Use of antidepressant medication following acquired brain injury: concise guidance*

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ABSTRACT – Depression is increasingly recognised as a common sequel to acquired brain injury and the use of antidepressant medication in this context has increased markedly over recent years. However, these drugs are not without side effects – some of them serious – and they should not be used without proper evaluation and monitoring. This set of concise guidance was developed jointly by the British Society of Rehabilitation Medicine, the British Geriatrics Society and the Royal College of Physicians, to guide clinicians working with people who have brain injury of any cause (ie stroke, trauma, anoxia, infection etc). The guidance covers (a) screening and assessment of depression in the context of brain injury, (b) issues to consider and discuss with the patient and their family before starting treatment, and (c) proper treatment planning and evaluation – including planned withdrawal at the end of treatment.

KEY WORDS: antidepressive agents, brain injuries, depression, practice guidelines

Box 1. Depression in acquired brain injury (ABI).

Reasons why depression may occur following ABI

- An emotional response to the sudden onset of disability and its associated life changes.
- A direct result of the brain injury leading to altered biochemical balance within the brain and resulting change in the background level of mood.
- Preceding tendency to depression or history of depressive illness.

*Reasons why symptoms that **mimic** depression may occur following ABI*

- Other emotional disorders associated with brain injury, such as apathy or emotional lability, may give the appearance of depression.
- Somatic symptoms which characterise depression in the normal population may occur as a result of hospitalisation or from the brain injury itself. These symptoms may include:
  - loss of energy, appetite and libido
  - altered sleeping habits
  - poor concentration, inability to make decisions, etc.
- Abnormal physical expressions of emotional status may give the appearance of depression, eg:
  - disorders of facial expression
  - flat speech patterns
  - general physical slowness.

Introduction and aims

Acquired brain injury (ABI) – whether due to stroke, trauma or any other cause – is frequently complicated by depression, which can interfere with rehabilitation, leading to poorer outcomes. The use of antidepressants in the treatment of depression following ABI is increasingly widespread. Because it may not be practical to involve a psychiatrist in all cases, first line management is usually undertaken by general clinicians. However, at present, many people are given antidepressant medication as a matter of routine – often without their knowledge and without any clear treatment plan.

The aim of these guidelines is to provide the general physician, GP or other clinician with a safe approach to managing *minor to moderate* depression in the context of rehabilitation or recovery from ABI, and to identify those individuals who require referral to mental health services.

The guidelines focus on the use of antidepressant drugs, but these are by no means the only way to manage depression following ABI, and it is important in any event to consider other contributing factors before reaching for the prescription pad. Alternative interventions may include simple measures to address environmental or other factors which contribute to low mood (such as missing their home and family, or worries about life outside hospital), and non-pharmacological interventions, such as 'talking therapies', for patients who have the cognitive and communicative abilities to engage successfully.

The guidelines have been prepared in accordance with the principles laid down by the AGREE Collaboration (Appraisal of Guidelines for REsearch and Evaluation).[1] A summary of the guideline development process is given in Table 1. Although developed specifically with brain injury in mind, the main principles applied here may also be applicable in other conditions, especially where the person's ability to interact is impaired.

*A fuller version of this guidance will be published by the Royal College of Physicians in June 2005. See end of paper for details.

The aetiology of depression in acquired brain injury

Reported frequencies of depression following ABI vary, but are generally around 30–40%.[2–7] Depression may remit between one and two years after injury,[8–10] at least in a proportion of cases. The aetiology of depression in the context of ABI is often multifactorial, and it is important to understand the reasons why it occurs in order to determine the circumstances in which antidepressants may or may not help (see Box 1). Antidepressants may be helpful for depression, and possibly other mood disorders such as emotional lability, but are unlikely to be helpful where clinical features of the brain injury itself mimic depression.

