Singapore Med J 2015; 56(6): 310-316
doi: 10.11622/smedj.2015088

CME ARTICLE

Ministry of Health Clinical Practice Guidelines: Anxiety Disorders

Leslie Lim, Hong Ngee Chan, Peng Hoe Chew, Sze Ming Chua, Carolyn Ho, Seow Khee Daniel Kwek, Tih Shih Lee, Patricia Loh, Alvin Lum, Yong Hui Colin Tan, Yi Min Wan, Matthew Woo, Hwa Ling Yap

ABSTRACT The Ministry of Health (MOH) has developed the clinical practice guidelines on Anxiety Disorders to provide doctors and patients in Singapore with evidence-based treatment for anxiety disorders. This article reproduces the introduction and executive summary (with recommendations from the guidelines) from the MOH clinical practice guidelines on anxiety disorders, for the information of SMJ readers. Chapters and page numbers mentioned in the reproduced extract refer to the full text of the guidelines, which are available from the Ministry of Health website: http://www.moh.gov.sg/content/moh_web/healthprofessionalsportal/doctors/guidelines/cpg_medical.html. The recommendations should be used with reference to the full text of the guidelines. Following this article are multiple choice questions based on the full text of the guidelines.

1.1 Background information

Anxiety disorders are known to be one of the most prevalent of psychiatric conditions, yet they often remain under-diagnosed and under-treated. Their chronic, disabling symptoms cause considerable burden not only to sufferers but also to their families, and contribute to poorer quality of life and considerable economic burden on society.

In many instances, there is a delay in seeking treatment and in some cases such delay may stretch up to nearly ten years. This may result from ignorance of the condition, fear of taking medications, and the stigma of receiving a psychiatric diagnosis, and or having to accept psychiatric treatment.

The anxiety disorders include panic disorder with or without agoraphobia, social anxiety disorder, specific phobia, obsessive-compulsive disorder, generalised anxiety disorder, acute stress disorder and post-traumatic stress disorder. In the clinical evaluation of anxiety disorders, it is important to ascertain the type of anxiety disorder present. This would allow treatment to be targeted at the specific type of disorder.

These guidelines are developed to provide practical, evidence-based recommendations to primary care physicians and specialists in psychiatry for the diagnosis and management of the anxiety disorders.

The first edition of the guidelines was published in 2003. In this edition, we present data from newer research as well as older data not previously reported in the earlier guidelines.

For example, we examine the efficacy of combining medications with psychological therapy over medications alone, or psychological therapy alone. In view of the majority of anxiety sufferers being female we have made recommendations for pharmacotherapy during pregnancy and breastfeeding. As these guidelines are intended for use in the Singapore context, we have omitted treatments that are currently not available in Singapore.

1.2 Aim

These guidelines are developed to facilitate the diagnosis and assessment of the anxiety disorders, and to ensure that their management is appropriate and effective.

1.3 Scope

These guidelines will cover the management of anxiety disorders in adults and address the issues of medication use during pregnancy and breastfeeding.

1.4 Target group

The content of the guidelines will be useful for all doctors treating patients with anxiety disorders. Efforts have been made to ensure that the guidelines are particularly useful for primary care physicians and specialists in psychiatry, including all those involved in the assessment and management of patients with anxiety disorders in the community. The doctor treating the patient is ultimately responsible for clinical decisions made after reviewing the individual patient's history, clinical presentation and treatment options available.

1.5 Development of guidelines

These guidelines have been produced by a committee of psychiatrists, a clinical psychologist, pharmacist, patient representative, and family practitioners appointed by the Ministry of Health. They were developed by revising the existing guidelines, reviewing relevant literature, including overseas clinical practice guidelines, and by expert clinical consensus of professionals with experience in treating patients in the local setting.

List of institutions in alphabetical order
Changi General Hospital, Duke-NUS Graduate Medical School, Institute of Mental Health, Jurong Health Services, Ministry of Health, National Healthcare Group Polyclinics, Parkway Health Primary Care Network (The Arcade), Shenton Family Medical Clinic, Singapore General Hospital, The Resilienz Clinic
Correspondence: A/Prof Leslie Lim, Senior Consultant, Department of Psychiatry, Singapore General Hospital, Outram Road, Singapore 169608. leslie.lim.e.c@sgh.com.sg

The following principles underlie the development of these guidelines:

- Treatment recommendations are supported by scientific evidence whenever possible (randomised controlled clinical trials represent the highest level of evidence) and expert clinical consensus is used when such data are lacking.
- Treatment should maximise therapeutic benefits and minimise side effects.

