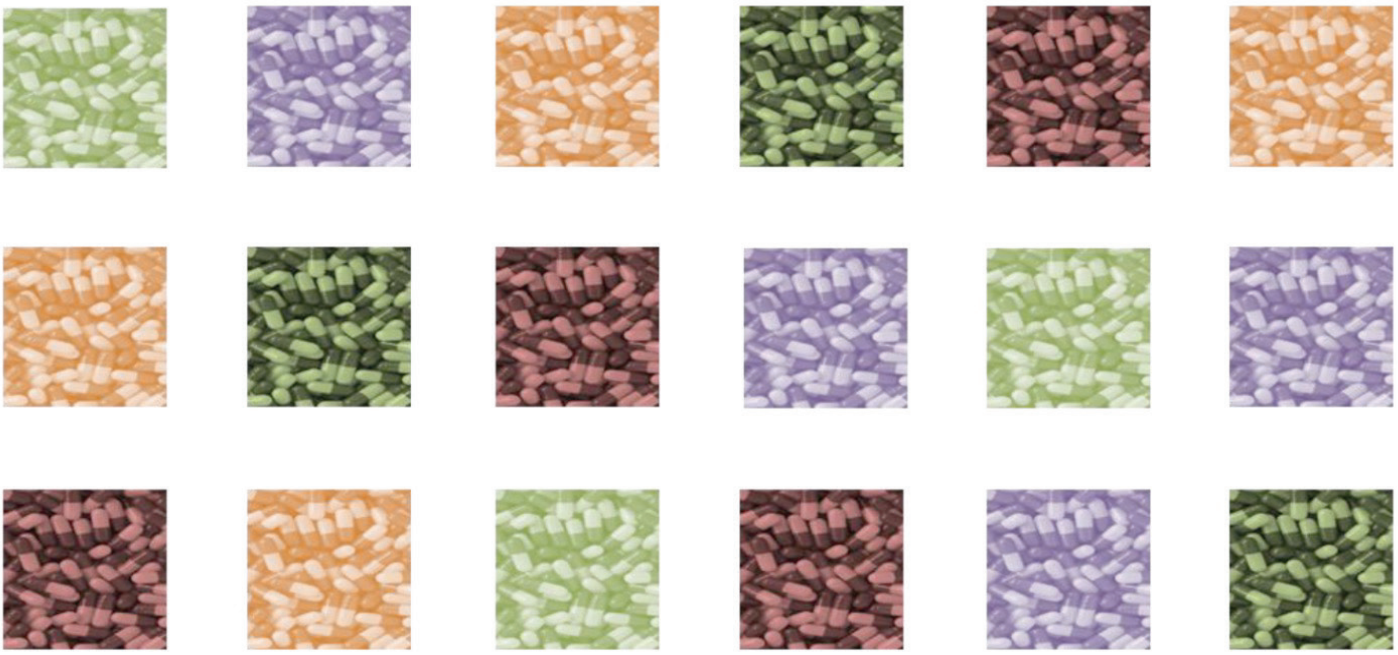
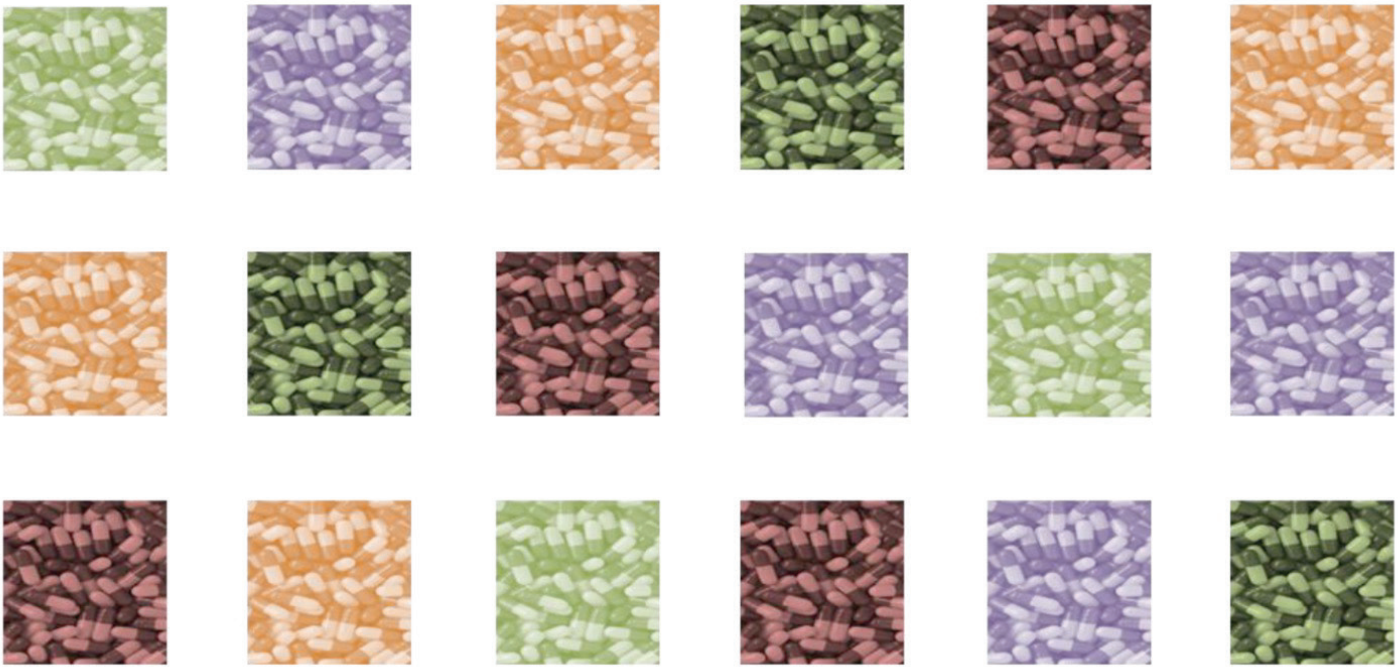


Quality Prescribing for Antidepressants

A Guide for Improvement 2024-2027



NHS SCOTLAND

REALISTIC MEDICINE

EFFECTIVE PRESCRIBING & THERAPEUTICS DIVISION

Scottish Government
Riaghaltas na h-Alba

Clinical foreword

We are delighted to present the Quality Prescribing for Antidepressants guide. This guide is welcomed as an opportunity to further improve the care of individuals receiving antidepressant medication and promote a holistic approach to person-centred care. It recommends supportive and collaborative discussions between individuals and prescribers when reviewing antidepressants, as well as highlighting the importance of addressing health inequalities and wider climate and sustainability challenges. The recommendations are aimed at supporting people receiving antidepressants, healthcare professionals, general practice clusters, health boards and health and social care partnerships and are designed to support improvements in healthcare service redesign and provision of care.

The prescribing of antidepressants continues to increase in Scotland, with many people receiving antidepressants for two years or more. This may be appropriate for some individuals, but it is important that ongoing treatment is reviewed regularly and that the risks and benefits of treatment are discussed. Treatment goals should be agreed with individuals, both at the time of initiation and when reviewing medication, and treatment plans should take a holistic approach to management and support. These should include discussions of non-pharmacological and wider community support options where these are available and indicated.

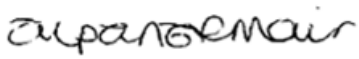
This prescribing advice is primarily intended to support and encourage the appropriate use of antidepressants for mental health and physical conditions, as part of the wider treatment options available. It supports appropriate initiation of antidepressants, regular and proactive reviews, reduction and stopping of treatment where it is ineffective or where treatment courses have been completed. Regular person-centred reviews can optimise the care of those receiving antidepressants and minimise avoidable medicine-related harm. These reviews can also support and enable appropriate continuation of antidepressant treatment where this is required, using the 7-Steps person-centred review approach.

This guide aims to maximise benefit and ensure safe, appropriate care from antidepressants. It is not intended to override other pharmacological or non-pharmacological prescribing treatment advice such as NICE, British Association for Psychopharmacology (BAP), Scottish Government Polypharmacy guidance or the principles outlined in the Realising Realistic Medicine report. It is intended to complement these and add practical advice for tailoring care to the needs and preferences of the individual.

This guide has been developed with a multidisciplinary team across Scotland, with clinical and policy expertise from NHS Scotland and Scottish Government and with experts by lived experience and patient groups.

We are extremely grateful to all those who contributed to the working group, the review and development of this guide.

Alastair Cook
Principal Medical Officer Psychiatric Adviser
Scottish Government



Alpana Mair
Head of Effective Prescribing and Therapeutics
Scottish Government

Professor Sir Gregor Smith
Chief Medical Officer for Scotland

Alison Strath
Chief Pharmaceutical Officer

Executive Summary

Antidepressant prescribing continues to increase in Scotland with one in five adults receiving one or more antidepressant prescriptions in a year. In part, this is due to the range of antidepressants available to treat conditions such as depression, neuropathic pain and anxiety disorders, as well as positive changes in attitudes towards mental health conditions. The number of people receiving long-term antidepressant treatment has continued to increase with more than half of those prescribed antidepressants (six in ten adults) receiving long-term (≥2 years) treatment (Chart 1).[1] Some of this prescribing is appropriate in providing people with better courses of treatment and enabling better outcomes, however some long-term use of antidepressants may be inappropriate, where medication is no longer required or where non-pharmacological treatment options may be preferred. It is known that the frequency of proactive review of antidepressants when people are not experiencing crises reduces with time and this guide encourages clinicians to proactively review antidepressants and their continued need when individuals are stable and well. It encourages people prescribed antidepressants, or any other medicine, to initiate discussions with healthcare professionals regarding the appropriate continuation, reduction and discontinuation of their medication [see Recommendations].

An important principle in improving the care of people taking antidepressant medicines is to consider the role of shared decision-making and adopting a person-centred approach, considering the ongoing need for treatment. This includes discussions of the risks and benefits of treatment and consideration of non-pharmacological and evidence based psychological interventions, where appropriate and in line with current clinical guidelines [see Recommendations]. When reviewing those receiving antidepressants, particular groups of people have been identified that could be prioritised for proactive reviews – List 1 [see Targeting reviews]. This can be done using clinical systems such as the Scottish Therapeutics Utility available within GP practice.

The 7-Steps medicines review process provides a clear structure for undertaking proactive person-centred reviews, both at the **initiation** of medicine and in the **review** of existing treatments. This ensures that the individual's concerns and preferences regarding continuation, reduction and/or cessation of antidepressants are considered and that treatment plans are centred around what matters to the individual.

The 7-Steps review process provides a framework for this, considering:

1. **Aim:** what matters to the person?
2. **Need**: identify essential medication.
3. **Need:** any unnecessary medication?
4. **Effectiveness**: are therapeutic objectives met?
5. **Safety:** any ADRs/ side effects or a risk of them?
6. **Sustainability**: cost-effective and environmentally sustainable
7. **Person-centred**: is the person willing and able to take drug therapy as intended?

Figure 1: The 7-Steps medicine review process

This prescribing guide does not override existing local and national guidelines for the treatment and management of pain or common mental health disorders [see Background]. It has been developed by the collaborative efforts of a multidisciplinary team of clinicians, academics, experts by experience, patient groups and policy makers from across Scotland, Scottish Government and NHS Scotland, who are already delivering work around antidepressant prescribing to improve outcomes for the people of Scotland.

Acknowledgements

Chairpersons

Alastair Cook	Principal Medical Officer Psychiatric Adviser, Scottish Government

Deputy Chair

Alpana Mair	Head of Effective Prescribing and Therapeutics Division, Scottish Government

Short-Life Working Group members

Ailsa Stein	SIGN Programme Manager, Healthcare Improvement Scotland
Andrew Walker	Scottish Mental Health Pharmacy Group
Ann Wales	Programme Lead, Knowledge and Decision Support, Digital Health & Care Innovation Centre
Beth Crozier	Senior Policy Officer, Effective Prescribing and Therapeutics, Scottish Government
Blair Smith	Clinical Professor and Consultant in Pain Medicine, NHS Tayside
Chris F Johnson	Clinical Pharmacist, General Practice and Specialist Mental Health Lead, Effective Prescribing and Therapeutics, Scottish Government
Claire Campbell	Consultant Clinical Psychologist, Aberdeenshire Alcohol and Drug Service (AADS)
David Revie	Community Link Worker, We Are With You
Denise McFarlane	GP and Chair Local Medical Committee: Grampian
Donald Macintyre	Consultant General Psychiatrist, Associate Medical Director, NHS 24
Duncan Hill	Specialist Pharmacist in Substance Misuse, NHS Lanarkshire
Kieran Dinwoodie	GP, NHS Lanarkshire
Iain Wilson	GP Clinical Lead, Effective Prescribing and Therapeutics, Scottish Government
Irene Oldfather	Director Strategic Partnerships and Engagement Health and Social Care Alliance Scotland, The ALLIANCE
Jackie Wiggins	Older Adults Mental Health, NHS Greater Glasgow and Clyde

Joe Lockhart	Administrative Support, Scottish Government
Laura Wilson	Policy and Practice Lead, Royal Pharmaceutical Society
Lesley Colvin	Prof of Pain Medicine and Hon Consultant in Anaesthesia and Pain Medicine, University of Dundee
Lise Hertel	Associate Medical Director, NHS Western Isles
Margaret Umeed	General Practice Nurse, and Advanced Nurse Practitioner Trainer
Paul Paxton	Senior Information Analyst, Public Health Scotland
Stephanie Cymber	Policy Officer, Mental Health Clinical Care Policy Team, Scottish Government
Stuart Law	Head of Policy & Research, Effective Prescribing and Therapeutics, Scottish Government
Stuart McTaggart	Principal Pharmacist, Public Health Scotland

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Sharon Pfleger	Consultant in Pharmaceutical Public Health, NHS Highland
Julius Cesar Alejandre	Doctoral Researcher and Hydro Nation Scholar, Glasgow Caledonian University

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Summary of recommendations

This guide recommends that clinicians:

- Undertake proactive medicine reviews and create the opportunity for people to be directed to and access non-pharmacological and psychological interventions, which may be needed to achieve better longer-term outcomes [see Recommendations].

- Code clinical records for people receiving antidepressant prescriptions with the indication for antidepressant treatment [see Recommendations].

- Consider different strategies for reducing, tapering and stopping antidepressants where indicated. These should be considered and applied depending on individual preferences and need [see Reducing and stopping].

- Review diagnosis, adherence with treatment and where appropriate consider switching to an alternative antidepressant if no response to antidepressant treatment at three to four weeks. All antidepressants show a pattern of response and rate of improvement greatest in the first one to two weeks [see Recommendations].

- Use optimal doses of antidepressants where '20's plenty and 50's enough'. Selective serotonin re-uptake inhibitors (SSRIs) demonstrate a flat dose response curve for the treatment of depression. Standard daily doses of 20mg citalopram/fluoxetine/paroxetine, 50mg daily of sertraline or 10mg escitalopram provide optimal antidepressant effectiveness [see Purpose of this advice].

- Proactively review those on antidepressants and long-term antidepressants. As individuals may not be proactively reviewed and present only at times of crisis, this may lead to doses being inappropriately increased in response to crisis. Long-term antidepressant use is associated with the use of higher antidepressant doses (Chart 2).

- When reviewing the management of depression consider the following [see Recommendations]:

    - The stepped-care approach should be used to help choose the most appropriate intervention - self-help, non-pharmacological, with or without antidepressant therapy.

    - Consider that for 50% of individuals depressive symptoms can spontaneously resolve within 12 weeks of diagnosis.

- Less severe depression (i.e. PHQ-9 score <16), commonly referred to as mild depression, may respond better to non-pharmacological approaches as antidepressants are not effective for less severe illness.
- Do not routinely offer antidepressant medication as first-line treatment for less severe depression, unless that is the person's preference.
- Antidepressants are effective for reducing symptoms of moderate to severe depression and/or helping people achieve remission, especially in combination with non-pharmacological treatment and/or self-help, see Figure 5 and Table 2.
- Combining antidepressants for depression is not recommended. Non-specialist psychiatry prescribers should not initiate these combinations, unless on the advice of specialist services. People initiated on combinations by psychiatry should be reviewed by specialist services.
- For people with dementia, antidepressants demonstrate limited benefits in treating depression. However, for some individuals they may reduce depressive symptoms and improve general functioning.

- When reviewing the management of anxiety disorders consider the following [see Recommendations]:
  - The stepped-care approach should be used to help choose the most appropriate intervention; self-help, non-pharmacological with or without antidepressants, see Figure 5.
  - Different antidepressants demonstrate variable efficacy depending on which anxiety disorder is being treated – generalized anxiety disorder (GAD), panic disorder, obsessive compulsive disorder (OCD), etc.
- When reviewing the management of pain consider the following [see Recommendations]:
  - Tricyclic antidepressants (TCAs) and duloxetine demonstrate modest effects in the treatment of neuropathic pain (Table 2).
  - Selective serotonin re-uptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs) and tricyclics antidepressants are not recommended in the management of lower back pain, with no evidence for the use of antidepressants in sciatica.
  - Antidepressants (amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine and sertraline) can improve quality of life, pain, sleep and psychological distress compared with placebo in the treatment of chronic pain, however the evidence is conflicting.

1. What is the purpose of this advice?

Background

This advice is intended to support healthcare professionals and those that provide support to people on antidepressant treatment to facilitate the appropriate use of antidepressants. It is not intended to override other prescribing and treatment advice such as NICE, British Association for Psychopharmacology (BAP), or Scottish Government Polypharmacy guidance, which follows the principles outlined in the Realising Realistic Medicines report. It is intended to complement and add practical advice and options for tailoring care to the needs and preferences of individuals.

Antidepressants are used for a variety of conditions and are commonly prescribed for people experiencing a range of comorbidities and diseases. This guide provides a range of options for individuals and clinicians to support proactive person-centred antidepressant reviews. From antidepressant initiation to treatment follow up and cessation, it includes advice for shared treatment plans, managed reduction and discontinuation of therapy for adults using a person-centred approach using the 7-Steps process.

What is the benefit of this prescribing advice to the person receiving an antidepressant?

This quality prescribing advice is intended to encourage supportive and constructive discussions between individuals and prescribers when reviewing antidepressants and their ongoing need. Where appropriate, the fears and apprehensions associated with initiation, continuing, reducing or stopping antidepressants should be considered and treatment tailored to the individual's needs.

As with all medicines – not just antidepressants – it is important to routinely and proactively monitor and review the ongoing needs and rationale for continued medicine use. Use the 7-Steps medication review process. For some individuals this may be on annual basis as part of their long-term conditions review (diabetes, asthma, etc.) while others may require more frequent reviews. However, it is known that long-term antidepressant use is increasing,[2,3] and that the longer someone receives an antidepressant the less frequently it, or the condition it is treating, is reviewed.[4,5] This can lead to inappropriate long-term prescribing for some individuals.

A large proportion of people with depression (receiving an antidepressant) have other comorbidities such as diabetes, cardiovascular disease, respiratory disease and therefore receive multiple prescribed medicines (known as polypharmacy).[6,7]

This is shown in Figure 2 comparing the likelihood in the most affluent and most deprived areas. These individuals may also be frail and more likely to experience

adverse drug effects and avoidable harms. Therefore, proactively reviewing antidepressant therapy creates an opportunity for a holistic person-centred assessment and review of the condition and medicine needs using the 7-Steps process. This can help reduce avoidable medication-related harms.

