). 64.2% of the respondents experienced psychological distress (54.3% of respondents' scores were between 28 - 51, and 9.9% of the respondents' scores were ≥ 52) in Table 3. The association of stress levels with demographic



Table 2. Reliability test results for CPDI, knowledge and attitude about self-medication during Pandemic Covid-19			
No.	Questions	Corrected Item - Total Correlation	Cronbach's Alpha if Item deleted
Covid-19 Peritraumatic Distress Index (CPDI)			
Q1	Compared to usual, I feel more nervous and anxious	0.412	0.918
Q2	I feel insecure and bought a lot of masks, medications, sanitizer, gloves and/or other home supplies	0.454	0.917
Q3	I can't stop myself from imagining myself or my family being infected and feel terrified and anxious about it	0.562	0.916
Q4	I feel empty and helpless no matter what I do	0.570	0.915
Q5	I feel sympathetic to the Covid-19 patients and their families. I feel sad about them	0.166	0.921
Q6	I feel helpless and angry about people around me, governors and media	0.563	0.915
Q7	I am losing faith in the people around me	0.502	0.917
Q8	I collect information about Covid-19 all day. Even if it's not necessary. I can't stop myself	0.429	0.918
Q9	I will believe the Covid-19 information from all sources without any evaluation	0.425	0.918
Q10	I would rather believe in negative news about Covid-19 and be skeptical about the good news	0.507	0.916
Q11	I am constantly sharing news about Covid-19 (mostly negative news)	0.481	0.917
Q12	I avoid watching Covid-19 news, since I am too scared to do so	0.598	0.915
Q13	I am more irritable and have frequent conflicts with my family	0.680	0.914
Q14	I feel tired and sometimes even exhausted	0.621	0.914
Q15	Due to feeling of anxiety, my reactions are becoming sluggish	0.740	0.913
Q16	I find it hard to concentrate	0.719	0.912
Q17	I find it hard to make any decisions	0.692	0.913
Q18	I feel uncomfortable when communicating with others	0.549	0.916
Q19	Recently, I rarely talk to my family	0.655	0.914
Q20	During this Covid-19 period, I often feel dizzy or have back pain and chest distress	0.667	0.914
Q21	During this Covid-19 period, I often feel stomach pain, bloating, and other stomach discomfort	0.497	0.917
Q22	I cannot sleep well. I always dream about myself or my family being infected by Covid-19	0.546	0.916
Q23	I lost my appetite	0.535	0.916
Q24	I have constipation or frequent urination	0.615	0.915
Knowledge Domain			
Q1	Excessive use of paracetamol causes liver toxicity	0.225	0.680
Q2	Changing the schedules for taking medication does not pose any danger	0.423	0.362
Q3	Food supplements can be taken without prescription because they do not cause any negative effects	0.477	0.290
Attitude Domain			
Q1	What do you think about self-medication for self-healthcare during pandemic?	0.548	0.649
Q2	Do you recommend self-medication to others?	0.659	0.582
Q3	It is acceptable to use Over-The-Counter medication for a short time	0.485	0.686
Q4	It is acceptable to use previously prescribed medications to treat the same symptoms	0.394	0.737

variables was analyzed using the Chi Square test. Based on the minimum expected counts, the variable for Area (town/countryside) was found to be statistically significant ($p < 0.05$) to be associated with the level of stress as shown in Table 4.

Maximum contribution towards stress was Negative mood with a mean score of 13.29 ± 4.27 , following the section of change in behavior and cognitive skills (8.91 ± 5.61). A linear regression model was carried out and showed that there was a statistically



significant difference ($p = 0.00$) in all domains, with highest influence recorded from the domain Tired and Hyperactivated ($B=0.89$) followed by a Change in behavior and cognitive skills ($B=0.845$) in table 5.