Diagnosis and measurement of depression

The possibility of depression should be considered in all patients following ABI. Screening and assessment of depression, however, carries no benefit if it is not followed through to appropriate treatment planning and continued monitoring to ensure response. A number of measures have been developed to quantify depression. These exist in several different formats which may be chosen to suit the patient's capabilities in response. Whatever the assessment process used, it must be timely and practical to allow for repeat use on subsequent occasions for comparison. The fuller version of this guidance (see end of paper) provides a more detailed account of the various scales available, but three simple and freely available scales are presented here for basic screening in clinical settings. These are:

- *Depression Intensity Scale Circles* (DISCs)[11] – a simplified visual analogue scale specifically designed for people with communication or cognitive difficulties, but who have adequately preserved visuo-spatial skills (Fig 1).
- *The Short-Form Geriatric Depression Scale* (GDS-15)[12*] – a simple questionnaire-based tool for people with adequate verbal and language skills (Box 2).

* Scales such as the Hospital Anxiety and Depression Scale (HADS) or the Beck Depression Inventory (BDI) are also widely used, but their use is restricted by copyright.

Table 1. Guideline development process.

Scope and purpose	
Overall objective of the guidelines	To clarify the main indications and contraindications to the use of antidepressants and provide guidance on a safe approach to managing mild to moderate degrees of depression in the context of recovery and rehabilitation following acquired brain injury (ABI).
The patient group covered	Adults with ABI of any cause, including stroke and other vascular injury, trauma, inflammation/infection, anoxia etc, who present with depression or low mood in the context of recovery or rehabilitation in inpatient or community settings.
Target audience	General physicians, GPs and other clinicians involved in the management and rehabilitation of patients with ABI.
Clinical areas covered	• Screening and assessment of depression in the context of ABI • Selection of patients for whom antidepressants are appropriate • Providing information and obtaining informed consent • Treatment planning and monitoring, including withdrawal • Which patients to refer for formal psychiatric advice.
Stakeholder involvement	
The Guideline Development Group (GDG)	A multidisciplinary working party representing: • physicians practising in stroke medicine, and rehabilitation for adults across the age ranges • liaison psychiatry, neuropsychiatry, clinical neuropsychology • primary care • representatives of patients and user groups.
Funding	The project was jointly funded by the British Society of Rehabilitation Medicine (BSRM) and the British Geriatrics Society (BGS).
Conflicts of interest	Conflicts of interest were fully declared and are summarised in Appendix 1 of the fuller version of this guidance.
Rigour of development	
Evidence gathering	Evidence for these guidelines was provided by review of Cochrane Library, Medline, Embase, conference proceedings and other guidelines up to October 2004. Articles not published in English were excluded. As part of the guideline development, a survey of consultant members of the BSRM and BGS was undertaken to establish current practice in the UK regarding the use of antidepressant medication in the context of rehabilitation following ABI.[23]
Review process	The evidence was evaluated by members of the GDG.
Links between evidence and recommendations	The system used to grade the evidence and guidance recommendations is that published by the Royal College of Physicians.[26] In the absence of specific research evidence on which to base the detailed advice, all recommendations in this set of guidelines are graded at level C.
Piloting and peer review	Not yet piloted.
Implementation	
Tools for application	Tools for implementation are included in the fuller version of this guidance.
Plans for update	The guidelines will be reviewed in 2008.

Instructions for administration

- This is a scale to measure depression. Please point to each of the circles in turn to make sure that you can see them all.
  [Continue only if satisfactorily accomplished]
- The grey circles show how depressed you feel.
  [Indicate the clear circle at the bottom]
- The bottom circle shows no depression.
  [Indicate the fully shaded circle at the top]
- The top circle shows depression as bad as it can be.
  [Pointing at each circle in ascending order]
- As you go from the bottom circle to the top, you can see that depression is becoming more and more severe.
- Which of these circles shows how depressed you feel today?

To the administrator:

In your opinion was the person able to understand this scale?

Yes ☐ No ☐

Comment

Fig 1. The Depression Intensity Scale Circles (DISCs).[11] The DISCs is displayed on a laminated card; each circle is 2 cm in diameter; the scale measures 15 cm from the centre of the bottom circle to the centre of the top circle; a pictorial version is also available.

