What's new in the Revised Depression CPG

Assoc Professor Leslie Lim
Senior Consultant
Department of Psychiatry
Singapore General Hospital

Levels of Evidence

Level	Type of Evidence
1++	High quality MA, SR of RCTs, or RCT with v. low risk bias
1+	Well conducted MA, SR of RCTs, or RCT with low risk bias
1-	MA, SR of RCTs or RCTs with high risk bias
2++	High quality SR, CC/ CS. High quality CC, CS with v. low risk bias, high probability r/s causal
2+	Well conducted CC/ CS, low risk bias, moderate probability r/s causal
2-	CC/cohort studies high risk bias, significant risk r/s not causal
3	Non- analytic studies e.g. case reports, case series
4	Expert opinion

Grades of Recommendation

Grade	Recommendation
A	At least one MA, SR of RCTs/ RCT rated 1++, body of evidence rated 1+
B	Body of evidence including studies rated 2++
C	Body of evidence including studies rated 2++ directly applicable to target population
D	Evidence 3 or 4; or extrapolated evidence from studies rated 2+
GPP	Recommended best practice based on clinical experience of guideline development group

CPG Depression 2004

Levels of evidence

Ia –MA or RCT

Ib-one RCT

IIa-controlled trial, non randomised

IIb-one other well designed quasi- experimental

III-descriptive studies

IV- expert reports or opinions

CPG Depression 2004

Grade	Recommendation
A	At least 1 RCT, good quality trial, body of good quality literature addressing the recommendation
B (evidence IIa, IIb,III)	Well conducted studies, no RCT
C (evidence level IV)	Expert committee reports or opinions, absence of clinical studies
GPP	Best practice based on clinical experience of CPG committee

Screening for Depression

Screening may be beneficial in high risk populations (individuals with significant physical illnesses causing disability) where benefits outweigh the risks.

The PHQ-9 (patient health questionnaire 9) may be used to screen for depression in primary care.

Grade C, Level 2+

Use of Antidepressants

Antidepressants should be recommended as 1st line treatment in moderate to severe

or sub-threshold depression that has persisted for 2 years or >

Grade A, Level 1+

Use of Antidepressants

Antidepressants are a treatment option in short duration mild depression in adults and should be considered in those with a history of moderate to severe recurrent depression or if depression persists > 2-3 months.

Grade D, level 4

Choice of Antidepressant

If the patient has previously responded well to and has had minimal side-effects with a drug, that drug is preferred.

Alternatively, if the patient has previously failed to respond to an adequate trial of one antidepressant or found the side-effects of an antidepressant intolerable, that medication should generally be avoided.

Grade D, Level 4

Dosing and monitoring

- Once antidepressant selected, start with low dose and titrate gradually to full therapeutic dose, monitor mental state and side- effects
- Frequency of monitoring depends on severity, suicide risk, cooperation, and social support.

Grade A, Level 1+

SSRIs

SSRIs should be prescribed as first line medication due to favourable risk-benefit ratio, tolerability, and safety in OD

(previous CPG: TCAs and SSRIs are 1st line)

Grade A, Level 1++

SSRIs should be prescribed as first line medication for depressed persons with cardiovascular diseases.

Grade A, Level 1++

Danger of Interactions

Where there are interactions with other drugs, use of escitalopram or sertraline should be considered as they have fewer propensities for interactions, appear to be safe and possibly protective of further cardiac events

Grade D, Level 4

TCAs

Due to their cardiotoxic adverse effect risks, tricyclic antidepressants (TCA) should be avoided in patients at high risk of cardiovascular disease, arrhythmias and cardiac failure.

Grade A, Level 1++

Failure of 1st line medications

TCAs and MAOIs should be used when 1st line medications have failed.

Grade A, Level 1+

Newer Options

- Serotonin and Norepinephrine Reuptake Inhibitors (SNRI) (e.g. venlafaxine)
- Noradrenergic and Specific Serotonergic Antidepressants (NaSSA) (e.g. mirtazapine)
- Norepinephrine and Dopamine Reuptake Inhibitors (NDRI) (e.g. bupropion))

Grade A, Level 1+

SNRI

Recent meta-analyses suggest SNRIs (venlafaxine) are more effective than SSRIs.

Einarson et al. Clin Ther 1999 Feb 21(2):296-308.

Alternative class

Melatonin agonist e.g. agomelatine, may also be considered as an alternative treatment for depression, if first-line medication is unsuitable or has failed

Grade B, Level 1+

Depression with physical health problems

When an antidepressant is to be prescribed, to the patient with depression and a chronic physical health problem take into account the following:

- the presence of additional physical health disorders.

Depression with physical health problems

- the side effects of antidepressants, which may impact on the underlying physical disease (in particular, selective serotonin reuptake inhibitors may result in or exacerbate hyponatraemia, especially in older people.
- interactions with other medications.

Grade D, Level 3

Switching

Process of switching (gradual tapering, washout and starting new, cross tapering and abrupt switch) depends on the type and the pharmacodynamic and pharmacokinetic properties of antidepressants getting switched from and to.

When switching, be vigilant for drug-drug interactions (serotonin syndrome) and drug discontinuation reaction.

GPP

Refer Annex VI pg 64-66 for recommendations for switching.