The overall prevalence of self-medication during the Pandemic Covid-19 was 70.6% which was slightly similar to the prevalence of self-medication before the Pandemic (71.9%). The association of Self-medication with demographic variables was analyzed using the Chi Square test. Based on the minimum

	n (%)	M (SD)
Total Sample	160	32.55 (15.98)
Gender		
Female	120 (75.0)	32.80 (16.22)
Male	40 (25.0)	31.80 (15.43)
Age		
18 - 24 years	5 (3.1)	26.60 (15.88)
25 - 34 years	56 (35.0)	34.32 (19.53)
35 - 44 years	54 (33.8)	32.13 (13.15)
45 - 54 years	33 (20.6)	33.76 (13.42)
55 - 64 years	12 (7.5)	25.33 (15.56)
Area		
Urban area (town)	47 (29.4)	35.21 (14.66)
Rural area (countryside)	113 (70.6)	31.44 (16.44)
Education		
Primary school	1 (0.6)	63.00
Secondary school	71 (44.4)	31.97 (13.54)
Diploma	46 (28.7)	29.74 (17.54)
Bachelor Degree	29 (18.1)	34.93 (16.34)
Master Degree	13 (8.1)	38.00 (19.57)
Marital Status		
Single	31 (19.4)	34.52 (16.07)
Married	116 (72.5)	33.34 (15.73)
Divorced/Widowed	13 (8.1)	20.85 (14.25)
Household Income		
Less than RM 2,500	61 (38.1)	33.41 (13.49)
RM 2,500 - RM 4,849	71 (44.4)	30.79 (17.35)
RM 4,850 - RM10,969	27 (16.9)	34.74 (17.60)
More than RM 10,970	1 (0.6)	46.00
Range of Covid-19 distress		
No Distress	56 (34.6)	15.61 (6.99)
Mild to Moderate	88 (54.3)	38.18 (6.92)
Severe	16 (9.9)	60.88 (11.70)

expected counts, the variable for Area (town/countryside) was found to be statistically significant ($p<0.05$) to be associated with self-medication during the pandemic (Table 6). Analysis showed that the association between CPDI groups was not

	<28 No Distress	28 >51 Mild, moderate, severe distress	p Value
Gender			
Female	11 (6.9)	29 (18.1)	0.251
Male	45 (28.1)	63 (39.4)	
Age			
18 - 24 years	3 (1.9)	2 (1.3)	0.744
25 - 34 years	19 (11.9)	37 (23.1)	
35 - 44 years	19 (11.9)	35 (21.9)	
45 - 54 years	10 (6.3)	23 (14.4)	
55 - 64 years	5 (3.1)	7 (4.4)	
Area			
Urban area (town)	11 (6.9)	36 (22.5)	0.047
Rural area (countryside)	45 (28.1)	68 (42.5)	
Education			
Primary school	0 (0.0)	1 (0.6)	0.392
Secondary school	22 (13.8)	49 (30.6)	
Diploma	21 (13.1)	25 (15.6)	
Bachelor Degree	8 (5.0)	21 (13.1)	
Master Degree	5 (3.1)	8 (5.0)	
Marital Status			
Single	10 (6.3)	21 (13.1)	0.112
Married	38 (23.8)	78 (48.8)	
Divorced/Widowed	8 (5.0)	5 (3.1)	
Household Income			
Less than RM 2,500	15 (9.4)	46 (28.7)	0.14
RM 2,500 - RM 4,849	30 (18.8)	41 (25.6)	
RM 4,850 - RM10,969	11 (6.9)	16 (10.0)	
More than RM 10,970	0 (0.0)	1 (0.6)	



Table 5. Linear regression among the four main domains of CPDI

Domains	Mean	Std Deviation	Adjusted R	Beta Coefficient	p-value
Negative mood	13.2938	4.2789	0.481	0.696	0.00
Change in Behavior and cognitive skills	8.9188	5.6155	0.711	0.845	0.00
Tired and Hyperactivated	7.2813	5.8515	0.791	0.890	0.00
Somatization	3.0563	3.9354	0.600	0.776	0.00

statistically significant with the practice of self-medication ($p = 0.196$; expected count 16.45).

