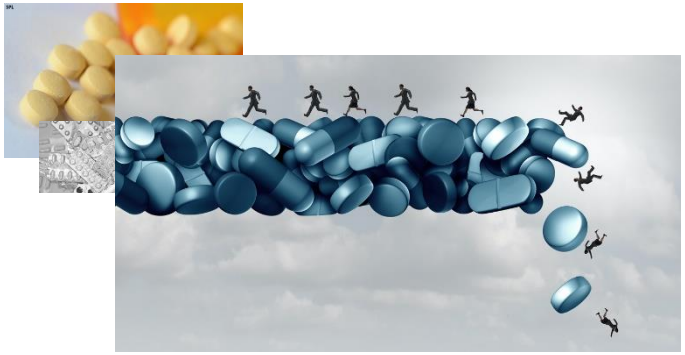
Bitesize Education and Training Session 3

Pharmacological Management of Depression and Anxiety in Primary Care: The SSRI's, SNRI's and Other Options.

19th February 2024

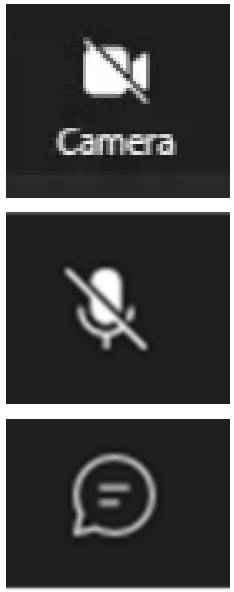


Speaker:
Vicki Jordan
Mental Health Practitioner
Independent Prescriber

Welcome & Housekeeping

Thank you for joining us today!

- ✓ The session is for 30-minutes (20-minute presentation and 10-minute Q&A session).
- ✓ Please switch off your cameras and put yourselves on mute.
- ✓ Please use the chat function if you want to ask a question or for comments.
- ✓ Please respect others' views and opinions. (We have prescribers from across the system on the call – primary, secondary care and community).
- ✓ Please use the chat function to network with your peers and share ideas.
- ✓ At the end of the session there is a short feedback questionnaire – the link to access this will be put into the chat.



Please note the 20-minute presentation will be recorded, and the slides and the recording will be uploaded to the LSC Training Hub website for you to download.

Guidance on Pharmacological Treatment for Depression and Anxiety in Primary Care

Vicki Jordan

- Mental Health Practitioner
- Independent Prescriber

Introduction

- Common mental health problems particularly anxiety and depression frequently present and are treated in primary care settings.
- They have a huge impact on society with people having extended periods of sickness absence from work and can have a negative impact on relationships.
- Depression can itself range from mild to severe but even in milder forms can cause distress and disruption to normal functioning.
- Anxiety commonly presents in combination with depression but anxiety disorders can present on their own and cause significant disruption to normal functioning.
- Even though NICE have recommended a broader range of treatment option in their updated depression guidance in 2022, antidepressants remain a routine treatment option in primary care.

Depression In Adults

- **Depression Guidelines 2022 Update – NICE NG222**
- Depression severity exists along a continuum and is essentially composed of 3 elements:
- • Symptoms (which may vary in frequency and intensity)
- • duration of the disorder
- • the impact on personal and social functioning. Severity of depression is therefore a consequence of the contribution of all of these elements.
- New episodes of depression should be categorized as *less severe* or *more severe.*
- *Less Severe* encompasses sub-threshold and mild depression
- *More severe* encompasses moderate and severe depression.
- Strengthened encouragement of a shared decision process from a broad menu of treatment options.
- Treatment should not be based on ‘symptom counts’
- Consistency of care and building a trusting therapeutic relationship is beneficial to both the patient and clinician.
- An emphasis on better quality information including benefits/harms/side-effects/withdrawal effects and patient concerns about stop/starting antidepressants.
- Guidance is strengthened on withdrawal reactions and the need to slowly taper medication when stopping
- Greater emphasis on risk assessment and asking directly on suicidal ideation and intent with appropriate safety netting. This should not deter the decision to start treatment.

Anxiety Disorders

- Anxiety can occur on its own or comorbid with other conditions including depression which is very common.
- It can also be a consequence of some physical illnesses (i.e. thyrotoxicosis) or drug induced.
- Psychological therapy is more effective than pharmacological approaches and should be used first line where possible
- Pharmacological therapy is also effective, with most evidence to support SSRI's in particularly Sertraline.
- Professionals need to provide good quality information on the benefits and risks of different treatment options.
- People with anxiety are more prone to adverse reactions to pharmacological treatment, with strong responses to initial doses of SSRI's.

