Child and Youth mental health: Pharmacological management of Depression/Anxiety in Adolescents

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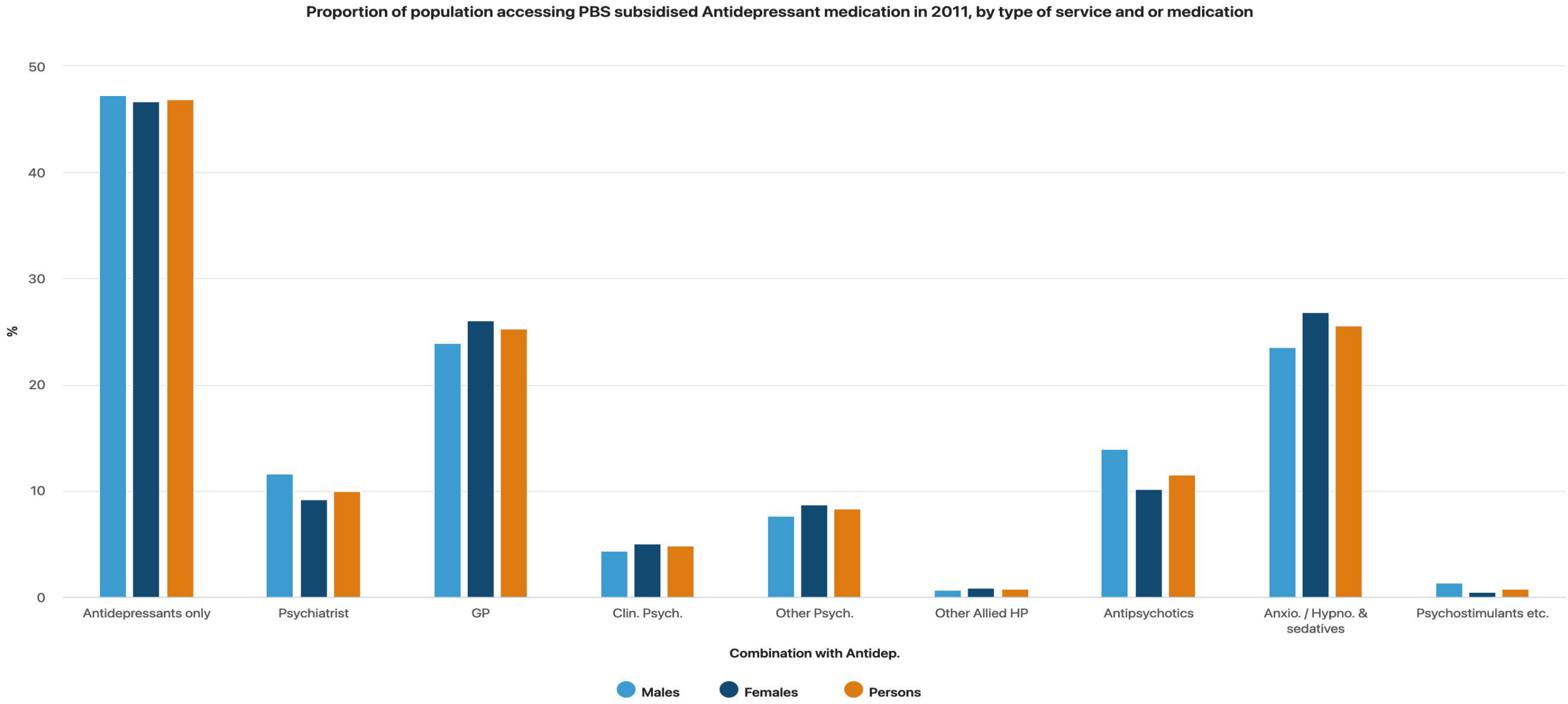
Expectations



Source(s): The Mental Health Services-Census Integrated Dataset

Source: Australian Bureau of Statistics, Patterns of Use of Mental Health Services and Prescription Medications 2011

Learning Points

Management of depression at different stages of presentation

- Acute
- Continuation
- Maintenance (and discontinuation)

Indications – When and why

General considerations when prescribing to Children and Adolescents

Assessing response to medication and setting expectations

First line choices as per guidelines, and therapeautic doses

Side Effects

Risks

Anxiety

Other presentations

Comorbidities

Introduction

- Redcliffe and Caboolture CYMHS is MNHHS' *only* Community Child and Youth Mental Health Service for …

RC-CYMHS

- Redcliffe and Caboolture CYMHS is MNHHS' ~~*only*~~ *Best* Community Child and Youth Mental Health Service for
  - Redcliffe, Caboolture and Kilkoy Hospital / Emergency Departments
  - Community Child and Youth Clinic
  - Consultation Liaison services for the hospitals
  - Working closely with out of hour Acute Care team
  - Providing such services to under 18's that may be covered in other catchment areas by additional teams such as early psychosis teams, specialist services, (e.g. eating disorders), and Acute Response Teams

CYMHS referral rates

- UK : In a typical UK NHS clinic (0–17 years), the number of children and adolescents in the catchment with depression per year will be:
  - circa 300 cases (0–17 years) per 100,000 all ages,
  - circa 30–45 (10–15%) new referrals to specialist CAMHS.

  So if a specialist clinic has a catchment population of 300,000 it could expect around 90–135 cases to be referred per annum.
- UK:

This article is more than **1 month old**

Children's NHS mental health referrals double in pandemic

Young people 'suffering terribly' in Covid crisis, with nearly 200,000 referred in just three months

The college analysed NHS Digital data on mental health referrals for children and young people aged 18 and under. It found that between April and June this year, 190,271 children aged 18 and under were referred to children and young people's mental health services – almost twice the number (97,342) referred during the same period in 2019.

Urgent referrals had also risen steeply. From April to June in 2019, 5,219 children and young people were referred for urgent care. This rose to 8,552 in 2021, the college said.

At the end of June, 340,694 people were in contact with children and young people's mental health services, up from 225,480 in June 2019.