Figure 2: Comorbidities comparison between most affluent and most deprived deciles [6]

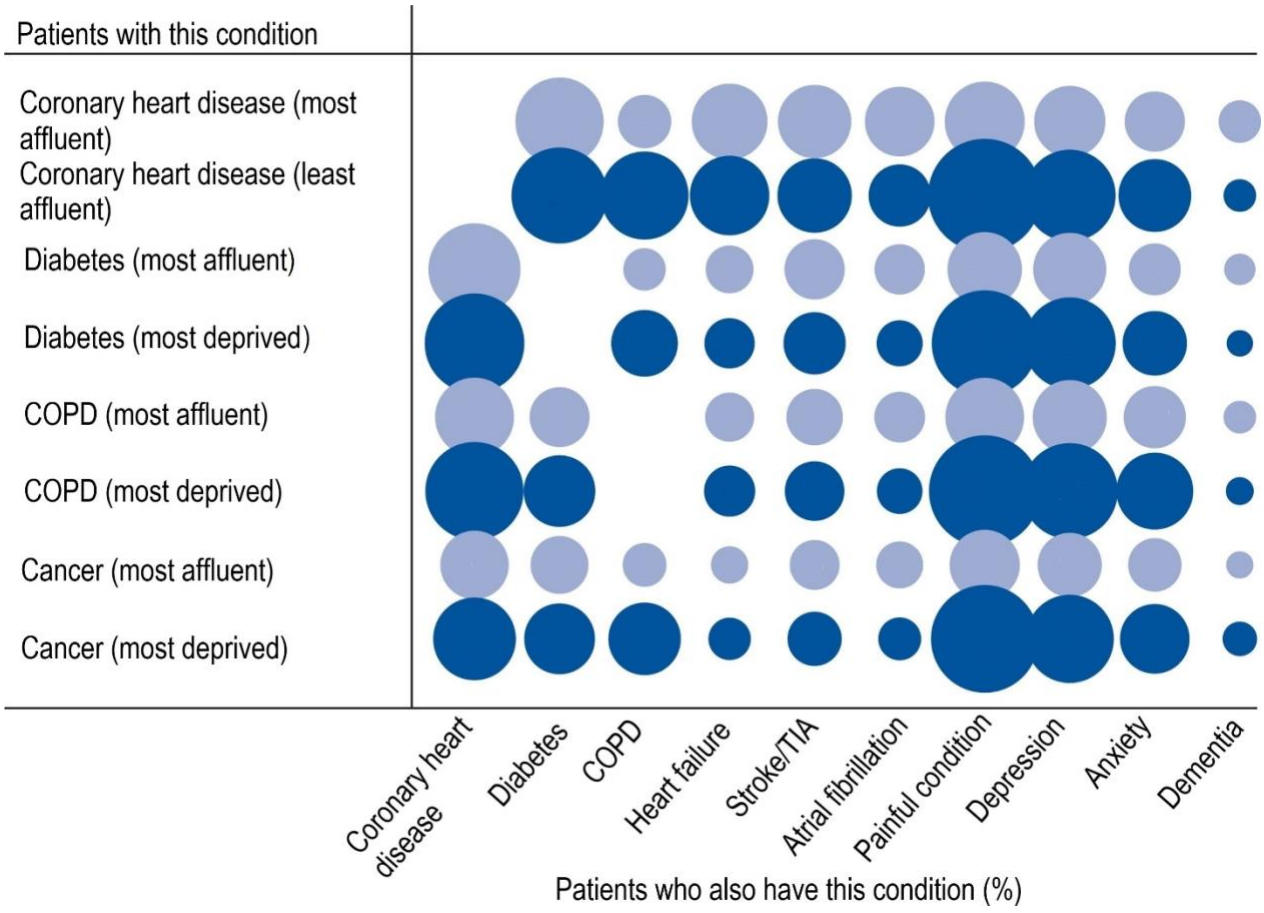


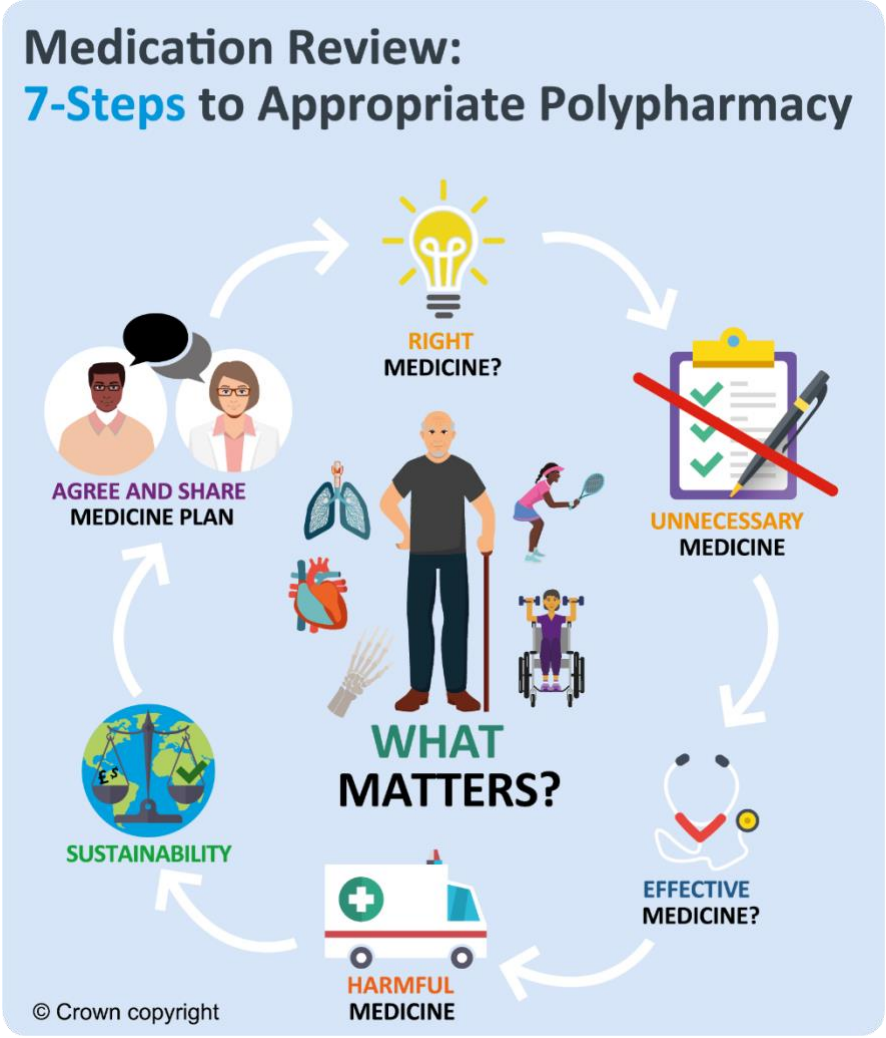
Table 1: Comorbidities comparison between most affluent and most deprived deciles[6]

Comorbidity	**CHD**	**Di**	**COPD**	**HF**	**S/TIA**	**AF**	**PC**	**Dep**	**A**	**Dem**
Coronary heart disease (most affluent)	-	19	7	14	13	12	16	13	9	4
Coronary heart disease (most deprived)	-	23	19	16	14	10	32	21	13	3
Diabetes (most affluent)	21	-	4	6	9	6	14	13	7	2
Diabetes (most deprived)	24	-	11	6	10	5	28	21	10	2
COPD (most affluent)	15	9	-	6	8	6	15	14	10	3
COPD (most deprived)	24	13	-	6	9	5	31	23	15	2
Cancer (most affluent)	12	8	5	3	6	5	12	10	7	2
Cancer (most deprived)	17	12	13	4	7	5	29	19	12	3

Key: CHD – Coronary heart disease; Di – Diabetes; COPD - Chronic obstructive pulmonary disease; HF - Heart failure; S/TIA - Stroke/TIA; AF - Atrial fibrillation; PC - Painful condition; Dep – Depression; A – Anxiety; Dem - Dementia

This guidance focuses on the quality prescribing of antidepressants to result in improvements in care. The 7-Steps medication review process promotes a shared decision-making approach to medicine reviews and places the individual at the centre, to ensure prescribing is effective and appropriate for them. People will be encouraged to self-manage their condition where appropriate and be asked 'what matters to you?'[8] to support a holistic approach to care in line with the Scottish Government's polypharmacy guidance.[9]

Figure 3: The 7-Steps medicine review process



Some prescribers may be less comfortable reviewing psychotropic medicines such as antidepressants and individuals may be fearful of reducing and stopping antidepressant therapy. This may be due to concerns about relapse or recurrence of their illness, and/or experiencing antidepressant discontinuation/withdrawal symptoms, all of which may result in inappropriate long-term use where treatment is no longer required.[5,10,11,12,13,14,15,16] Proactive medicines reviews also create an opportunity for people to be directed to and access non-pharmacological and

psychological interventions, which may be needed to achieve better longer-term outcomes.[17,2]

Overall, proactive medicines reviews will help to:

- reduce inappropriate medicines use e.g. where medicines are no longer needed
- reduce avoidable adverse drug effects and harms
- optimise care and outcomes
- enable people to take the medicines they need
- direct to non-pharmacological interventions where appropriate

Where appropriate, and when applied to practice, this prescribing advice may help provide structure to support people who are anxious about reducing and/or stopping antidepressant therapy, and who worry about discontinuation/withdrawal symptoms.

'Discontinuation symptoms' or 'withdrawal effects'?

The term 'discontinuation symptoms' is used to describe symptoms experienced on stopping medicines that are not drugs of dependence. There are important semantic differences in the terms 'discontinuation' and 'withdrawal' symptoms – the latter implying addiction, the former does not.[18] While the distinction is important for precise medical terminology, it is irrelevant when it comes to personal experiences and how an individual may describe their signs and symptoms. Regardless of this, proactive medicines reviews create an opportunity for individuals and prescribers to discuss and address potential fears and worries, alongside developing appropriate shared management plans for the use of antidepressants and other medicines as part of a realistic prescribing plan.

What are the benefits of this prescribing advice to healthcare professionals?

This prescribing guide provides practical structured advice and examples of good practice approaches for health professionals to:

- identify individuals who may benefit from review (see List 1)
- review antidepressant therapy and
- routinely support people in their care

Prescribers have identified and reported that it can be:

> '…easier to start [psychotropic medicines] than to stop [them]'[10]

and that

> '…what we're [prescriber] probably not good enough, at the moment, is sort of the long-term managing and the coming-off part'[14]

This may be due to a range of perceived and actual barriers, such as some healthcare professionals lacking confidence, knowledge and skills to support and enable proactive antidepressant review and discontinuation.[10,13,14,16,19] Lack of knowledge may include time to onset of action,[5] as antidepressants demonstrate their effects within one to two weeks of use.[18,20] Despite this, some prescribers wait eight weeks or more before optimising doses or switching antidepressant treatments in poor or non-responders.[5,21]

Identifying individuals for review can be limited by some of the electronic clinical systems routinely used in clinical practice. However, the Scottish Therapeutics Utility (STU) has been developed for use in general practice in Scotland, to identify people who may benefit from a medication review. General practice staff can routinely use STU to identify and plan antidepressant review work. While there is no consensus on the optimal method for antidepressant withdrawal,[22,23] this guidance provides a range of options for reducing and withdrawing antidepressants. More detail is available in Section 5.

What are the benefits of this prescribing advice to organisations?

Implementation and use of this advice will help improve care and outcomes with:

- a range of prescribing indicators and measures which focus attention and resources on areas that would benefit from action
- resources and examples within the case studies of what has already been trialled in clinical practice

These measures will be of use to health boards, health and social care partnerships (HSCPs), general practice clusters and individual general practices.

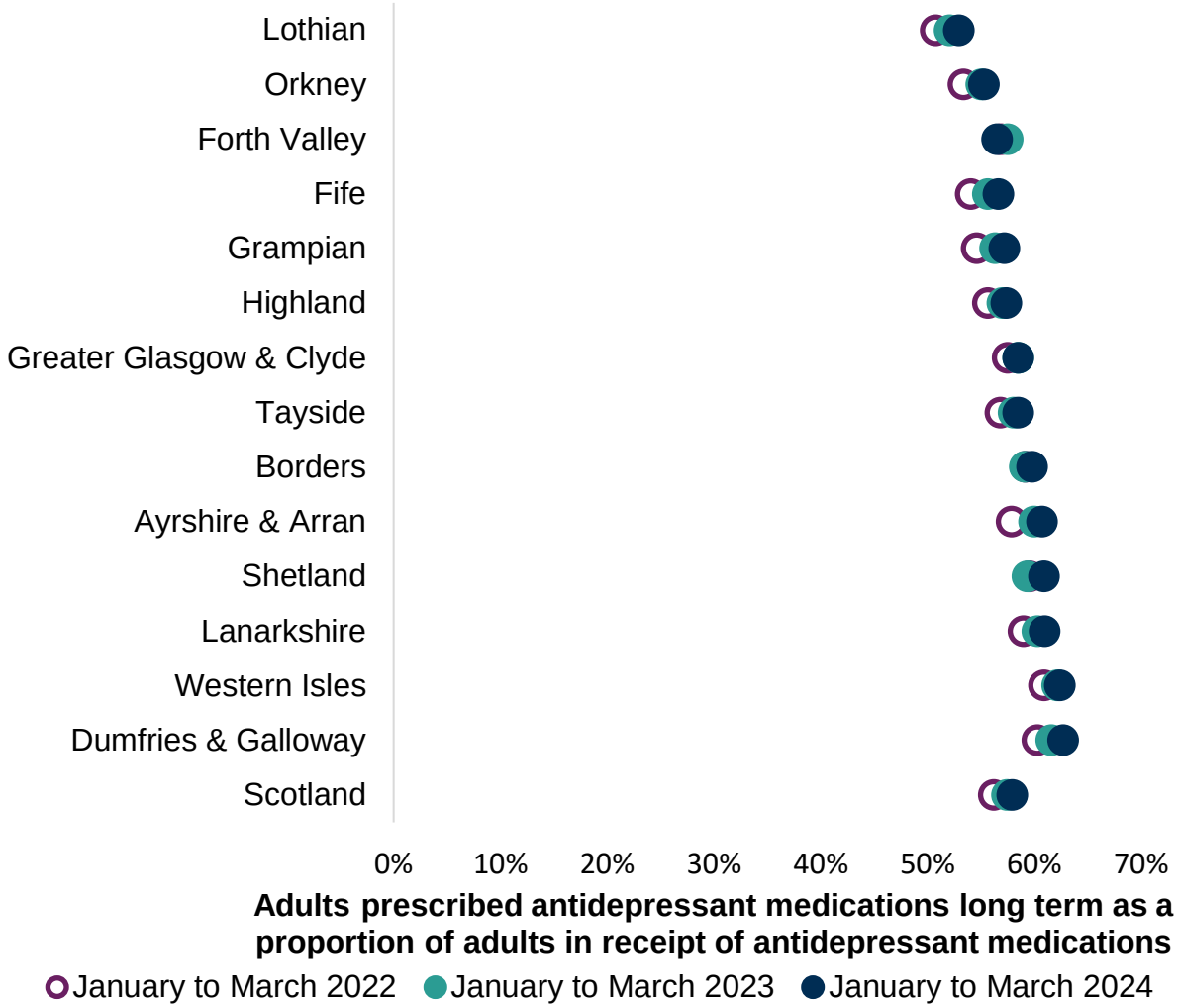
Why is proactively reviewing antidepressants important?

In Scotland, as with other Westernised societies, antidepressant prescribing has increased over the last 30 years and continues to increase,[1] with one in five adults receiving one or more antidepressant prescriptions in a year, and more than half of those (six in ten adults) receiving long-term (≥2 years) treatment (Chart 1).[1]

This has been due to:

- the availability of different antidepressants,[24,25] some of which are better tolerated and safer than others[26,27]
- people's expectations[28,29] and changes in society's attitudes towards mental health conditions[30]
- greater willingness to prescribe for a variety of mental health and non-mental health conditions[31,32,33]
- increased long-term use,[2] and use of higher doses[17,34]
- lack of regular medicine reviews[5,35]
- more people receiving antidepressant therapy[1]

Chart 1: Adults (≥18 years old) prescribed all long-term (≥2 years) antidepressants as a proportion of adults in receipt of antidepressant medications, by NHS board



While the majority of antidepressants are prescribed for the treatment of 'common mental health conditions' such as depression and anxiety disorders, they are usually only one aspect of a complex multidimensional treatment plan to care for and support people to achieve recovery.[20,36] The lack of regular review reduces the opportunity to advise the use of non-pharmacological approaches that may aid in recovery and can lead to inappropriate long-term antidepressant use.[5,36,37,38,19]

Long-term antidepressant use is associated with the use of higher antidepressant doses (Chart 2), and while this may be appropriate for some antidepressants, it can be inappropriate for others.

For example:

- Selective serotonin re-uptake inhibitors (SSRIs) demonstrate a flat dose response curve for the treatment of depression.
    - standard daily doses: 20mg citalopram/fluoxetine/paroxetine, 50mg daily of sertraline or 10mg escitalopram provide optimal antidepressant effectiveness – '20's plenty and 50's enough'[20,39,40,41,42]
    - as individuals may not be proactively reviewed when stable and well, presenting only at times of crisis, this may lead to doses being inappropriately increased in response to the crisis[5]
    - for SSRIs, higher than standard doses are known to cause more adverse effects and avoidable harms (i.e. anxiety, insomnia, falls, etc) and are possibly associated with more withdrawal effects.[20,39-42,43] Higher than standard doses are not more effective at reducing depressive symptoms in poor and/or non-responders[41,42,44,45,46]
- Mirtazapine also demonstrates optimal effects for the treatment of depression at 30mg daily[40]
    - however, its use is associated with 5-7 kg weight gain[47,48]
    - lower doses (15mg daily) are more sedating[49]
- Tricyclics antidepressants (TCAs) demonstrate a dose response for the treatment of depression where higher doses can be more effective e.g. increasing to 100mg to 125mg per day.[18,20,39]
    - doses as low as 10mg daily can be effective for the treatment of neuropathic pain, while 50mg to 75mg daily provide optimal effects for the majority of people with neuropathic pain[33,50]
    - higher doses are known to cause more adverse drug effects and avoidable harms such as sedation, confusion and QTc prolongation, amongst others[51]

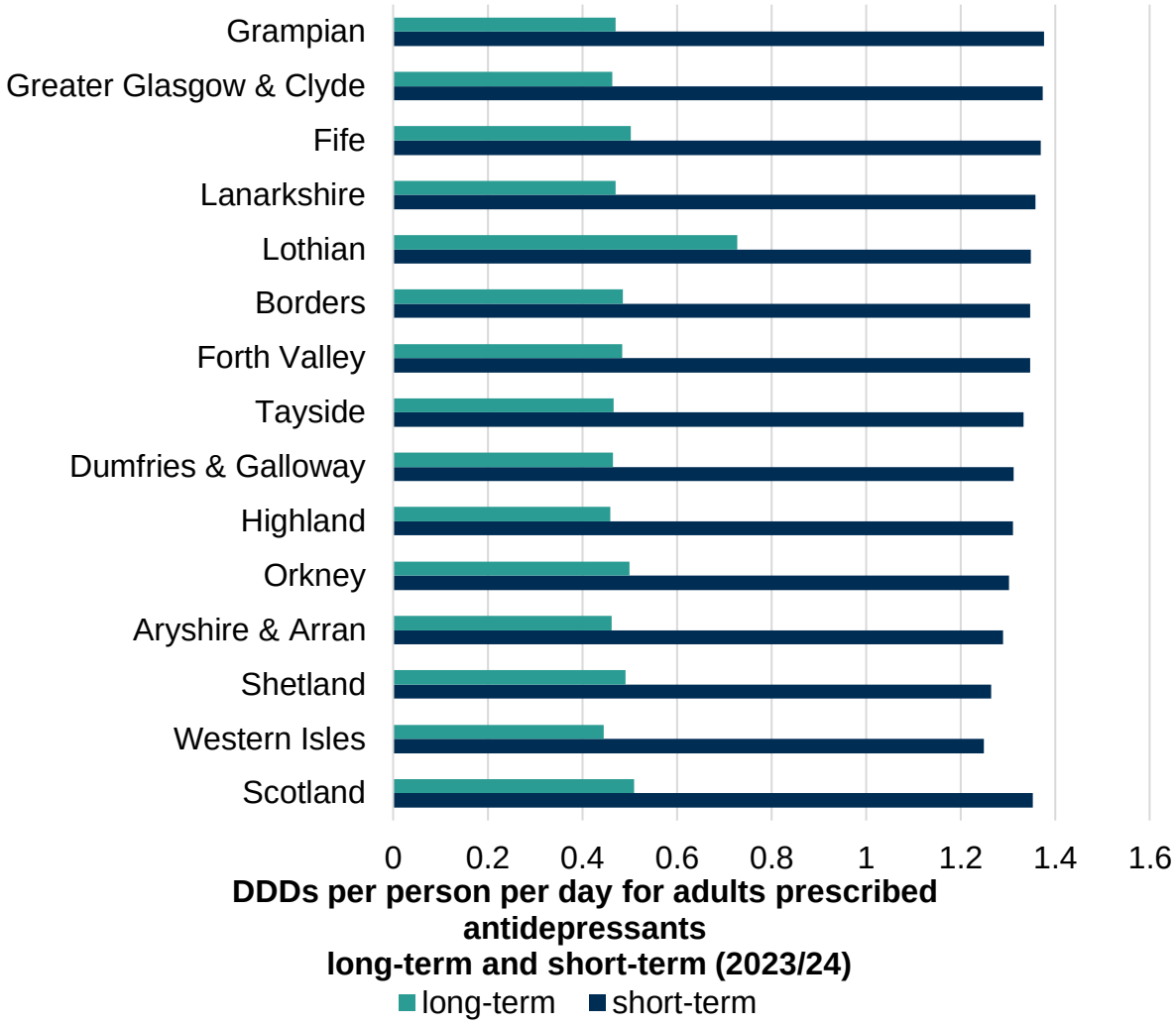
Note: QTc prolongation: QTc prolongation is of concern as it is associated with ventricular tachycardia and sudden cardiac death. The QT interval on an electrocardiogram describes the manifestation of ventricular depolarization and repolarization. The QT interval is influenced by heart rate therefore the QT interval should be measured for rate correction, allowing the calculation of the corrected QT interval (QTc). Intervals of 440 to 460 milliseconds in men and 440 to 470 milliseconds in women are considered to be at the top limit of normal range. Bazett's formula is considered the gold standard for QTc calculation. QTc prolongation is associated with ventricular tachycardia and sudden cardiac death.[50]

- Serotonin and noradrenaline re-uptake inhibitors (SNRIs) demonstrate a dose response effect for the treatment of depression where higher doses can be more effective.[39,40,49,52,53,54]
    - For example, venlafaxine exhibits predominantly serotonin ceiling effects at doses <150mg daily, with noradrenaline (>150mg daily), and dopamine (>225mg daily) effects becoming more significant as doses are increased.[49,52]
    - Duloxetine demonstrates similar effects.[53,54] Higher doses are known to cause more adverse drug effects and avoidable harms including insomnia, weight loss and sexual dysfunction.[40,55,56]

While in certain conditions it may be appropriate to increase the antidepressant dose, prescribers should always consider limitations of medications and the risks associated with the use of higher doses of medicines. Proactive review of individuals when their condition is stable creates an opportunity to review the need for continued antidepressant treatment regardless of the indication to reduce inappropriate or ineffective antidepressant use.

Chart 2 below shows higher daily doses for individuals on long-term antidepressants (equal to or more than two years), in comparison to those who are on short-term (less than two years) antidepressant therapy.

Chart 2: Average defined daily doses (DDDs) per person per day for adults (≥18 years old) prescribed an antidepressant long-term (≥2 years) or short-term (<2 years), by NHS board for 2023/24



All antidepressant classes are included. Note TCAs are more commonly prescribed for the treatment of neuropathic pain (e.g. amitriptyline 10mg to 50mg daily, equating to 0.13 to 0.67 DDD) rather than depression (100 to 150mg daily, equating to 1.3 to 2.0 DDD). The majority of SSRIs however, are prescribed for the treatment of depression (e.g. citalopram 20mg to 40mg daily, equating to 1.0 to 2.0 DDD).[57]

Environmental impact

The healthcare industry is increasingly asked to account for the negative climate and environmental impact generated through providing medical care.