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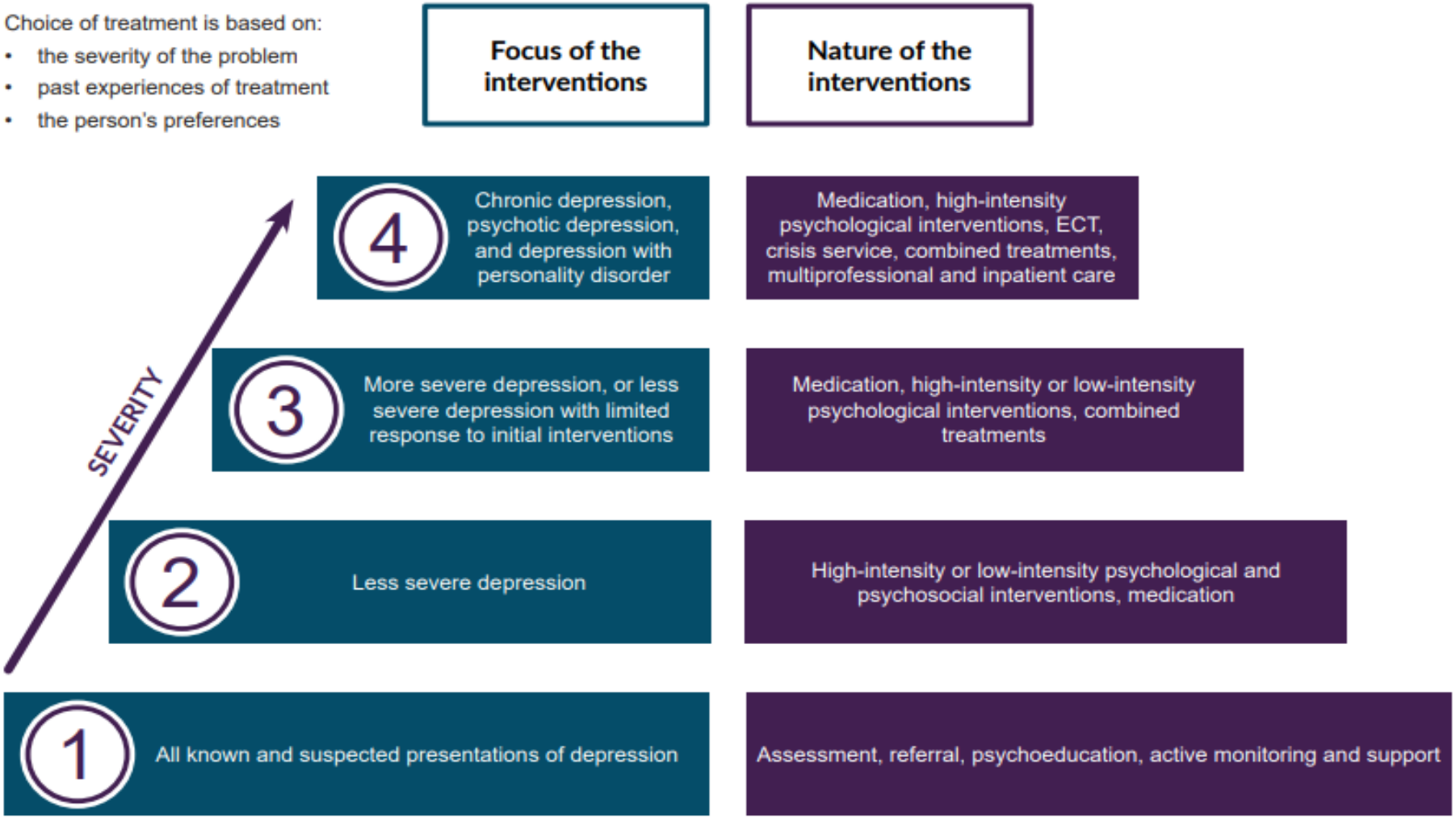
Depression in adults: the matched care model

Choice of treatment is based on:

- the severity of the problem
- past experiences of treatment
- the person's preferences



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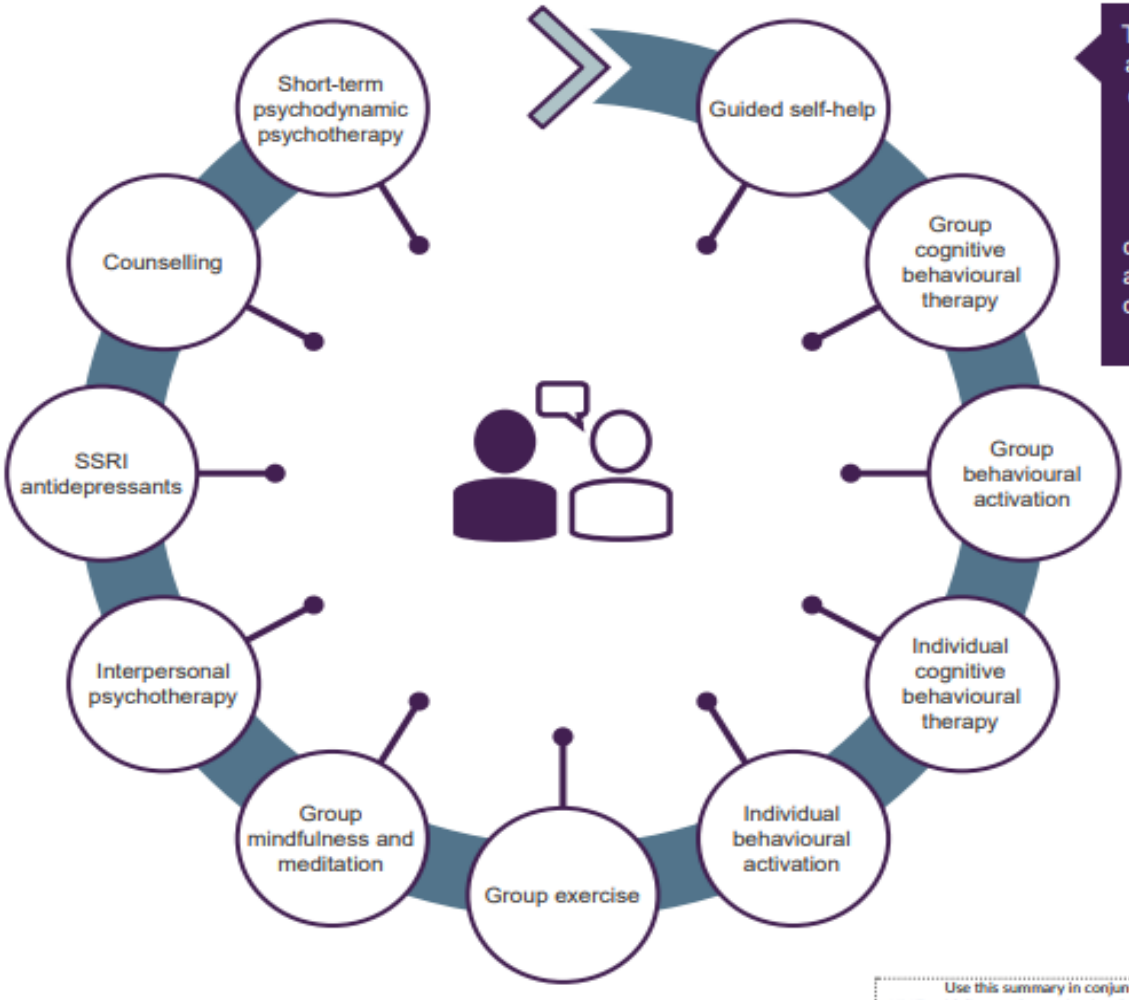
Depression in adults: discussing first-line treatments for less severe depression

Discuss treatment options and match the choice of treatment to clinical needs and preferences, taking into account that any option can be used as first line, but consider the least intrusive and least resource intensive treatment first (guided self-help).

If the person has a clear preference, or experience from previous treatment to use as a guide: support the person's choice, unless there are concerns about suitability for this episode of depression.