1.6 What's new in the revised guidelines

This edition of the guidelines contains updated recommendations based on latest evidence, as well as detailed discussions and recommendations on the management of anxiety disorders in adult populations.

The following represent changes to the revised guidelines

- An extensive review of the literature, including new evidence. This involved the re-writing and extensive revision of the chapters.
- Length of treatment, which provides answers to a pertinent question.
- Use of medications during pregnancy and breastfeeding. Given that females are more likely to be at risk of being diagnosed with anxiety disorders, this is an important subject.

We are aware that the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) was released in 2013. In DSM-5, post-traumatic stress disorder and obsessive-compulsive disorder have been removed and classified separately from the rest of the anxiety disorders. If we were to adhere strictly to DSM-5, this would entail omitting discussion on post-traumatic stress disorder and obsessive-compulsive disorder. As it is our aim to provide an update on the 2003 guidelines, post-traumatic stress disorder and obsessive-compulsive disorder have been included in this edition of the guidelines.

In addition, anxiety conditions in children are included in DSM-5. Since the present guidelines are meant to address only adult anxiety disorders, guidelines on children's anxiety conditions are not included here.

Hence, for purposes of these guidelines, we will continue to use classifications based on the International Classification of Diseases-10 (ICD-10) and DSM-IV-TR criteria.

1.7 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or when new evidence appears that requires substantive changes to the present recommendations.

EXECUTIVE SUMMARY OF RECOMMENDATIONS

Details of the recommendations listed can be found in the main text as the pages indicated. Key recommendations are shaded in grey.

Clinical Evaluation and Overview

No.	Recommendation	Grade, Level of evidence	CPG page no.
1	A diagnosis of anxiety disorder should be considered only after appropriate clinical evaluation and investigation to rule out general medical conditions have been done. Figure 1 summarises how the various anxiety disorders are diagnosed.	GPP	16
2	The initial management of anxiety disorders should ideally be instituted at the primary care level. The recommended framework for the management of anxiety disorders in primary care is described in Figure 2.	GPP	22
3	The following may be instituted in primary care immediately after diagnosis: • Educating patient on nature and origin of anxiety symptoms and providing appropriate reassurance, e.g., not having a 'heart attack' or 'going crazy' • Suggestion of lifestyle changes as appropriate, i.e., stress reduction strategies, reducing alcohol and caffeine intake, avoiding nicotine and drug use, regular exercise • Supportive counselling • Symptomatic relief with medication prescribed on a short-term basis • Evaluation and mobilisation of family and social resources • Monitoring and addressing early signs of relapse	Grade D, Level 4	22
4	Psychiatric evaluation and treatment is appropriate when there is serious risk of suicide, there are psychotic symptoms, co-occurring drug/alcohol problems exist, symptoms are severe/complex or if symptoms fail to improve on initial treatment and follow-up.	GPP	27
5	Consider transferring patients with anxiety disorders from psychiatric to primary care for long-term management if they have the following characteristics: • Aged 18 or older • Stabilised for the past 3 months • No psychiatric hospitalisation in the past 6 months • No history of forensic or substance abuse • No disruptive personality disorders • Non suicidal • No history of aggressive behaviour • Not currently receiving clozapine, lithium, valproate, hypnotics (including benzodiazepines, zopiclone, zolpidem) or formal psychotherapy treatment	GPP	27

(*Contd...*)

No.	Recommendation	Grade, Level of evidence	CPG page no.
6	All patients should receive education about their disorder, including aetiology, treatment choices and prognosis.	GPP	28
7	As local patients may show higher propensity for initial side effects of antidepressants (e.g. paradoxical excitation), starting doses for local patients should be lower than those suggested by overseas guidelines.	GPP	30
8	The Clinical Global Impression scales (both severity and improvement sub-scales) may be used to measure illness severity and treatment progress during consultations for anxiety disorders.	Grade B, Level 2++	31