(RCPSYCH CPD module, updated in 2018), https://www.theguardian.com/society/2021/sep/23/childrens-nhs-mental-health-referrals-double-in-pandemic, https://www.rcpsych.ac.uk/news-and-features/latest-news/detail/2021/09/23/record-number-of-children-and-young-people-referred-to-mental-health-services-as-pandemic-takes-its-toll

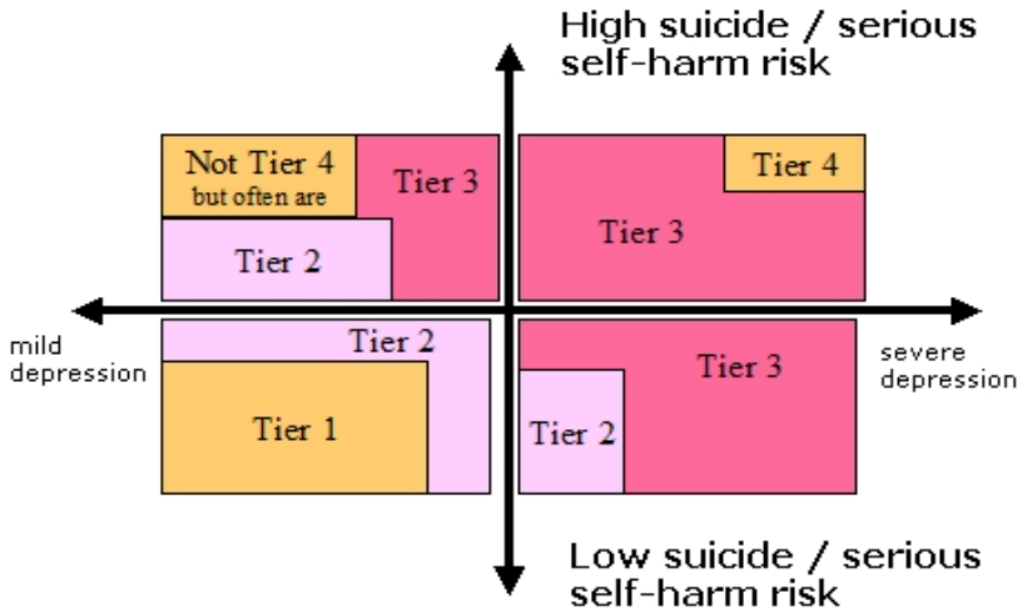
RC-CYMHS referral rates

	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec	Total
2019	103	124	171	109	125	136	111	122	124	130	147	108	**1510**
2020	100	161	146	121	153	199	143	205	178	202	213	116	**1937**
2021	111	162	199	150	211	189	170	199					1391

- RCCYMHS had a 30% increase in referrals from 2019 to 2020 (166 referrals per month)
- 2021 YTD - a further 13% increase on 2020 figures (173 referrals per month)
- 58% of all referrals to RCCYMHS are through the EDs (60% CAB ED, 40% RED ED)
- 21% of all CYMHS presentations to the EDs reside out of RedCab catchment

- Detection and management:
  - IMPACT – Goodyer 2017 – 0-12% depressed cases reach CAMHS every year
  - No more than 25% of cases of any severity the whole community are ever detected. (Garber 2009)

(1.7) Alternative representation



An alternative representation can highlight issues familiar to clinicians working with this patient group.

For example – those cases that can sometimes be referred for in-patient care because high suicidality may have been assumed to index high depression severity, when in fact depression was milder in severity, if present (but suicidality was nevertheless high).

https://learnit.ranzcp.org/course/877293/module/1361860/Scorm?LPId=0 Dr R Kelvin

Case Scenario 1

- 15 year old girl presents to emergency department, reporting an increase in suicidal ideation and recent self harming behaviour. She is frustrated that after having two different antidepressants over the past four weeks, she isn’t feeling happier. Her father is FIFO and currently working away from home. She is living with her father's partner. School’s Guidance officer used to be a source of support, but off late her attendance at school has been poor. The guidance officer is also believed to have gone on maternity leave.

Depression

- Depression is a broad diagnosis that can include different symptoms in different people. Depressed mood or loss of pleasure in most activities, are key signs of depression. Psychological themes include
  - Learned helplessness
  - Impaired problem solving
  - Distorted conflict resolution
  - Tendency to negatively ruminate (Park et al, 2004)
  - *Irritability*

- It is unlikely that the severity of depression can be understood in a single symptom count or visit
  - Develop safety plan at the earliest

https://acamh.onlinelibrary.wiley.com/doi/full/10.1111/j.1469-7610.2004.t01-1-00291.x

Longitudinal assessment

- Heterogenecity in psychiatry
  - DSM-V symptom criteria for PTSD could present in 636,120 combinations (DSM-IV PTSD criteria = 79,794 combinations) (https://doi.org/10.1177/1745691613504115)
  - DSM-V criteria for Major Depressive Disorder + PTSD = **270 million combinations** (Young et al, 2014)

- In young persons, illness may evolve over a period of time

- Symptom overlap
  - Social withdrawal of depression vs social avoidance due to anxiety
  - Altered concentration – ADHD vs Depression
  - Irritability – also prominent symptoms of oppositional defiant disorder or conduct disorder
  - Neurovegetative symptoms related to substance abuse, medical conditions
- Severity of symptoms
- Comorbidities : ADAPT study – comorbidity –anxiety avg 40% ,conduct disorders 25%, eating disorders, substance misuse, ocd etc

Longitudinal assessment

- Symptom overlap
  - Social withdrawal of depression vs social avoidance due to anxiety
  - Altered concentration – ADHD vs Depression
  - Irritability – also prominent symptoms of oppositional defiant disorder or conduct disorder
  - Neurovegetative symptoms related to substance abuse, medical conditions
- Severity of symptoms
- Environmental Factors:
  - Parental depression and family discord
  - Childhood maltreatment
  - Bullying/peer victimization
  - Sexual minority status
  - Bereavement