Do not routinely offer antidepressants as a first-line treatment, unless that is the person's preference.



Treatment options are listed in order of recommended use, based on the committee's interpretation of their clinical and cost effectiveness and consideration of implementation factors.

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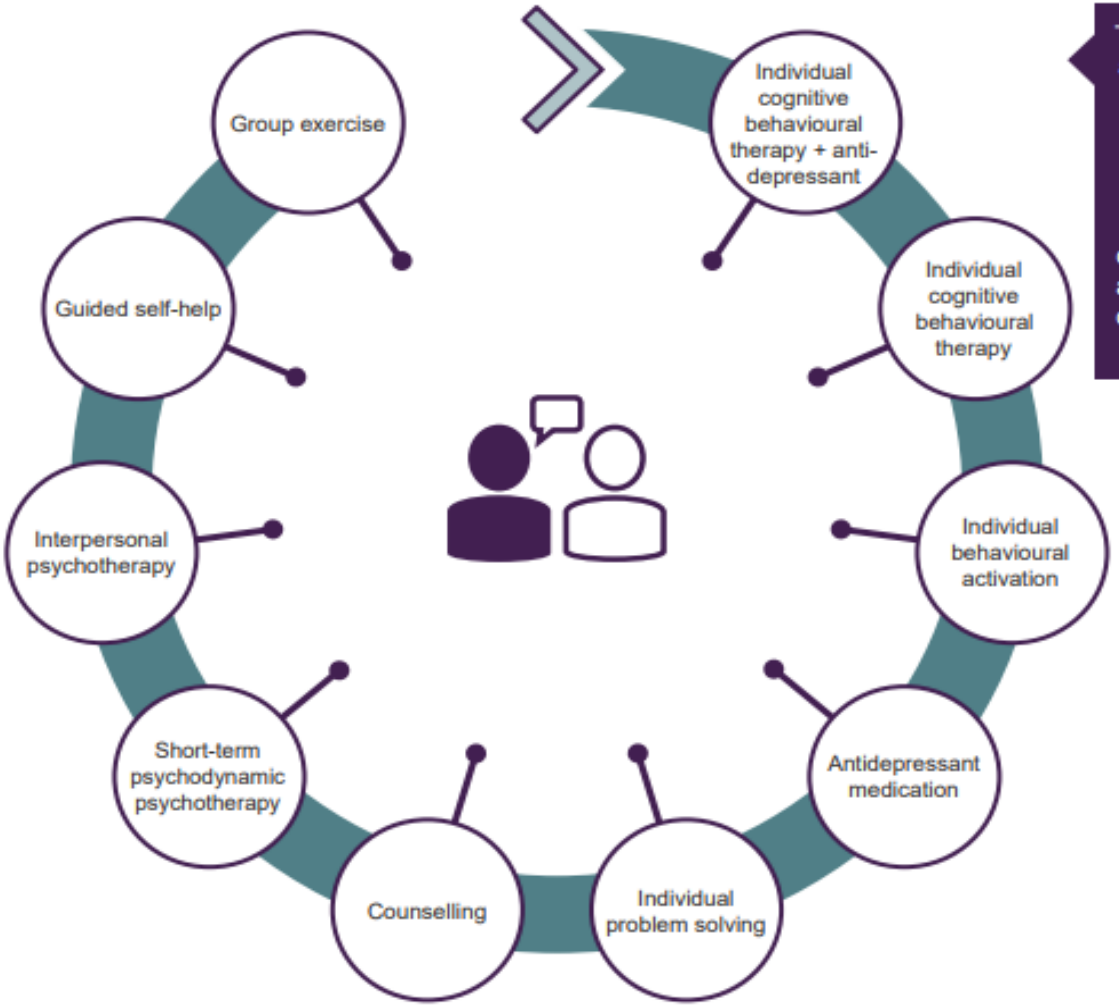
Depression in adults: discussing first-line treatments for more severe depression

Discuss treatment options with people who have a new episode of more severe depression. Match their choice of treatment to their clinical needs and preferences.

If the person has a clear preference, or experience from previous treatment to use as a guide: support the person's choice, unless there are concerns about suitability for this episode of depression.



Treatment options are listed in order of recommended use, based on the committee's interpretation of their clinical and cost effectiveness and consideration of implementation factors.

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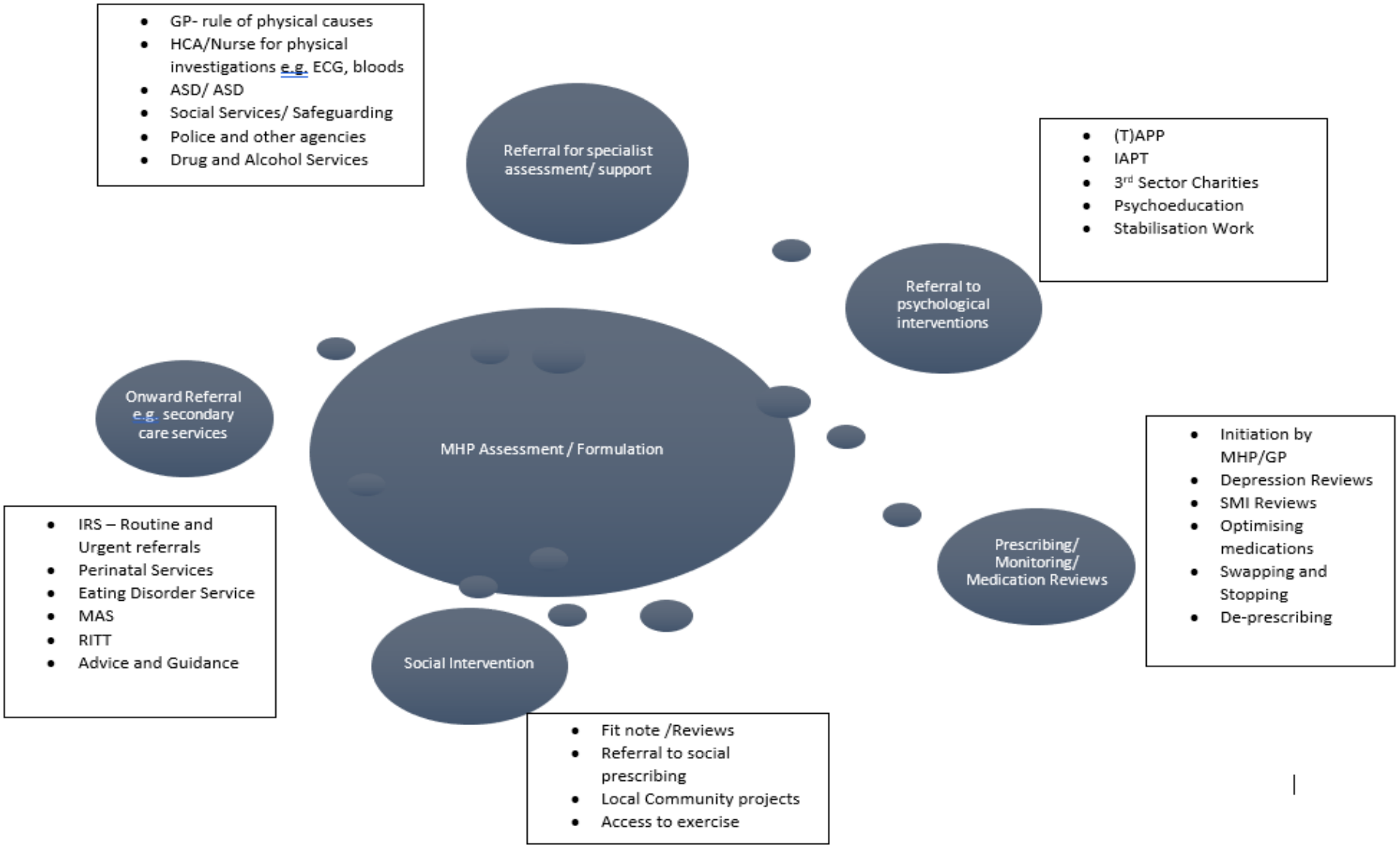
NICE GUIDANCE SUMMARY & PRINCIPLES FOR PRESCRIBING IN DEPRESSION

