Anxiety disorders in intellectual disability: medication use and evidence-based practice

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Anxiety vs fear vs anxiety disorder

Anxiety has 2 components-

- Physiological sensations
- Awareness of being nervous/ frightened

Anxiety is a normal adaptive response to survive danger, through fight, flight or freeze.

Anxiety is response to impending danger.

Pathological anxiety is anxiety disorder

- Inappropriately triggered
- Maladaptive

Definition of anxiety disorder

ICD11 Anxiety or fear-related disorder-

‘’ excessive fear and anxiety and related behavioural disturbances, with symptoms that are severe enough to result in significant distress or significant impairment in personal, family, social, educational, occupational, or other important areas of functioning’’

Definition of anxiety disorder

ICD11- Anxiety or fear-related disorder	DSM 5- Anxiety disorders
Generalised anxiety disorder	Generalised anxiety disorder
Panic disorder	Panic disorder
Agoraphobia	Agoraphobia
Specific phobia	Specific phobia
Social anxiety disorder	Social anxiety disorder
Separation anxiety disorder	
Selective mutism	
Unspecified	

Associated disorders

Anxiety disorders can occur in isolation

Co-morbid with other psychiatric disorders like depression

Consequence of physical illness like thyrotoxicosis

Substance induced like alcohol, cannabis, opioid, cocaine, stimulant, caffeine (a separate category under anxiety disorders in ICD11)

Epidemiology-

People with ID are at higher risk

In general population,

- Most prevalent mental disorder.
- Lifetime prevalence 31% (Katzman et al 2014)
- Incidence 9.7 per 1000 person-years in UK primary care (Martín-Merino et al 2010).
- Anxiety symptoms- 4-5%

In people with ID,

- Anxiety disorder could be underreported and underdiagnosed.
- But prevalence rates similar to general population (Cooray et al, 2022)
- Anxiety symptoms- 22% compared to 4-5% in general population (Edwards et al, 2022).

Aetiology

Clinical presentation

Psychological (Cognitive)	Physical (autonomic arousal)	Behavioural (motor)
Poor concentration	GI- Dry mouth Difficulty swallowing Epigastric discomfort Excessive wind Frequent or loose stools	Restlessness
Worrying thoughts	Respiratory- Difficulty inhaling Chest constriction Hyperventilation	Inability to sit or stand still for long
Fearful anticipation	Cardiovascular- Chest discomfort Palpitations	
Irritability	Muscle tension- Headache Tremor Muscle ache	
	Sleep- Insomnia Night terrors	

How presentation is different in ID

Commonly noticed behavioural patterns-

- Agitation, screaming, crying, withdrawal, regressive/ clingy behaviour, freezing.
- Restless, easily fatigued, irritable, sleep disturbance.
- Increased drinking, hyperventilation, sweating, urinary frequency, hyperactivity, vomiting, tremulousness.

Diagnostic criteria for psychiatric disorders for use in adults with learning disability (2001) by Royal college of psychiatrists &