In Scotland, every 10 days a 10-tonne truck of medicines waste is transported for incineration. There are associated costs with incineration; travel costs and environment impact (see Figure 4 below). This is in addition to the direct costs of unused medicine.

Figure 4: Annual cost of managing medicines waste in Scotland

There are many factors which contribute to medicines waste and a Department of Health and Social Care report in September 2021[58] showed that over prescribing is commonplace, accounting for at least 10% of all prescribed medications.

This guidance supports reducing inappropriate prescribing by recommending person-centred medicine reviews; providing guidance and support for clinicians and promoting the use of non-pharmacological alternatives where available and effective. This may involve physical and social activities, lifestyle change and regular medicine reviews for those with long-term health conditions.

The Royal Pharmaceutical Society policy, 'Pharmacy's role in climate action and sustainable healthcare',[59] identifies medicines as contributing 25% of carbon emissions in the NHS. This can be reduced by:

- improving prescribing and medicines use
- tackling medicines waste
- preventing ill health and
- improving infrastructure and ways of working

The Royal College of General Practitioners[60] has identified that prescribing accounts for over 60% of general practice's carbon footprint.

Reduction of medicines waste can be achieved by ensuring appropriate prescribing and initiation of medicines, regular person-centred medication reviews to ensure continued effectiveness and deprescribing medicines where appropriate.

Reducing waste from medicines has a double carbon and environmental benefit by:

- reducing upstream emissions, e.g. those associated with distribution, and
- downstream emissions, where fewer medicines need to be disposed of

Medicines that are disposed of in general waste, poured down the sink or flushed down the toilet, increase the risk of environmental harm. Residues from medicines which are unused, not properly disposed of, or from those that pass through the body, can be found in water, soil and sludge and in organisms at all stages of their lifecycles.[61]

Unused or unwanted medicines should be returned to community pharmacy for safe disposal or recycling where available.

The Sustainable Markets Initiative established in 2020 identify seven levers to reduce carbon emissions in care pathways:[62]

1. Decarbonising facilities and fleets
2. Preventing disease onset
3. Diagnosing early
4. Optimising disease management
5. Improving the efficiency of interventions
6. Delivering care remotely or closer to home when appropriate – digital innovations
7. Using lower-emission treatments where available

Pharmaceuticals in the water environment

The Royal Pharmaceutical Society's Sustainability Policies also point to the occurrence of pharmaceuticals in the water environment.[59] Every oral dose of a medicine taken is excreted unchanged or converted to a metabolite with 30-100% entering our wastewater system, which cannot effectively remove all traces. The occurrence of pharmaceuticals in the environment is of global concern and the extent of the risks and impacts on human health and biota is growing. There is already evidence that they can affect aquatic wildlife, increase microbial resistance and enter the human food chain.

The consumption of antidepressants has increased on a global scale and continues to do so. These compounds have been detected in wastewater treatment plants and

surface waters, raising concerns about their potential impacts on the environment. After exposure to antidepressants, aquatic life has been found to have behavioural, physical, cardiovascular and reproductive changes.[63]

Current research using estimated risk quotients to predict levels of toxicity to aquatic life indicates that sertraline (RQ4.88), followed by citalopram (RQ 1.55) and bupropion (RQ 1.12) pose the highest known risk from antidepressant therapy to the aquatic environment.[63] Research into this area is evolving but highlights the need to prescribe medicines appropriately and consider non-pharmacological interventions where they are available and effective.

There is some existing evidence around the environmental impact of antidepressants globally and the need to ensure appropriate prescribing of antidepressants where indicated, alongside non-pharmacological interventions where available and appropriate.[64] However, a comprehensive Scotland-based environmental profile of antidepressants needs to be developed for use in the Scottish context.

2. Recommendations and guidance for healthcare professionals

Healthcare professionals should:

Consider non-medicalised and non-pharmacological options where appropriate

Non-medicalised and psychosocial [65,66,67]

While a range of activities may help with common mental health problems and pain management, these will vary with individuals' preferences, capabilities, and locality. Some of the following may be appropriate and should be considered and discussed before initiating an antidepressant, as well as when continuing an antidepressant for more severe illness. Where appropriate and available, a Community Link Worker may be able to support and enable individuals to access or develop some of the options below.

- exercise and regular physical activity e.g. 30-minute walks
- debt advice and/or money management e.g. seeking advice from appropriate agencies such as Citizens Advice
- hobbies and interests e.g. gardening, crafts, etc.
- ensuring a healthy work-life balance
- lunch clubs and other activities which help to reduce social isolation
- discussing problems, where appropriate, with a close friend or confidante that is willing and able to listen

Psychosocial and psychological Interventions

The Psychological Therapies Matrix (2015) outlines a matched care approach to support the safe and effective delivery of evidence based psychological interventions. Both the Matrix and clinical guidelines advocate decisions regarding psychological interventions based on a comprehensive assessment of need and suitability, individual preferences, availability of trained practitioners and cultural appropriateness.[36,37] This matched care model considers 'high volume', low intensity interventions for mild to moderate symptoms, in addition to high intensity and highly specialist interventions delivered by practitioners with additional competences, for those presenting with more complex presentations. The Matrix acknowledges those in primary care who regularly identify and support those presenting with psychological issues and mental health disorders. They are often able to provide support for low intensity interventions and referral to specialist mental health services where indicated.

Low intensity interventions

For mild to moderate symptoms of depression and/or anxiety these include guided self-help and computerised cognitive behavioural therapy (cCBT). Psychoeducation can support self-management. A range of evidence based cCBT programmes and telephone supports are available to support general mental wellbeing, sleep problems (including insomnia) and mild to moderate symptoms of depression. Links to these programmes can be accessed via NHS Inform (Mental Health). Please refer to Appendix 1 and 2 for a detailed description and links to these resources.

High intensity and highly specialist interventions

For those individuals who present with moderate to severe symptoms of depression and/or anxiety, a referral for High Intensity and/or Highly Specialist Interventions may be indicated and may include CBT. These interventions are usually delivered within NHS or non-NHS specialist services. (Note: non-NHS services: ensure non-NHS practitioners providing psychological therapies are registered with appropriate professional bodies e.g. Health and Care Professions Council, British Association of Behavioural and Cognitive Psychotherapy, British Association of Counselling and Psychotherapy.)

Follow a person-centred approach to initiating antidepressants

A holistic assessment that includes assessment of severity of symptoms and discussion of the risks, benefits and limitations of prescribing, should inform decisions to initiate antidepressants, considering the psychological components of care. This can be done using the 7-Steps medication review process.

- Consider comorbidities prior to initiating an antidepressant as part of the biopsychosocial assessment and the potential for interactions with other medicines and diseases e.g. QTc prolongation, etc.
- Depression:
    - The stepped-care approach should be used to help choose the most appropriate intervention - self-help, non-pharmacological, with or without antidepressant therapy.[36]
    - Consider that for 50% of individuals depressive symptoms can spontaneously resolve within 12 weeks of diagnosis.[68]
    - Less severe depression (i.e. PHQ-9 score <16) commonly referred to as mild depression, may respond better to non-pharmacological approaches as antidepressants are not effective for less severe illness.[20,36]

        ‘Do not routinely offer antidepressant medication as first-line treatment for less severe depression, unless that is the person's preference’.

- Moderate to severe depression. Antidepressants are effective for reducing symptoms of moderate to severe depression and/or helping people achieve remission, especially in combination with non-pharmacological treatment and/or self-help, see Figure 5 and Table 2.[20,36]

- Anxiety disorders:
  - The stepped-care approach should be used to help choose the most appropriate intervention; self-help, non-pharmacological with or without antidepressants,[37,38] in supporting individuals to achieve a reduction in anxiety symptoms and/or achieve remission, see Figure 5.
  - Different antidepressants demonstrate variable efficacy depending on which anxiety disorder is being treated – generalized anxiety disorder (GAD), panic disorder, obsessive compulsive disorder (OCD), etc.[37,69]

- Pain:
  - Neuropathic pain. Tricyclic antidepressants (TCAs) and duloxetine demonstrate modest effects for the treatment of neuropathic pain (Table 2).[33]
  - Low back pain and sciatica. NICE indicates that 'there was no evidence on the use of antidepressants for sciatica. The committee agreed that antidepressants were commonly prescribed for sciatica, and clinical experience suggests they may be of benefit in some people. The committee considered the potential for harm to be less than the harms of prolonged use of opioids.'[70]
  - Chronic pain. The evidence for use of antidepressants (amitriptyline, citalopram, duloxetine, fluoxetine, paroxetine and sertraline) in chronic pain is conflicting. Antidepressants improved quality of life, pain, sleep and psychological distress compared with placebo.[71,72]

Discuss:

- individual and prescriber's expectations
- stepped-care and watchful-waiting for common mental health conditions
- effective non-pharmacological interventions (e.g. physical activity, self-help)
- drug effects and limitations (e.g. dose response) including dose ranges for treatment of different conditions (e.g. SSRI flat dose response effects for depression: meaning that '20's plenty and 50's enough' – using standard doses of 20mg daily of citalopram/fluoxetine/paroxetine or 50mg daily of sertraline – to provide the full antidepressant effect,[40-42,44] or for neuropathic pain response TCAs at doses ≤75mg per day)[33]

- the potential for short and long-term adverse drug effects e.g. nausea, agitation, sedation, sexual dysfunction. It is also important to discuss and consider how and when the antidepressant will be reduced and stopped in the future to minimise potential drug-related harms

Provide appropriate information about the condition (NHS Inform website), antidepressant treatment and stopping. The Choice and Medications website contains a variety of information and leaflets which may be helpful.

Plan and agree follow up in relation to the condition being treated

In depression, it is a widely held belief that antidepressants do not exert their effects for four to six weeks. However, all antidepressants show a pattern of response and rate of improvement which is greater in the first one to two weeks.[18,20,73] Therefore, for those with no response at three to four weeks, review diagnosis; adherence with treatment; and where appropriate consider switching to an alternative antidepressant. Studies demonstrate that prescribers may change the antidepressant or optimise the dose at eight weeks, which creates a lag in treatment and may slow recovery.[5,21] Where appropriate, communicate changes in prescribing to the individual's specialist in secondary care.

Agree, plan and record the criteria for reducing and stopping the antidepressant in the future, or if adverse drug effects become intolerable e.g. severe restlessness, more frequent thoughts of suicide or deliberate self-harm. Although younger people less than 25 years old are considered at greatest risk of antidepressant associated self-harm, there are multiple age, gender and regional effects that are associated with self-harm and suicide,[74,75] therefore these should also be explored.

Encourage people that are prescribed antidepressants, or any other medicine, to initiate open discussions regarding the appropriate continuation, reduction and discontinuation of pharmacological treatment.

Review effectiveness, tolerability and adherence on an ongoing basis as part of a medication review, and where appropriate reduce the number and doses of medicines to minimise avoidable adverse effects and harms and to optimise adherence. Consider inviting individuals for proactive medication reviews. See Appendix 3 for an example review invite letter.

In relation to mental health and emotional distress, where appropriate complete and record a biopsychosocial assessment including:

- asking individuals directly about thoughts and/or plans of self-harm or suicide, and record severity as outlined in appropriate guidelines.[37,76]

- consider and exclude physical causes of signs and symptoms including:
    - alcohol (FAST tool)
    - problem substance use
    - bereavement
    - organic disease as a cause for symptoms

As depression and other mental health conditions are associated with an increased risk of deliberate self-harm and suicide, ask the individual directly about any thoughts or plans for self-harm or suicide. Although some individuals may have suicidal thoughts when visiting their health professional, they may withhold and not share their thoughts.[11,77] Where healthcare professionals are uncomfortable asking directly about self-harm or suicide, the PHQ-9 assessment tool includes a self-harm question that may help facilitate and enable further discussion around this. As outlined in guidelines, such as the NICE depression guidelines, antidepressants may be appropriate in treating depression as part of the stepped-care model for the treatment of moderate to severe depression.[36] Continue to use and record the results of valid assessment tools such as PHQ-9, CORE 10 or other suitable rating scales to support continuity of care.

Develop a clear management plan collaboratively with the individual and carers where appropriate

Prescribers and individuals should aim to develop mutually supportive and constructive discussions when reviewing antidepressants and ongoing treatment needs. Where appropriate consider the fears and apprehensions associated with reducing/stopping antidepressant therapy and tailor treatment to the individual's needs.

The stepped-care approach should be used to tailor the most appropriate intervention to the individual's needs. This can be done according to the severity of the condition being treated, such as self-help resources or non-pharmacological interventions with or without antidepressant therapy.[36,37]

Include realistic expectations and review dates that can be read coded for recall and pre-planned follow-up.

Figure 5: Interventions to aid reduction of symptoms and recovery

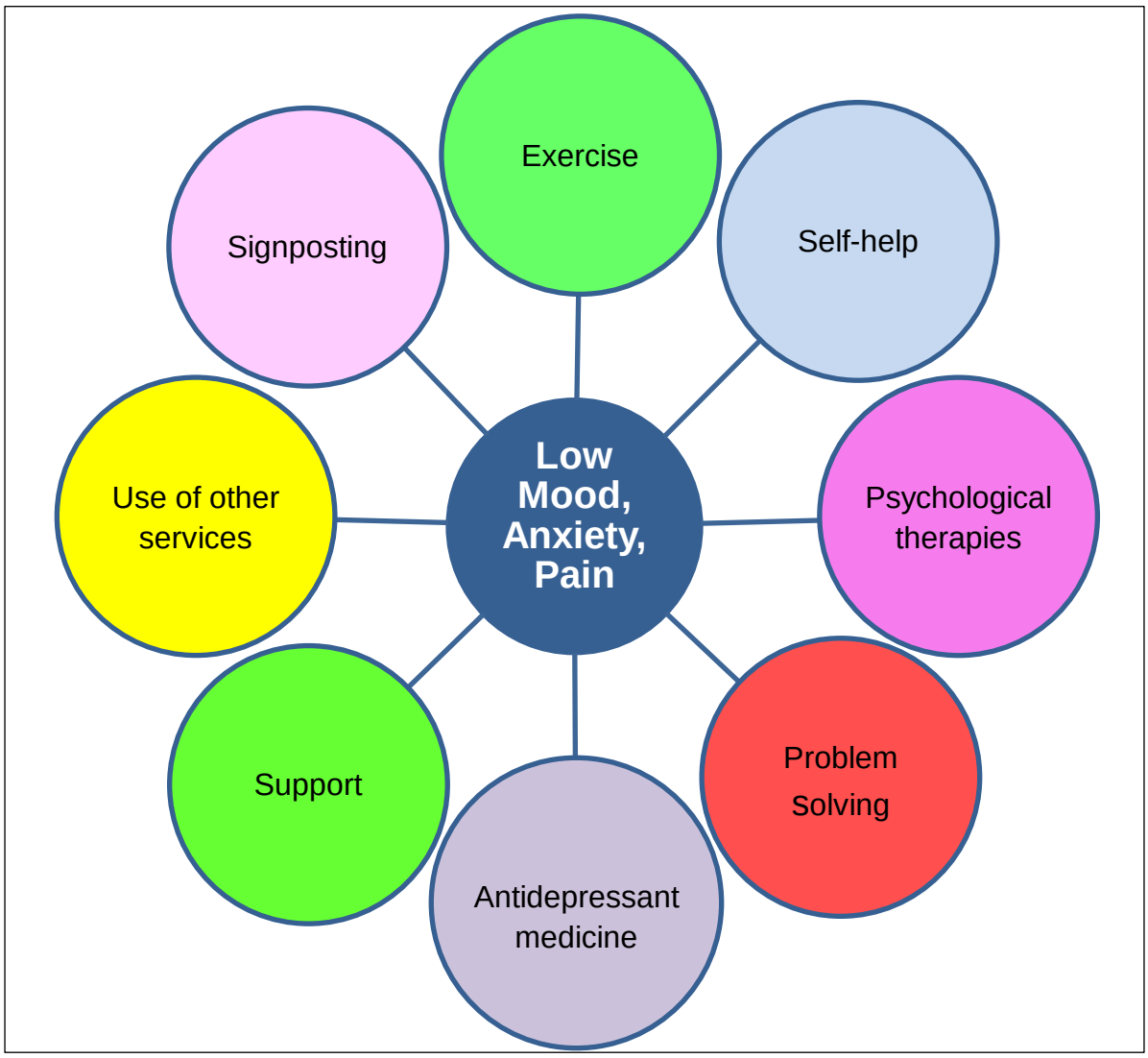


Table 2: Numbers needed to treat (NNT), and numbers needed to harm (NNH)

Indication	Antidepressant	NNT	NNH	Reference
Depression	Antidepressants	5 to 7*	-	Cleare et al 2015[20]
Depression	TCA	8.5*	-	Arroll et al 2016[78]
Depression	SSRI	6.5*	-	
Depression	TCA	4*	4 to 30†	Arroll et al 2009[79]
Depression	SSRI	6*	20 to 90†	
Neuropathic pain	TCA	4+	13†	Finnerup et al 2015[33]
Neuropathic pain	SNRI	6+	12†	
OCD	SSRI	6 to 12±	-	Soomro et al 2008[80]
Bipolar depression	Antidepressants	4*	-	Leucht et al 2012[81]

* Response: usually defined as a ≥50% reduction in depression rating scale scores or remission.
† Withdrawal from study due to adverse drug effects
+ ≥50% reduction in pain intensity scores
± ≥25% reduction in Yale Brown Obsessive Compulsive Scale

Common adverse drug effects/harms from antidepressants

Antidepressants are associated with a variety of adverse drug effects. Short-term effects can include symptoms such as nausea, with long-term effects including weight gain, weight loss or cognitive effects. Other short- or long-term drug effects include sexual dysfunction, insomnia, sedation, anxiety, falls, fatigue, gastric bleeding, hyponatraemia and QTc prolongation.[82] People may experience weight changes during antidepressant treatment. Weight gain may be associated with depression recovery and improved appetite on one hand and undesirable antidepressant effects on the other;[83] however, many placebo controlled studies report no weight data making it difficult to accurately estimate weight changes.[82] SSRIs have been seen as weight neutral, or in some cases associated with weight loss in the short-term (≤8wk studies) and weight gain in the long-term.[83,49,84,85]

Ensure individuals are assessed and read coded for the condition being treated

Only a minority of individuals have a clear electronically recorded (read code) indication for receiving an antidepressant.[7] Although the indication for the antidepressant can be identified from free-text entries in electronic and paper clinical notes, these are not easily identified unless an individual's clinical record is accessed and specifically searched for.[7] Therefore, appropriately coding of individuals' records

would support easier identification for proactive medication reviews in general practice and specialist services, as prescribers have indicated that:

> '...patients can get lost in the system, and that systems which adequately prompt medication reviews would be useful in broaching discontinuation with patients.'[14]

Healthcare practitioners and clinical teams should ensure individuals are appropriately coded in their electronic clinical systems:

- Depression (code E2B), anxiety with depression (E2003), bipolar affective disorder (Eu32), etc.
- Anxiety disorder such as generalised anxiety disorder (GAD, E2002), post-traumatic stress disorder (PTSD, Eu431), etc.
- Chronic pain (1M52), neuropathic pain (N2423), diabetic neuropathic pain (1M8) and chronic pain review recorded as 66n when a review is undertaken.
- For a polypharmacy review, if reviewing existing treatment prior to initiation of antidepressant medicines, use read code 8B31B Polypharmacy medication review.
- Where the condition has resolved and the antidepressant has been stopped, please use the appropriate read code e.g. depression resolved (212S), anxiety resolved (2126J). (Other read codes for resolution of symptoms are not currently available on general practice systems.)

Boards and HSCPs should:

Consider the prescribing advice within this guidance alongside local prescribing and clinical data to plan, resource and drive quality improvement and prescribing initiatives.

Nominate local leads/champions – one medical and one within or with strong links to medicines management teams, or equivalent, to drive delivery and recommendations within this guidance.

Consider and engage a whole system approach to delivering quality improvements in prescribing

- **Ensure primary and secondary care are informed** to support continuity of care and overall goals of reviewing and minimising inappropriate prescribing, especially given the significant influence of secondary care.
- **Work with third sector (non-medicalised) organisations** to further develop support and capacity for self-management.

Hospitals and specialist outpatient clinics should:

Secondary care specialists should ensure that prescribing records reconcile with the individual's current prescription and review what medicines they are taking. It is known that prescribing discrepancies can occur between primary and secondary care records.[86,87,88] Where appropriate, specialists should access, check and update current prescribing information using the individual's Emergency Care Summary.

Secondary care should establish and communicate changes in antidepressant prescriptions started in hospital, stating intended treatment duration or where a drug has been reduced or stopped, including the rationale for the prescriber's actions.

General practice clusters:

Engage with local prescribing support teams, who have a wealth of experience improving the quality of prescribing using local and national measures, datasets and tools.

3. Which groups of people should be targeted for review?

This may vary depending on practice populations and prescriber preferences, however, we would advise that the following groups should be considered for review. The Scottish Therapeutics Utility (STU) is available in all general practices in Scotland to allow case finding and identification of the higher risk groups below.