Management of Panic Disorder

No.	Recommendation	Grade, Level of evidence	CPG page no.
9	Either selective serotonin reuptake inhibitors (SSRIs) or venlafaxine should be used as first-line agents for the pharmacological treatment of panic disorder.	Grade A, Level 1+	33
10	Imipramine and clomipramine are effective and may be used as second-line treatment of panic disorder.	Grade A, Level 1+	33
11	Benzodiazepines may be added to antidepressants in the short term to produce a more rapid therapeutic response in the treatment of panic disorder. In view of addictive potential, benzodiazepines should be tapered and withdrawn by 4 weeks.	Grade A, Level 1+	35
12	Depending on availability of treatment and patient preference, cognitive behaviour therapy (CBT) or combination therapy (i.e. CBT and SSRIs or venlafaxine) may be used for the treatment of panic disorder.	Grade A, Level 1++	36

Management of Generalised Anxiety Disorder (GAD)

No.	Recommendation	Grade, Level of evidence	CPG page no.
13	Either SSRIs or venlafaxine should be used as first-line pharmacological treatment for patients with GAD.	Grade A, Level 1++	38
14	Imipramine may be considered as a second-line treatment for GAD, in view of the possibility of poor tolerability and the danger of fatal overdosage.	Grade A, Level 1+	38
15	Mirtazapine may be considered as a second-line treatment for GAD due to its anxiolytic effects.	Grade A, Level 1+	38
16	Benzodiazepines should not be used for the long-term treatment of GAD.	Grade B, Level 1+	39
17	Pregabalin may be prescribed for patients with GAD as it has anxiolytic effects which may be more rapid acting. Due caution must be exercised when prescribing to patients who are at risk of abusing substances.	Grade B, Level 2++	39
18	Hydroxyzine may be used as adjunctive treatment together with other anxiolytic agents for treatment of GAD.	Grade C, Level 2+	39
19	Propanolol is not recommended for the long-term treatment of generalised anxiety disorder.	Grade B, Level 1+	39
20	Drug treatment for GAD needs to be continued for at least 32 weeks as high relapse rates were reported after discontinuing medications.	Grade A, Level 1+	40
21	CBT may be used as first-line psychotherapy treatment for GAD.	Grade A, Level 1++	40
22	A specialist's opinion should be sought for patients with complex GAD and/or with marked functional impairment, or at high risk of self-harm.	GPP	40

Management of Specific Phobia

No.	Recommendation	Grade, Level of evidence	CPG page no.
23	CBT should be used as first-line treatment of specific phobia.	Grade A, Level 1++	41
24	Benzodiazepines may be used on a short-term basis for temporary anxiety relief in specific phobia, pending resolution of symptoms with other forms of treatment.	Grade B, Level 1+	42

Management of Social Anxiety Disorder (SAD)

No.	Recommendation	Grade, Level of evidence	CPG page no.
25	Either pharmacotherapy or psychotherapy alone may be used as first-line treatment for SAD, depending on patient preferences, values and economic considerations.	Grade A, Level 1++	43
26	Either SSRIs or venlafaxine should be used as first-line pharmacotherapy for SAD.	Grade A, Level 1+	44
27	Moclobemide may be used for the treatment of SAD if treatment with SSRIs or venlafaxine has not been effective.	Grade A, Level 1+	44
28	Benzodiazepines may be used on a short-term basis for temporary anxiety relief pending resolution of phobic symptoms with other forms of treatment.	Grade A, Level 1+	44
29	Beta-blockers (e.g. atenolol, propranolol) are not recommended for the treatment of SAD, as they have been found ineffective. However, they may be used for the treatment of performance anxiety (e.g. playing an instrument, giving a speech).	Grade B, Level 2++	45
30	CBT should be used as first-line psychotherapy treatment of SAD.	Grade A, Level 1+	45
31	Pharmacotherapy with SSRIs, venlafaxine, or moclobemide in SAD should be continued for at least 12 months to prevent relapse.	Grade B, Level 2++	45

Management of Obsessive-Compulsive Disorder (OCD)

No.	Recommendation	Grade, Level of evidence	CPG page no.
32	Either pharmacotherapy or psychotherapy alone may be chosen as first-line treatment for OCD, depending on patient preferences, values and economic considerations.	Grade A, Level 1++	46
33	The first-line pharmacological treatment for OCD should be a 10-12 week trial with an SSRI at adequate doses.	Grade A, Level 1++	47
34	Clomipramine may be used as a treatment for OCD after an adequate trial of SSRI treatment has failed.	Grade A, Level 1++	47
35	An adequate treatment trial in OCD should last for at least 12 weeks. If the patient does not respond to treatment in adequate dosages, the medication may be changed or specialist opinion sought.	Grade D, Level 4	48
36	Venlafaxine may be considered in patients who have not responded to SSRIs and clomipramine. Monitor blood pressure during treatment as venlafaxine at high doses can raise blood pressure.	Grade A, Level 1+	48
37	CBT may be used as first-line treatment for OCD if patients prefer psychological treatment over pharmacotherapy.	Grade A, Level 1+	49
38	CBT augmentation of serotonergic antidepressants (e.g. SSRIs, clomipramine) in the treatment of OCD may be considered for those who are treatment-resistant or partially responsive to medications.	Grade B, Level 1+	49
39	Patients with OCD who respond to antidepressants in the acute phase should be continued on their medication for at least 12 months.	Grade A, Level 1+	49