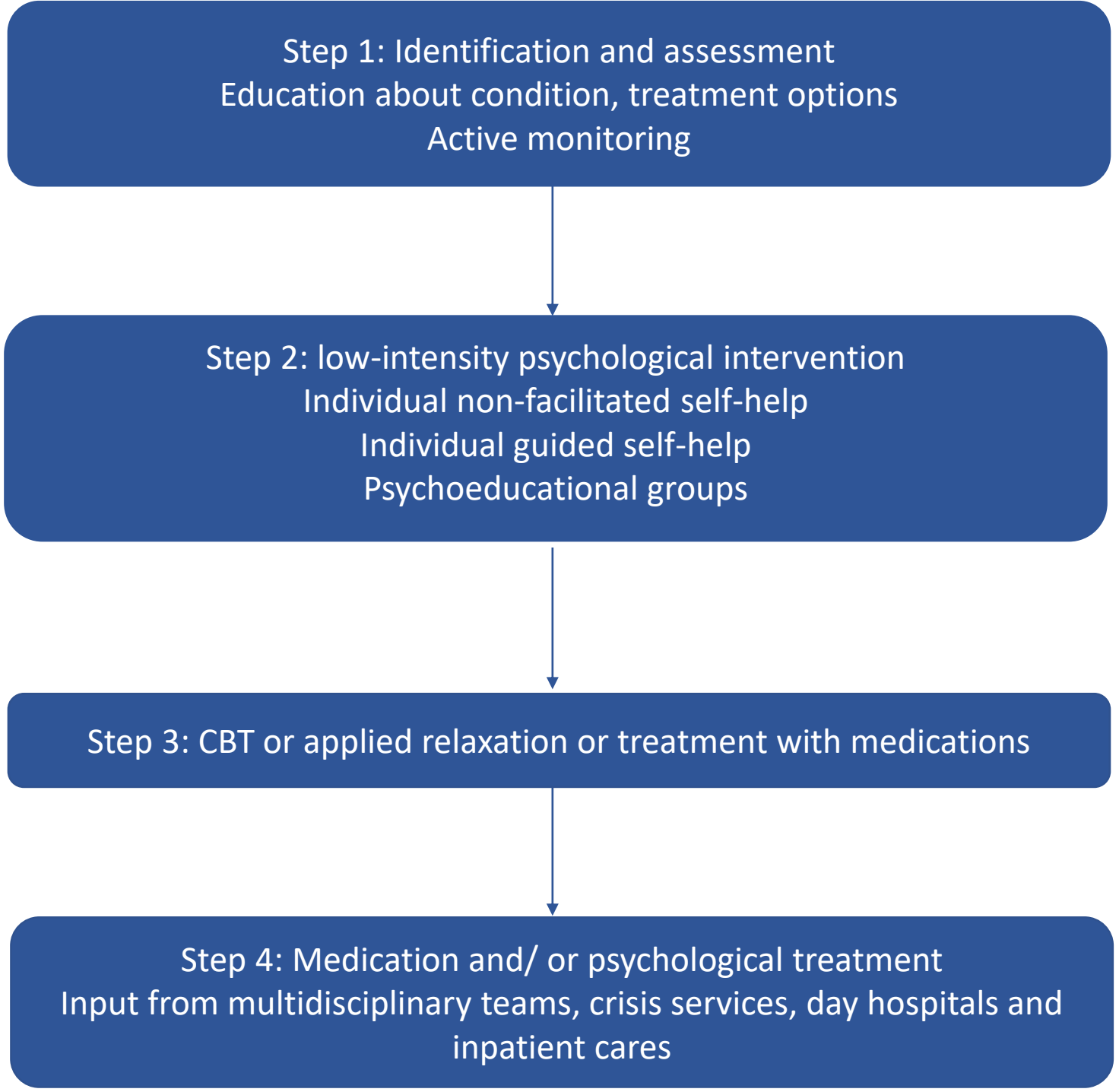
Diagnostic manual- intellectual disability (2007) by NADD and APA

Diagnostic framework

- the 5-P model of the presenting problem, predisposing, precipitating, perpetuating and protective factors (Macneil et al, 2012)

- the HELP framework of Health, Environment, Lived experience and Psychiatric problems (Green et al., 2018)

Treatment guidelines in general population for GAD and Panic disorders



Medication use in general population as per NICE

First line: SSRI like sertraline

Second line: Alternative SSRI or SNRI

Third line: Pregabalin

Not to use Benzodiazepines unless for short-term
Not to use antipsychotics in primary care

Treatment guidelines in ID

- Specific evidence base limited
- Similar to general population
- Choice determined by symptoms, associated impairment and distress, co-morbid physical/ psychological symptoms/ patient characteristics and preferences, availability of interventions, clinician experience, response to previous treatments.

Overview of non-pharmacological treatment

- Reassurance, counselling, relaxation therapy, anger management, guided self-help.
- NICE- relaxation therapy for anxiety symptoms and graded exposure to treat anxiety symptoms or phobias.
- Low intensity Psychological Interventions
  - individual non-facilitated self-help
  - individual guided self-help
  - psychoeducational groups.
- High Intensity Psychological Interventions
  - CBT
  - Applied relaxation

Treatment guidelines in ID

Evidence base for pharmacological treatment in GAD

SSRI, SNRI, TCA, Trazodone, agomelatine-

- Systematic reviews and randomised placebo-controlled trials, acute treatment with these antidepressants for GAD:

  Substantial evidence for their efficacy (Baldwin et al., 2011a, Baldwin et al., 2011b; National Institute for Health and Clinical Excellence, 2011)