- Antidepressants are not recommended as a first line treatment in a recent onset, mild depression- Active monitoring, individual guided self-help/CBT and exercise are preferred.
- Antidepressants are recommended for moderate to more severe depression and dysthymia.
- When prescribing an antidepressant, a generic SSRI is recommended. Prescribe a dose that is likely to be effective.
- Discuss likely outcomes including the gradual relief of depression symptoms over several weeks
- All patients should be informed of the potential withdrawal (discontinuation) effects of antidepressants.
- For a single episode of depression, look to treat for at least 6-9 months once symptoms have resolved.
- Look to treat for at least 2 years for someone who may have had two or more prior episodes with functional impairment.

Outcomes of MHP Assessment



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What Should We Tell Patients?

-Antidepressants are Effective
-Antidepressants are not addictive (although withdrawal symptoms can be expected)
-Antidepressants are not “happy pills”
-Antidepressants do take time to work, but this time varies from person to person.
-Consistency and perseverance is key, the benefits will come.
-Antidepressants are not known to lose their effectiveness over time
-Antidepressants are not known to cause any new long term side-effects.
-Antidepressants should not be stopped too soon or abruptly

Choice and Medication Website

https://www.choiceandmedication.org/lancashirecaretrust/

Lancashire and South Cumbria NHS Foundation Trust's Choice and Medication website provides people with information about medicines used in the mental health setting to help people make informed decisions about medication.

Use the site on your own or use it together with your family or someone you care for or your doctor, nurse or pharmacy team.

Choice Of Antidepressant

Drug	Licensed Indication	Drug Class	Formulation	Additional Prescribing Information
Citalopram	-Major Depression -Panic Disorder	SSRI	10mg, 20mg, 40mg tablets 40mg/ml oral drops (1 drop=2mg) 4 drops (8mg) = 10mg tablet	SSRI with least propensity for drug interactions Suitable choice in renal impairment. Citalopram: QT interval prolongation—new maximum daily dose restrictions (including in elderly patients) Citalopram most toxic of SSRI's in overdose (coma, seizures, arrhythmia) Contraindicated with other QT prolonging medications. Baseline ECG advised in patients with cardiac disease.
Fluoxetine	-Major Depression -Bulimia Nervosa -Obsessive- Compulsive Disorder -Menopausal symptoms, particularly hot flushes, in women with breast cancer (except those taking tamoxifen)	SSRI	20mg capsules 20mg/5ml oral liquid (can also be used sublingually)	60mg capsules NOT approved. Good option for patents with poor medication compliance due to its long half-life.
Paroxetine	-Major depression -Social anxiety disorder -PTSD -GAD	SSRI	20mg and 30mg tablets 10mg/5ml oral suspension	Less preferred choice. Poorly tolerated. SSRI with greatest risk of withdrawal reactions.
Sertraline	-Depressive Illness -Obsessive-Compulsive Disorder	SSRI	50mg and 100mg tablets	Drug of choice for those with cardiovascular disease (recent MI or unstable angina) or renal impairment. Reduced propensity for drug interactions

Duloxetine	-Major Depression -GAD -Diabetic Neuropathy -Moderate to severe stress urinary incontinence	SNRI	30mg and 60mg capsules	Second line SNRI only after venlafaxine
Venlafaxine	-Major Depression -GAD -Social Anxiety -Panic Disorder -Menopausal symptoms, particularly hot flushes, in women with breast cancer	SNRI	37.5mg and 75mg tablets 37.5mg, 75mg, 150mg and 225mg MR tablets	Immediate-release venlafaxine (BD dosage) is considerably less expensive than once daily (MR) formulations. The MR formulation should only be used if the immediate-release formulation is not tolerated or if concordance with a twice daily regimen is difficult. If MR preparation is required then MR tablets should be prescribed rather than MR capsules as these are more cost effective. Existing patients on MR preparations must not be switched to IR tablets without involvement/agreement of psychiatrist. Avoid use in patients with high risk of cardiac arrhythmia. Monitor blood pressure in doses above 150mg. Consider ECG at higher dose. Do not prescribe venlafaxine for patients with: • Uncontrolled hypertension • Recent myocardial infarction • High risk of cardiac arrhythmia • Monitor BP at initiation and regularly during treatment (particularly during dose titration) Monitor for signs and symptoms of cardiac dysfunction • Doses of 300 mg daily or more should only be prescribed under the supervision or advice of a specialist mental health practitioner