List 1: Potential groups of people that receive antidepressants and may benefit from being prioritised for a regular, proactive medicines review

- People receiving the same antidepressant continuously, long-term (≥2 years)
- Older adults (≥65 years) and/or frail adults
  - Receiving a SSRI plus antiplatelet/NSAIDs/DOAC/warfarin without gastro-protection, due to the increased risk of gastric bleed with this combination.
  - Receiving >1 defined daily dose per day of citalopram (>20mg per day) or escitalopram (>10mg per day) due to QTc prolongation
  - Diagnosed with dementia,
    - Antidepressants may provide limited effects for depression
    - Receiving antidepressants for behavioural and psychological symptoms of dementia
  - Receiving TCAs and other anticholinergics – reduce the anticholinergic drug burden, to reduce the risk of falls and confusion
- People receiving combinations:
  - Antidepressant plus long-term benzodiazepines (≥8 weeks) and/or z-drugs (B-Z)
    - B-Z are associated with an increased risk of depressive symptoms, paradoxically worsen anxiety, and reduce the effectiveness of psychological treatments. Review reducing B-Z use prior to assessing antidepressant need where appropriate.
    - B-Z prescribing and use is associated with use of higher doses of SSRIs
  - Combination antidepressant treatment e.g. mirtazapine with SSRI/SNRI. There is a lack of evidence demonstrating the efficacy of this combination to treat depression. People initiated on combinations by psychiatry should be reviewed by specialist services.
  - Higher risk of QTc prolongation combinations:
    - Citalopram or escitalopram or TCAs plus: methadone, antipsychotics, quinine, some antinausea medicines, etc
- People receiving high dose SSRIs for the treatment of depression
- People receiving low dose mirtazapine or trazodone for insomnia or subtherapeutic doses of mirtazapine (<30mg per day) for the treatment of depression

Note: DOAC: direct oral anticoagulant. NSAID: non-steroidal anti-inflammatory drug. SSRI: selective serotonin re-uptake inhibitor. TCA: Tricyclic antidepressant QTc prolongation see Section 1 for more information.

People receiving the same antidepressant long-term, for two or more years

As already acknowledged, this is a growing population.[2,3] This group is less likely to have their antidepressant reviewed than people who have recently been initiated on treatment or are receiving a shorter course.[4,5] For some they may be 'lost in the system' and inadvertently continue treatment that is no longer needed.[14,22] For others their antidepressant treatment may be ineffective or causing adverse effects. Therefore, it is necessary to proactively review individuals' progress, and while some guidelines provide clear advice regarding the frequency of review,[36,37,89] others remain vague.[20,50,90,91] For those with chronic illness, where long-term treatment is considered necessary, annual reviews may provide an optimal method e.g. assessing the need for TCA/duloxetine treatment of neuropathic pain from diabetes.

For those under the care of specialist secondary care services (e.g. Pain Clinics, Alcohol and Drug Rehabilitation Services, Community Mental Health, Learning Difficulties, etc.), it is important that the specialist services update primary care prescribers about the appropriateness of continuing treatment. In some cases, this will facilitate the availability of prescribing information on the patient's Emergency Care Summary.

Reviewing people receiving the same antidepressant for two or more years can result in one in four people having a change in treatment and some reducing and/or stopping their antidepressants.[17]

Frail and older adults: avoidable adverse drug events, dementia and polypharmacy and high-risk combinations

All antidepressants are associated with increasing risk of falls in older adults.[43] SSRIs are also associated with an increased risk of gastrointestinal bleed, which is further increased when they are used in combination with antiplatelets, non-steroidal anti-inflammatory drugs (NSAIDs), direct oral anticoagulants (DOACs), and/or warfarin.[92,93,94,95] Reviewing people in this group can ensure appropriate use and minimise avoidable adverse drug events and harms. For some individuals initiation of appropriate gastro-protection such as proton pump inhibitors may be advised in local and national guidelines.[20,77]

QTc prolongation can occur with a range of antidepressants and other medicines.[96,97] However, higher doses of citalopram and escitalopram are associated with an increased risk of QTc prolongation. Therefore, all older adults (>65 years) prescribed more than citalopram 20mg or escitalopram 10mg daily should be reviewed and considered for dose reduction and/or cessation where appropriate.[98] Where it is considered clinically appropriate, or people refuse to

reduce their citalopram or escitalopram dose, discuss and document the risk of harm and arrange regular cardiac QTc monitoring as per List 2. Older and/or frail adults are at higher risk of QTc prolongation which is associated with ventricular tachycardia and sudden cardiac death.[51] In part this due to ageing but can be exacerbated by comorbidities and multiple medicines e.g. antibiotics, cardiac, diuretic, psychotropics, respiratory, etc.[6] Therefore, proactively reviewing polypharmacy will also help to reduce the risk of QTc prolongation and sudden death.

A list of medications known to prolong the QT interval[99] can be found on Stockley's Drug Interactions and the Credible Meds website.

List 2: Monitoring criteria for citalopram and escitalopram[98]

- People with cardiac disease, consider an ECG review before starting treatment with citalopram and escitalopram.
- Electrolyte disturbances (e.g. hypokalaemia and hypomagnesaemia) should be corrected before treatment with citalopram and escitalopram. Monitoring of serum magnesium is advised, particularly in older adults, who may be taking diuretics or proton pump inhibitors.
- If cardiovascular symptoms, such as palpitations, vertigo, syncope, or seizures develop during treatment, cardiac evaluation including an ECG should be undertaken to exclude a possible malignant cardiac arrhythmia.
- If QTc interval is >500 milliseconds, treatment should be withdrawn gradually.
- If QTc interval duration is between 480 milliseconds and 500 milliseconds, the balance of benefits and risks of continued treatment should be carefully considered, alongside options for dose reduction or gradual withdrawal.

Dementia

For dementia, antidepressants demonstrate limited benefits in treating depression.[18,100,101,102] However, for some individuals they may reduce depressive symptoms and improve general functioning.[103] There are relatively few studies of antidepressants for the treatment of agitation and psychosis in dementia, however sertraline, citalopram and trazodone have been used and are associated with modest reductions in symptoms of agitation and psychosis.[104,105] Antidepressants also demonstrate mixed and limited effects for the treatment of behavioural and psychological symptoms of dementia,[18] therefore, routine reviews may help to appropriately minimise doses and optimise non-pharmacological management.

Polypharmacy and anticholinergic effects

TCAs have strong to very strong potential for anticholinergic risk.[106] Consider TCA use in relation to other prescribed and non-prescribed medicines with anticholinergic effects. These include antihistamines, anti-Parkinson's medicines, urinary antispasmodics and some antinausea medicines, etc. [see Polypharmacy Guidance for more information].[9] TCA anticholinergic effects include an increased risk of dry mouth, blurred vision, cognitive dysfunction, urinary retention and falls, etc.[31]

People receiving antidepressants in combination with other psychotropics

Benzodiazepines and z-drugs (B-Z) with antidepressants

All B-Z use can lead to long-term regular use, sometimes lasting for years.[107] This is contrary to good practice guidance[36,37] and the terms of their licence[31,69] therefore, consider reviewing appropriateness where:

- B-Z are initiated to treat anxiety or insomnia prior to starting antidepressant therapy, or to treat agitation, anxiety or insomnia symptoms associated with starting an SSRI.[20,36] B-Z only demonstrate marginal benefits for short-term relief of insomnia and some anxiety disorders.
- B-Z are initiated to treat avoidable adverse drug effects caused by higher SSRIs doses (e.g. insomnia, agitation),[39,40,42] or for signs and symptoms of poorly controlled depression, anxiety or back pain.
- B-Z use is known to worsen depressive symptoms, cause cognitive dysfunction and other avoidable adverse effects, and reduce the efficacy of some psychological therapies.[107,108,109,110] This should be considered one of the priority groups for review.
- Long-term B-Z have been prescribed, to review and gradually withdraw using an agreed structured and planned reduction schedule. A small minority of individuals may require longer-term B-Z treatment with regular review to optimise care and minimise street B-Z use, see the Benzodiazepine and Z-drugs Quality Prescribing Guidance for more detail.
- Accompanying this guide are a suite of National Therapeutic Indicators allowing identification of variation in prescribing at NHS board or GP practice level with accompanying case finding STU searches to allow identification of individuals at risk of harm from within general practice. For example, those on antidepressant medication in combination with other psychotropic medication.

Combining antidepressants for depression

Combining antidepressants for depression is not recommended. Non-specialist psychiatry prescribers should not initiate such combinations, unless on the advice of specialist services.

- Consultant psychiatrists may initiate combined therapy for their regular patient(s), e.g. for treatment of treatment resistant depression. The quality of evidence supporting combination antidepressant treatment is poor. For example, SSRIs or serotonin and noradrenaline re-uptake inhibitors (SNRIs) plus mirtazapine (30-45mg) demonstrate marginal benefits in observational studies to no difference in randomised placebo-controlled studies.[20,111,112]
- Antidepressant augmentation with an antipsychotic or lithium therapy (as per guidance from the Directorate of the Chief Medical Officer)[113] can be more effective; providing clearer benefits, but these are not without risks and the requirement of extra monitoring which is often lacking.[20,114,115] Monitoring for antipsychotic therapy may include regular cardiometabolic risk assessment, including HbA1c, lipids, weight, blood pressure and lifestyle advice.[116]

Low dose mirtazapine added to SSRI/SNRIs therapy:

- This combination to reduce antidepressant induced sexual dysfunction is supported by limited evidence of efficacy.[117,118] Clinicians should assess the efficacy of such strategies and record this as the mirtazapine indication where appropriate.
- This combination has also been used for short-term sedating antihistamine effects (also seen with trazodone). In part, these additional antidepressants are possibly being used to treat SSRI/SNRI induced insomnia, agitation etc., and as an alternative to B-Z. However, this combination is of questionable benefit, and it may be more appropriate to reduce the dose of the SSRI/SNRI to minimise potential adverse effects and drug-related harms, rather than adding additional psychotropics, especially as tolerance can develop quickly to mirtazapine and trazodone sedating effects.[84,119.] This avoids the prescribing cascade.

Specialists should be conscious of their prescribing actions potentially influencing prescribing habits in general practitioners.[5] Specialists should consider providing clear rationale and therapeutic goals, alongside withdrawal strategies when initiating psychotropic combinations as outlined above.

Neuropathic pain plus depression/anxiety:

- At times prescribers switch from a TCA and an effective antidepressant (for depression for example) to a TCA or duloxetine to treat both pain and mood. In these cases the TCA or duloxetine may only be effective for one condition, and not the other, or individuals may not tolerate higher doses of TCAs or duloxetine which can be more effective for treating depression.[20,39,53,54] For non-neuropathic

pain prescribers should also consider avoiding concomitant antidepressant and tramadol use, due to the risk of serotonin syndrome.[94]

- Two antidepressants (e.g. TCA for neuropathic pain and an antidepressant for depression such as a SSRI) may be appropriate to reduce symptoms (not two TCAs). However, use should be reviewed regularly, considering interactions, adverse and synergistic effects, e.g. sedating effects, TCA dose related QTc prolongation (greater risk of prolongation with higher doses).[96]

High dose SSRIs for the treatment of depression

Standard SSRI doses provide the optimal balance between efficacy and minimising adverse effects and harms. This is due to their flat dose response curve for the treatment of depression, meaning that '20's plenty and 50's enough' to provide the full antidepressant effect. (Standard doses provide optimal serotonin transporter occupancy.)[120] Previously prescribers have been heavily criticised for prescribing subtherapeutic licensed doses of TCAs for the treatment of depression. (Licensed dose is the approved dose or dose range that medicines are licensed to be prescribed at by the regulatory authority – Medicines and Healthcare products Regulatory Agency (MHRA) – for the condition that they approved to treat, e.g. sertraline for depression treatment has a dose range of 50mg to 200mg per day.[121,122] While TCAs and SNRIs demonstrate dose response effects, with larger doses being more effective for depression treatment,[39,40,53] higher than standard daily doses of SSRIs (20mg citalopram/fluoxetine/paroxetine, 50mg sertraline or 10mg escitalopram) do not provide better response rates, not even for poor or partial responders.[39-42,44]

While a range of campaigns and guidelines for depression have heavily promoted the message 'to increase the dose' of antidepressants for poor and non-responders,[36,123,124,125] a minority of guidelines have highlighted the differences in response and efficacy between SSRIs and other antidepressants.[20,126] Individuals and prescribers may have expectations that higher doses are more effective for routine treatment of depression,[5,11] in part this may be due to guidelines or training, as well as individual or societal expectations and beliefs regarding medicines.[29,127,128] For a small minority of individuals, where a trial of higher dose SSRI is considered appropriate, follow up review within two to four weeks should be arranged to assess response to treatment and address any adverse effects. It is known that early improvement predicts a stable response.[73,129] For anxiety disorders SSRI dose response effects are mixed. GAD guidelines indicate no clear indication of a dose response relationship, whereas obsessive compulsive disorder guidelines indicate that higher SSRI doses can be more efficacious.[37,69,89]

In 2011, in the UK, the MHRA issued advice regarding new maximum daily dose restrictions, contraindications, and warnings for citalopram and escitalopram use.[98]

Health boards issued local advice on reviewing citalopram/escitalopram doses: reviewing, reducing doses and if necessary switching to an alternative antidepressant where appropriate.[130] Anecdotally from prescribers and general practice feedback, of those individuals that were reviewed: some stopped, some required a switch to an alternative antidepressant; while the vast majority that were required to continue treatment were continued on lower doses, as per MHRA advice, without worsening of their depressive symptoms.

Low dose mirtazapine and trazodone for sedation

Low daily doses of mirtazapine (15mg) or trazodone (100mg or less), are commonly used to treat insomnia and anxiety symptoms due to their sedating antihistamine effects.[84,119] However, people commonly develop tolerance (usually within a couple of weeks) to such sedating effects and therefore longer-term use – as with B-Z drugs – may be inappropriate.

Antidepressants demonstrate mixed and limited effects for the treatment of behavioural and psychological symptoms of dementia,[18] therefore, routine reviews may help to appropriately minimise doses and optimise non-pharmacological management.

The routine use of low dose mirtazapine for the treatment of depression should be reviewed, as the majority of clinical trials demonstrated efficacy with doses ≥30mg daily.[26,40,131] Therefore, if mirtazapine is considered as appropriate and necessary then increasing to 30mg per day within the first week of treatment with an agreed plan for follow up within two to four weeks to assess efficacy and tolerance may help to provide an optimal response.

Pharmacogenomic testing and antidepressant therapy

Pharmacogenomic testing has the potential to improve medicines optimisation by providing information on the individual's response to treatment, improving effectiveness and safety of treatment by reducing the risk of adverse drug reactions (ADRs). People have on average four gene variants that influence medication effectiveness and risk of ADRs, with 99% of individuals having at least one gene variant that affects drug metabolism. The use of pharmacogenetics to guide treatment choices could reduce the likelihood of medication related harm and improve patient outcomes from safer personalised medication regimes. Some studies have shown that this approach could be more cost effective, and that pharmacogenomics can be used to support antidepressant prescribing,[132] however more evidence is needed together with a tested framework for implementation.

4. The 7-Steps medication review

The 7-Steps person-centred medication review process can be used at both initiation of new medications and when reviewing existing treatments, including non-pharmacological approaches. This process ensures a shared decision-making approach to prescribing, with discussion of risks and benefits of treatments and enable safe, sustainable and effective person-centred care.

Steps	Process	Person specific issues to address
1. **Aims** What matters to the individual about their condition(s)?	**Review diagnoses and consider:** • Therapeutic objectives of drug therapy • Management of existing health problems • Prevention of future health issues, including lifestyle advice **Ask person to complete PROMs** (questions to prepare for my review) **before their review**	• Ensure person-centred approach • Consider non-pharmacological options where appropriate • Before initiation of treatment discuss the risk of dependency/ withdrawal reaction with use
2. **Need** Identify essential drug therapy	**Identify essential drugs (not to be stopped without specialist advice)** • Medicines that have essential replacement functions (e.g. levothyroxine) • Medicines to prevent rapid symptomatic decline (e.g. drugs for Parkinson's disease, heart failure)	• Although not classed as an essential medicine, prescribers should be aware of the potential for dependence and withdrawal reaction with these medicines
3. Does the individual take unnecessary drug therapy?	**Identify and review the continued need for drugs** • what is medication for? • with temporary indications • with higher than usual maintenance doses • with limited benefit/evidence for use	• consider non-pharmacological approaches where appropriate, either alone or as an adjunct to medicines (e.g. CBT) • if first episode of depression treated for six months and course complete, consider managed reduction and stop

	• with limited benefit in the person under review (see Drug efficacy & applicability (NNT) table)	• Ensure optimum dose of therapy e.g. 20's plenty (fluoxetine, citalopram) or 50's enough (sertraline) for depression
4. Effectiveness Are therapeutic objectives being achieved?	**Identify the need for adding/intensifying drug therapy to achieve therapeutic objectives** • to achieve symptom control • to achieve biochemical/clinical targets • to prevent disease progression/exacerbation • is there a more appropriate medication to achieve goals?	• With SSRIs there is limited additional benefit and increased risk of adverse effects with increasing doses (see dose response curve). Review and decrease dose where appropriate • If no response to optimal dose within two to four weeks consider change to alternative medication, rather than increase dose further • Consider non-pharmacological approaches
5. Safety Does the individual have or is at risk of ADR/ Side effects? Does the person know what to do if they're ill?	**Identify individual safety risks by checking for** • appropriate individual targets e.g. HbA1c, BP • drug-disease interactions • drug-drug interactions (see ADR table) • monitoring mechanisms for high-risk drugs • risk of accidental overdosing **Identify adverse drug effects by checking for** • specific symptoms/laboratory markers (e.g. hypokalaemia) • cumulative adverse drug effects (see ADR table) • drugs used to treat side effects caused by other drugs • **Medication Sick Day guidance**	• Consider combinations of high-risk medications e.g. NSAIDs and SSRIs • Some antidepressants can have a high anticholinergic burden that can be additive • Consider the increased potential for harm in combination with other CNS depressants • Co-prescribing of benzodiazepine or z-drugs for antidepressant induced insomnia is no longer recommended • Co-prescribing of two antidepressant agents for depression should be for specialist initiation only

6. **Sustainability** Is drug therapy cost-effective and environmentally sustainable?	**Identify unnecessarily costly drug therapy by** • considering more cost-effective or environmentally sensitive alternatives, but balance against safety, convenience and individual preferences **Consider the environmental impact of** • inhaler use • single use plastics • medicines waste • water pollution	• Are all medicines formulary choices? • Advise to dispose of medicines through community pharmacy to ensure safe disposal • Medicines should not be disposed of in household waste, pouring down sink or flushing down toilet • Advise to only order what is needed, do not stockpile medicines
7. **Person-centredness** Is the person willing and able to take drug therapy as intended?	**Does the person understand the outcomes of the review?** • Consider Teach back **Ensure drug therapy changes are tailored to individual's preferences. Consider** • is the medication in a form they can take? • is the dosing schedule convenient? • what assistance is needed? • are they able to take medicines as intended? **Agree and communicate plan** • discuss and agree with the individual/carer/welfare proxy therapeutic objectives and treatment priorities • include lifestyle and holistic management goals • inform relevant health and social care providers of changes in treatments across the transitions of care	**Agreed plan** • Consider review period for management of depression • If there is dosage reduction, agree a reduction plan and agree with individual to prevent withdrawal • Signpost appropriate non-pharmacological support and resources (e.g. NHS Inform)

Ask person to complete the [post-review PROMs questions] after their review

Key concepts in this case

- Take a holistic person-centred approach with regular reviews of treatment
- Consider the use of non-pharmacological options where appropriate
- For a polypharmacy review, if reviewing existing treatment prior to initiation of antidepressant medicines, use read code 8B31B Polypharmacy medication review.

5. Reducing and stopping antidepressants

Quick links

- Standard reduction: SSRI, SNRI, TCA, Other antidepressants
- Difficulty withdrawing SSRI/SNRI
- Significant difficulty/fear of withdrawing SSRI/SNRI

Discontinuation

All classes of antidepressants can cause discontinuation/withdrawal symptoms, especially when stopped abruptly. Therefore, this advice is intended to provide prescribers and individuals with a range of options to appropriately support and enable successful antidepressant reduction and discontinuation.

Discontinuation/withdrawal effects may also occur to a lesser extent when doses are missed or reduced. It is, however, unknown what the specific incidence and prevalence is – as this can vary by individual antidepressant (e.g. more commonly occurs with paroxetine and venlafaxine), duration of treatment, the condition being treated and study design – studies have indicated that that up to 17% of people receiving placebo and up to 15-56% of people receiving different antidepressants may be affected.[133,134,135,136] It is also estimated that 3% of people may experience severe withdrawal effects.[136] However, some individuals may be more sensitive to withdrawal than others, and unfortunately, it is difficult to know who will or will not experience discontinuation/withdrawal effects.