Management of Post-Traumatic Stress Disorder (PTSD)

No.	Recommendation	Grade, Level of evidence	CPG page no.
40	Either the SSRIs or venlafaxine may be used as first-line pharmacological treatment for PTSD.	Grade A, Level 1++	51
41	Mirtazapine may be considered as a second-line treatment for PTSD.	Grade B, Level 1+	51
42	Either amitriptyline or imipramine may be considered for PTSD if the first-line and second-line treatments are ineffective or poorly tolerated.	Grade A, Level 1+	52
43	Benzodiazepines should not be used for the treatment of PTSD.	Grade A, Level 1+	52
44	Risperidone, olanzapine, quetiapine, and lamotrigine may be prescribed as adjunctive treatments for PTSD in conjunction with the SSRIs.	Grade B, Level 1+	52
45	Pharmacological treatment for PTSD should be continued for at least 12 months.	Grade D, Level 4	53

(*Contd...*)

No.	Recommendation	Grade, Level of evidence	CPG page no.
46	CBT should be used as the first-line psychological treatment for PTSD.	Grade A, Level 1+	53
47	Eye Movement Desensitisation and Reprocessing therapy may be used as second-line treatment for PTSD.	Grade B, Level 2++	54
48	If CBT or eye movement desensitisation and reprocessing therapy for PTSD are contraindicated or have failed, combination therapy (i.e. CBT plus pharmacotherapy) may be used as an alternative treatment.	Grade B, Level 1+	54

Management of anxiety disorders in pregnancy

No.	Recommendation	Grade, Level of evidence	CPG page no.
49	If a woman is planning a pregnancy or becomes pregnant while on medication for an anxiety disorder, consider: • Stopping medication and starting CBT, if necessary and if not already tried. • Switching to a safer drug, if the decision is to maintain her on medication.	Grade D, Level 4	55
50	When prescribing a drug for a woman with an anxiety disorder who is planning a pregnancy, already pregnant, or breastfeeding: • Choose drugs with the lowest risk potential for the mother and foetus/infant • Start at the lowest effective dose, and slowly titrate upwards • Continue for the shortest possible duration • Use monotherapy instead of combination treatment	Grade D, Level 4	56
51	Sertraline, paroxetine and citalopram should be avoided during pregnancy.	Grade C, Level 2+	57
52	Benzodiazepines should not be routinely prescribed for pregnant and breastfeeding women, except for the short-term treatment of extreme anxiety and agitation.	Grade D, Level 4	59
53	The risk-benefit ratio of prescribing benzodiazepines should be assessed on a case-by-case basis; use the lowest dose for the shortest time, or avoid prescribing at all during the first trimester.	GPP	59
54	Atypical antipsychotics should be prescribed with caution in patients suffering from or at risk of gestational diabetes.	Grade D, Level 3	59
55	Medication for nursing mothers should be maintained at the lowest effective dose to minimise infant exposure.	Grade D, Level 3	60
56	When antidepressant treatment is indicated in the postpartum period, women should generally not be advised to discontinue breastfeeding.	Grade D, Level 3	60
57	Treatment with paroxetine or sertraline should be preferred over other SSRIs in treatment-naive breastfeeding women due to the low infant exposure to these drugs	Grade D, Level 3	61
58	Drugs for which little data exist, such as fluvoxamine, venlafaxine, bupropion and mirtazapine, should not be considered as first-line therapies in breastfeeding women, but they may be used in special cases.	Grade D, Level 4	61
59	If mothers have been successfully treated with a particular SSRI, TCA or SNRI, this drug should be the first-line treatment if there are no contraindications. An individual risk-benefit assessment should always be done before starting antidepressants.	Grade D, Level 4	61
60	Women on long term treatment with high dose benzodiazepines should continue to breastfeed, as stopping of benzodiazepine may precipitate withdrawal symptoms in the infant. Gradual tapering and stopping of benzodiazepines may be attempted at a later stage when the infant has grown bigger.	GPP	62
61	During maternal treatment with benzodiazepines, infants should be monitored for signs of sedation, lethargy, poor feeding and weight loss.	Grade D, Level 4	62