Longitudinal assessment

- Symptom overlap
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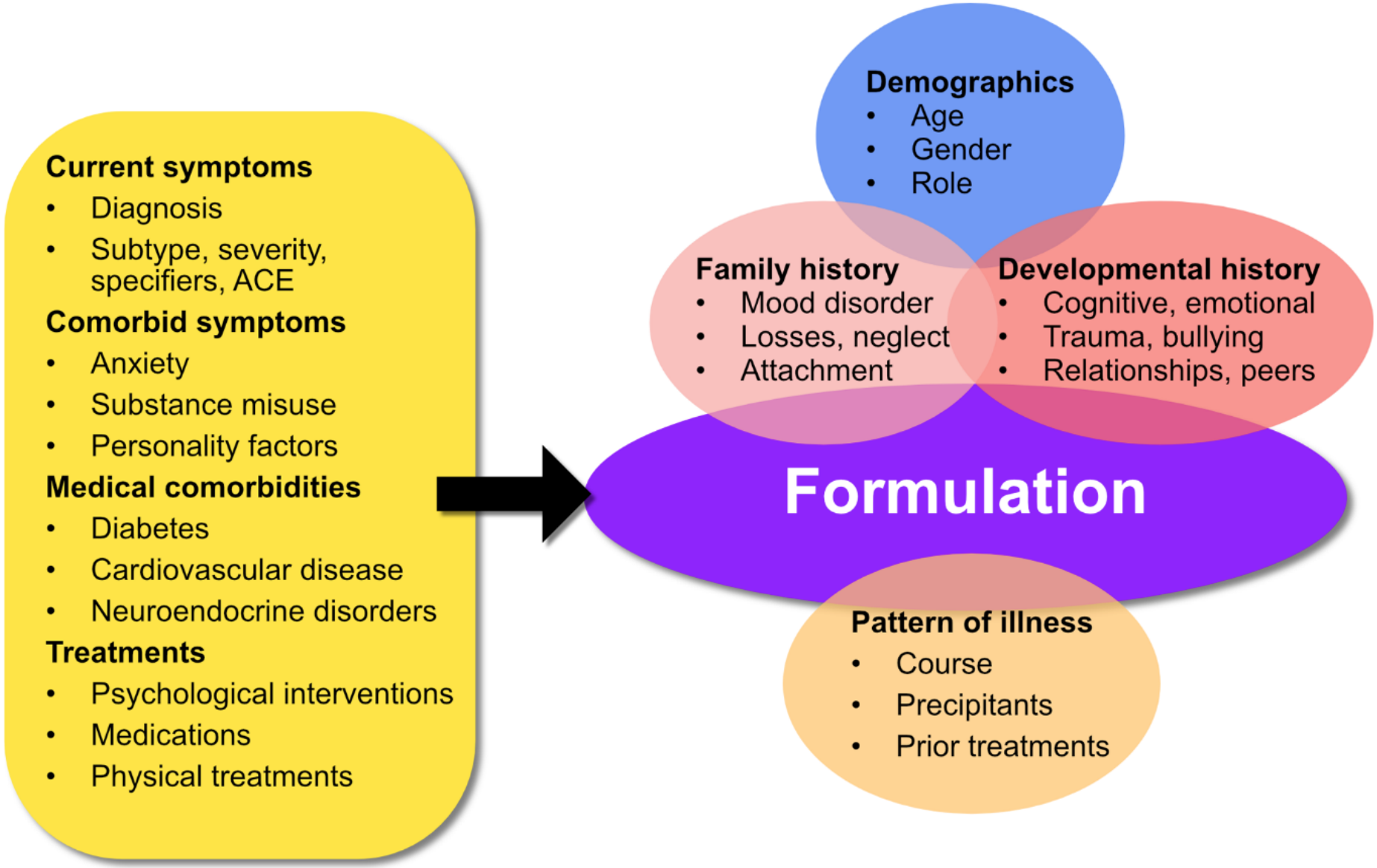
- Environmental Factors:
  - Parental depression and family discord
  - Childhood maltreatment
  - Bullying/peer victimization
  - Sexual minority status
  - Bereavement
- Identify Strengths and supports
- Inform management plans
  - Eg: substance abuse is more likely to lead to depression than vice versa (Bolden & Fergussen, 2011; Horwood et al, 2012)
  - Treatment of maternal depression, for example, has been shown to lead to symptomatic improvement in offspring (Gunlicks & Weissman, 2008)


Current symptoms
• Diagnosis
• Subtype, severity, specifiers, ACE
Comorbid symptoms
• Anxiety
• Substance misuse
• Personality factors
Medical comorbidities
• Diabetes
• Cardiovascular disease
• Neuroendocrine disorders
Treatments
• Psychological interventions
• Medications
• Physical treatments
Demographics
• Age
• Gender
• Role
Family history
• Mood disorder
• Losses, neglect
• Attachment
Developmental history
• Cognitive, emotional
• Trauma, bullying
• Relationships, peers
Formulation
Pattern of illness
• Course
• Precipitants
• Prior treatments

RACGP Red Book:

Table 10.1.2. Test to detect depression

Test	Technique	References
Question regarding mood and anhedonia	Asking two simple questions may be as effective as longer instruments: • 'Over the past two weeks, have you felt down, depressed or hopeless?' • 'Over the past two weeks, have you felt little interest or pleasure in doing things?' Asking a patient if help is needed in addition to these two screening questions improves the specificity of a GP diagnosis of depression (IV) In adolescents, consider use of HE²ADS³ assessment tool (refer to Chapter 3. Preventive activities in children and young people)	42 33 43

Practice Point	Comment
m	Assess for risky behaviours Promoting health and minimising harm is a whole-of-community opportunity and responsibility. Celebrating strengths, explaining confidentiality (including its limits) and using the HE²ADS³ framework[60] (refer to below) to explore with young people the context in which they live are strategies that are likely to improve the clinician's capacity to promote health and minimise morbidity (C):[61,62] – **H**ome – **E**ducation/employment – **E**ating and exercise – **A**ctivities – **D**rugs – **S**exuality – **S**uicide – **S**afety • Young people who present frequently are at higher risk of having a mental health problem[63] • Provide messages that encourage delay in initiation of potentially risky behaviours and, at the same time, promote risk-reduction strategies if adolescents choose to engage or are already engaging in the behaviour • Use principles of motivational interviewing in the assessment and discussion of risky health behaviours with adolescent patients (including safe practice for those who are sexually active) • Be familiar with the resources in the community that provide harm reduction programs for substance abuse, pregnancy prevention, injury prevention and road safety • Be familiar with resources in the community that provide parenting skills training for parents of young people • Advocate for the introduction, further development and evaluation of evidence-based prevention and treatment programs that use a harm reduction philosophy in schools and communities (C)

https://www.racgp.org.au/clinical-resources/clinical-guidelines/key-racgp-guidelines/view-all-racgp-guidelines/guidelines-for-preventive-activities-in-general-pr/psychosocial/depression

Severity of Depression

Table 63.1 Levels of severity of depression.