Using Multinomial Regression analysis in Table 7 showed that between CPDI score and Yes to Self-medication: OR is 1.085 with $P < 0.05$ ($p = 0.004$); for every increase of CPDI score, there is statistically significant increase by 1.085 times (8.5%). The variable for Area (town/countryside) was found to be positively associated with self-medication (OR = 2.06; $p = 0.05$) at Table 8.

Table 6. Chi-square Results on Association of Demographics with self-medication

	X ² value (df=1)	P Value
Gender	1.697	0.193
Age	11.207 ^b	0.024
Area	3.917	0.048
Education	3.803 ^b	0.433
Race	2.076 ^b	0.722
Marital Status	0.286 ^b	0.867
Occupation	2.790 ^b	0.732
Healthcare workers	3.383	0.066
Frontliners	0.054	0.816
Household Income	1.020 ^b	0.796

b. Fisher's Exact Test because of low expected counts.

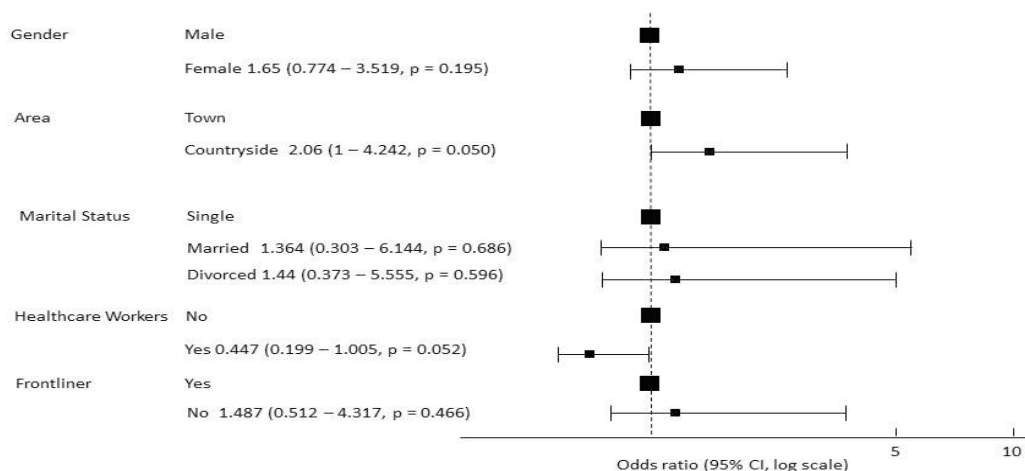
This questionnaire included a few main reasons for self-medication during the pandemic. Fear of being infected by Covid-19 was the highest with 77 respondents, followed by Difficulty getting to Clinic/Hospital due to MCO (n=44) and Time Saving (n=38). The highest observed medication used in self-medication were Vitamin C, Vitamin D, Zinc supplements (n=99), followed by Antipyretics such as Paracetamol and Ibuprofen (n=58) and multivitamin supplements (n= 28). It was interesting to find out that seven (7) respondents consumed Lianhua Qingwen products and two (2) respondents consumed Ivermectin. Majority consumed mention medication as prevention of Covid-19 (n=40) and as other reasons than Covid-19 (n=32).

The data revealed the level of knowledge of respondents, where 33% (n=53) of them have good knowledge and both 27.5% (n=44) of respondents scored moderate and fair respectively. Furthermore, 47% (n=54) of respondents who practiced self-medication understand the instructions fully on the medication

Table 7. Multinomial Regression Analysis on Yes to Self-medication

	B	Sig	Exp (B)	95% CI
Intercept	-2.017	0.284		
CPDI Scores	0.082	0.004	1.085	1.027-1.147
No Distress	-0.169	0.888	0.845	0.081-8.844
Mild Distress	1.373	0.387	3.946	0.176-88.23

Table 8. Shows factors associated with self-medication during the Pandemic Covid-19 in WP Labuan in a binary logistic multivariable model



while 14% did not understand at all or understand poorly on the instruction of the medication. Most medication procured or obtained by respondents were from Pharmacies, beauty shops and panel clinics (n=107), followed by friends and families (n=29) and Online shopping (n=20).