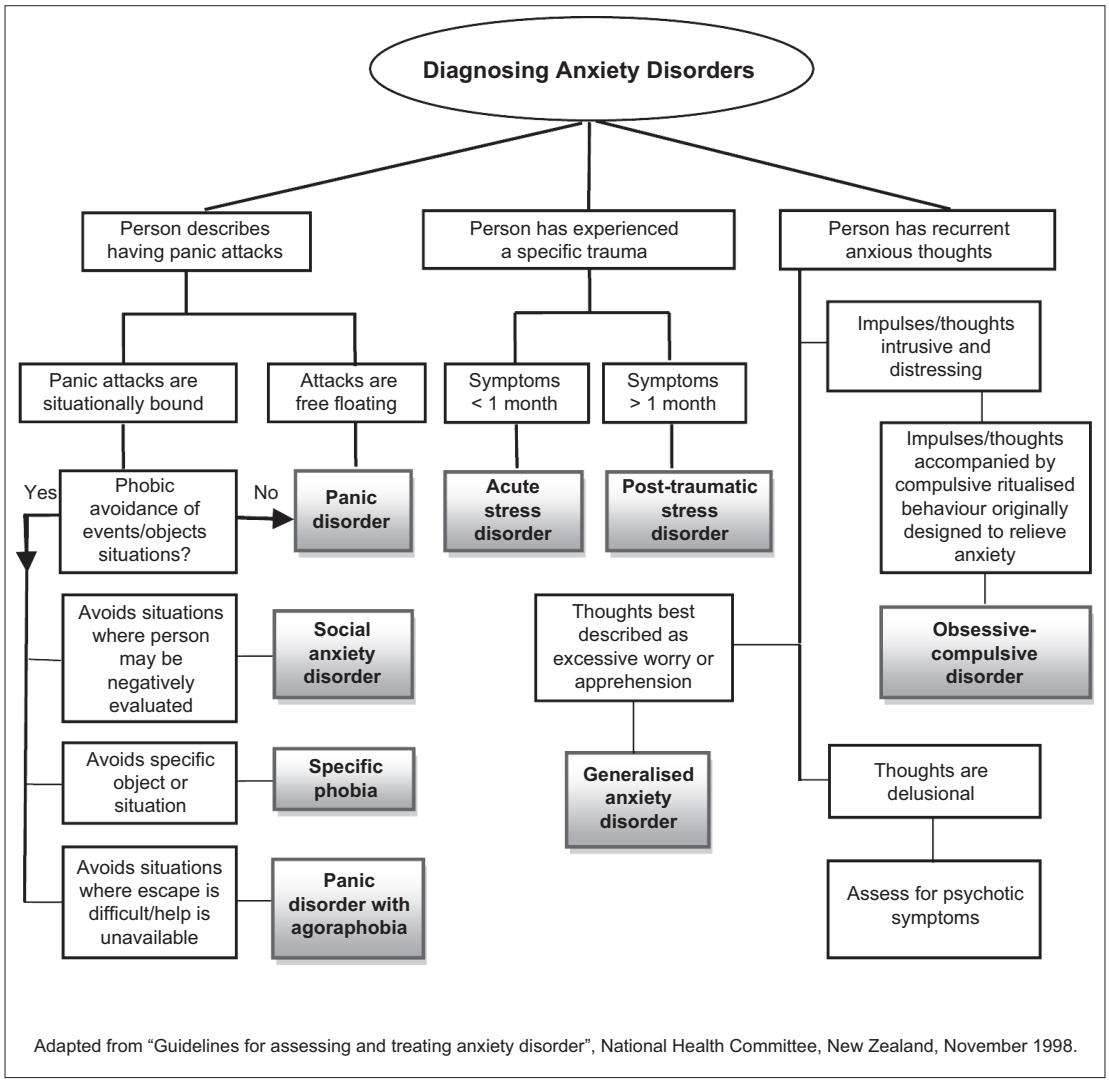

Fig. 1 Differentiating anxiety disorders.