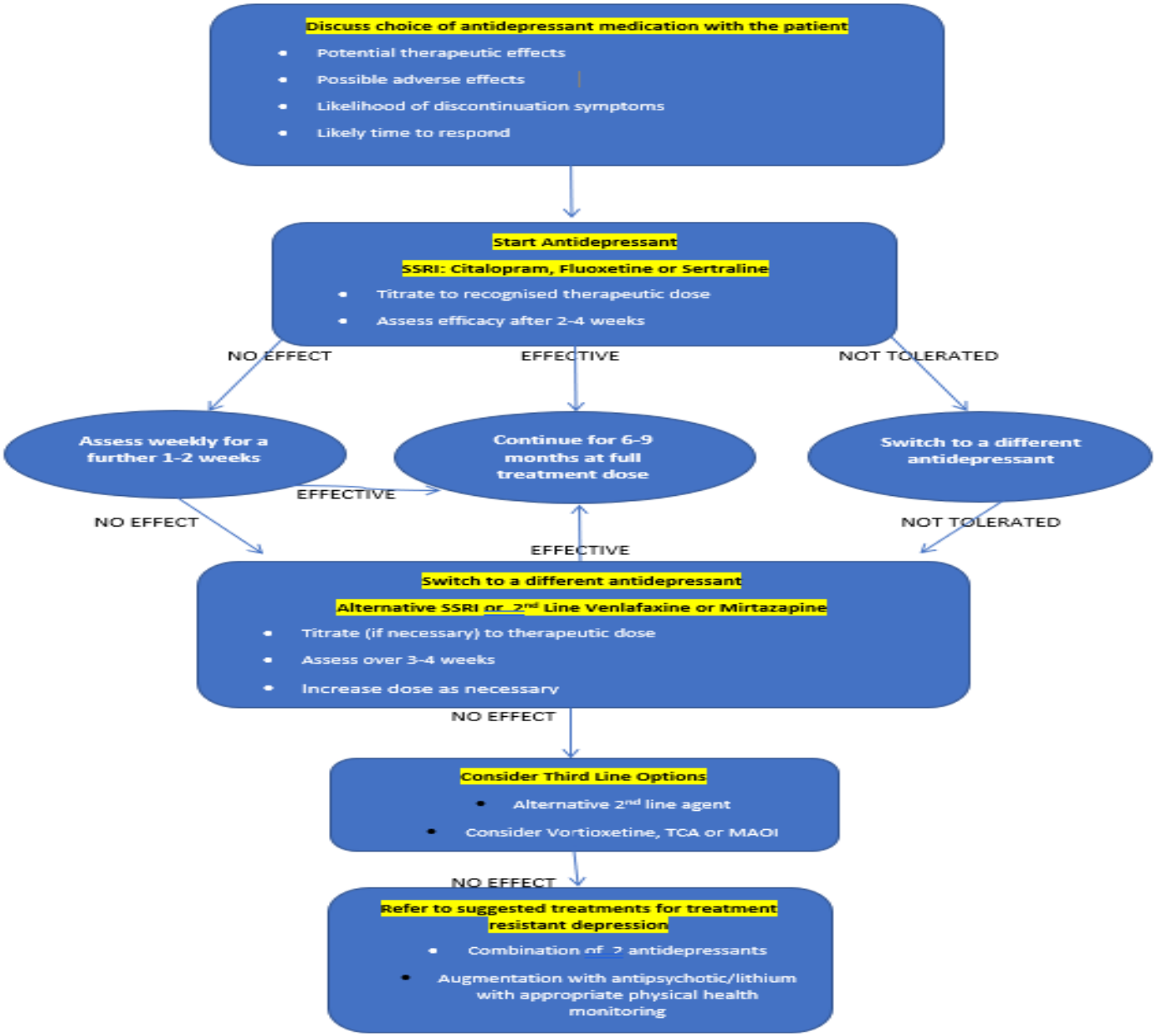
Mirtazapine	-Major Depression	Noradrenaline and specific serotonin antidepressant (NaSSa)	15mg, 30mg and 45mg tablets and orodispersible tablets 5mg/ml oral solution	Oral solution should only be used when orodispersible tablets are unsuitable. Safer option in patients at high risk of GI bleed e.g. older adults + NSAIDs. Consider if SSRI has not benefited or SSRI not appropriate. Good choice if sedation required.
Reboxetine	-Major Depression	Selective inhibitor of noradrenaline re-uptake	4mg tablets	Reboxetine should be used with caution in patients with renal or hepatic impairment. It should also be used under close supervision in patients with bipolar disorder, urinary retention, benign prostatic hyperplasia, glaucoma, or a history of epilepsy or cardiac disorders.
Vortioxetine	-Major Depression	Serotonin modulator and stimulator (SMS) This multimodal activity appears to be associated with antidepressant and anxiolytic-like effects.	5mg, 10mg and 20mg tablets	NICE recommends that vortioxetine is an option for treating major depression in adults who have responded inadequately to two antidepressants within the current episode of depression. However, NICE considered that there was no convincing evidence that vortioxetine was more or less effective than other antidepressants. Low toxicity in overdose. Dose adjustment not required in renal impairment although caution in severe renal impairment and in severe hepatic impairment as data is limited. Trial data suggest no effect on QTc or on coagulation parameters. Treatment can be stopped abruptly as it has a long half-life (66hours) and there is no evidence of clinically important discontinuation symptoms.

Trazodone		Tricyclic Related Antidepressant	50mg and 100mg capsules 150mg tablets 50mg/5ml sugar free oral solution	Oral liquid significantly more expensive than tabs/caps. Restricted to those unable to swallow solid dose forms.
Amitriptyline Nortriptyline Imipramine Trimipramine Lofepramine Clomipramine	Major Depression [not recommended– increased risk of fatality in overdose]	TCA	10mg, 25mg and 50mg tablets 25mg/5ml and 50mg/5ml oral solution	Consider TCAs in patients presenting with pain and physical symptoms. Avoid in patients at risk of arrhythmias. Consider ECG at higher dose or when co-administered with other drugs that may increase the risk e.g. fluoxetine. Increased cholinergic burden, especially when co-prescribed with other anticholinergic drugs.