Suicidal thoughts and Antidepressants

The emergence of suicidal thinking and behaviour, or unusual changes in behaviour should be monitored during the early phases (generally the first 1-2 months) of antidepressant treatment, especially in children, adolescents and young adults between 18 to 24 years old.

Grade C, Level 2+

Duration of Treatment

All antidepressants once started should be continued for at least 4-6 weeks.

Some show effects end of 1st week- 2nd or 3rd week. If effective at least partial symptomatic response by 4-6 weeks

Grade C, Level 2+

Duration of treatment

Patients with first episode of depression without psychotic symptoms should be treated with antidepressants at full treatment dose for 6-9 months after remission of symptoms.

Grade A, Level 1++

Duration of treatment

Patients who have a second episode of depression should be maintained on treatment for 1-2 years - the duration may depend on the risk factors for recurrence and the patient preference.

Grade B, Level 1+

Duration of treatment

Patients with >2 episodes of depression should be maintained on treatment for 2 years or longer, or even lifelong - the duration may depend on the risk factors for recurrence and the patient preference (pg 31).

Grade C, Level 2+

Combining Benzodiazepines and Antidepressants

Initial and short-term (2-4 week) usage of a benzodiazepine together with an antidepressant may be considered where anxiety, agitation and/or insomnia becomes problematic to patients with depression.

Grade A, Level 1++

Combining Benzodiazepines and Antidepressants

A systematic review found that patients with combination treatment of antidepressants and benzodiazepines were more likely to show response at 1 and 4 weeks than patients with antidepressant treatment only (although the difference was no longer significant at 6-8 weeks).

Furukawa, Streiner, Young. Cochrane Database Syst Rev 2002

Combining Benzodiazepines and Antidepressants

The benefits of using benzodiazepines have to be balanced against the risk of developing dependence, tolerance and increased accident probabilities. The review concluded that early time-limited use of benzodiazepines in combination with an antidepressant drug may accelerate treatment response.

Furukawa, Streiner, Young. Cochrane Database Syst Rev 2002

Discontinuation of antidepressants

When discontinuing antidepressants, slowly taper the medication instead of suddenly stopping them, to avoid discontinuation symptoms.

Grade A, Level 1++

No changes

Psychoeducation, psychotherapy, couple/marital Therapy, ECT.

ECT may be considered when rapid response is required e.g. in pregnancy, comorbid medical conditions, that preclude use of antidepressants. (Grade D, Level 3)

Depression in Children and Adolescents

Psychosocial interventions are recommended in initial treatment based on the literature and local clinical experience

Grade A, Level 1+

Depression in Children and Adolescents

- Psychosocial interventions and medications have been shown to be useful.
- Psychosocial interventions include close supervision and monitoring by Dr, engaging support networks, schools, and psychological treatments (CBT, and IPT).

Depression in Children and Adolescents

Medication should not be the only treatment modality.

Pay attention to self esteem, coping skills, adaptation to changes, and relationships

Grade D, Level 3

Depression in Children and Adolescents

Medications are usually indicated in severe depression, psychotic symptoms, or failed psychotherapy.

Grade D, Level 3

SSRIs in children and adolescents

SSRIs should be used with caution.

Grade C, Level 2+

SSRIs in children and adolescents

Only Fluoxetine has been approved by US and UK regulatory bodies. There are reports of increased suicidal thinking with Paroxetine.

Schneeweiss et al. Pediatrics 2010; 125(5): 876-88.

Combination approach

Combination psychosocial interventions and SSRIs may be considered for moderate to severe depression.

Grade A, Level 1+

Venlafaxine

Considered as second line treatment .
(previous CPG stated that TCA, MAOIs, VLF not so effective)

Grade A, Level 1++

Referral to Child Psychiatrist

- Failure to improve with psychosocial interventions or requiring specialised psychological interventions
- Failure to improve after 4 weeks of medications at maximum tolerated dose
- Suicidal intentions, disruptive psychotic symptoms.

GPP

Depression in Pregnancy

Screening and early recognition

During the past month have you often been bothered by:

- “feeling down depressed or hopeless?”
- “having little interest or pleasure in doing things?”

Depression in Pregnancy

If ‘yes’ to either question, ask:

- “Is this something you feel you need or want help with?”

Depression in Pregnancy

It is strongly recommended that specialist psychiatric care be arranged for pregnant or postpartum women with:

- Past history of SMI e.g. schizophrenia, BPD, postnatal psychosis and severe depression.
- Previous treatment by a psychiatrist, including inpatient care.
- F/H maternal perinatal mental illness
- Grade D, Level 4

Scales for Children and Adolescents

- Center for Epidemiologic Studies Depression Scale (CESD)
- Child Development Inventory (CDI)
- Asian Children Development Scale (ACDS)
- Patient Health Questionnaire-2 (PHQ-2)

Screening Tools

- Hamilton Depression Rating scale HAM-D
- Hospital Anxiety and Depression Scale (HADS)
- Montgomery- Asberg Depression Rating Scale (MADRS)
- Beck Depression Inventory (BDI)
- Patient Health Questionnaire -9 (PHQ-9)

Monitoring of outcomes

The Clinical Global Impression (CGI) rating scales are commonly used measures of symptom severity, treatment response and treatment efficacy in studies of patients with mental disorders. The scales are quick to administer and helps clinicians to monitor patient progress in a consistent, systematic manner. Two questions i.e. severity, gpbal improvement. Each with 7 responses.

GPP

THANK YOU