Discontinuation symptoms

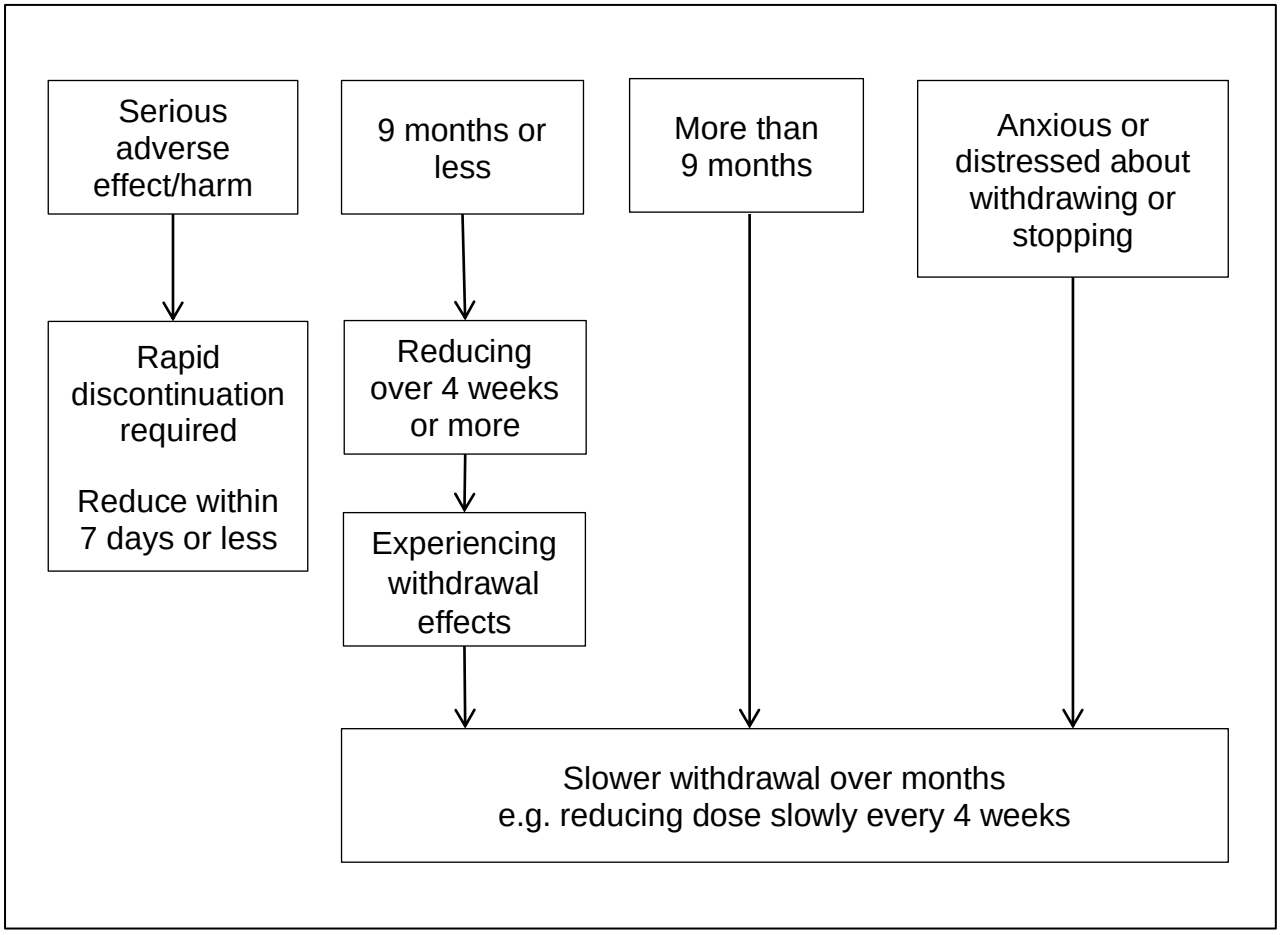
The term ‘discontinuation symptoms’ is used to describe symptoms experienced on stopping medicines that are not drugs of dependence, although there are important semantic differences in the terms ‘discontinuation’ and ‘withdrawal’ symptoms – the latter implying addiction, the former does not.[18] While the distinction is important for precise medical terminology, it is irrelevant when it comes to personal experiences and how an individual may describe their signs and symptoms.

The optimum rate of taper to prevent withdrawal effects is unknown.[22,23] Therefore, the prescriber and individual should discuss and agree on the most appropriate approach to reducing the dose and reviewing progress – for some this will mean ‘low and slow reductions’. This will vary depending on individual’s needs, circumstances, age, clinical condition and other comorbidities being treated, as well as the duration of antidepressant treatment. However, some individuals who stop antidepressant treatment for depression may experience a depressive relapse. A recent large robust trial by Lewis et al.[137] assessed the risk of relapse for people who indicated that they were ready to stop their antidepressant which they had taken for two years or more. During a 52 week follow up period 39% of people continuing antidepressant

treatment experienced a depressive relapse, with 56% of those discontinuing treatment. Of the latter group 39% subsequently restarted antidepressant treatment

Considerations for reduction and/or stopping an antidepressant

Figure 6: Reducing and stopping antidepressants



Note: Nine months was assessed as being an appropriate point when an individual may have completed a six-month course of treatment for first episode of depression and account for the time required to receive an effective antidepressant and dose. For example, first antidepressant partially effective at four weeks, then required to switch to alternative antidepressant, dose titration where appropriate, then six-month course for people achieving remission.

The strategy for reducing/stopping antidepressants should be guided and informed by the individual's preferences and needs. Consider the clinical situation when reviewing and discussing reducing/stopping antidepressants. Encourage individuals to discuss stopping their antidepressants with their prescriber before doing so.

By discussing and planning withdrawals, the most appropriate rate of reduction can be agreed and planned with the individual, according to their preferences and needs:

- If experiencing serious adverse effects/harms - may require rapid discontinuation within seven days or less (Table 3).
- Completed a nine month or less course of antidepressant treatment e.g. with first episode of moderate to severe depression – reduce over a minimum of four weeks. Some individuals may need a slower reduction e.g. four weekly stepped reductions. (Shorter courses of antidepressant treatment may be less likely to be associated with discontinuation/withdrawal effects. However the rate of reduction should be guided by the individual's preferences and needs.)
- Completed a longer course (nine months or more) of antidepressant treatment, and/or a history of recurrent depression or anxiety. Reducing and tapering the dose at a slower rate over months may be more appropriate, e.g. for people with anxiety disorders who have responded to antidepressants and received long-term treatment a minimum of three months or longer, tapered reduction is recommended.
- Anxious about reducing/withdrawing antidepressants or history of experiencing discontinuation effects. Reducing and tapering the dose at a slower rate over months may be more appropriate.

Where people experience significant or unbearable withdrawal effects during reduction, increasing back to the previous dose that did not cause withdrawal symptoms, and after stabilising, considering a slower rate of reduction may help.

Table 3: Serious adverse effects/harms which may require rapid discontinuation

Adverse effect	Drugs	Symptoms/Signs
Serotonin syndrome (very rarely occurs)	SSRI, SNRI, clomipramine, moclobemide, and other medicines e.g. triptans, tramadol, fentanyl, etc.	**Mild** (individual may/may not be concerned): insomnia, anxiety, nausea, diarrhoea, hypertension, tachycardia, hyperreflexia **Moderate** (causes distress): agitation, myoclonus, tremor, mydriasis, flushing, diaphoresis, low fever (<38.5°C) **Severe** (medical emergency): severe hyperthermia, confusion, rigidity, respiratory, coma, death
QTc interval prolongation	Citalopram, escitalopram, TCAs, and other medicines e.g. quinine, methadone, antipsychotics, antibiotics etc.	ECG changes in QTc interval

Note: Serotonin syndrome, for more detail see Buckley et al. 2014[138] and Isbister 2007[139] QTc prolongation is of concern as it is associated with ventricular tachycardia and sudden cardiac death, see Kallergis et al. 2012.[51]

Assess the individual's readiness to reduce and/or stop

It is important that an individual's motivation and readiness for reduction and/or discontinuation is adequately assessed. Where agreed a tailored dose reduction should be planned, and where implemented, regularly reviewed. Signposting or referral for interventions to support changes to prescribing should also be considered, including psychosocial or psychological interventions.

What is the risk-benefit balance of continuing current antidepressant dose?

Example considerations may be:

- balancing anticholinergic effects versus neuropathic pain control
- reducing the signs and symptoms of the condition it was prescribed for

or the

- need to stop the antidepressant due to increased risks e.g. cardiovascular disease, QTc prolongation risk or a newly diagnosed condition

Has the individual completed the planned and agreed course or trial of treatment?

For example, in relation to depression, is the individual experiencing residual symptoms such as sleep issues, irritability and ruminating, motivation (have they managed to do something they like to do) and do they have plans for the future (moving on from depressive episode)? These factors may indicate that an individual is suitable to consider reducing and stopping their antidepressant after completing an appropriate course of treatment. This can be six months for the first episode of depression or 12 or 24 months of treatment, depending on the number of depressive episodes and relapses.

Discontinuation/withdrawal symptoms: These may begin on average within two days (up to five days) after stopping and occasionally following dose reduction or missed doses. Generally, these symptoms subside within seven to ten days,[18,20] but may include a wide range of symptoms which can vary in intensity, depending on which antidepressant is being stopped (Tables 4 and 5). For some people these symptoms are mild and self-limiting, however, others may experience severe or prolonged discontinuation or withdrawal symptoms e.g. flu-like symptoms, electric shocks (brain zaps), vivid dreams, dizziness or diarrhoea. Unfortunately, the optimum rate of taper to prevent discontinuation/withdrawal symptoms is unknown.[22,23]

Table 4: Clinical presentation of discontinuation/withdrawal symptoms

-	**Symptoms**
Systemic, cardiac effects	Flu-like symptoms*, **dizziness/drowsiness*,** tachycardia (fast heart rate)*, **impaired balance, fatigue,** weakness, **headache**, dyspnoea (breathlessness)
Sensory	Paraesthesia (burning, prickling sensation)*, electric shock–like sensation (“brain zaps/body zaps”)*, sensory disorders, dysesthesia (abnormal unpleasant sensation e.g. burning, itching), itch, tinnitus, altered taste, blurred vision, visual changes
Neuromuscular	Muscle tension*, myalgia (muscle pain)*, neuralgia (nerve pain)*, agitation*, ataxia (lack of muscle co-ordination)*, tremor, akathisia (inner restlessness, urgent need to constantly move, inability to stand/sit still)
Vasomotor	Perspiration*, flushing*, chills*, impaired temperature regulation
Gastrointestinal	Diarrhoea*, abdominal pain*, anorexia, **nausea, vomiting**
Sexual	Premature ejaculation*, genital hypersensitivity*
Sleep	**Insomnia,** nightmares, vivid dreams, hypersomnia (excessive sleepiness)
Cognitive	Confusion*, disorientation*, amnesia*, reduced concentration
Affective	**Irritability,** anxiety, agitation, tension, panic, depressive mood, impulsivity, sudden crying, outbursts of anger, mania, increased drive, mood swings, increased suicidal thoughts, derealization, depersonalization
Psychotic	Visual and auditory hallucinations
Delirium	Typically only with tranylcypromine

Adapted from Henssler et al 2019[133] and Haddad et al.[140] Symptoms in bold occur more frequently. *Serotonin related

Table 5: Antidepressant discontinuation/withdrawal symptoms

Antidepressant class	Most commonly associated[a]	Common symptoms[b]	Occasional symptoms[b]
SSRI, Clomipramine (TCA)	Paroxetine	Flu-like symptoms (chills, myalgia, excess sweating, nausea, headache), 'shock-like' sensations, dizziness exacerbated by movement, insomnia, excess (vivid) dreaming, irritability, crying spells	Movement disorders, concentration, memory difficulties
SNRIs	Venlafaxine	Same as above, due to serotonin effects	Same as above
TCAs	Amitriptyline Imipramine	Flu-like symptoms, insomnia, excess dreaming Anticholinergic rebound – more common in older adults: headache, restlessness, diarrhoea, nausea and vomiting	Movement disorders, mania, cardiac arrhythmias
Other	Mirtazapine[c]	Anxiety, panic attacks, insomnia, irritability, nausea	-
Other	Agomelatine	-	No discontinuation symptoms have been reported[d]
Other	Trazodone	-	Rarely SSRI type withdrawals[e]
Other	Vortioxetine	-	No discontinuation symptoms have been reported[f]

a. Although most commonly associated with the listed medicines, other medicines in the group may cause similar symptoms.
b. Symptoms: As individuals may or may not experience discontinuation/withdrawal symptoms, and the intensity and range of symptoms may vary by individual, people may experience or identify symptoms not listed above.
c. Limited data: mirtazapine case studies, see Cosci et al. 2017.[141]
d. At time of writing no case reports in literature. Agomelatine rarely used.
e. See Haddad et al. 2001[140] and Otani et al. 1994[142] for more detail.
f. Adapted from and informed by Maudsley and Psychotropic Drug Directory. Vortioxetine rarely used.

Standard reduction approaches

Standard reduction approaches may be appropriate for individuals taking antidepressants that have no past history of distressing withdrawal, and no particular fear of withdrawing and/or stopping antidepressants over four to six weeks.

Review and reduce dose every one to four weeks, or as guided by the individual's needs and/or preferences. However, reducing by one step every four weeks may be more practical for individuals due to their carer, family and work commitments, as well as for collecting prescriptions and enabling appropriate face-to-face or telephone review follow-up.

Selective serotonin re-uptake inhibitors (SSRIs)[143]

Due to the long half-life, the following can be stopped at standard daily doses: citalopram 20mg, escitalopram 10mg, fluoxetine 20mg and sertraline 50mg per day. However, individuals may prefer or require a slower reduction with lower doses.

Table 6: Example SSRI dose reduction steps

SSRIs	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Citalopram	40mg	30mg	20mg	10mg	Stop	-
Escitalopram	20mg	15mg	10mg	5mg	Stop	-
Fluoxetine	40mg	30mg*	20mg	10mg**	Stop	-
Fluvoxamine	300mg	200mg	100mg	50mg	Stop	-
Sertraline	200mg	150mg	100mg	50mg	25mg	Stop
Paroxetine†	40mg	30mg	20mg	10mg	5mg††	Stop

Steps: the rate of withdrawal will vary with individual needs e.g. weekly to four weekly reductions for some.
All doses are single daily doses
*Alternate day dosing 40mg/20mg
**Alternate day dosing with 20mg capsule, or consider using fluoxetine liquid
† Some individuals may require to be switched to an alternative SSRI if experiencing significant withdrawals, see below.
†† Half a 10mg tablet

Serotonin and noradrenaline re-uptake inhibitors (SNRIs)
Most individuals will be able to slowly withdraw and discontinue duloxetine and venlafaxine without any adverse effects. Where individuals experience discontinuation/withdrawal effects after stopping, it may be appropriate to restart the antidepressant at the previous dose and frequency for seven days then switch to a long-acting SSRI if interactions and contra-indications allow.

Table 7: Example SNRI dose reduction steps

SNRI	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Duloxetine[a]	120mg	90mg	60mg	30mg	Stop	-
Venlafaxine MR[b]	300mg	225mg	150mg	75mg	37.5mg	Stop
Venlafaxine[c]	150mg twice daily	150mg morning 75mg night	75mg twice daily	37.5mg twice daily	Stop[d]	-

Steps: the rate of withdrawal will vary with individual needs e.g. weekly to four weekly reductions for some, or longer and slower reductions for others.
Note: Venlafaxine 300mg daily used as example, as individuals on higher doses are usually under the care of community mental health teams who should be involved in decisions to reduce or withdraw.

a. BNF only has 60mg dose listed for treatment of major depressive order. Duloxetine SmPC (data sheet) quotes up to 120mg daily. However, there is no clinical evidence suggesting that individuals not responding to the initial recommended dose may benefit from dose up-titrations.[144]
b. If receiving modified-release (MR) preparations as split dose e.g. twice daily, please consider that MR preparations are intended as once daily preparations.
c. Some individuals may have a preference for reducing the night-time or morning dose first.
d. If needed venlafaxine 37.5mg MR daily could be used for another step before stopping.

Tricyclic antidepressants (TCAs)

Frail and/or older adults may require and need slower reduction to minimise the risk of cholinergic rebound (nausea, vomiting, headache, restlessness). Therefore, slow reduction over longer than six weeks, or months, may be needed for some individuals depending on their preference and/or needs.

Table 8: Example TCA dose reduction steps

TCAs	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	Step 7	Step 8
Amitriptyline[a]	150mg	100mg	50mg	Stop	-	-	-	-
Amitriptyline[a,b]	150mg	125mg	100mg	75mg	50mg	25mg	10mg[c]	Stop
Lofepramine[d]	210mg	140mg	70mg	35mg[e]	Stop	-	-	-

a. The same reduction schedule could be advised for:

Clomipramine	Dosulepin (dothiepin)	Doxepin
Imipramine	Nortriptyline	Trimipramine

b. Older adults and some individuals may require reductions using smaller dose increments to minimise the risk of adverse withdrawal effects/harms.
c. Dosulepin and doxepin not available as 10mg dose, therefore, consider if necessary, using 25mg capsules on alternate days, then stop.
d. If dose is split morning and night, consider reducing and stopping morning dose first, and then continuing reduction with nighttime dose.
e. Tablets are less suitable for halving as they have a film coating. If necessary, a 35mg dose can be given using lofepramine 70mg/5ml oral suspension.

Other antidepressants and monoamine oxidase inhibitors (MAOIs)

Table 9: Example dose reduction steps for other antidepressants and MAOIs

Other antidepressants/MAOIs		Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	Step 7
Agomelatine		50mg	25mg	Stop	-	-	-	-
Mirtazapine		45mg	30mg	15mg[a]	Stop	-	-	-
Trazodone		300mg[b]	250mg	200mg	150mg	100mg	50mg	Stop
Vortioxetine		20mg	10mg	Stop	-	-	-	-
Isocarboxazid[c]	Morning	60mg	50mg	40mg	30mg	20mg	10mg	Stop
Moclobemide[d]	Morning	300mg	300mg	150mg	150mg	Stop	-	-
	Night	300mg	150mg	150mg	Stop	-	-	-
Phenelzine[c]	Morning	30mg	30mg	30mg	15mg	15mg	15mg	Stop
	Afternoon	30mg	15mg	15mg	15mg	Stop	Stop	-
	Night	30mg	30mg	15mg	15mg	15mg	Stop	-
Tranylcypromine[c]	Morning	30mg	20mg	10mg	Stop	-	-	-

Steps: the rate of withdrawal will vary with individual needs e.g. weekly to four weekly reductions for some.

a. Some individuals may find the 15mg dose more sedating than higher doses due to greater antihistamine effects at lower doses.
b. For higher doses consider reducing at each step by 50mg. However, clinical need and/or individual preferences may require larger reduction steps e.g. 100mg.
c. Isocarboxazid, phenelzine and tranylcypromine inhibit monoamine oxidase A and B for up to two weeks after stopping. Consider risk of interactions for two weeks after stopping.
d. Moclobemide is a reversible inhibitor of monoamine oxidase A.

Difficulty withdrawing SSRI/SNRI

For individuals with difficulty withdrawing SSRI/SNRIs, or those who are fearful of withdrawing, switching to a longer half-life (longer acting) SSRI (e.g. fluoxetine) may enable a smoother reduction in antidepressant blood levels. This may be of use, especially for individuals who are having difficulty stopping short half-life antidepressants: paroxetine, venlafaxine or duloxetine. Venlafaxine and duloxetine act as SSRIs at low dose.

Convert to long-acting SSRI, then reduce and stop[143]

Reduce the total daily dose in a stepwise fashion to: paroxetine 20mg, venlafaxine 75mg, duloxetine 30mg daily (see SSRI and SNRI). Then convert to an approximate dose equivalent* of fluoxetine, citalopram or sertraline (Step 1), using standard

capsules, tablets or liquid. Switch by taking the last dose of paroxetine/venlafaxine/duloxetine today, and then starting the new dose of fluoxetine tomorrow at the same time of day.[18,20] Then stabilise on that dose for three to seven days then stop, as per previously reported.[145,146] For example, duloxetine 30mg daily changed to fluoxetine 20mg daily and continued for three to seven days then stopped. However, some individuals may prefer or need slower reductions.

Table 10: Half-lives and time to almost complete elimination - Selective serotonin re-uptake inhibitors (SSRIs) [49,147]

SSRI	**Half-life ($T_{1/2}$)**	**Time to almost complete elimination (five half-lives) (hours, unless specified)**
Citalopram	35 hours	7.3 days
Escitalopram	30 hours	6.25 days
Fluoxetine [Norfluoxetine]*	4-6 days [4-16 days]	20-24 days [20-80 days]
Paroxetine**	24 hours	5 days
Sertraline	26 hours	5.4 days

*Active metabolites
**Paroxetine and venlafaxine are associated with a greater incidence of withdrawal effects. There are mixed reports of discontinuation symptoms with Duloxetine.

Table 11: Half-lives and time to almost complete elimination - Serotonin and noradrenaline re-uptake inhibitors (SNRIs) [49,147]

SNRI	**Half-life ($T_{1/2}$)**	**Time to almost complete elimination (five half-lives) (hours, unless specified)**
Duloxetine	12 hours	60 hours (2.5 days)
Venlafaxine [Desmethylvenlafaxine]*	5 hours [11 hours]	1 day [2.3 days]

*Active metabolites

Alternate day dosing – half-life of antidepressants

The half-life of an antidepressant determines if it is appropriate for alternate day dosing. In general, most medication effects will be considered negligible/insignificant after three half-lives and will be eliminated from the individual`s system after five half-lives, but there are exceptions to this.

Citalopram, escitalopram, fluoxetine and sertraline all have long half-lives (see Table 10 above). If active metabolites are considered this can be up to 48 days (3 x 16

days) for fluoxetine. Therefore, alternate day (48 hour) dosing is possible with these drugs.

Venlafaxine and duloxetine are inappropriate for alternate day dosing due to their short half-life. For some people it may be appropriate to switch from ordinary release twice daily dosing of venlafaxine to once daily modified release (MR) preparations, to allow further reduction prior to stopping. For example, venlafaxine 37.5mg twice daily to 75mg MR once daily, then reducing to 37.5mg MR daily before stopping.[148]

Paroxetine causes more withdrawal/discontinuation effects than sertraline even though their half-lives are comparable.[149] This is due to complex pharmacokinetics.[150] The high affinity of paroxetine for muscarinic receptors can lead to cholinergic rebound, contributing to withdrawal/discontinuation syndrome.[151]

Table 12: Example conversion from short half-life antidepressant: Duloxetine (30mg), Paroxetine (20mg) (daily dose) or Venlafaxine MR 75mg (37.5mg twice daily) to SSRI with long half-life

Daily dose		**Step 1***	**Step 2**	**Step 3**	**Step 4**	**Step 5**	**Step 6**
Duloxetine 30mg Or Paroxetine 20mg Or Venlafaxine MR 75mg (37.5mg twice daily)	To any of the SSRIs in Step 1	Fluoxetine 20mg	20mg alternate days	20mg every third day	Stop†	-	-
		Citalopram 20mg	10mg	10mg alternate days	Stop	-	-
		Sertraline 50mg	25mg	12.5mg (half a 25mg tablet)	Stop	-	-
		Fluoxetine liquid[a,b,c] (20mg in 5ml)	16mg (4ml)	12mg (3ml)	8mg (2ml)	4mg (1ml)	Stop

Steps: the rate of withdrawal will vary with individual needs e.g. weekly to four weekly reductions for some.