Box 2. Geriatric Depression Scale (Short Version).[12]

	Choose the best answer for how you felt over the past week.	Points for Response: Yes	No
1	Are you basically satisfied with your life?	0	1
2	Have you dropped many of your activities and interests?	1	0
3	Do you feel that your life is empty?	1	0
4	Do you often get bored?	1	0
5	Are you in good spirits most of the time?	0	1
6	Are you afraid that something bad is going to happen to you?	1	0
7	Do you feel happy most of the time?	0	1
8	Do you often feel helpless?	1	0
9	Do you prefer to stay at home, rather than go out and do new things?	1	0
10	Do you feel you have more problems with memory than most?	1	0
11	Do you think it is wonderful to be alive now?	0	1
12	Do you feel pretty worthless the way you are now?	1	0
13	Do you feel full of energy?	0	1
14	Do you feel that your situation is hopeless?	1	0
15	Do you think that most people are better off than you are?	1	0
	Total score		

Interpretation of scores:
0-5: 'normal' for older people;
6-9: borderline depression;
10-15: probable depression.

- *The Signs of Depression Screening Scale* (SDSS)[13] – a simple tool based on observation of behaviour such as crying, withdrawal, or apathy which may be useful where the individual is unable to respond to either of the above (Box 3).

More detailed assessment is then required for those in whom depression is suspected, to distinguish symptoms of depression from the general effects of ABI, and to quantify the severity of depression prior to considering treatment. A schema for assessment is outlined in Fig 2.

Capacity and consent

The capacity to consent to treatment requires the patient to be able to:

(a) understand and retain information about the treatment proposed and any alternative options that may be available, and

(b) weigh up the benefits and risks associated with treatment, including any possible consequences of declining treatment.

Box 3. Signs of Depression Screening Scale (SDSS).[13]

1	Does the patient sometimes look sad, miserable or depressed?	Yes/No
2	Does the patient ever cry or seem weepy?	Yes/No
3	Does the patient seem agitated, restless or anxious?	Yes/No
4	Is the patient lethargic or reluctant to mobilise?	Yes/No
5	Does the patient need a lot of encouragement to do things for him/herself?	Yes/No
6	Does the patient seem withdrawn, showing little interest in the surroundings?	Yes/No
	Total score	

Score 1 for 'yes' and 0 for 'no'.