First Line Drug Treatment

ANXIETY DISORDER	CLINICAL PRESENTATION	RECOMMENDED FIRST LINE DRUG TREATMENT- IN ORDER OF PREFERENCE
GAD	• Excessive uncontrollable worry • Motor tension, restlessness, irritability • Somatic symptoms (hyperventilation, sweating, tachycardia) • Often comorbid with depression, panic disorder and OCD.	• SSRI'S- MAY INITIALLY EXACERBATE SYMPTOMS- FLUOXETINE AND SERTRALINE PREFERRED OPTIONS • SNRI'S- MAY INITIALLY EXACERBATE SYMPTOMS- LOWER STARTING DOSE RECOMMENDED • PREGABALIN (150mg- 600mg)– RESPONSE MAY BE SEEN IN FIRST WEEK OF TREATMENT
PANIC DISORDER	• Sudden, unpredictable episodes of anxiety, usually 30-45 minutes in duration. • Shortness of breath and other autonomic symptoms • Fear of suffocation/dying • Urgent desire to flee	• SSRI's- Any SSRI, Citalopram licensed Therapeutic effect can be delayed and sometimes symptoms are exacerbated in early treatment. • Venlafaxine- Initiate at 37.5mg for first 7 days
PTSD	• Exposure to traumatic event • Emotional numbing/detachment • Intrusive flashback, nightmares, vivid dreams • Disabling fear of re-exposure and subsequent avoidance	• SSRI's- Paroxetine, Sertraline or Fluoxetine favoured. • Venlafaxine – Modified-release (37.5mg- 300mg)
OCD	• Obsessional thinking • Compulsive Behaviour	• SSRI'S – Any SSRI and may try more than 1, Fluoxetine and Sertraline licensed. • Clomipramine- Due to poor tolerability, recommended to try at least 1 SSRI
SOCIAL PHOBIA	• Extreme fear of situations • Fear of humiliation or embarrassment • Avoidant behaviour • Anxious Anticipation	• SSRI's – If no response to first SSRI, try - alternative SSRI • Venlafaxine- Modified Release (75mg- 225mg)

Pharmacological Management of Depression



Take Home Messages

NICE 2022:

Everything on the menu in terms of options.

Useful guidance on further line treatment:

- Allow adequate treatment time (anywhere between 6-12 weeks to get the full benefit)
- Consider factors that might reduce response (personal, social, physical factors)
- Consider switching/ adding in exercise or psychological therapy
- Considering referring on
- Consider dose or switching drug
- Consider adding in another medication

Medication Reviews

Patients with depression should be regularly reviewed to check for beneficial and adverse effects of medications or psychological interventions and to review the risk of self-harm and suicide.

Determine follow up plan timings on the assessed risk of suicide/the need to review medication

Arrange to review the person after starting antidepressant medication to check symptom response, concordance with treatment, any adverse effects or harms of treatment, or suicidal ideas. This will usually be within 2-4 weeks to check their symptoms are improving and for side effects.

Arrange initial review 1 week after starting antidepressant medication if the person is aged 18–25 years or there is a particular concern for risk of suicide and ensure a risk management strategy is in place.

- Ensure the person has a crisis plan identifying potential triggers and strategies to help.
- Consider limiting the amount of medication available, depending on clinical judgement.

Arrange subsequent reviews as needed and within 4 weeks of starting antidepressant treatment.

What To Include In A Review

Ask about and manage:

- Any ongoing symptoms of depression, impact on daily functioning including work, relationships, and any carer role for a child or vulnerable adult(s).

- Response of symptoms to any psychosocial intervention(s) or antidepressant drug treatment, including adherence to treatment, and any adverse effects.

Consider using a validated depression questionnaire to assess for depression, severity of symptoms, and response to treatment, such as PHQ-9/ GAD-7

- Any thoughts, plans, or intent to self-harm or commit suicide and any other risks to others or risk of self-neglect.

Ensure the person has a crisis plan identifying potential triggers and strategies to help
Any new symptoms of other mental health disorders, including anxiety, eating disorders, bipolar disorder, or psychosis.

Case Study 1

Lucy, 28 years old.

Been on Sertraline 50mg for 6 months for an episode of mixed anxiety and depression. Did initially respond well, but now feels it isn't working.

Would like to try Fluoxetine.

What would you do?

How do we go about switching?

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Based on **NICE NG22 Depression in Adults**

Continued management

- For all treatments for people with depression, review how well the treatment is working between 2 to 4 weeks after starting treatment and monitor therapeutic response and side effects.
- *Facilitate continuity of care.*
- Monitor suicidal ideation, especially in the early weeks of treatment.
- Consider routine outcome monitoring e.g. PHQ-9 or similar symptom score.
- **Remission**: if treatment achieves full or partial remission, make a shared decision as to whether or not continue on treatment for relapse prevention:
  - If people have been treated with antidepressants and considered higher risk of relapse, consider continuing treatment for up to 2 years to prevent relapse, with or without a course of psychological therapy such as mindfulness based cognitive therapy MBCT.
  - If they do not wish to continue on medication offer MBCT for relapse prevention.
- **No treatment response:** if patients have not responded after 4 weeks of psychological therapy, switch to an alternative therapy with or without an SSRI or mirtazapine alone:
  - Note CKS Guidance on Switching Antidepressants for cross-tapering advice.
  - If patients have not responded to an antidepressant drug consider:
    - Increasing the dose of the current drug if it is well-tolerated, OR
    - Switch to another in the same class, OR
    - Switch to another medication in a different class (e.g. SSRI, SNRI, TCA or MAOI).
  - If still fail to respond, **consider combination therapy** with an additional antidepressant from a different class, an atypical antipsychotic or lithium but *'combination therapy should be initiated in specialist mental health settings or after consulting a specialist.'* Antipsychotics should be prescribed under shared care arrangements.