Level of severity	Number and type symptoms	Impairment
Mild	≤4, no suicidal ideation or psychosis	Able to function in most ways, but takes more effort
Moderate	5–6, suicidal ideation	Impairment in at least one domain
Severe	7, imminent suicidal risk, could have psychosis, mixed features	Unable to function adequately, with impaired self-care

Rutter's Child and Adolescent Pscychiatry

Stepped Care : Tier System

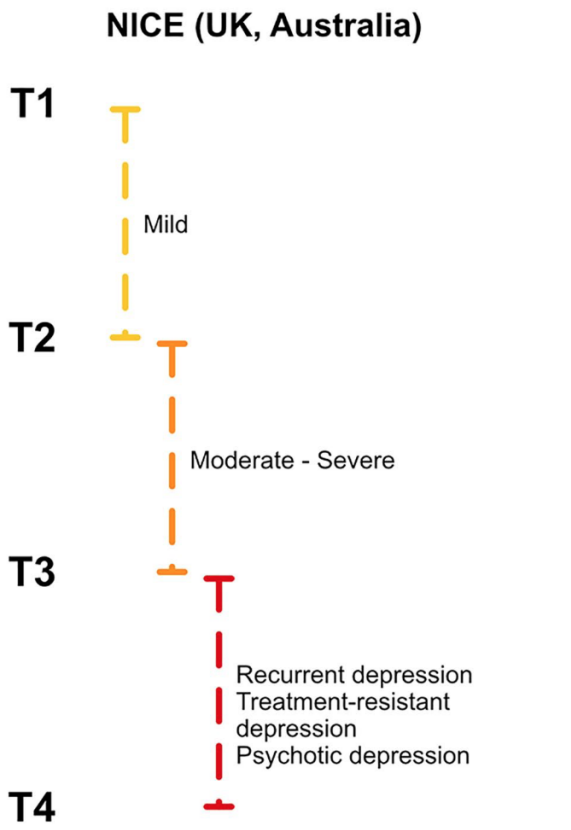


Table 3. Tier system for setting of care for children and adolescents.

Tier 1	General advice and treatment for less severe problems by non-mental health specialists working in general services, such as GPs, school nurses, social workers and voluntary agencies.
Tier 2	Usually CAMHS specialists working in community and primary care, such as mental health workers and counsellors working in clinics, schools and youth services.
Tier 3	Usually a multi-disciplinary team or service working in a community mental health clinic providing a specialised service for more severe disorders, with team members including psychiatrists, social workers, board certified behaviour analysts, clinical psychologists, psychotherapists and other therapists.
Tier 4	Highly specialist services for children and young people with serious problems, such as day units, specialised outpatient teams and in-patient units.

Source: Department for Children Schools and Families (2010).
CAMHS: child and adolescent mental health services.

NICE Guidelines (UK)

- Stepped care Model

- **2 weeks of Watchful Waiting** (after assessing for risks and comorbidities):
  - Provide information
  - Involve family and child in decision making
  - take time to build a supportive and collaborative relationship with both the patient and the family or carers
  - always ask the patient and their parents or carers directly about the child or young person's alcohol and drug use, any experience of being bullied or abused, self-harm and ideas about suicide.
  - Sleep hygiene, exercise, anxiety management and nutrition

- 1:1 therapy, CBT , or family therapy, IPT,

- **Medication - Monotherapy (SSRI)** + psychotherapy

- Tier III = CAMHS/CYMHS

https://www.nice.org.uk/guidance/ng134/chapter/Recommendations#stepped-care

The stepped-care model of depression draws attention to the different needs of children and young people with depression – depending on the characteristics of their depression and their personal and social circumstances – and the responses that are required from services. It provides a framework in which to organise the provision of services that support both healthcare professionals and patients and their parents or carers in identifying and accessing the most effective interventions (see table 1).

Table 1 The stepped-care model

Focus	Action	Responsibility
Detection	Risk profiling	Tier 1
Recognition	Identification in presenting children or young people	Tiers 2 to 4
Mild depression (including dysthymia)	Watchful waiting Digital CBT, group CBT, group IPT or group NDST If shared decision making based on full assessment (including maturity and developmental level) indicates needs not met, individual CBT or attachment-based family therapy	Tier 1 Tier 1 or 2
Moderate to severe depression (5- to 11-year-olds)	Family-based IPT, family therapy (family-focused treatment for childhood depression and systems integrative family therapy), psychodynamic psychotherapy, or individual CBT With or without fluoxetine	Tier 2 or 3
Moderate to severe depression (12- to 18-year-olds)	Individual CBT With or without fluoxetine If shared decision making based on full assessment (including maturity and developmental level) indicates needs not met, IPT-A, family therapy (attachment-based or systemic), brief psychosocial intervention or psychodynamic psychotherapy With or without fluoxetine	Tier 2 or 3
Depression unresponsive to treatment/recurrent depression/psychotic depression	Intensive psychological therapy With or without fluoxetine, sertraline, citalopram, augmentation with an antipsychotic	Tier 3 or 4

Acute Treatment (first 2-3 months)

- Mild severity
  - many patients with mild depression respond to assessment and education alone (Birmaher et al., 2007)
  - Non specific interventions – family education, supportive counselling, case management and problem solving (Renaud *et al.*, 1998; Goodyer *et al.*, 2007; Bridge *et al.*, 2009).

“Upto 20% of moderate to severe depressive episodes, even with varying lengths of episode prior to treatment will remit within the first 2-3 appointments in BPI (Goodyear et al 2007, Wilkinson et al, 2011)”

- Moderate to Severe Depression (>4 symptoms)
  - Antidepressant after 2-3 months of psychological therapy
    - Brief Psychological Intervention:

assessment, formulation, case management

  - Other coexisting factors
    - comorbid conditions,
    - persisting psychosocial risk factors such as family discord,
    - or the presence of parental mental ill-health,

  - Offer fluoxetine if moderate to severe depression in a young person (12–18 years) is unresponsive to a specific psychological therapy after 4 to 6 sessions. [2015]
    - Medication is to enable recovery, not passively deliver symptoms resolution
    - “Part of the solution”
    - Exert more caution for under 12

Consolidation of treatment (next 3-6 months)

- If partial or non-response after eight weeks of the maximum recommended (or highest tolerated) therapeutic dose of an SSRI, consider the medication changes
- "CBT performs better than supportive, family and relaxation techniques in acute trials but alternative treatments catch up during longer term follow up" (Wood *et al.*, 1996; Brent *et al.*, 1997; Birmaher *et al.*, 2000)
- **At least 9 sessions** may be needed for adequate response, and in 18 weeks, CBT may have similar outcomes to other active treatments including medication (march et al, 2007)
- "for patients with a history of abuse or current parental depression, CBT is no better, and sometimes worse, than alternative treatments (Brent *et al.*, 1998; Curry *et al.*, 2006; Asarnow *et al.*, 2009).

Medication – Principles of prescribing
(Maudsley Guidelines 2021) & Rutter's Child and Adolescent Psychiatry

- Targets for medication are Symptomatic rather than diagnosis. (eg: Antidepressant for PTSD)
  - Diagnosis is difficult in children and comorbidity is common
  - It may take time for the illness to evolve
- Start low, go slow
- Monitor for adverse effects and efficacy
  - Adverse reactions are more common in Children and Adolescents
- **Allow time for an adequate trial**
- Monitor response in more than one setting
  - Problems may be different across settings
- Patient and family education is ESSENTIAL
- Ultimately people are treated, not symptoms (Eg medication for tics vs learning to accept , manage and be resilient)

Prescribing "off label"

- The practice is common, with rates up to 40% in adults and up to 90% in paediatric patients.
- Three broad categories of appropriate off-label use are identified:
  - off-label use justified by high-quality evidence;
  - use within the context of a formal research proposal; and
  - exceptional use, justified by individual clinical circumstances.