Pregabalin (Wensel et al 2012), some Benzodiazepines (Martin et al 2007), Busipirone (Chessick et al 2006), some Antipsychotics (Lalonde and Van Lieshout 2011), Hydroxyzine- an antihistamine (Guaiana et al 2010)-

- Placebo- controlled acute treatment studies:

  Showed good efficacy

Beta blockers

- Placebo-controlled study in acute treatment:

  Minimal efficacy (Meibach et al 1987)

Evidence base for pharmacological treatment in GAD

SSRIs as first line-

- Broad-spectrum efficacy in short term and long term treatment
- Generally well tolerated

Duration-

- Acute treatment studies indicate steady increase in response over time (Baldwin et al 2011a)
  - Escitalopram or paroxetine from 8-24 weeks (Bielski et al 2005)
  - Sertraline from 4-12 weeks (Allgulander et al 2004a)
  - Venlafaxine from 8-24 weeks (Montgomery et al 2002)
- Several RCTs:
  - Response is likely only if there is an onset of effect within four weeks of treatment (Pollack et al., 2008, Baldwin et al., 2009, Baldwin et al., 2011a)
- Randomised placebo-controlled relapse prevention studies:
  - Significant benefit on treatment for 6-18months ((Baldwin et al., 2011b, 2012; Katzman et al., 2011; Rickels et al., 2010)

Evidence base for pharmacological treatment in GAD

- Some patients who have not responded to an initial low dosage may respond to a higher daily dose e.g. the efficacy of pregabalin is more marked at higher daily doses (Bech, 2007; Lydiard et al., 2010).
- The addition of pregabalin to SSRI or SNRI is superior to continued treatment with SSRI or SNRI alone (Rickels et al., 2012).
- Augmentation of antidepressants with antipsychotics may be beneficial (Brawman-Mintzer et al., 2005; Pollack et al., 2006; Altamura et al., 2011).

Evidence base for pharmacological treatment in Panic disorder

All SSRIs, Venlafaxine (SNRI), Reboxetine (NARI), Phenelzine (MAOI), some Benzodiazepines and Anticonvulsants, Gabapentin, Sodium valproate-

- Randomised double blind placebo-controlled trials:

  Efficacious in acute treatment (Batelaan et al 2012)

Pharmacological, psychological and combination-

- Systematic reviews:

  Effective in acute treatment (Andrisano et al., 2013; Batelaan et al., 2012; Schmidt and Keough, 2010; Furukawa et al., 2007; Watanabe et al., 2007).

Some SSRIs (Fluoxamine, paroxetine) more effective than some NARIs (maprotiline, reboxetine) as per some RCTs (Bertani et al., 2004; Den Boer and Westenberg, 1988).

Evidence base for pharmacological treatment in Panic disorder

Buproprion, Propranolol, Busipirone

Lack efficacy in acute treatment (Sheehan et al., 1983; Munjack et al., 1989; Sheehan et al., 1988).

Unknown potential value of antipsychotic monotherapy in acute treatment (Depping et al 2010).

Duration

- Increase in steady response over time (Batelaan et al 2012)
- SSRI or clomipramine 12-52 weeks

  Increased response rates in double blind studies ((Ballenger, 1998; Lecrubier and Judge, 1997; Lepola et al., 1998).
- Fluoxetine, Impramine, Paroxetine, Sertraline, Venlafaxine 6months

  Significant advantage in placebo-controlled and other relapse-prevention studies.

Evidence base for pharmacological treatment in Panic disorder

Acute treatment-

- Psychotherapy and antidepressant combination superior than either alone (Furukawa et al., 2007; Koszycki et al., 2011; Van Apeldoorn et al., 2010)

Relapse prevention-

- Combination more effective than antidepressant alone, but no different than psychological treatment alone (Furukawa et al 2007)

Evidence base for pharmacological treatment in Social anxiety disorder

- Meta-analyses and RCTs indicate that a range of approaches are efficacious.
- Antidepressant drugs with proven efficacy include most SSRIs, the SNRI venlafaxine, phenelzine, and moclobemide
- Nefazodone is not efficacious and the evidence for mirtazapine is inconsistent (De Menezes et al., 2011).
- Bromazepam and clonazepam, gabapentin and pregabalin, including olanzapine also appear efficacious in acute treatment (Blanco et al., 2013).
- Buspirone and beta-blocker atenolol are not efficacious in generalised social anxiety disorder (Blanco et al., 2013) but some benefit with beta-blockers in performance anxiety.
- Duration-

  SSRI or SNRI 12-24 weeks increased response rates (Lader et al., 2004; Stein et al., 2002a, 2003).