Swapping And Stopping

Tapering regimes:

Switch from:	Switch to TCA (except clomipramine)	Switch to SSRI (except fluoxetine)	Switch to fluoxetine	Switch to SNRI	Switch to mirtazapine
TCA (except clomipramine)	Direct switch possible	gradually reduce TCA to 25-50mg daily then start SSRI and slowly withdraw TCA over next 5-7 days	Halve dose of TCA, add fluoxetine and then slowly withdraw TCA	Cross taper cautiously with low dose SNRI	Cross taper cautiously
SSRI (except fluoxetine)	Cross taper cautiously with low dose TCA	Direct switch possible	Direct switch possible	Direct switch possible (caution if paroxetine used)	Cross taper cautiously (see below for example)
Fluoxetine	Stop fluoxetine, start TCA low dose 4-7 days later and increase dose very slowly	Stop fluoxetine, start other SSRI at low dose 4-7 days later	N/A	Stop fluoxetine, start SNRI at low dose 4-7 days later	Cross taper cautiously
SNRI	Cross taper cautiously with low dose TCA	Direct switch possible	Direct switch possible	Direct switch possible	Cross taper cautiously
Mirtazapine	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously	Cross taper cautiously	N/A

- Example for cross tapering regime from citalopram to mirtazapine:

	Pre-switch dose	Week 1	Week 2	Week 3	Week 4
Withdrawing citalopram	40mg daily	20mg daily	10mg daily	Nil	Nil
Introducing mirtazapine	Nil	15mg daily	30mg daily	30mg daily	45mg daily (if needed)

Case Study 2

Jason, 41 years old.

- **Been on Fluoxetine 40mg for 4 months and still severely depressed.**
- **Prior to Fluoxetine, Jason has tried Citalopram and Sertraline, both ineffective.**

What are the further options for depression?

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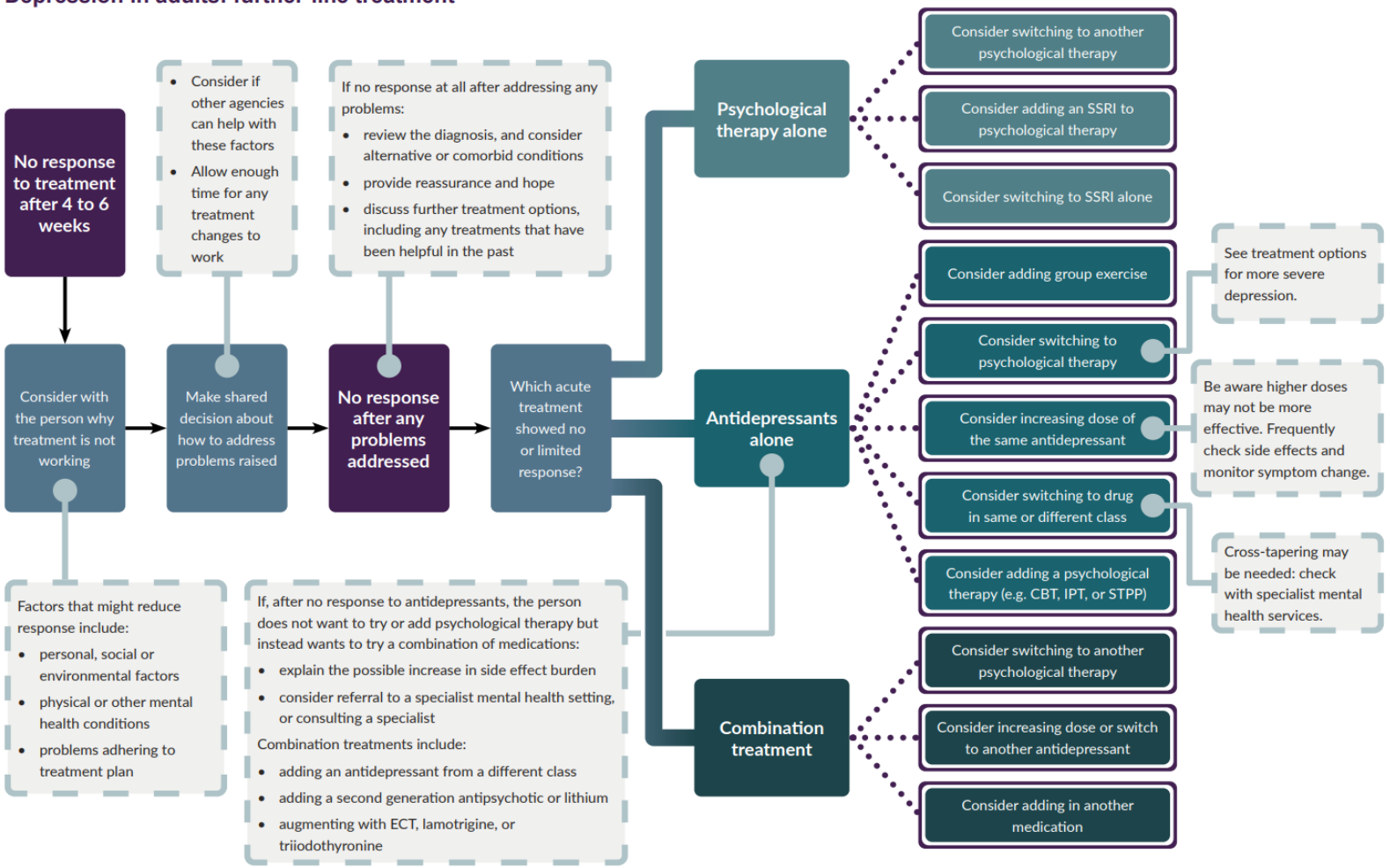
Depression in adults: further-line treatment