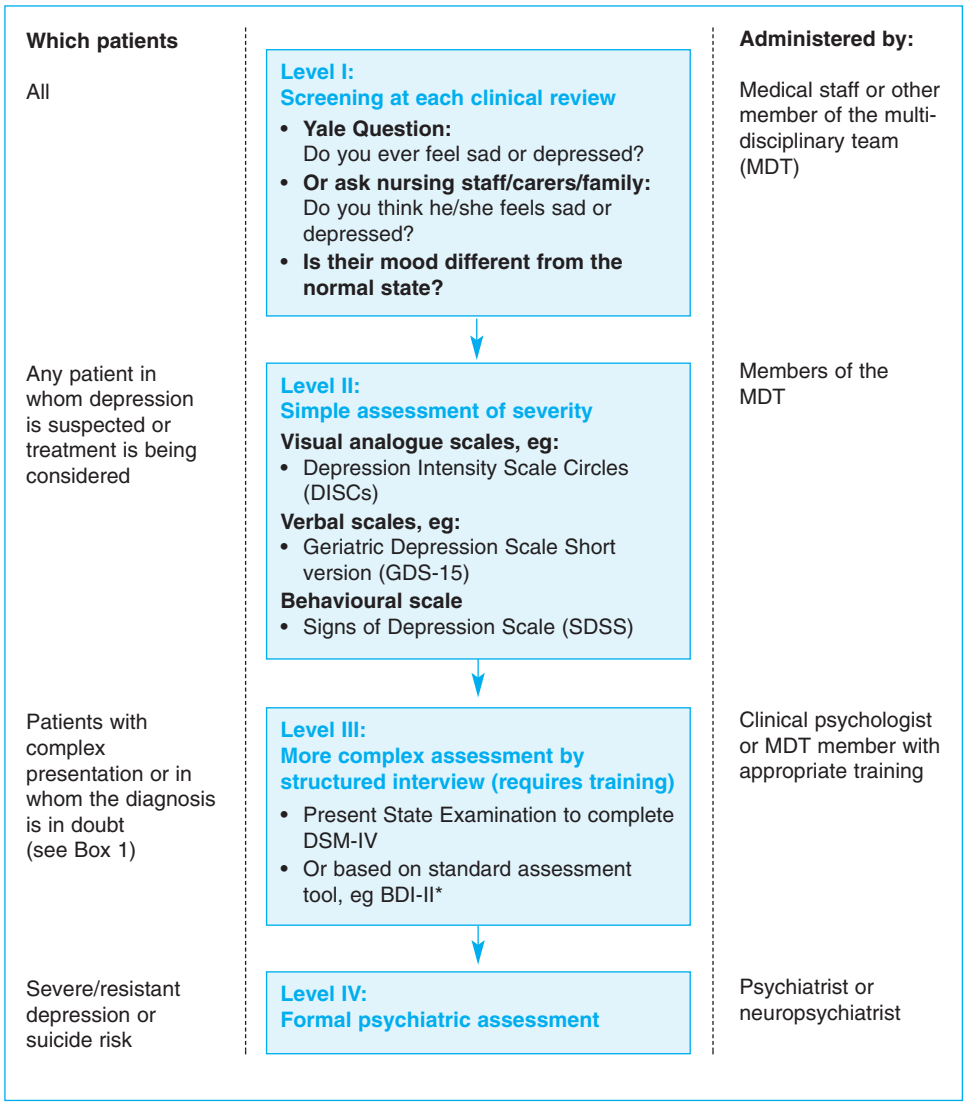

Fig 2. Screening and assessment of depression in ABI.
DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders*, American Psychiatric Association, 1994. BDI = Beck Depression Inventory II.
*Use of the Beck Depression Inventory scales is restricted by copyright. It is necessary to purchase a licence to use them. Obtainable from Harcourt Assessment. Halley Court, Jordan Hill, Oxford OX2 8EJ. Tel: 01865 888188. Fax: 01865 314348 Email: info@harcourt-uk.com

People who have ABI may have cognitive and communicative difficulties that limit their capacity to make informed decisions about their treatment and to give consent, or their judgement may be clouded by the depression itself. In these situations, assessment may be complex and formal psychiatric advice may be required.

Even when patients can give consent, they may feel uncertain about why treatment is being recommended. Every effort should be made to provide the right information at the right time and in an accessible format (see fuller version for sample information sheet).

The evidence for use of antidepressants in people with ABI

Systematic review and assimilation of the evidence for use of antidepressants in ABI is confounded by heterogeneity in research design, time-points of measurement and instruments used to assess depression. Most studies to date have examined short-term effects only, with no standardised assessment of adverse effects. There is little or no formal research-based evidence to date to inform the most appropriate regimen or length of treatment. However, the following general conclusions may be drawn from the literature:

- Antidepressants are reasonably safe and acceptable to patients, but probably less effective than originally supposed. Overall, approximately four patients would need to be treated to produce one recovery, and one in ten patients would drop out because of side-effects.[14]
- All antidepressant drugs lower the threshold for seizures, which is a particular concern in the context of ABI.
- Improvement in symptoms of depression or lability is often reported,[15–19] but actual gains in function or quality of life are harder to demonstrate.[20]
- Selective serotonin re-uptake inhibitors (SSRIs) appear generally to be about as effective as tricyclic antidepressants (TCAs), but have fewer reported side-effects,[21] and are probably therefore cost efficient despite the slightly higher drug costs.[22]

Table 2. Concise guidelines on the use of antidepressant medication following acquired brain injury.
These guidelines are summarised in Fig 3.

Grade of recommendation

1 Screening* — **C**

The possibility of depression should be considered for any patient with acquired brain injury.

- At the very least the patient should be asked 'Do you often feel sad or depressed?' at each assessment.
- For individuals who are unable to respond, staff should consider whether their behaviour suggests depression (eg apathy, withdrawal, non-compliance, excessive crying etc).
- Assessment should include inquiry for prior psychiatric history or any previous use of antidepressant medication, and should take into account previous personality and emotional traits, and change from normal personality.
- The cause of apparent distress should be explored with the patient by an appropriate professional.

2 More detailed assessment of mood* — **C**

For patients in whom depression is suspected, more detailed assessment of mood should be undertaken:

- using validated instruments, interview and/or observation
- to determine the severity of depression and contributing factors.