  Clonazepam, escitalopram, paroxetine, pregabalin, sertraline 6months beneficial for relapse prevention (Blanco et al 2013)

Evidence base for pharmacological treatment in ID

Antidepressants (SSRI citalopram & SNRI mirtazapine)-

- Retrospective study of 17 patients with pervasive developmental disorders, aged 4-15, treated in open-label trial of citalopram:
  - 59 % much improved or very improved on anxiety and aggression, using CGI (Couterier & Nicolson 2002)
- Retrospective chart review of 15 children and adolescents with pervasive developmental disorders (asperger's, autism, PDD NOS), treated with citalopram:
  - 66 % showed significant improvement in anxiety symptoms (Namerow et al. 2003)
- Open-label trial with SNRI mirtazapine in 26 patients with pervasive developmental disorders:
  - 34.6% (9 patients) much improved or very much improved on CGI scale (Posey et al. 2001)

Evidence base for pharmacological treatment in ID

Risperidone

- Double-blind, placebo-controlled trial of atypical antipsychotic risperidone in adults with pervasive developmental disorders and comorbid anxiety:
  - Treatment group demonstrated significant reduction in anxiety and other psychiatric symptoms compared to control group (McDougle et al 1998)
- Case study of 14 children and adolescents with developmental disorders treated with risperidone:
  - 10-14 patients showed marked reduction in anxiety (Fisman & Steele, 1996)

Evidence base for pharmacological treatment in ID

Busipirone

- Open-label trial of busipirone for anxiety in 22 children, aged 6-17 with pervasive developmental disorders:
  - 9 showed marked therapeutic response on CGI,
  - 7 showed moderate response on CGI (Buitelaar et al 1998)
- Study of 6 adults with ID:
  - Showed reduction in aggression and anxiety (Ratey et al 1991)

Evidence base for pharmacological treatment in ID

- These studies are mostly in those with ASD/pervasive developmental disorder and quite dated now.
- NICE recommends referring to NICE guidelines on specific mental health problems.
- A large multi-centre, placebo-controlled, RCT in UK and Australia to compare sertraline and placebo in anxiety for autistic adults (Rai 2022)- currently under way.

Assessment

- Step 1
- Detailed diagnostic assessment (Alexander et al, 2010; Chester et al., 2023)-

Degree of ID
Cause of ID
Behavioural phenotypes
ASD or other neurodevelopmental disorders
Mental illness including anxiety disorder
Personality disorders
Substance misuse
Physical health condition
Psychosocial stressors
Challenging behaviour

- Followed by formulation as detailed earlier

Non-pharmacological interventions

- Step 1 and step 2-

Education to both patients and support staff

Low-intensity psychological interventions

- Step 3 and step 4:

High intensity psychological interventions like relaxation training and or cognitive therapy.

Medication use recommendations

- Step 3 and 4
- Medication history including OTC
- Self-medication with alcohol or drugs
- Check for potential drug interactions
- History of sensitivity to side-effects
- Discussion with patient and carers/family about target symptoms, monitoring and follow ups.

Medication choice for different anxiety disorders in ID

Anxiety Disorder	First Line	Second Line	Third Line	Fourth Line (No order of preference)
Generalized Anxiety Disorder	CBT; other Psychosocial and Environmental Interventions	SSRIs	SNRIs then, Pregabalin	TCAs, Buspirone, Quetiapine, Mirtazapine (Consider Propanolol if significant autonomic symptoms)
Panic Disorder	CBT; other Psychosocial and Environmental Interventions	SSRIs	SNRIs	TCAs, Mirtazapine
Social Phobia	CBT; other Psychosocial and Environmental Interventions	SSRIs (Atenolol helpful for autonomic symptoms in performance situations)	SNRIs	Olanzapine, Benzodiazepines on a PRN basis