Tips for considering off-label use of a medicine

The medicine I want to use is more appropriate for my patient than any TGA-approved alternative.
There is adequate evidence or experience with the medicine's use to demonstrate that it works and is safe; I understand the product information may be of limited help to me in establishing this.
I take responsibility for prescribing the medicine and overseeing its use in my patient, including providing sufficient information to the patient or their carers.
I have documented the informed consent process together with a clear, accurate record of reasons for prescribing the medicine in the patient's notes.

1. Off-label use of medicines: consensus recommendations for evaluating appropriateness|
2. Prescribing for children - AMH Children's Dosing Companion

Box 5.1 Summary of pharmacotherapy for depression in children and adolescents[3,4,21,25]

	Medication	Starting dose	Therapeutic dose range
First line	Fluoxetine (FDA approved for 8 years and over)	10mg/day	20–60mg/day
Second line	Sertraline or Citalopram*	25–50mg/day 5–10mg/day	50–200mg/day 10–40mg/day
Third line	Escitalopram (FDA approved for 12 years and over)	5–10mg/day	10–20mg/day

Maudsley Prescribing Guidelines 2021

Medication

- FLUOXETINE
  - NICE Guidelines,
  - US FDA for preadolescent and adolescent depression

- Escitalopram
  - USFDA for adolescent depression

- Sertraline superior to placebo

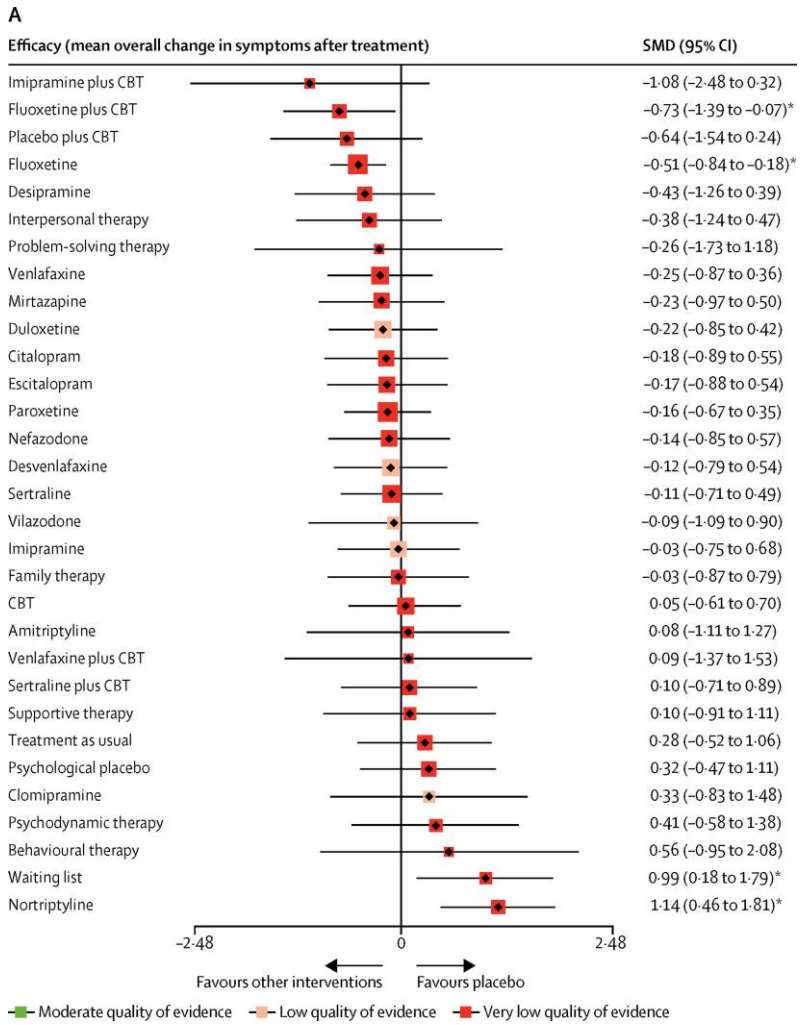
- Placebo
  - Paediatric antidepressant trials also show high placebo response (49%), (Bridge et al 2007)

Safety:

- NNT for SSRI : 2-10, average = 6.
- NNTH for SSRI : 112 ("11 times as many adolescents will benefit from antidepressant rather than experience a suicidal event", Bridge et al 2007)

Comparative efficacy and acceptability of antidepressants, psychotherapies, and their combination for acute treatment of children and adolescents with depressive disorder: a systematic review and network meta-analysis (JULY 2020)

- We found that, of all the included active interventions, only fluoxetine plus CBT and fluoxetine were significantly more efficacious than pill placebo in children and adolescents with depressive disorders.



https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(20)30137-1/fulltext

Which medication :SSRI.
Doses and how to titrate: (Case Scenario 1)

Expectations – eg Fluoxetine

- 10mg/day 1 to 3 weeks. Therapeutic dose 10 – 20mg/day.
- Response after 2-4 weeks of **stable therapeautic dose**
- Common side effects may take 1-6 weeks to resolve
- Improvement in executive functioning and rumination
- Others may notice changes before the patient does. Compare to baseline

- Fluoxetine – 10- 20mg (max dose 40mg/day)
- Second Line – Sertraline. Start at 25mg, and then increase in steps to 50-200mg/day.
- Escitalopram – starting at 5 – 10 mg , increase to 10-20mg/day
- Mirtazapine (only mentioned in Maudsley guidelines 2021) - after trial of 2 ssri, if sleep is poor

Paradigm (Case Scenario 1)

In practice there is a substantial delay, usually a matter of weeks, following the commencement of an antidepressant before there is any significant improvement in depressive symptoms. This delay is a problem for several reasons.