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Case Study 3

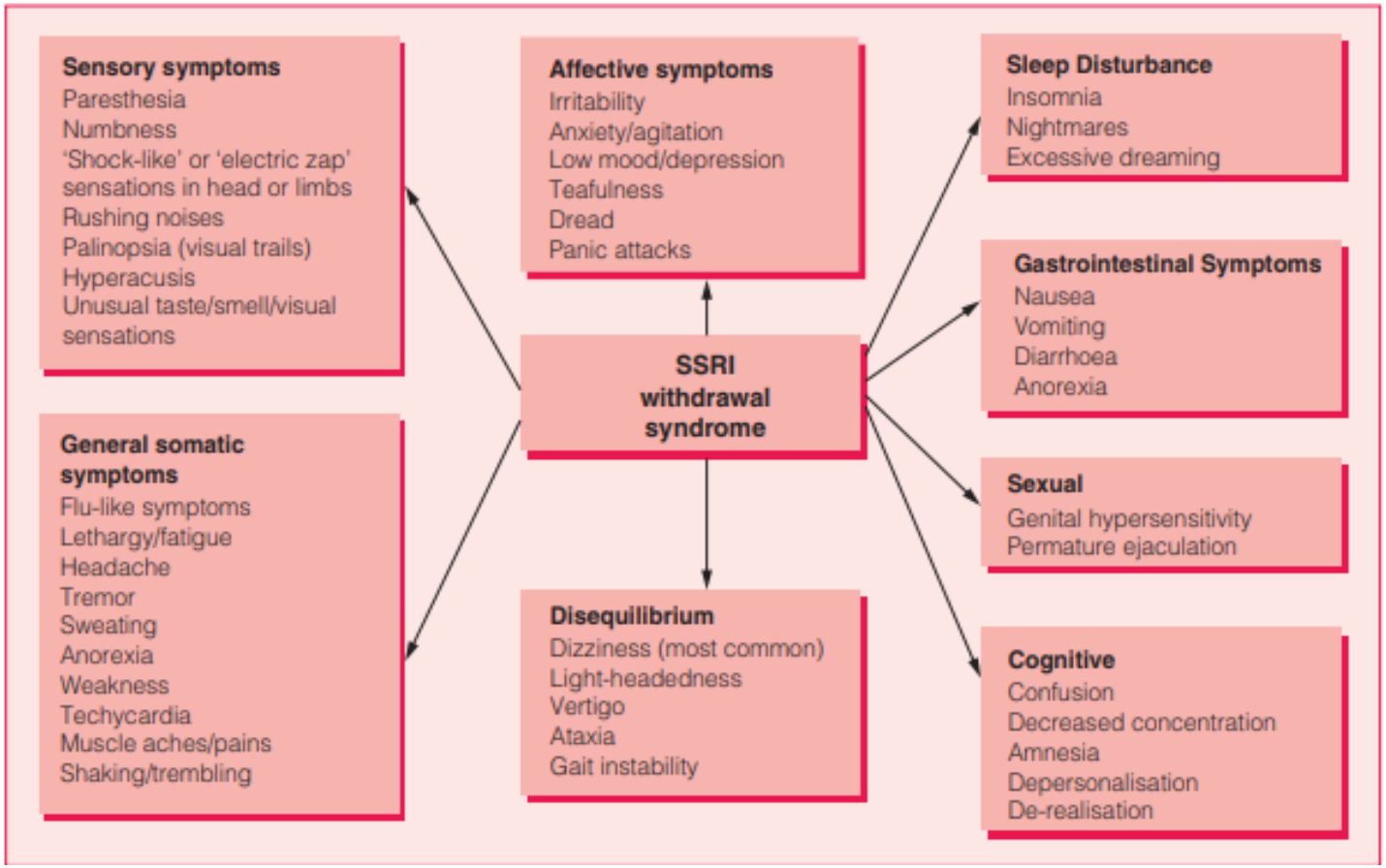
Dani, 32-year-old.

- **Been on Sertraline 100mg for many years, stopped very recently in order to conceive.**

- **Feels dreadful, dizzy, shaky and anxious.**

What advice do we give?

Antidepressant Withdrawal Symptoms



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RC PSYCH ROYAL COLLEGE OF PSYCHIATRISTS

Appendix 1: Risk of withdrawal symptoms with individual antidepressant

Highest Risk	Moderate Risk	Low Risk	Lowest Risk
Amitriptyline	Citalopram	Bupropion	Agomelatine
Clomipramine	Escitalopram	Fluoxetine	
Paroxetine	Fluvoxamine		
Venlafaxine	Imipramine		
Duloxetine	Lofepramine		
	Nortriptyline		
	Mirtazapine		
	Reboxetine		
	Sertraline		
	Trazodone		
	Vortioxetine		

What to Include in Discussions with Pregnant Women

- The woman's ability to be treated with non-pharmacological interventions and previous response
- The potential impact of an untreated mental disorder on the foetus or infant
- The risks from stopping medication abruptly
- Severity of previous episodes, response to treatment and the woman's preference
- The background risk of foetal malformations for pregnant women without a mental disorder
- The increased risk of harm associated with drug treatments during pregnancy and the postnatal period (and acknowledge uncertainty with regards to risk)
- The possibility that stopping a drug with known teratogenic risk after pregnancy is confirmed may not reduce the risk of malformations
- Breastfeeding
- https://www.medicinesinpregnancy.org/

Case Study 4

Derek, 68 years old.

- **Been on Citalopram 40mg for 15 years following a divorce.**
- **Symptoms in remission for a long time, just continued taking the medication without question.**

- **How do we go about stopping??**

Influencing Factors for the incidence and severity of antidepressant withdrawal symptoms

- **Pharmacological Factors:** pharmacokinetics, drug half life, pharmacodynamics, receptor affinity.

Symptoms are typically more severe with drugs that have a short half life (e.g. Paroxetine, Venlafaxine)

- **Treatment Factors:** Duration of treatment, dose, tapering method

Generally, the slower the better, particularly if someone has been in treatment for several years

- **Patient Specific Factors:** Prior experiences and anticipation effects

- handyfactsheetstoppingantidepressantsuk.pdf (choiceandmedication.org)

Tapering Advise

- Withdrawal symptoms can be mild, may appear within a few days of reducing or stopping antidepressant medication, and usually go away within 1 to 2 weeks
- Withdrawal can sometimes be more difficult, with symptoms lasting longer (in some cases several weeks, and occasionally several months)
- Withdrawal symptoms can sometimes be severe, particularly if the antidepressant medication is stopped suddenly.
- Reduce the dose by 25-50% each week over a 2-4 weeks period. This can be done slower if required by reducing the frequency of the reducing dose or reducing in smaller increments.
- If a person has more severe withdrawal symptoms, consider restarting the original antidepressant medication at the previous dose, and then attempt dose reduction at a slower rate with smaller decrements after symptoms have resolved.

- https://www.rcpsych.ac.uk/mental-health/treatments-and-wellbeing/stopping-antidepressants

- handyfactsheetstoppingantidepressantsuk.pdf (choiceandmedication.org)

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Question and Answer

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Thank you for listening

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Please complete our short feedback questionna by clicking on the link that has been put into the chat.

Please note: all feedback will be anonymous

Next session: 19th March 2024
Impact of SMRs: stopping medication and reducing costs, reducing polypharmacy, ACB reduction and decreasing CO2 emissions.
Speaker: Andrea McGuinness: PCN Lead Pharmacist, Skelmersdale

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