3 Before considering treatment for depression: — **C**

The clinician should consider the following questions:**

- Is depression interfering with the patient's quality of life or progress in rehabilitation?
- Is antidepressant treatment really needed at this time or are other interventions more appropriate in the first instance?
  For example, are there simple interventions which would improve quality of life and hence boost the patient's mood?
- Has a period of watchful waiting (ie at least 2–3 weeks) demonstrated that the problem is not resolving spontaneously?
- Has the patient and their family (where appropriate) been properly informed about the nature of depression and different treatment options?

4 Before starting an antidepressant: — **C**

The clinician should consider the following questions:†

- Are there any contraindications to treatment?
- Do the likely benefits outweigh the risks?
- Has the patient given informed consent – or, if unable to consent, have appropriate procedures been followed?
- How will you know if the antidepressant has worked?

5 Formulating the treatment plan‡ — **C**

Antidepressants should be prescribed according to an agreed treatment plan which includes:

a Baseline assessment using an appropriate validated measure of depression
b Baseline urinalysis, and blood samples for FBC, U&E and LFTs
c Selection of an appropriate agent
d Clinical review of initial response to optimise dose at 2–3 weeks
e Repeat assessment of mood after 6–8 weeks (using the same measure as in (a)) to assess the effect
f In the case of a positive treatment response, an agreed treatment plan outlining:
  – length of treatment (usually 6 months)
  – procedure for withdrawal at the end of treatment and who will supervise this.
g If the response to an appropriate dose of medication is poor or absent at 6–8 weeks, the drug should be withdrawn and alternative treatment or referral considered.

6 During treatment — **C**

- Patients should see their doctor regularly during treatment (at least every 2 months) and any clinical deterioration during treatment should be investigated. In particular, the following should be considered as possible side-effects of treatment:
  – hyponatraemia, seizures, GI bleeding, anti-cholinergic symptoms, sexual dysfunction, sedation, hallucinations, increased confusion, headache.
- Antidepressant medication should not be given under automatic repeat prescription, and no more than 2 months supply should be given in any prescription.

7 Referral for formal psychiatric review — **C**

The patient should be referred for formal psychiatric review if:

- Depression is very severe or resistant to treatment
- There is a past history of psychiatric disorder
- The patient shows evidence of suicidal ideation or intent – this should trigger emergency referral
- It seems likely that the patient needs to be treated under section of the Mental Heath Act 1983 or equivalent.

8 Withdrawal from treatment — **C**

At the end of the treatment period (4 to 6 months) there should be a planned withdrawal of antidepressant medication, which should be undertaken gradually over a period of 1 to 2 months.

Prior to withdrawal:

- The patient's mood should be re-evaluated using the same measure as at baseline
- The patient/family should be warned to expect rebound symptoms.

In the event of significant longer-lasting relapse of depression, the need for long-term treatment should be considered and formal psychiatric advice sought.

* See Fig 1 and the fuller version for further details.
** See checklist in the fuller version.
† The checklist in the fuller version may be freely photocopied to assist in this process
‡ This process is summarised in Fig 2.
FBC = full blood count; LFT = liver function tests; U&E =.Urea and electrolytes.

- TCAs, however, may still have a role, particularly in the presence of symptoms such as neuropathic pain, hyper-salivation or insomnia, where their 'side-effects' may actually be desirable.[23]

Choice of antidepressant

There are important pharmaco-kinetic differences between the six SSRIs currently available, notably in their ability to inhibit hepatic cytochrome P450 iso-enzymes which are responsible for the metabolism of many drugs.[24] Citalopram and sertraline are among the more specific agents and *in vitro* studies suggest they are least likely to inhibit these iso-enzymes. A recent survey of rehabilitation consultants and geriatricians in the UK[23] has demonstrated these two agents to be the most common first choice for management of depression following ABI at present. More detailed information about the choice of antidepressant is given in the fuller version. Recent preliminary data in non-brain-injured patients suggest that St John's Wort may be as effective and better tolerated than paroxetine, but there is as yet no data on patients with ABI, or in comparison with the more specific agents which are preferred in this context.[25]

The guidelines

The guidelines are laid out in Table 2 and summarised systematically in Fig 3.