- Risk that treatment may be stopped as the individual feels it is not of benefit
- If the treatment is not effective, then the underlying illness continues to cause impairment
- This is associated with ongoing risks such as the possibility of self-harm or suicide

VS

- Expectation Bias:
- “If you lower the risk of exposure to placebo, then the apparent therapeutic effect with the antidepressants and placebo is greater.”
- “Sinyor et al (14) reported that, if there was no placebo control in an antidepressant trial comparing two antidepressants, the magnitude of symptom reduction was 65.7%. If the trial included two antidepressant treatments and one placebo arm (33% placebo exposure risk), the magnitude of symptom reduction with the antidepressants was 57.7%, while that with placebo was 44.6%. If the antidepressant trial included one antidepressant arm and one placebo arm (50% placebo exposure risk), the magnitude of symptom reduction with antidepressant was 51.7% and that with placebo was 34.3%.”

- **Antidepressants versus placebo in major depression: an overview .** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4592645/

Paradigm

- 1/4 of RC-CYMHS patients are not on antidepressant medication
- ½ to 1/3 of RC-CYMHS medicated patients are on monotherapy, or have additional PRN medication
- Most common ADT prescribed in RC-CYMHS –
  - SSRI (Fluoxetine > Sertraline),
  - ocassionally Fluvoxamine, Escitalopram,
  - less frequently Mirtazapine
  - Exceptional circumstances Duloxetine
  - TCA?

Response to Monotherapy

- 20% show a good response the first few weeks

- 20% will not show improvement or get worse after specialist care (UK)

- Predictors of poor response:
  - Clinical severity, comorbidity, family conflict (Emslie *et al.*, 1998; Curry *et al.*, 2006; Asarnow *et al.*, 2009; Emslie *et al.*, 2012).
  - Non adherance
  - Substance abuse

Medication to avoid

- Paroxetine and venlafaxine should not be used for the treatment of depression in children and young people. **[2005]**
  - Paroxetine is now not recommended for the treatment of pediatric depression because the aggregate trial data do not support efficacy (Bridge *et al.*, 2007).

- 1.6.27 Tricyclic antidepressants should not be used for the treatment of depression in children and young people. **[2005]**
  - Tricyclic antidepressants are not efficacious against child or adolescent depression (Hazell *et al.*, 2002)

Case Scenario 2

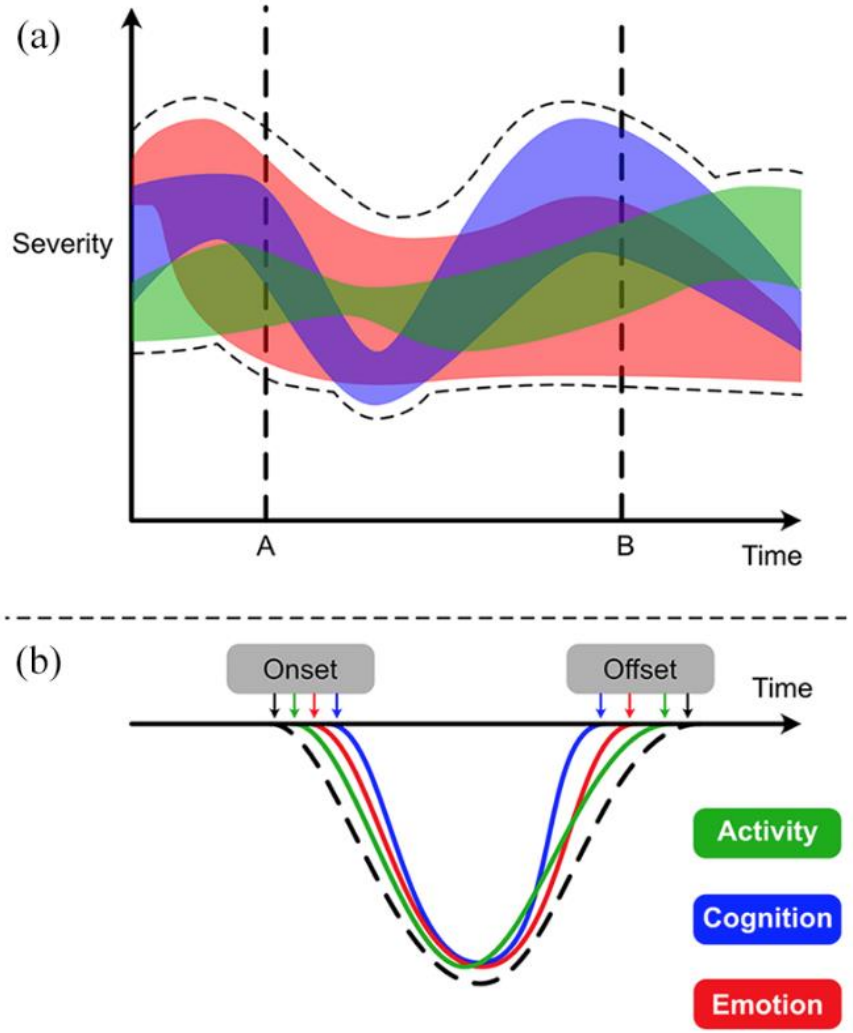
- Patient managed by Redcliffe Caboolture CYMHS, successfully discharged on a single antidepressant, on 150mg/day Sertraline.
- Patient was offered case management after they had been treated sequentially by GP, Private paediatricians, private psychiatrists.
- Past medication history included SSRI, Venlafaxine, Mirtazapine (and combination of the above)
- along with antipsychotic, (and multiple sessions of TMS + inpatient admission arranged to consider Lithium/ECT)