Duration of treatment and related issues

- **STOMP by NHS 2016-**

clinicians to prescribe only when appropriate and for appropriate time

- **Benzodiazepine-**

Used only if severe, disabling

Use lowest possible dose

No longer than 4 weeks

- **SSRIs and SNRIs-**

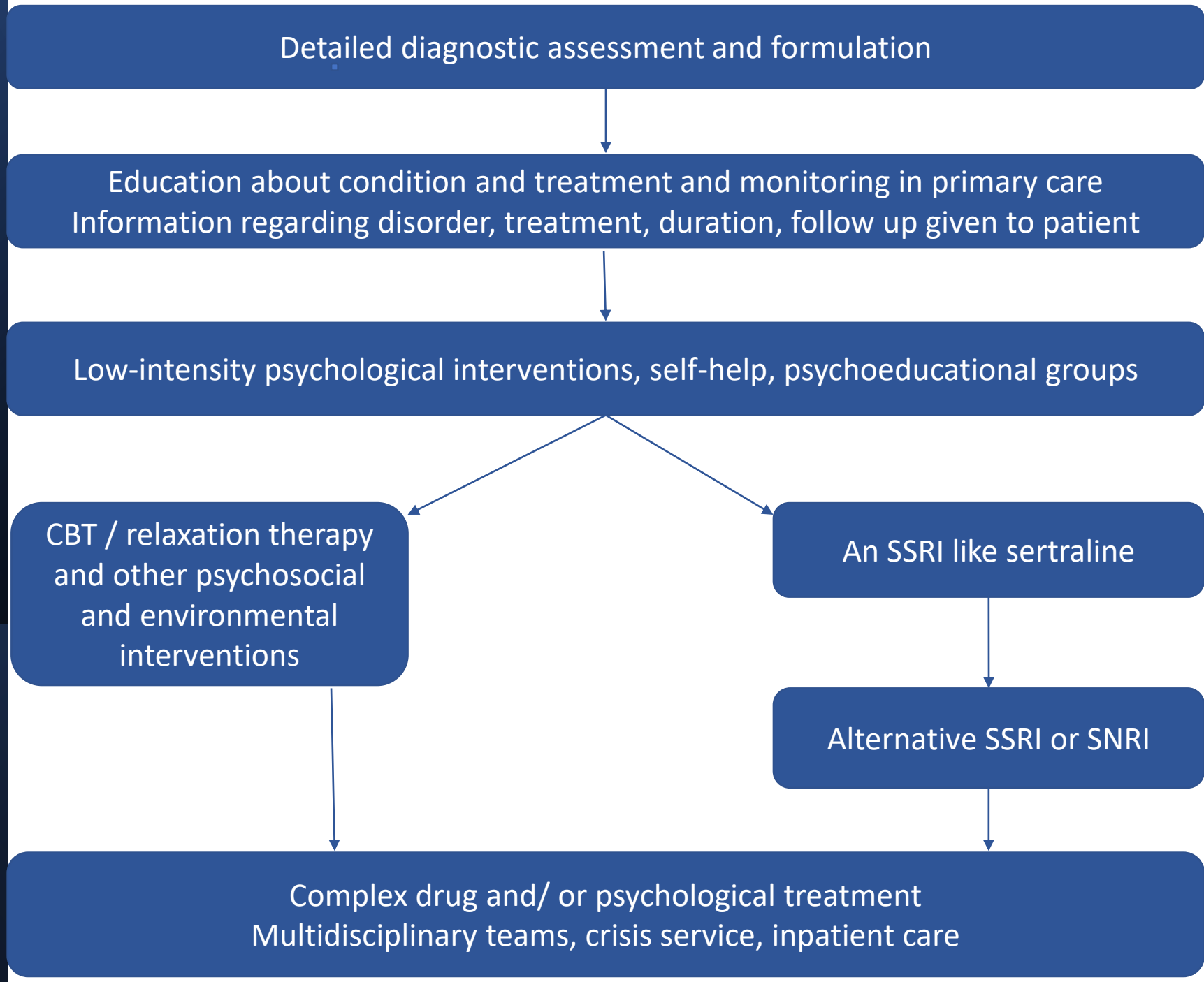
Some benefit expected in 6 weeks, and increasing with time

Duration unclear but can continue for a year

If effective, continue as abrupt discontinuation can precipitate relapse

Review 3-6monthly (Rcpsych 2016) or at least yearly (NICE 2016)

Treatment algorithm



Thank you