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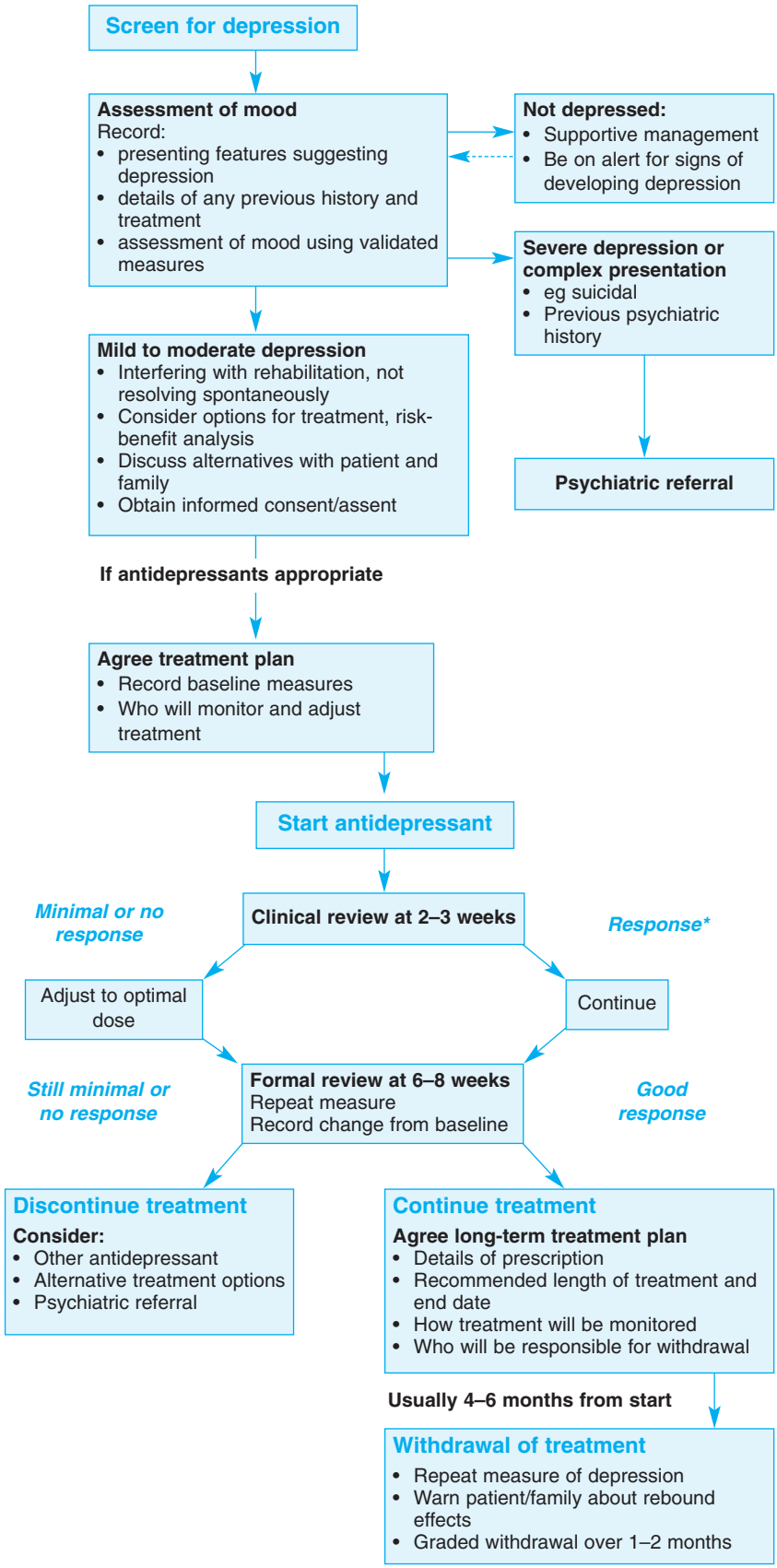

Fig 3. Depression management flowchart (see Guidelines, Table 2). *Response to SSRIs is often seen within 1–2 weeks of starting treatment, but TCAs may take longer to have effect.

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