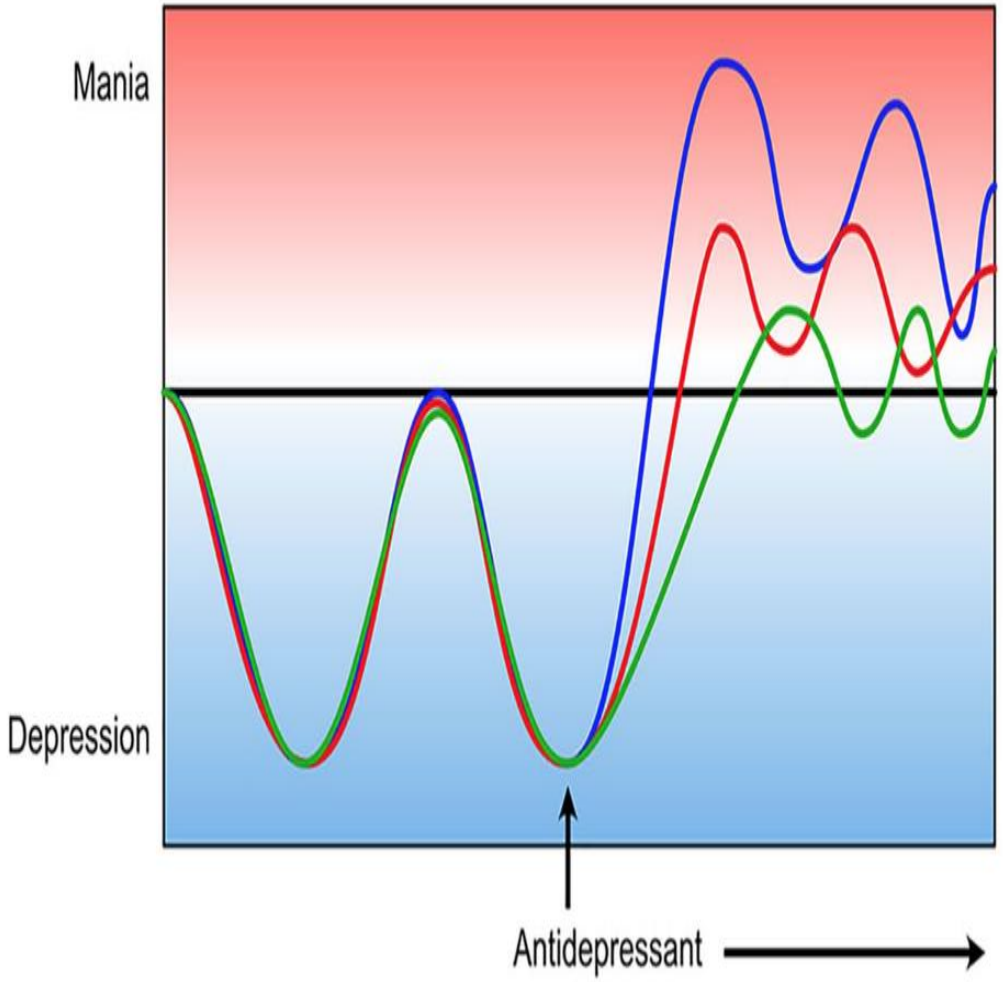
Interpreting response to treatment (RANZCP)

Activity

Cognition

Emotion





Continuation (12+ months)

- Continue medication for 8 months (ie 8 weeks + 6 months)
- A Cochrane review found that the likelihood of relapse was 41% in those maintained on an antidepressant versus 67% in those on placebo (OR = 0.34, NNT = 4) (Cox *et al.*, 2012b).
- The addition of a wellness-oriented CBT to fluoxetine during the continuation phase resulted in an even lower risk of relapse or recurrence compared to medication continuation alone (Kennard *et al.*, 2014).

Prescribing antidepressant during an Emergency/ high risk presentation

- Suicidal events tend to occur within the first 3-5 weeks . More common in those
  - do not respond to antidepressant treatment,
  - experience family conflict,
  - have a history of nonsuicidal self-injury
  - use of drugs or alcohol (Brent *et al.*, 2009b; Vitiello *et al.*, 2009; Wilkinson & Goodyer, 2011).

- A meta-analysis of trials of fluoxetine showed that both adolescents and adults showed a decrease in depressive symptoms but only the adults also showed a decline in suicidal events
  - For adolescents, "**antidepressant treatment alone may not be sufficient to reduce suicidal ideation** "(March *et al.*, 2004, 2007).

Side effects

- Common Side Effects
- Headache
- Sleep Changes
- Nausea
- Less common side effects
- GI symptoms – decreased appetite, nausea, diarrhoea, constipation , dry mouth
- CNS – tremors, agitation
- Bruising, rare bleeding
- Dangerous SE
- Allergies
- Mania
- Increased suicidal ideation (for under 18 (or under 24) years of age)

What to do
. If safe –
Give patient psychoeducation and choice to :

‘wait’, ‘wait’, ‘wait’ (Stahl’s Essential Psychopharmacology)

Especially for anxious patients start at v low dose, eg 25mg fluvoxamine, and go v slow.

Review timing of dose/consider split dose

Take medication with some food

Check for comorbidities, substance abuse, other medication (CYP450 inhibitor)

and even compliance.

Table 2. Approximate relative frequency (not intensity) of common adverse effects of antidepressants[1]

Note: This table lists the approximate relative frequency of adverse effects, not the intensity with which they occur.

Drug	Agitation	Gastrointestinal effects[2]	Insomnia	Hypertension	Orthostatic hypotension / dizziness	Sedation	Sexual dysfunction[3]	Weight gain (more than 6 kg)
Selective serotonin reuptake inhibitors (SSRIs)								
citalopram	+	++	++	–	+	++	+++	+
escitalopram	–	++	++	–	+	+	++	–
fluoxetine	+	++	++[4]	?	++	++	+++[5]	+[6]
fluvoxamine	+	+++	++	?	+	++	+++	+[6]
paroxetine	+	++	++	+	++	++	+++[5]	++[6]
sertraline	+	+++	++	–	++	++	+++[5]	+[6]
Serotonin and noradrenaline reuptake inhibitors (SNRIs)								
desvenlafaxine	+	+++	++	+	++	++	+	?
duloxetine[7]	+	++	++	–	++	++	+++	+
venlafaxine	+	+++	++[4]	+	++	++	+++[5]	+[6]

continued next page

Table 2. Approximate relative frequency (not intensity) of common adverse effects of antidepressants[1] (cont.)

Drug	Agitation	Gastrointestinal effects[2]	Insomnia	Hypertension	Orthostatic hypotension / dizziness	Sedation	Sexual dysfunction[3]	Weight gain (more than 6 kg)
Others								
agomelatine[8]	–	+	+	?	+	–	–	–
mirtazapine	?	+	+	?	+	+++[9]	+	+++
moclobemide	?	++	++[4]	–	++	+	+	–
reboxetine	+	+	+++	+	+	–	+	–

Approximate frequencies of adverse effects: ? = little or no information reported; – = negligible or absent; + = infrequent; ++ = moderately frequent; +++ = frequent

1 The information in this table is based on a combination of reported adverse effect data and expert opinion; it is intended only as a guide and should be interpreted in the context of the patient's particular situation (eg concurrent drugs, drug history, physical health, the considerable interindividual variation in elimination half-lives) and the doses of the drugs. See 'Tricyclic antidepressants' (p.33), 'Irreversible nonselective monoamine oxidase inhibitors' (p.34) and 'Mianserin' (p.34) for their adverse effects.

2 Gastrointestinal adverse effects may include nausea, anorexia, diarrhoea and abdominal discomfort.

3 Sexual dysfunction may include decreased libido, anorgasmia and ejaculatory disturbance.

4 Insomnia is more likely if the antidepressant is dosed in the evening.

5 Priapism has been reported.

6 Weight loss reported initially.

7 Avoid duloxetine in patients with liver impairment.

8 Increase in serum transaminases has been reported with agomelatine and, rarely, hepatitis can occur so avoid agomelatine in patients with liver impairment. Liver biochemistry should be performed in all patients at baseline; then 3, 6, 12 and 24 weeks after starting treatment with agomelatine; then as clinically indicated. Stop treatment if the increase in serum transaminases exceeds 3 times the upper limit of normal.