† Consider risk of interactions for two weeks after stopping

a. Some community pharmacies may not stock 1ml graduated 5ml oral syringes, but they can order if given advance notice.
b. Citalopram 40mg/ml drops and escitalopram 20mg/ml drops are not recommended due to the difficulty with accurately measuring small doses with drops.
c. Sertraline liquid is not recommended as it is unlicensed in the UK, and individuals may experience oral numbness on their tongue and mouth due to the anaesthetic effects of non-tablet formulations.

***Approximate dose equivalents and switching considerations:**[18,49,134]

Due to inter-patient variability and differing half-lives, this means that these are approximate dose equivalents, not exact equivalence.

- The drug and dose equivalents can never be exact and should be interpreted considering your clinical knowledge and the individual's needs.
- Drug interactions and drug-disease interactions should be considered
- Fluoxetine liquid may be required for a few individuals that require or prefer a slower reduction at weekly to four weekly intervals.

Significant difficulty or fears withdrawing SSRI/SNRI

For a very small minority of individuals, slower graduated reduction may be appropriate. For example, where standard reduction and/or discontinuing/withdrawing SSRI/SNRI has been unsuccessful. This approach will help flatten the reductions in plasma drug concentrations at lower doses (Chart 3).

First, reduce current antidepressant to standard dose as per SSRI or SNRI. Then convert to an approximate dose equivalent of fluoxetine 20mg/5ml liquid.

Fluoxetine 20mg is approximately dose equivalent* to:

- Citalopram 20mg
- Escitalopram 10mg
- Fluvoxamine 50mg
- Paroxetine 20mg
- Sertraline 50mg
- Duloxetine 30mg
- Venlafaxine 75mg

***Approximate dose equivalents and switching considerations:**[18,49]

Due to inter-patient variability and differing half-lives, this means that these are approximate dose equivalents, not exact equivalence.

- The drug and dose equivalents can never be exact and should be interpreted considering your clinical knowledge and the individual's needs.
- Drug interactions and drug-disease interactions should be considered prior to any switch in therapy.

For example, if switching paroxetine 20mg daily to fluoxetine 20mg daily, or paroxetine 10mg daily to fluoxetine 8mg daily (step 3 below). Switch by taking the last dose of paroxetine today, and then start the new dose of fluoxetine tomorrow at

the same time of day.[18,20] Agree on an appropriate rate of reduction e.g. weekly or monthly and time for face-to-face or telephone review follow-up.

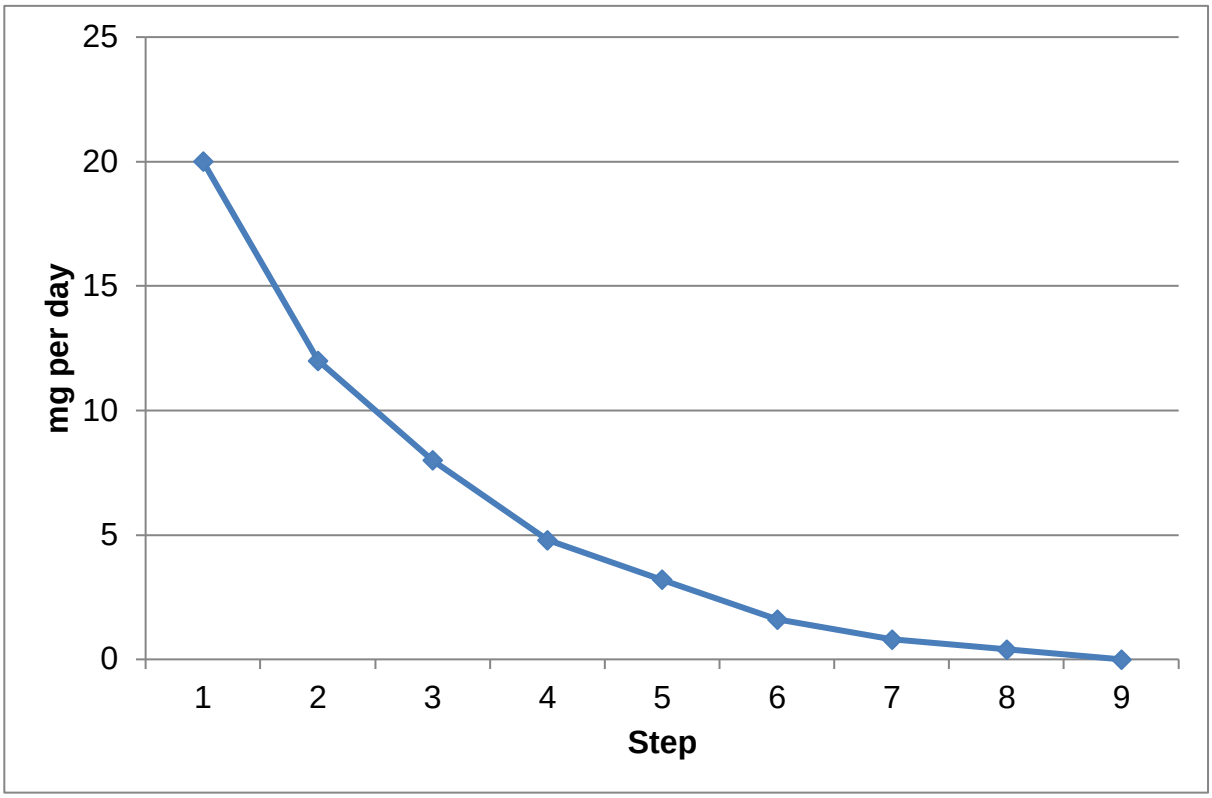
Table 13: Example dose reduction using fluoxetine liquid 20mg/5ml

Step	mg/d	ml/d	Step down Difference (mg)
1	20	5	-
2	12	3	8
3	8	2	4
4	4.8	1.2	3.2
5	3.2	0.8	1.6
6	1.6	0.4	1.6
7	0.8	0.2	0.8
8	0.4	0.1	0.4
9	Then stop	0	0.4

Note:

- Steps: the rate of withdrawal will vary with individual needs e.g. weekly to four weekly reductions for some.
- Citalopram 40mg/ml and escitalopram 20mg/ml liquid are not recommended due to the difficulty with accurately measuring small doses.
- Sertraline liquid is not recommended as it is unlicensed in the UK, and individuals may experience oral numbness on their tongue and mouth due to the anaesthetic effects of non-tablet formulations
- Table 13 adapted with consideration of Horowitz et al,[152] Ruhe et al,[153] Selvaraj et al,[154] and The Maudsley Prescribing Guidelines in Psychiatry 14th edition.[18]

Chart 3: Fluoxetine hyperbolic dose reduction



6. Examples from practice and case summaries

Lived Experience 1

I am learning that my experience of psychiatric drug prescribing is not an unusual one. In May 2013, I suffered a two-week period of insomnia due to work-related stress and visited my GP. I was prescribed mirtazapine, an antidepressant. Unfortunately, I had a bad reaction to the drug; very increased anxiety within one week, and suicidal thinking within two weeks. I was then prescribed antipsychotics and a benzodiazepine. The benzodiazepine helped with the anxiety, but provided short lived relief, and I realised it was possibly an addictive medicine which I then tried to avoid.

The anxiety remained; I had no relief. I was then prescribed imipramine, a tricyclic antidepressant, and was told I should slowly increase the dose over six weeks when the relief would begin to be felt. After six weeks there was no improvement. My GP told me that I needed to 'believe in the antidepressant and then it would work'. At this point I began to descend into severe depression.

During periods of depression, the anxiety would lessen, but as the depression eased the anxiety would return – like two sides of the same coin. With no relief from the drugs, I experienced multiple admissions to different mental hospitals over a number of months. First to a mental hospital, where different drug combinations were tried. Then another where a further ten different psychiatric drugs were tried. Then finally two admissions to the same hospital, as a precaution to prevent suicide attempts. During these two admissions I was given 15 courses of electroconvulsive therapy (ECT). These treatments did not work either. There would be a day of hyperactivity and then a plunge back into even deeper depression. I volunteered to stop all ECT treatments. My Hamilton Depression rating was frequently close to the maximum of 45. I was very seriously ill, and the psychiatrist at that time diagnosed me as chronic treatment resistant bi-polar depressed, and promptly put me onto lithium. Before long I was having trouble with shaking hands, acute nervous agitation and unbearable anxiety.

Every day was a struggle to survive. My mind was constantly occupied with ways to kill myself and there were many attempts, which very luckily were not successful. Only time spent with the excellent nurses and other individuals in the hospital garden eased my suffering and despair.

Eight years later, I am fully recovered. How did this happen? I was very lucky to have had psychotherapists visit me every day and talking therapy with a psychotherapist in the health centre once a week. These talking sessions kept me alive. After three and a half years of being prescribed psychiatric drugs of all descriptions, my psychiatrist referred me to a brilliant psychologist. Talking with her helped to keep me alive.

But finally, it was clear to me that the only thing we had not tried was coming off all psychiatric drugs. My psychiatrist eventually agreed to help me do this. Within eight weeks, on a slow reducing dose I was lifted out of depression for the first time in four years. Three months later I was allowed to stop the last drugs. I have never taken a single pill of any description ever since. While coming off the drugs, I started low sugar, low carbohydrate, high fibre diet with some minerals and vitamins to build up my immune system. I lost 3 stone of weight that had accumulated on the antidepressants and restored my physical health as well as my mental health. Before reducing the psychiatric drugs, my wife had enrolled me into an art group. Although I was severely depressed at the time, the simple act of joining a group of people who enjoyed art had a great positive effect on me; I began to enjoy learning to be better at drawing and painting. I found myself looking back at previous art work and being amazed that I had actually achieved something. My wife also enrolled me in the volunteers gardening group where I enjoyed meeting others in the public garden, we would do small jobs that gave us all a sense of achievement and belonging. I then joined a choir. The atmosphere was always friendly, and I began, very slowly, to begin to look forward. My mind was slowly shifting from endless rumination towards normal thought processes of linear continuity. Finally, Tai Chi and weekly walks with the local walking club all helped me to recover full health.

Lived Experience 2

In 2014, my GP prescribed sertraline to help alleviate my anxiety. Following a traumatic experience, and an operation, I was petrified of being left by myself. I was started on 50mg a day which, after an assessment by Psychiatry, was stepped up to 200mg over the course of four months. At the same time, I attended a six-week group CBT course through primary care mental health services and started receiving regular counselling. Concurrently, I was seen and assessed by cardiology, gastroenterology and genetics which ultimately compounded my anxiety and increased the medicine burden to around 20 tablets a day.

Fast forward to August 2021 and I remain on the same daily dose. I am subject to annual medicines reviews by my GP where the question of lowering the dose is discussed. The first time I panicked, as I hadn't even considered it, so naturally any adjustment was put on hold. I have never felt pressurised or been made to feel guilty for 'failing to cut back'. I have a supportive GP who understands I have no desire to ever feel the way I did before I started taking antidepressants. I have done behavioural therapy and learned the tools to change my way of thinking, but for me there has always been a huge physical element to my anxiety, they called it 'Double Anxiety' at the time. Add to that the physical health problems, additional drugs, and changes in my personal circumstances. So far, the time has never been right to start

cutting back. When the time is right, however, I know I have a GP who is mindful of my reservations and who will let me go at my own pace.

NHS Greater Glasgow and Clyde[17]

GPs were asked to proactively review a proportion of their practice patients prescribed the same antidepressant continuously long-term (≥2 years), as current guidelines advise up to two years' treatment for some individuals with depression. Amitriptyline was excluded as it is more commonly used to treat neuropathic pain. Prescribing support pharmacists and technicians created the opportunity for proactive reviews by identifying potential patients for review, using data extraction tools, enabling >150-hour audits to be completed within two to four hours, November 2009 to March 2010. The GPs then decided which of their patients to review.

78 of 96 practices participated. 8.6% (33,312/388,656) of all registered patients were prescribed an antidepressant, 47.1% (15,689) were defined as long-term users and 2,849 (18%) were reviewed. 811 (28.5%) patients reviewed had a change in antidepressant therapy: 7% stopped, 13% reduced dose, 5% increased dose, and 3% changed antidepressant, resulting in 9.5% (95% CI = 9.1% to 9.8% P<0.001) reduction in prescribed daily dose and 8.1% reduction in prescribing costs. 6% were referred onwards, half to NHS mental health services. Pre-review SSRI doses were 10–30% higher than previously reported.

Since 2009, this work has continued as a local prescribing initiative, enabling over 8,000 people in more than 180 general practices to be reviewed between 2009/10 and 2014/15. However, this represents less than 2% (8,000/451,084) of people receiving long-term treatment,[155] and lacked long-term follow-up to assess relapse and recurrence rates. (Estimate calculated from: previous studies indicate approximately 50% of people receive long-term treatment.17 Current medicines use in mental health indicates that 902,168 people received antidepressants in 2017/18. Therefore approximately 451,084 people are receiving long-term treatment in Scotland.)

Strengths: Enabled GPs to proactively review their own patients, enabling more people to be reviewed in a short period of time. Demonstrated use of electronic systems in enabling appropriate people to be identified and called for review. Demonstrated the effectiveness of pharmacy general practice teams in supporting and facilitating proactive GP reviews.

Limitations: Prescribers were asked to use their own clinical judgement for reviewing and reducing antidepressants, however they did not have structured

advice as outlined in this guideline which may help overcome some of the barriers outlined in 2.3 above. Limited numbers of people reviewed. Limited resources and long-term follow-up to assess longer-term impact.

Systematic review summary from Maund et al[23]

Maund et al. have completed a systematic review regarding published studies that focused on reviewing, reducing and stopping antidepressants.

Of the 15 studies outlined, 12 were included in the synthesis (eight randomized controlled trials, two single-arm trials, two retrospective cohort studies). None were rated as having high risk for selection or detection bias.

Two studies prompting primary care clinician discontinuation with antidepressant tapering guidance found 6% and 7% of patients discontinued versus 8% for usual care.

Six studies of psychological or psychiatric treatment plus tapering reported cessation rates of 40% to 95%.

Two studies reported a higher risk of discontinuation symptoms with abrupt termination.

At two years, risk of relapse/recurrence was lower with cognitive behavioural therapy (CBT) plus taper versus clinical management plus taper (15% to 25% vs 35% to 80%: risk ratio = 0.34; 95% CI, 0.18-0.67; two studies).

Relapse/recurrence rates were similar for mindfulness-based cognitive therapy with tapering and maintenance antidepressants (44% to 48% vs 47% to 60%; two studies).

CBT or mindfulness-based cognitive therapy can help patients discontinue antidepressants without increasing the risk of relapse/recurrence but are resource intensive.

Strengths: Included a range of studies with different methodologies and different populations. Highlighted that a complex intervention with tapering and psychological support may be more effective.

Limitations: Variation in study methodologies across different healthcare systems, and small sample numbers. Not always clear how long individuals had been receiving the antidepressant for; ranged from three months to more than nine months for the majority of studies.

Case study 1: Depression

Background (age, sex, occupation, baseline function)

- 54-year-old male
- Recent loss of employment

History of presentation/ reason for review

- Attended for review of his antidepressant started two months ago for first depressive episode
- Attends with a supportive friend who is concerned about him, as the individual has cancelled plans to meet and avoiding contact with others. Appears more socially isolated
- Signs of self-neglect
- Has lost over half a stone in weight due to reduced appetite
- Reports early morning wakening, increased rumination and a loss of motivation

Current medical history and relevant comorbidities

- Depressive episode – started antidepressant therapy two months ago
- Asthma (diagnosed in childhood) currently well controlled

Current medication and drug allergies (include over the counter (OTC) preparation and herbal remedies)

- Citalopram 20mg tablets - one tablet daily
- Clenil® (beclomethasone) 100microgram MDI - two puffs twice a day
- Salbutamol 100microgram MDI - two puffs up to four times a day (two ordered in last 12 months)
- No known drug allergies

Lifestyle and current function (include frailty score for >65yrs), alcohol, smoking, diet, physical activity

- Recent loss of employment
- Supportive friend
- At review:
    - Avoidant of eye contact and when asked becomes tearful reporting fleeting, occasional thoughts of ending his life. Whilst he has no active plan for suicide, he has disclosed he has thought about different ways of ending his life. Is adamant he would not act on these, citing his father and dog as protective factors
    - He reports taking his citalopram as prescribed every day for eight weeks but little/no benefit
    - Does not drink alcohol or use recreational substances

“What matters to me” (ideas, concerns and expectations of treatment)

- When asked about his goals he struggles to identify any, other than he wants to feel better but feels helpless as to how to change his situation
- Invited to complete the Patient Reported Outcome Measures (PROMs) prior to his review to identify any additional areas for discussion

Results e.g. biochemistry, other relevant investigations or monitoring
Note: local lab reference ranges may vary

- Recent bloods within normal range, including thyroid function tests
- During consultation indicates a worsening of symptoms. PHQ-9 score 14/27 eight weeks ago to 18/27 today (moderately severe depression)

Most recent relevant consultations

He is agreeable to a review of his medication and psychological supports are discussed. He was signposted to the NHS inform self-help guide at first presentation to the practice, which he had taken time to explore. He found understanding the links between his thoughts, feelings and behaviours helpful but would feel more comfortable if able to discuss this in person.

Steps	Process	Person specific issues to address
1. **Aims** What matters to the individual about their condition(s)?	**Review diagnoses and consider:** • Therapeutic objectives of drug therapy • Management of existing health problems • Prevention of future health issues, including lifestyle advice • Ask person to complete PROMs in preparation for their review	• Wants to “feel better” • Wants to regain motivation and appetite • Wants to walk his dog more often
2. **Need** Identify essential drug therapy	**Identify essential drugs (not to be stopped without specialist advice)** • Drugs that have essential replacement functions (e.g. levothyroxine) • Drugs to prevent rapid symptomatic decline (e.g. drugs for Parkinson’s disease, heart failure)	• none identified as essential medicines • inhaled corticosteroids required for asthma control • consider the need for gradual withdrawal/ cross tapering with antidepressants where necessary
3. Does the individual take unnecessary drug therapy?	**Identify and review the continued need for drugs** • what is medication for? • with temporary indications • with higher than usual maintenance doses • with limited benefit/evidence for use • with limited benefit in the person under review (see Drug efficacy & applicability (NNT) table)	• episode of depression, possibly related to loss of employment. Trial of citalopram 20mg daily – ineffective after two months

4.
Effectiveness
 	
Are therapeutic objectives being achieved?
	Identify the need for adding/intensifying drug therapy to achieve therapeutic objectives
	
	• to achieve symptom control
	• to achieve biochemical/clinical targets
	• to prevent disease progression/exacerbation
	• is there a more appropriate medication to achieve goals?
		• Moderate severe depressive episode, worsening signs and symptoms, citalopram ineffective.
		• Combination of:
		  ○ switch antidepressant as no effect at eight weeks of therapeutic dose. Should be reviewed two to four weeks after initiation.
		  ○ psychological intervention (e.g. cCBT)
		  ○ lifestyle interventions e.g. exercise such as walking
		• Asthma well controlled

5. **Safety** Does the individual have or is at risk of ADR/ Side effects? Does the person know what to do if they're ill?	**Identify individual safety risks by checking for** • appropriate individual targets e.g. HbA1c, BP • drug-disease interactions • drug-drug interactions (see ADR table) • monitoring mechanisms for high-risk drugs • risk of accidental overdosing **Identify adverse drug effects by checking for** • specific symptoms/laboratory markers (e.g. hypokalaemia) • cumulative adverse drug effects (see ADR table)	• Worsening symptoms and possible increasing self-harm/suicide risk • Worsening symptom advice and out-of-hours numbers provided (e.g. NHS 24, Breathing Space). • Follow-up review within one to two weeks, or sooner if considered appropriate • Current medicines have low overdose fatality risk

	• drugs used to treat side effects caused by other drugs **Medication Sick Day guidance** Ensure discussion and clear information on which medicines to withhold at times of dehydrating illness	
6. **Sustainability** Is drug therapy cost-effective and environmentally sustainable?	**Identify unnecessarily costly drug therapy by** • considering more cost-effective alternatives, safety, convenience **Consider the environmental impact of** • inhaler use • single use plastics • medicines waste • water pollution	• Formulary preferred options being prescribed • Asthma well controlled, salbutamol ordering/use appropriate and inhaler technique checked • Consider option of dry powder inhalers at a later consultation if suitable (prioritise depression management) • Dispose of unwanted and expired medicines at community pharmacy • Advised not to dispose of medicine via household or water waste
7. **Person-centredness** Is the person willing and able to take drug therapy as intended?	**Does the person understand the outcomes of the review?** • Consider Teach back • Involve the adult where possible. If deemed to lack capacity, discuss with relevant others, e.g. welfare guardian, power of attorney, nearest relative if one exists. Even if adult lacks capacity, adults with Incapacity Act still requires that the adult's	**Agreed plan** • Switch antidepressants: last dose of citalopram today, start sertraline 50mg daily tomorrow. • Referral to adult mental health services for high intensity psychological interventions • Safety information - suicide prevention advice, provide emergency contact

	views are sought. Ensure "Adults with Incapacity Documentation" in place **Ensure drug therapy changes are tailored to individual's preferences. Consider** • is the medication in a form they can take? • is the dosing schedule convenient? • are they able to take medicines as intended? **Agree and communicate plan** • discuss and agree with the individual/ carer/welfare proxy therapeutic objectives and treatment priorities • include lifestyle and holistic management goals • inform relevant health and social care providers of changes in treatments across the transitions of care **Ask person to complete the post-review PROMs questions after their review**	telephone numbers for out-of-hours services for crisis support if required. • Low intensity exercise recommended – e.g. walking his dog may help • Friend attending with him is supportive, safety information provided as above