76% of respondents (n=86) reported feeling better after self-medication, followed by a similar response of 8% to feeling unsure (n=14) and no difference (n=13) respectively. Only two (2) respondents reported experiencing side effects after self-medication which was diarrhea or stomach upset. 11.5% respondents reported not sure after self-medication while the majority (86%; n=98) have not experienced any side effects.

The respondents' attitudes toward the statements about self-medication during the Pandemic have been presented in Table 9. Overall mean score for the attitudes towards self-medication and usage of previously prescribed medication showed about 50% respondents were positively agree. However, data showed that there was a lower mean score on attitude towards recommending self-medication to others and acceptability on using Over the Counter medication for a short period of time.

	Attitudes towards self-medication Mean (SD)
What do you think about self-medication for self-health care during the pandemic?	3.523 (1.238)
Do you recommend self-medication to others?	2.800 (1.237)
It is acceptable to use Over the Counter medication for a short time	2.725 (1.307)
It is acceptable to use previously prescribed medications to treat the same symptoms	3.343 (1.288)

DISCUSSION

The main aim in this study was to develop a valid and reliable questionnaire to effectively measure psychological distress during a pandemic in WP Labuan general public. In this study, it was found that general population of WP Labuan practiced self-medication as a preventative measure as they are fearful of being infected with Covid-19. Participants who practiced self-medication reported higher level of psychological distress and may be more panicked and worried about the potential infection. It is possible that self-medication may be seen as a health security to those who practiced in managing the potential threat of contracting the virus.¹⁵

During the peak cases in WP Labuan in 2021, vaccine was introduced the public. However, the fear of infected by Covid-19 may have been influenced by the social media regarding misinformation of available treatments, and this may lead to public and confusion and increase the practice of self-medication. Another factor which was location may have played a role as it has strong association to the level of distress during pandemic, and may lead to self-medication as people from the rural area may have disadvantage in seeking medical help. Other trigger factors of self-medication may come

from friends, family, previous prescriptions and experience, pharmacist and the media.⁶

The use of vitamin supplements, antipyretics, antihistamines, antibiotics, were seen in this study, including medicinal herbs. The interests in vitamin and mineral supplements, and other foods such as garlic was increased during the Covid-19 pandemic. Vitamin D and Vitamin C was showed to have inflammatory response and strong antioxidant, as well as antiviral properties.¹⁶

CONCLUSION

The development of the questionnaire for this pilot study was a valid and reliable instrument for assessment of psychological effects on Self-medication during the Pandemic Covid-19. Overall, this study showed that Self-medication is commonly practiced and positively associated with psychological distress associated with the Pandemic Covid-19. The current questionnaire can be used as a tool in research to measure distress level of the general population during a pandemic and can help government agencies and healthcare professionals toward the development of an effective educational intervention to improve general and mental health and wellbeing.

DECLARATION OF INTEREST STATEMENT

The author(s) declare that there are no conflicts of interest.

AUTHOR CONTRIBUTION STATEMENT

Tan ML, Rahman MS, Robinson F, and Sani MHM contributed equally to this work. All co-conceived the study and finalized the structural questionnaire. Tan ML analyzed the data and drafted the manuscript. All authors read and approved the final manuscript.

DATA ACCESS STATEMENT

Corresponding authors currently have the direct access to the study data.

DATA AVAILABILITY STATEMENT

All data are incorporated into the article and its online supplementary material.

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