9 Sedation is decreased at higher doses of mirtazapine (more than 15 mg daily).

Seretonergic syndrome – overactivation of central and peripheral 5HT1a and 5HT2a receptors

Serotonin syndrome – symptoms[11]

Increasing severity

Severity	Symptoms
Mild	Insomnia, anxiety, nausea, diarrhoea, hypertension, tachycardia, hyper-reflexia
Moderate	Agitation, myoclonus, tremor, mydriasis, flushing, diaphoresis, low fever (<38.5°C)
Severe	Severe hyperthermia, confusion, rigidity, respiratory failure, coma, death

Discontinuation

- 8 week of nil symptoms + 6 months
- Best considered under a period of low stress
  - Not one week before exams
  - Not when they are starting uni
  - Not when parents are separating

Symptoms associated with withdrawal of selective serotonin reuptake inhibitors[6]

Gastrointestinal	nausea, vomiting, diarrhoea, loss of appetite, abdominal pain, abdominal distress
General somatic distress	lethargy, flu-like symptoms
Sleep disturbance	insomnia, abnormal dreams including nightmares and decreased need for sleep
Affective symptoms	irritability, anxiety symptoms, agitation
Problems with balance	dizziness, vertigo, light-headedness, ataxia
Sensory abnormalities	paraesthesia, numbness, blurred vision/diplopia, 'electric shock', visual lag

- “Where antidepressant medication is to be discontinued, the drug should be phased out over a period of 6 to 12 weeks based on extent of discontinuation symptoms. Discontinuation more likely with medication with shorter half life (within 3-5 half lives of the drug)
  - Fluoxetine < Sertraline < Citalopram
  - Longer half-life (Fluoxetine), symptoms may appear after 2-6 weeks. Shorter half life – symptoms may arise in 1-2 day
  - Some indications that half life of sertraline and citalopram is shorter in C&A population
- Discontinuation symptoms consists of diverse physical and psychological symptoms, the commonest being dizziness, nausea, lethargy and headache.

- - Safest method of tapering (not always practical) is to reduce by 10 to 20 percent of most recent dose every 2-4 weeks (As opposed t olinear reduction – half tablet to quarter tablet and so forth.

https://www.nps.org.au/australian-prescriber/articles/stopping-antidepressants-1#dd text

Anxiety

- Fear and Anxiety may be part of normal development in children
- Anxiety as well as Anxiety disorders often begin in childhood and adolescence.
- Even more common in children with neurodevelopmental disorders
- Guidelines recommend – psychoeducation, CBT, and for chronic, or moderate to sever anxiety – medication : SSRI
- Before prescribing, again, rule out comorbidity, assess severity.
- Medication of choice- SSRI
- **Neither benzodiazepine nor tricyclic antidepressant use is supported by controlled trials in children . Benzodiazepines may cause paradoxical disinhibition in some children**
- Start low dose. SSRI first choice. **Anxious patients may report worsening of anxiety symptoms, agitation and disinhibition**
- Trial of medication should be started at period of low stress/demands (eg not one week before exams)
- Therapeutic effect may be noticed in 6-8 weeks
- Maintenance treatment for at least one year.

Table 5.5 Typical dosage of medications for treatment of anxiety disorders in children and adolescents

Medication	Starting dose (mg)	Dose range (mg/day)
SSRI		
Sertraline	12.5–25	25–200
Fluoxetine	5–10	10–60
Fluvoxamine	12.5–25	50–200 (BD if >50)
Paroxetine	5–10	10–40
Citalopram*	5–10	10–40
SNRI		
Venlafaxine XR	37.5	37.5–225
Duloxetine	30	30–120
Alpha$_2$ agonist		
Guanfacine	1	1–6
5-HT$_{1A}$ partial agonist		
Buspirone*	5 TDS	15–60
Benzodiazepine (PRN)		
Clonazepam*	0.25–0.5	–
Lorazepam*	0.5–1	–

*Treatments not supported by RCT evidence.
Note: Always check dose with latest formal guidance, for example British National Formulary for Children (in the UK).
BD - twice daily
TDS - three times daily

Maudsley prescribing guidelines

Psychotic depression vs hallucinations in children

- Hallucinations may be reported but are often a marker of traumatic experiences rather than psychosis (Hielscher et al., 2018; Nam et al., 2016)
- Depression may present with psychotic features with depressive, self deprecatory, mood syntonic or paranoid content
- Main difference – prodromal symptoms of schizophrenia
- Often only determined through longitudinal follow up
- Schizophrenia is rare in children, more common in adolescence

- ----
- Algorithms for management similar to that of adult guidelines , but
- Detailed developmental and physical assessment is often needed
- First generation antipsychotic should be avoided. Most second generation antipsychotics are effective
- Children may need lower range of lower than adult doses
- Medication in conjunction with family interventions and CBT

- Manage expectations – Explain that hallucinations may often be the primary reason for seeking help, a broader understanding of their developmental needs, mental health difficulties will be needed to understand the relevance and impact of hallucinations.

- Hallucinations could be benign, developmental phenomenon or smptoms of a developing mental health issue

- Antipsychotic medication : Halluciations are not an indiction for the use of antipsychotic medication. When hallucinations are a symptom of psychotic disorder, but also when hallucincations are a symptom or signal of decompensation of underlying conditions (such as an autism spectrum disorder or borderline personality disorder) antipsychotic may be considered according to related guideline

doi:10.1093/schbul/sby119

Bipolar Affective Disorder

- Only 25% of young people with clinically significant mania in one epidemiological study met criteria for Bipolar spectrum disorder (Findling et al, 2010)

Table 5.3 Recommended first-line treatments for acute mania*

Aripiprazole	10mg daily
Risperidone	0.5–2.5mg daily
Olanzapine	5–20mg daily
Quetiapine	Up to 400mg daily
Asenapine	2.5–10mg twice daily

*Continue acutely effective dosing regimen as prophylaxis, and consider need for lithium.

Table 5.4 Recommended first-line treatments for bipolar depression*

Lurasidone	18.5(20)mg–74(80)mg a day
Olanzapine/fluoxetine	6/25–12/50mg daily
Quetiapine	Up to 300mg daily

*Continue acutely effective dosing regimen as prophylaxis, and consider need for lithium.

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