Key concepts in this case

- Ensure timely review of new antidepressant treatment to assess effectiveness
- Review following changes to antidepressant therapy to ensure effectiveness
- Potential medication side-effects: loss of appetite could be caused by both depression and/or antidepressants
- Ongoing symptoms of depression including suicidal thoughts, despite antidepressant, indicates the need for review of therapy
- Importance of non-pharmacological therapies, such as psychological interventions, cCBT, exercise
- Holistic review could include inhaler use and environmental sustainability. However, these may be more suitable for future discussions when depression has stabilised

Case study 2: Anxiety

Background (age, sex, occupation, baseline function)

- 24-year-old female
- Office administrator

History of presentation/ reason for review

- Reports a 12-week history of increasing anxiety including worry, mild irritability, difficulties concentrating and marked sleep disturbance
- Increasingly difficult to control her worries which is having an impact on her work. She has been going in early and staying late as taking extra time to both complete and then check over her work due to concerns she may make a mistake
- Parents have noticed she is more on edge, restless and seems tired all the time

Current medical history and relevant comorbidities

- No mental or physical health comorbidities

Current medication and drug allergies (include over the counter (OTC) preparation and herbal remedies)

- None

Lifestyle and current function (include frailty score for >65yrs), alcohol, smoking, diet, physical activity

- Single, no dependents
- Lives at home with her parents
- Social drinker
- Non-smoker
- Very supportive close group of friends, parents, and older brother that she has been able to talk to about her anxiety

“What matters to me” (ideas, concerns and expectations of treatment)

- Keen to reduce the time she spends worrying, improve sleep, and feel less tense
- Although she is experiencing some difficulties at work, she is keen to avoid time off and is still managing to go to the gym
- Keen to avoid medication
- Invite individual to complete questions to prepare for the review (PROMs)

Results e.g. biochemistry, other relevant investigations or monitoring
Note: local lab reference ranges may vary

- GAD-7 score 8 (mild-moderate anxiety). However, as the anxiety is affecting her daily tasks of living, she is experiencing moderate anxiety

Most recent relevant consultations

- Presents as very motivated, has clear goals that including reducing the time she spends worrying, improved sleep, and feeling less tense
- Caffeine intake assessed and discussed
- Medication options are explored alongside psychological options. Has avoided coming into the practice as she is keen to avoid medication however expresses an interest in accessing CBT which she has looked up online. Comfortable using computers, see this as a flexible way to receive support that she can manage around her work and social commitments
- Reports no family history of suicide. No plans or intent to harm herself or others
- **Agreed plan:**
  - Medication options will not be commenced at this stage. Sleep hygiene discussed and written information given
  - Referral to Daylight, a cCBT package for Generalised Anxiety Disorder (GAD) with a review in the practice in four to six weeks' time or if symptoms worsen

Steps	Process	Person specific issues to address
1. **Aims** What matters to the individual about their condition(s)?	**Review diagnoses and consider:** • Therapeutic objectives of drug therapy • Management of existing health problems • Prevention of future health issues, including lifestyle advice • Ask individual to complete PROMs to prepare for the review	• Motivated and keen to reduce anxiety and time spent worrying • Improve focus at work • Improve sleep • Prefers to avoid medication
2. **Need** Identify essential drug therapy	**Identify essential drugs (not to be stopped without specialist advice)** • Drugs that have essential replacement functions (e.g. levothyroxine) • Drugs to prevent rapid symptomatic decline (e.g. drugs for Parkinson's disease, heart failure)	• None
3. Does the individual take unnecessary drug therapy?	**Identify and review the continued need for drugs** • what is medication for? • with temporary indications • with higher than usual maintenance doses • with limited benefit/evidence for use • with limited benefit in the person under review (see Drug efficacy & applicability (NNT) table)	• None

4. **Effectiveness** Are therapeutic objectives being achieved?	**Identify the need for adding/intensifying drug therapy to achieve therapeutic objectives** • to achieve symptom control • to achieve biochemical/clinical targets • to prevent disease progression/exacerbation • is there a more appropriate medication to achieve goals?	• Medication options explored but not appropriate at present, interested and preference for cCBT and non-pharmacological management (e.g. sleep hygiene, physical activity, caffeine reduction)
5. **Safety** Does the individual have or is at risk of ADR/ Side effects? Does the person know what to do if they're ill?	**Identify individual safety risks by checking for** • appropriate individual targets e.g. HbA1c, BP • drug-disease interactions • drug-drug interactions (see ADR table) • monitoring mechanisms for high-risk drugs • risk of accidental overdosing **Identify adverse drug effects by checking for** • specific symptoms/ laboratory markers (e.g. hypokalaemia) • cumulative adverse drug effects (see ADR table) • drugs used to treat side effects caused by other drugs **Medication Sick Day guidance** Ensure discussion and clear information on which medicines to withhold at times of dehydrating illness	• No current plans or intent to harm herself or others • No family history of suicide • Has good family and friends support network • Prefers non-pharmacological treatment to start with • Reducing the use of medicines that are not indicated or appropriate avoids the risk of ADRs

6. **Sustainability** Is drug therapy cost-effective and environmentally sustainable?	**Identify unnecessarily costly drug therapy by** • considering more cost-effective alternatives, safety, convenience **Consider the environmental impact of** • inhaler use • single use plastics • medicines waste • water pollution	• No medicines prescribed. Reducing the use of medicines that are not indicated or appropriate reduces the environmental impact from medicines
7. **Person-centredness** Is the person willing and able to take drug therapy as intended?	**Does the person understand the outcomes of the review?** • Consider Teach back • Involve the adult where possible. If deemed to lack capacity, discuss with relevant others, e.g. welfare guardian, power of attorney, nearest relative if one exists. Even if adult lacks capacity, adults with Incapacity Act still requires that the adult's views are sought. Ensure "Adults with Incapacity Documentation" in place **Ensure drug therapy changes are tailored to individual's preferences. Consider** • is the medication in a form they can take? • is the dosing schedule convenient? • are they able to take medicines as intended?	**Agreed plan** • Medication options will not be commenced at this stage • Sleep hygiene and non-pharmacological options discussed. Written information given with links to self-help resources • Referral made to a cCBT program (e.g. Daylight) for GAD. Review in the practice planned for four to six weeks' time

Agree and communicate plan

- discuss and agree with the individual/carer/welfare proxy therapeutic objectives and treatment priorities
- include lifestyle and holistic management goals
- inform relevant health and social care providers of changes in treatments across the transitions of care

Ask person to complete the post-review PROMs questions after their review

Key concepts in this case

- Moderate GAD
- Non-pharmacological option preferred by patient, and matches with stepped-care model as per NICE guidelines
- Online computerised CBT fits with individual's preference, needs and ease of access

Case study 3: Falls with osteoporosis

Background (age, sex, occupation, baseline function)

- 74-year-old female
- Retired

History of presentation/ reason for review

- Falls – no dizziness or light headedness. Has experienced a number of falls over the years. Main cause is balance and mobility. Has been referred to falls team
- At review:
  - Pains in feet. States that 'lack of feeling in feet possibly to do with plantar fasciitis'
  - Higher dose of sertraline (100mg daily) 'made no difference' Depression resolved
  - Sometimes forgets to take alendronate – due to timing of dose

Current medical history and relevant comorbidities

- Osteoporosis – one year
- Fractured neck of femur (right). Total hip replacement – two years ago
- Depression – three years. Related to death of husband after long illness
- Plantar fasciitis – four years
- Acne rosacea
- High blood pressure – five years
- Chronic kidney disease stage three to seven years
- Lower back and knee pain – chronic
- Dyspepsia – eight years
- Cerebral lacunar infarct – seven years

Current medication and drug allergies (include over the counter (OTC) preparation and herbal remedies)

- Aspirin 75mg tablets - one tablet daily
- Alendronate 70mg tablets – one tablet once weekly (takes before breakfast)
- Co-codamol 30/500mg tablets - two tablets up to four times a day if needed
- Co-codamol 8/500mg tablets - two tablets up to four times a day if needed
- Fludrocortisone 50mcg tablets – one tablet daily
- Salicylic acid 2.0%, mucopolysaccharide polysulfate (MPS) 0.2% gel (Movelat®) - apply up to three times a day if needed
- Omeprazole 20mg capsules – one capsule daily
- Senna 7.5mg tablets – two tablets at night (last ordered 12 months ago)

- Sertraline 100mg tablets – one tablet daily (initiated two years ago after death of husband)
- Simvastatin 40mg tablets - one tablet at night
- Colecalciferol 1000 unit tablets – one tablet daily

Lifestyle and current function (include frailty score for >65yrs), alcohol, smoking, diet, physical activity

- Lives alone
- Supportive family and neighbours. Contact with sister and brother regularly
- Ex-smoker
- Does not drink alcohol
- Walks with stick

"What matters to me" (ideas, concerns and expectations of treatment)

- Reducing frequency of falls
- Invite individual to complete questions to prepare for the review (PROMs)

Results e.g. biochemistry, other relevant investigations or monitoring
Note: local lab reference ranges may vary

- U&Es, LFTs, bone profile, HbA1c and FBC – all within normal range. eGFR = 45ml/min - over estimating renal function
- Weight 65kg, Height 1.62m IBW 54.2kg. Estimated creatinine clearance 35ml/min (CKD G3b)
- DEXA scan – one year ago, severe osteoporosis
- BP 143/91 mmHg sitting, 116/78 mmHg standing. No symptoms of postural BP drop
- Pulse 74 bpm, regular

Most recent relevant consultations

- Fall in garden one week ago. Laceration to forehead. Six stitches in situ. Wound closed and dry with large black scab. No signs of infection. Six stitches removed, no issues. Care advice given. No dressing.

Steps	Process	Person specific issues to address
1. **Aims** What matters to the individual about their condition(s)?	**Review diagnoses and consider:** • Therapeutic objectives of drug therapy • Management of existing health problems • Prevention of future health issues, including lifestyle advice • Ask person to complete PROMs to prepare for the review	• Reduce frequency of falls • Where appropriate reduce/minimise prescribed medicines that may add to the risk of falls
2. **Need** Identify essential drug therapy	**Identify essential drugs (not to be stopped without specialist advice)** • Drugs that have essential replacement functions (e.g. levothyroxine) • Drugs to prevent rapid symptomatic decline (e.g. drugs for Parkinson's disease, heart failure)	• None considered essential
3. Does the individual take unnecessary drug therapy?	**Identify and review the continued need for drugs** • what is medication for? • with temporary indications • with higher than usual maintenance doses • with limited benefit/evidence for use • with limited benefit in the person under review (see Drug efficacy & applicability (NNT) table)	• First episode of depression after death of husband – states 'higher dose sertraline not made much difference'. Consider a tapered reduction. SSRIs and higher doses associated with increased risk of falls • Hypertensive while sitting. Previous stroke • Unclear indication for fludrocortisone. Consider stopping if no indication as increases blood pressure

		• Osteoporosis – forgets to take alendronate. Advised to take at 11am on Fridays (two hours before and after meals) • Senna not required – stop
4. **Effectiveness** Are therapeutic objectives being achieved?	**Identify the need for adding/intensifying drug therapy to achieve therapeutic objectives** • to achieve symptom control • to achieve biochemical/clinical targets • to prevent disease progression/ exacerbation • is there a more appropriate medication to achieve goals?	• Depression resolved – trial stopping sertraline – taper gradually • As required co-codamol, using both strengths depending on pain intensity, finds effective – not causing drowsiness, constipation • Stroke prevention medicines: simvastatin, aspirin, hypertension control • Osteoporosis treatment: alendronic acid and colecalciferol • Forgetting to take alendronic acid - discuss strategies to help, such as calendar reminder or phone alarm
5. **Safety** Does the individual have or is at risk of ADR/ Side effects? Does the person know what to do if they're ill?	**Identify individual safety risks by checking for** • appropriate individual targets e.g. HbA1c, BP • drug-disease interactions • drug-drug interactions (see ADR table) • monitoring mechanisms for high-risk drugs • risk of accidental overdosing **Identify adverse drug effects by checking for** • specific symptoms/laboratory	• Two strengths of co-codamol for knee and back pain. Paracetamol only is ineffective. Takes 8/500 during day and 30/500 at night. Knows not to take both at same time. Uses sparingly • Fludrocortisone increasing risk of high blood pressure – stop • GI protection – aspirin and sertraline, GI bleed risk • Omeprazole to continue as needed for GI protection

	markers (e.g. hypokalaemia) • cumulative adverse drug effects (see ADR table) • drugs used to treat side effects caused by other drugs **Medication Sick Day guidance** Ensure discussion and clear information on which medicines to withhold at times of dehydrating illness	
6. **Sustainability** Is drug therapy cost-effective and environmentally sustainable?	**Identify unnecessarily costly drug therapy by** • considering more cost-effective alternatives, safety, convenience **Consider the environmental impact of** • inhaler use • single use plastics • medicines waste • water pollution	• Formulary preferred list medicines options being prescribed. • Advise to take unused or expired medicines back to community pharmacy for safe disposal • Unnecessary/ineffective medicines stopped
7. **Person-centredness** Is the person willing and able to take drug therapy as intended?	**Does the person understand the outcomes of the review?** • Consider Teach back • Involve the adult where possible. If deemed to lack capacity, discuss with relevant others, e.g. welfare guardian, power of attorney, nearest relative if one exists. Even if adult lacks capacity, adults with Incapacity Act still requires that the adult's	**Agreed plan** • Trial reduction of sertraline, reducing every four weeks: 100mg to 50mg to 25mg then stop • Osteoporosis – forgets to take alendronate. Advised to take at 11am Fridays (two hours before and after meals) • Plantar fasciitis – refer for podiatry review • Understands and agrees to changes to medicines

views are sought. Ensure “Adults with Incapacity Documentation” in place

Ensure drug therapy changes are tailored to individual’s preferences. Consider

- is the medication in a form they can take?
- is the dosing schedule convenient?
- are they able to take medicines as intended?

Agree and communicate plan

- discuss and agree with the individual/ carer/welfare proxy therapeutic objectives and treatment priorities
- include lifestyle and holistic management goals
- inform relevant health and social care providers of changes in treatments across the transitions of care

Ask person to complete the post-review PROMs questions after their review

- Poor sleep since retired – uses sleep hygiene techniques: low caffeine intake, reads when has insomnia/night-time wakening
- Has capacity and is independent and capable of looking after her own medicines

Key concepts in this case

- Importance of regular review of long-term antidepressant therapy
- Higher dose SSRIs associated with increased risk of falls[43]
- eGFR overestimating renal function. Although eGFR is routinely reported with U&Es it does not routinely reflect older adults’ renal function therefore it may be prudent to calculate individual’s creatinine clearance – see BNF Prescribing in Renal Failure section

- Minimise the number of unnecessary medicines
- Fludrocortisone – increases blood pressure, and borderline hypertensive with a previous history of stroke. Fludrocortisone may have increased the risk of future strokes
- Podiatry assessment not included in routine falls team review therefore referral was needed

Case study 4: Long-term antidepressant use

Background (age, sex, occupation, baseline function)

- 60-year-old female
- Works part-time

History of presentation/ reason for review

- Identified from 'long-term antidepressant use" search using STU within the GP practice and invited for review. Receiving paroxetine 20mg daily for over two years
- At review tells you her mood is good and asks if she can stop her antidepressant

Current medical history and relevant comorbidities

- Mixed anxiety and depression following death of son four years ago

Current medication and drug allergies (include over the counter (OTC) preparation and herbal remedies)

- Paroxetine 20mg tablets – one tablet daily (approximately 2.5 years)
- Temazepam 10mg tablets – one tablet at night (approximately 3 years - does not over order)
- Drug allergies: Nitrofurantoin – rash

Lifestyle and current function (include frailty score for >65yrs), alcohol, smoking, diet, physical activity

- Lives alone
- No alcohol
- Good concentration, appetite and weight stable, sleeping well
- Helps to look after grandson to support her daughter-in-law
- Looking forward to the future and seeing her grandson growing up
- No thoughts of suicide/deliberate self-harm

"What matters to me" (ideas, concerns and expectations of treatment)

- Would like to stop antidepressant as has been taking a long time
- Ask person to complete questions to prepare for the review (PROMs)

Results e.g. biochemistry, other relevant investigations or monitoring

Note: local lab reference ranges may vary

- Blood tests at diagnosis (including TFT's) all within normal range

Most recent relevant consultations

- Urinary tract infection six months previously

Steps	Process	Person specific issues to address
1. **Aims** What matters to the individual about their condition(s)?	**Review diagnoses and consider:** • Therapeutic objectives of drug therapy • Management of existing health problems • Prevention of future health issues, including lifestyle advice • Ask person to complete PROMs to prepare for the review	• Would like to stop her antidepressant, as has been taking for over two years
2. **Need** Identify essential drug therapy	**Identify essential drugs (not to be stopped without specialist advice)** • Drugs that have essential replacement functions (e.g. levothyroxine) • Drugs to prevent rapid symptomatic decline (e.g. drugs for Parkinson's disease, heart failure)	• no essential medicines • if reducing or stopping paroxetine or temazepam, consider gradual reduction to avoid withdrawal symptoms

3.
 	
Does the individual take unnecessary drug therapy?
	Identify and review the continued need for drugs
	• what is medication for?
	• with temporary indications
	• with higher than usual maintenance doses
	• with limited benefit/ evidence for use
	• with limited benefit in the person under review (see Drug efficacy & applicability (NNT) table)
		• temazepam no longer needed
		  ○ insomnia – related to bereavement, sleep now improved.
		  ○ temazepam loses efficacy after two to four weeks. Licensed for a maximum of four weeks
		• paroxetine no longer needed
		  ○ Completed six-month course of treatment. Mood improved

4. **Effectiveness** Are therapeutic objectives being achieved?	**Identify the need for adding/intensifying drug therapy to achieve therapeutic objectives** • to achieve symptom control • to achieve biochemical/clinical targets • to prevent disease progression/exacerbation • is there a more appropriate medication to achieve goals?	Ensure appropriate non-pharmacological options discussed to maintain wellbeing
5. **Safety** Does the individual have or is at risk of ADR/ Side effects? Does the person know what to do if they're ill?	**Identify individual safety risks by checking for** • appropriate individual targets e.g. HbA1c, BP • drug-disease interactions • drug-drug interactions (see ADR table) • monitoring mechanisms for high-risk drugs • risk of accidental overdosing **Identify adverse drug effects by checking for** • specific symptoms/ laboratory markers (e.g. hypokalaemia) • cumulative adverse drug effects (see ADR table) • drugs used to treat side effects caused by other drugs **Medication Sick Day guidance**	• Temazepam – increased risk of cognitive effects, falls, lower mood, etc. Plan to stop • Paroxetine – GI bleed risk, emotional blunting, etc. Risk of withdrawal effects higher than with other antidepressants. Plan appropriate reduction schedule

	Ensure discussion and clear information on which medicines to withhold at times of dehydrating illness	
6. **Sustainability** Is drug therapy cost-effective and environmentally sustainable?	**Identify unnecessarily costly drug therapy by** • considering more cost-effective alternatives, safety, convenience **Consider the environmental impact of** • inhaler use • single use plastics • medicines waste • water pollution	• Temazepam dose reduction and stop - oral solution significantly more expensive than tablets. Consider switch to diazepam to aid reduction - longer half-life and a number of preparations available

7.
Person-centredness
 	
Is the person willing and able to take drug therapy as intended?
	Does the person understand the outcomes of the review?
	• Consider Teach back
	• Involve the adult where possible. If deemed to lack capacity, discuss with relevant others, e.g. welfare guardian, power of attorney, nearest relative if one exists. Even if adult lacks capacity, adults with Incapacity Act still requires that the adult's views are sought. Ensure "Adults with Incapacity Documentation" in place
	
	Ensure drug therapy changes are tailored to individual's preferences. Consider
		Agreed plan
		• Continue non-pharmacological support to maintain recovery: physical activity, minimise social isolation, etc. Signpost to resources e.g. local groups or online support
		• Temazepam to reduce and stop, due to lack of efficacy and risk of ADR:.
		  ○ Switch to diazepam 10mg at night and reduce by 1mg every two to four weeks.
		  ○ Alternative: Temazepam 10mg/5ml oral solution, reducing by 1mg (0.5ml) every two to four weeks. (oral solution higher acquisition cost)
		• Paroxetine withdrawal schedule options (after stopping temazepam):

- is the medication in a form they can take?
- is the dosing schedule convenient?
- are they able to take medicines as intended?