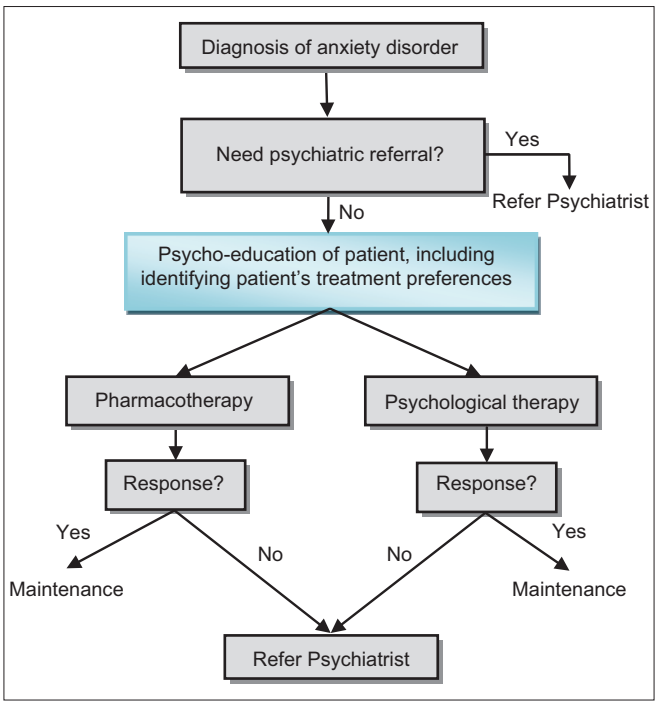

Fig. 2 Anxiety disorders management algorithm.

SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

(Code SMJ 201506B)

These questions are based on the full text of the guidelines which may be found at http://www.moh.gov.sg/content/moh_web/healthprofessionalsportal/doctors/guidelines/cpg_medical.html

	True	False
Question 1. After diagnosis of an anxiety disorder in the outpatient setting, the following immediate steps should be instituted at the primary care level:		
(a) Reassurances and psycho-education about the nature and origin of anxiety.	☐	☐
(b) Lifestyle changes, such as regular exercise.	☐	☐
(c) Treat psychotic symptoms if present.	☐	☐
(d) Refer to a psychiatrist.	☐	☐
Question 2. Psychiatric referral is appropriate when:		
(a) Risk of suicide is serious.	☐	☐
(b) Anxiety disorder is first diagnosed.	☐	☐
(c) Pharmacological treatment for anxiety disorder is needed.	☐	☐
(d) Anxiety symptoms have stabilised.	☐	☐
Question 3. For panic disorder:		
(a) Treatment response can be quantified and documented with the Panic Disorder Severity Scale (PDSS).	☐	☐
(b) About two-thirds of patients with panic disorder suffer from agoraphobia.	☐	☐
(c) Combination therapy is as efficacious as monotherapy.	☐	☐
(d) Cognitive behaviour therapy is not useful.	☐	☐
Question 4. For post-traumatic stress disorder:		
(a) Alprazolam and clonazepam have been found to be superior to placebo.	☐	☐
(b) Amitriptyline may be considered as first-line treatment.	☐	☐
(c) Risperidone and lamotrigine may be prescribed as adjunctive treatments.	☐	☐
(d) Combination therapy is superior to trauma-focused cognitive behaviour therapy.	☐	☐
Question 5. Evaluate the following statements:		
(a) Beta-blockers have been shown to be often useful in the treatment of social phobia.	☐	☐
(b) Moclobemide should be used as first line treatment for social anxiety disorder.	☐	☐
(c) Phobic symptoms respond best to exposure therapy to the feared situation or object.	☐	☐
(d) Cognitive behaviour therapy components such as systematic desensitisation, imaginal exposure and in-vivo exposure are useful in the treatment of specific phobia.	☐	☐

Doctor's particulars:

Name in full : _____

MCR number : _____ Specialty: _____

Email address : _____

SUBMISSION INSTRUCTIONS:

(1) Log on at the SMJ website: http://www.sma.org.sg/publications/smjcurrentissue.aspx and select the appropriate set of questions. (2) Provide your name, email address and MCR number. (3) Select your answers and click "Submit".

RESULTS:

(1) Answers will be published in the SMJ August 2015 issue. (2) The MCR numbers of successful candidates will be posted online at the SMJ website by 31 July 2015. (3) Passing mark is 60%. No mark will be deducted for incorrect answers. (4) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council. (5) One CME point is awarded for successful candidates.

Deadline for submission: (June 2015 SMJ 3B CME programme): 12 noon, 24 July 2015.