Agree and communicate plan

- discuss and agree with the individual/ carer/welfare proxy therapeutic objectives and treatment priorities
- include lifestyle and holistic management goals
- inform relevant health and social care providers of changes in treatments across the transitions of care

Ask person to complete the post-review PROMs questions after their review

- Reduce to 10mg daily for four weeks, then 5mg daily for four weeks, then stop.
- If problematic withdrawal or apprehensive: switch to equivalent dose of fluoxetine (20mg/5ml) oral solution for seven days, then reduce by 4mg (1ml) every four weeks

Key concepts in this case

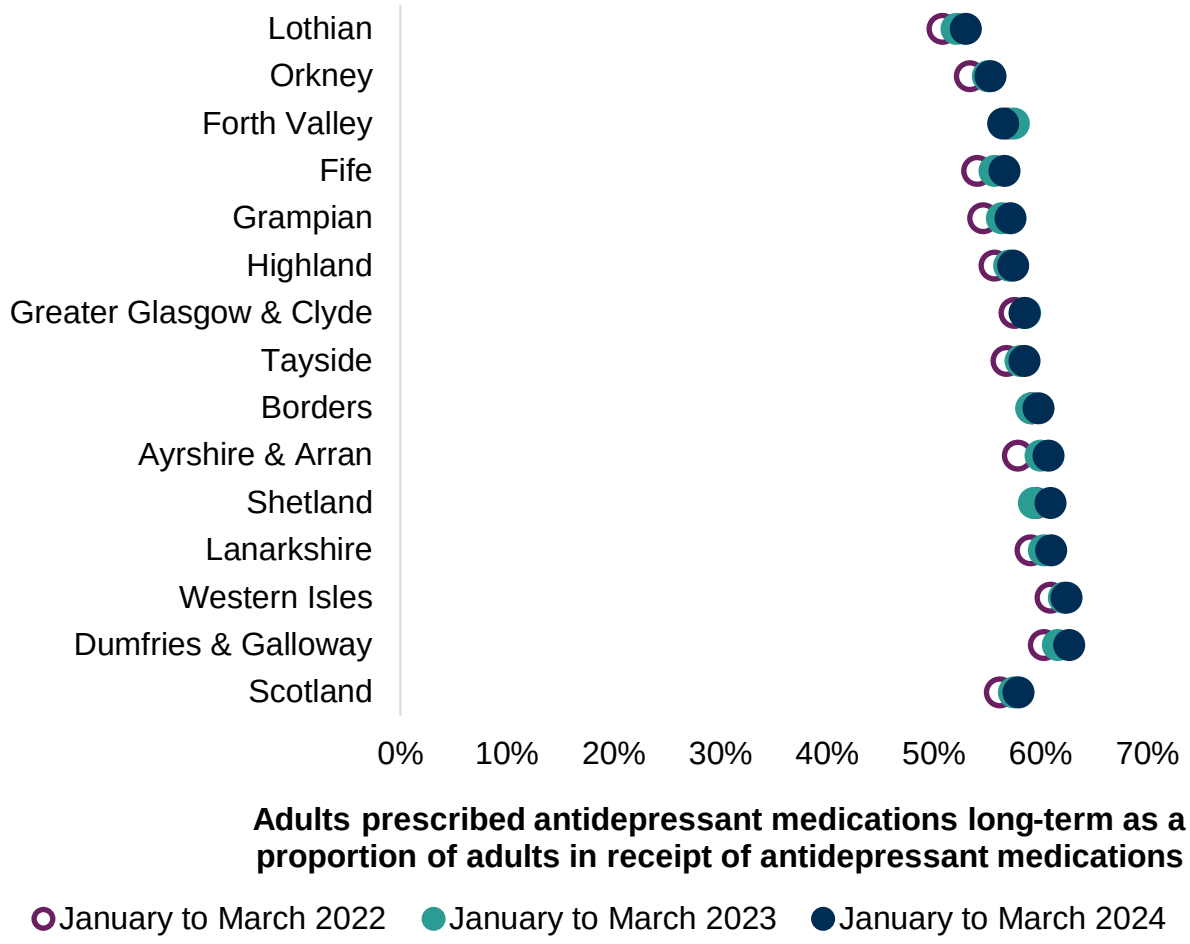
- Benzodiazepines are associated with an increased risk of depression and are only licensed for a maximum of four weeks use. Stopping temazepam is a priority due to increased risk of avoidable ADRs. Reducing temazepam may require gradual reduction to assist with stopping.
- Switching from a short acting SSRI to a longer half-life SSRI may enable reduction and stopping.
- Paroxetine is associated with withdrawal effects. Therefore, have a range of options and agree the most appropriate approach to reducing and stopping, to improve chances of a successful withdrawal

7. Data – National Therapeutic Indicators (NTIs) and the Scottish Therapeutics Utility (STU)

National Therapeutic Indicators

To identify where your health board, GP cluster or GP practice benchmark in relation to prescribing indicators, please use the following National Therapeutic Indicator dashboard. Here you will find the three-point timeline allowing you to benchmark your health board, GP cluster or GP practice against similar areas or the Scottish average in a wide range of prescribing areas.

Chart 4: Adults (≥18 years old) prescribed all long-term (≥2 years) antidepressants as a proportion of adults in receipt of antidepressant medications, by NHS board



The full list of current National Therapeutic Indicators for antidepressants is listed in Appendix 6, and a set of related searches have been developed in the Scottish Therapeutics Utility (STU) to help you identify these patients within your GP practice.

Once you have identified where your health board, GP cluster or GP practice sits in relation to similar clusters and the Scottish average, use the Scottish Therapeutics

Utility (STU) tool in your practice to identify these individuals for review of treatment where necessary. The Scottish Therapeutics Utility tool is available to download within all general practices in Scotland and provides a suite of case finding prescribing indicators to help you identify individuals who could benefit from review. STU links to the patient record, allowing you to make changes to medication within Vision and EMIS from the toolkit itself. It can be downloaded on your practice computer using the installation guide on the Effective Prescribing and Therapeutic website.

Users can click on the required prescribing indicator and select a specific patient medication record and any acute prescriptions issued in the last 84 days. Acute prescriptions are annotated with (a). The data can then be sorted by any of the columns by clicking on the column heading. As STU uses more accurate practice level and near real time data, the number of patients identified in general practice may differ from the benchmarking numbers displayed on the National Therapeutic Indicators. NTIs use a different data source, updated on a quarterly basis, and as a result any changes made at a practice level on STU may take time to be reflected on the NTI dashboard.

Any additional STU searches that could help you or your practice in identifying issues around prescribing can be suggested to the STU team for consideration using the email nti.stu@gov.scot.

Abbreviations

A&A	Ayrshire and Arran Health Board
ADRs	Adverse drug reactions
BAP	British Association for Psychopharmacology
BP	Blood pressure
B-Z	Benzodiazepines and/or z-drugs
CBT	Cognitive Behavioural Therapy
cCBT	computerised Cognitive Behavioural Therapy
COPD	Chronic obstructive pulmonary disease
DDD	Defined daily dose
D&G	Dumfries and Galloway Health Board
DOAC	Direct oral anticoagulant
ECT	Electroconvulsive therapy
eGFR	Estimated glomerular filtration rate
FBC	Full blood count
FV	Forth Valley Health Board
GAD	Generalised Anxiety Disorder
GAD-7	Generalised Anxiety Disorder questionnaire
GGC	Greater Glasgow and Clyde Health Board
GP	General practitioner
HbA1c	Glycated haemoglobin
HSCP	Health and Social Care Partnership
IBW	Ideal body weight
LFTs	Liver function tests
MAOI	Monoamine oxidase inhibitor
MDI	Metered dose inhaler
MHRA	Medicines and Healthcare products Regulatory Agency
MR	Modified release
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NNH	Number needed to harm
NNT	Number needed to treat
NSAID	Non-steroidal anti-inflammatory drug
NTI	National Therapeutic Indicator
OCD	Obsessive compulsive disorder
OTC	Over the counter
PHQ-9	Patient Health Questionnaire
PROMs	Patient Reported Outcomes Measures
PTSD	Post-traumatic Stress Disorder
SNRI	Serotonin and noradrenaline re-uptake inhibitor
SSRI	Selective serotonin re-uptake inhibitor

STU	Scottish Therapeutics Utility
TCA	Tricyclic antidepressant
TIA	Transient ischaemic attack
U&Es	Urea and electrolytes
WI	Western Isles Health Board

Appendix 1. Sleep hygiene: Patient information leaflet

Things to consider that can help and improve your quality of sleep and reduces anxiety.

- **How much caffeine do you take?** Remember that caffeine is a stimulant which is alerting and will affect your sleep quality and any anxiety. Common products that contain caffeine are tea, coffee, Irn-Bru®, cola, Red Bull®, Pro Plus® tablets and some energy drinks. Some pain medicines also contain caffeine: Solpadeine®, Propain®, Panadol Plus®, Veganin® etc. Therefore, try to avoid all caffeine containing products after 6pm in the evening.
- **Alcohol** will affect the quality of your sleep, which may add to problems of anxiety and depression.
- Other things that affect sleep
    - Watching television stimulates your brain with sound, light and motion. All of these stimulate your body and reduce fatigue.
    - Watching television in your bedroom. This can affect sleep quality as your body gets out of the habit of being trained to go to bed to sleep. Therefore, remove TV from bedroom.
    - Noisy neighbours – difficult to deal with but ear plugs may help.
- How to improve sleep
    - **Establish a routine** Go to bed and get up at the same time each day.
    - **No naps** Try not to sleep during the day.
    - **Unwind the mind** May help writing down problems and filing them away until the next morning. Address problems the next day, e.g. money/family problems.
    - **Take regular exercise** such as a brisk 20 minute walk. Natural chemicals (endorphins) produced during exercise have a calming and relaxing affect after you have exercised. Do not exercise before going to bed or for three hours before going to bed as this can have the opposite effect.
    - **Hot caffeine free drinks** will warm you and help your body relax.
    - **Make time to relax** Quiet time reflecting, listening to calming music such as classical, transient house, etc. 20-30 minutes a day would be enough. Watching TV does not help as it can be over stimulating.
    - **Consider using ear plugs** for noise that is affecting you which you cannot control.
    - **If all else fails get out of bed** and do something (read, etc) and then go back to bed.

Other information:

- NHS Inform: Sleep problems and insomnia self-help guide
- NHS How to get to sleep: Sleep and tiredness
- The Sleep Charity: Information for adults
- The Sleep Charity: Teen Sleep Hub

Appendix 2. Resources to support low intensity psychosocial and/or psychological interventions

The NHS Inform (Mental Health) website provides information regarding a range of mental health difficulties. In addition to self-help guides, NHS Inform provides links to evidence based digital/online resources and telephone support based on CBT principles, see options below. Decisions regarding interventions should be based on an assessment of need and consider both suitability and acceptability for the individual. Regular review is necessary to monitor progress and to step up care as and when required. There may also be a number of wellbeing resources available across localities.

Beating the Blues	cCBT programme for mild to moderate symptoms of depression and/or anxiety: Eight sessions
Living Life	Appointment based telephone support for anxiety and depression for ≥16 years: Four to nine sessions. Tel: 0800 328 9655
SilverCloud	Range of online psychoeducational programmes to support wellbeing, stress and mild to moderate anxiety and low mood
Sleepio	Online resource for Insomnia
Daylight	Online resource for Anxiety

Note: Silvercloud see 'How to assess for patient suitability for online mental health and wellbeing programs' for more detail.[156]

Appendix 3. Example practice invitation letter for review

PRACTICE LETTERHEAD

Private & Confidential

Patient Name
Patient Address

Date

Dear

From reviewing your records, we note that you are currently prescribed [drug name(s)].

With all medicines it is important that your [drug name(s)] is routinely reviewed in line with current guidelines and safety advice.

We are now inviting you to contact the practice to arrange a routine appointment where we can discuss your current use of [drug name(s)] and answer any questions and/or concerns you may have about your medications.

Yours sincerely

Drs A, B and C

Appendix 4. Patient information leaflet

Background

Antidepressants can be effective for the treatment of moderate to severe depression, moderate to severe anxiety disorders and nerve pain caused by diabetes and other conditions. However, there are concerns that some individuals may experience dependence and withdrawal associated with antidepressant use. Effective non-pharmacological treatments and lifestyle changes are also an important consideration. It is also known that some individuals may receive an appropriate course of treatment, while others may continue antidepressants inappropriately due to a lack of routine review.

What is the purpose of the antidepressant quality prescribing guide?

It is intended to:

- Empower and help people who receive antidepressants and prescribers to review antidepressants and get the best out of the medicines for individuals.
- Improve the support available from the healthcare system for people experiencing dependence on, or withdrawal from, prescribed medicines.
- Help prescribers identify people who may benefit from an antidepressant review, and support routine antidepressant reviews.
- Provide a range of options, where appropriate, for people who have completed their course of antidepressant treatment, and/or are appropriate to reduce and stop their antidepressants.

Do I need to have my antidepressant reviewed?

- Antidepressants are no different to any other medicines. It is important to have your medicines routinely reviewed. For some individuals once a year review may be enough, for others more regular review will be needed.
- Having medicines reviewed regularly creates an opportunity to discuss if a medicine needs to continue. Consider effective non-pharmacological treatments and lifestyle changes that may help.
- Prior to your medicines review you may wish to complete the questions for your review section on the manage medicines app or website, to help you prepare for your review and identify 'what matters to you' about your treatment.

Do I need to stop my antidepressant?

- It may be appropriate for some individuals to stop their antidepressant, but not for others.
- Continuing your antidepressant may be appropriate because there are more benefits to continuing than risks of stopping e.g. recurrence of severe depression.

- Reducing and/or stopping your antidepressant may be necessary to reduce the risk of avoidable adverse drug effects and harms e.g. falls, confusion, sedation. Or where you have completed your course of antidepressant treatment and recovered e.g. six months of antidepressant treatment due to a single episode of depression.

How should I stop my antidepressant?

If you are ready to stop your antidepressant:

- Arrange a review with your general practice doctor, pharmacist or nurse.
- Complete the questions for my review section on the manage medicines app or website to help you prepare for your review and identify "what matters to you"
- Discuss stopping your antidepressant and agree if this is appropriate.
- If appropriate to stop, then plan and agree the best way to do this for you, considering the options outlined in the antidepressant quality prescribing guide.

Appendix 5. Data tables from indicator charts

Table 14: Adults (≥18 years old) prescribed long-term (≥2 years) antidepressants as a proportion of adults in receipt of antidepressant medications, by NHS board (Chart 1)

NHS Board	Jan to Mar 2022	Jan to Mar 2023	Jan to Mar 2024
NHS Ayrshire & Arran	57.9%	60.0%	60.7%
NHS Borders	59.2%	59.1%	59.8%
NHS Dumfries & Galloway	60.3%	61.6%	62.7%
NHS Fife	54.0%	55.7%	56.7%
NHS Forth Valley	56.9%	57.5%	56.5%
NHS Grampian	54.6%	56.4%	57.2%
NHS Greater Glasgow & Clyde	57.6%	58.6%	58.5%
NHS Highland	55.7%	57.0%	57.4%
NHS Lanarkshire	59.0%	60.3%	61.0%
NHS Lothian	50.8%	52.1%	53.0%
NHS Orkney	53.4%	55.1%	55.3%
NHS Shetland	59.6%	59.4%	61.0%
NHS Tayside	56.8%	58.1%	58.5%
NHS Western Isles	61.0%	62.2%	62.4%
Scotland	56.2%	57.5%	58.0%

Table 15: Average defined daily doses (DDDs) per person per day for adults (≥18 years old) prescribed an antidepressant long-term (≥2 years) or short-term (<2 years), by NHS board for 2023/24 (Chart 2)

NHS Board	Long-term	Short-term
NHS Ayrshire & Arran	1.29	0.46
NHS Borders	1.35	0.49
NHS Dumfries & Galloway	1.31	0.47
NHS Fife	1.37	0.50
NHS Forth Valley	1.35	0.48
NHS Grampian	1.38	0.47
NHS Greater Glasgow & Clyde	1.37	0.46
NHS Highland	1.31	0.46
NHS Lanarkshire	1.36	0.47
NHS Lothian	1.35	0.73
NHS Orkney	1.30	0.50
NHS Shetland	1.27	0.49
NHS Tayside	1.33	0.47
NHS Western Isles	1.25	0.44
Scotland	1.35	0.51

Appendix 6. NTI Indicators

NTI: Adults (18 years and over) prescribed antidepressant medications long-term (two years and more), as a proportion of people in receipt of antidepressant medications (variants excluding tricyclics and showing tricyclics only)

An appropriate course of treatment for depression can be six months for the first episode of depression, or 12 or 24 months of treatment, depending on the number of depressive episodes and relapses. Long-term use is considered as more than two years of treatment and encompasses a growing number of people less likely to have their antidepressant reviewed, than those who have recently been initiated on treatment or receiving a shorter course. The longer an individual receives an antidepressant, the less frequently it, or the condition it is treating, is reviewed. For some they may be 'lost in the system' and inadvertently continue treatment that is no longer needed, and in others the antidepressant treatment may be ineffective or causing adverse effects.

Some prescribers may be less comfortable reviewing psychotropic medicines such as antidepressants, and may be apprehensive of reducing or stopping antidepressant therapy. This may be due to concerns about relapse or recurrence of illness, and/or antidepressant discontinuation/withdrawal symptoms, all of which may result in inappropriate long-term use where treatment is no longer required.

Reviewing people receiving the same antidepressant for two years or more can result in one in four people having a change in treatment, reduction, or stopping their antidepressants.

Actions:

- Health boards and prescribers to ensure appropriate use of antidepressants, considering licensed indications and duration of therapy
- The 'What matters to you' approach should assist the individual to achieve goals which have been identified and developed in partnership with clinicians.
- Access to and availability of non-pharmacological options, including psychosocial and/or psychological interventions, should be encouraged and pursued where appropriate
- Review effectiveness, tolerability and compliance on an ongoing basis
- Any reduction/stop should be gradual to minimise discontinuation effects
- Some individuals may be more sensitive to discontinuation than others
- Review and reduce dose every one to four weeks, or as guided by the individual's needs and/or preferences. See guidance for suggested dose reductions
- The 7-Steps review process should be used for all medication reviews

- Individuals can be identified using the Scottish Therapeutics Utility (STU) in GP practices.

Notes:

1. Age limited to 18 years and over due to licensing, however there may be some individuals under 18 years who are prescribed off-licence and should have regular follow-up by specialists. These individuals will not be identified in current STU searches.
2. In NTIs, two years or more treatment is assessed as those received more than 10 prescriptions in a 24-month period of the same antidepressant medication, with medicine issued at any point in the first three months and an issue in the last three months. It does not include anyone who may have changed antidepressant during that time. This is measured against the count of people prescribed an antidepressant at the midpoint of the last three months.
3. Antidepressants included are those in BNF legacy section 4.3, including tricyclic and related antidepressants, monoamine-oxidase inhibitors, SSRIs, other antidepressant drugs. Exclusions: injectables

NTI: All people prescribed an SSRI in combination with an antiplatelet, NSAID, DOAC or warfarin without gastro-protection, as a proportion of people prescribed an SSRI

Selective serotonin reuptake inhibitors (SSRIs) are associated with an increased risk of gastrointestinal bleed. This is further increased when they are used in combination with non-steroidal anti-inflammatory drugs (NSAIDs) and/or antiplatelets and/or direct oral anticoagulants (DOAC)/warfarin. These individuals should be prescribed gastro-protection such as proton pump inhibitors as advised in local and national guidelines.

This indicator should have a low value to ensure safe prescribing.

Actions:

- Health boards and prescribers to ensure appropriate use of SSRIs in conjunction other medication with may increase the risk of GI bleeds
- Reviewing people in this group will help to ensure appropriate use and help reduce avoidable adverse drug events and harms
- The 'What matters to you' approach should assist the individual to achieve goals which have been identified and developed in partnership with clinicians
- It is appropriate to ensure that there is an ongoing valid indication for all medication, as it may be more appropriate to stop the SSRI, rather than add PPI,

if the depression/anxiety has resolved. Any reduction/stop of SSRI should be gradual to minimise discontinuation effects

- If continued SSRI use is required, non-pharmacological options, including psychosocial and/or psychological interventions, should be encouraged and pursued where appropriate, e.g. regular physical activity, cognitive behavioural therapy
- Consider the use of NSAID and whether alternative analgesia, e.g. paracetamol, is more appropriate, or when required topical NSAID
- Ongoing need for SSRI and other medication will require appropriate gastro-protection such as proton pump inhibitors. Note the interaction between clopidogrel and omeprazole/esomeprazole, when selecting PPI
- Review effectiveness, tolerability and compliance on an ongoing basis
- The 7-Steps review process should be used for all medication reviews
- Individuals can be identified using the Scottish Therapeutics Utility (STU) in GP practices.

Notes:

NTI searches include:

- SSRI: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, but not dapoxetine as when required use and side effects do not list haemorrhage risk
- Aspirin 75mg considered as antiplatelet dosing
- NSAID preparations exclude those including misoprostol, omeprazole and esomeprazole

Exclusions: injectables

NTI: All people prescribed an antidepressant (all) in combination with a long-term benzodiazepine or z-drug (>8 weeks) as a proportion of people prescribed an antidepressant (BNF section 4.3)

Benzodiazepines and/or z-drugs (B-Z) are sometimes prescribed to treat:

- anxiety and/or insomnia symptoms prior to starting an antidepressant for depression or anxiety
- symptoms of poorly controlled depression, anxiety or back pain
- agitation, anxiety or insomnia symptoms associated with starting a selective serotonin reuptake inhibitor (SSRI)
- avoidable adverse drug effects such as insomnia and/or agitation caused by higher SSRIs doses

This can lead to regular long-term (≥8 weeks) B-Z use, sometimes lasting for years.

B-Z only demonstrate marginal benefits for short-term relief of insomnia and some anxiety disorders.

Long-term chronic use is:

- contrary to good practice, guidance, and terms of the licence
- known to worsen depressive symptoms, cause cognitive dysfunction and other avoidable adverse effects
- known to reduce the efficacy of some psychological therapies.

Therefore the prescribing of B-Z should generally be limited to short-term use with regular review.

There should be a low level of prescribing for this indicator.

Actions:

- Health boards and prescribers to ensure appropriate use of B-Z in conjunction with antidepressants; promoting person-centred reviews, and appropriate continuation, reduction and stopping of them
- The 'What matters to you' approach should assist the individual to achieve goals which have been identified and developed in partnership with clinicians.
- The long-term B-Z should be reviewed first.
  - where appropriate gradually withdraw using an agreed structured and planned reduction schedule
  - a small minority of individuals may require longer-term B-Z treatment with regular review to optimise care and minimise street/illicit B-Z use
- Non-pharmacological options, including psychosocial and/or psychological interventions, should be encouraged and pursued where appropriate, e.g. regular physical activity, cognitive behavioural therapy
- Any reduction/stop should be gradual to minimise discontinuation effects
- Review effectiveness, tolerability and compliance on an ongoing basis
- The 7-Steps review process should be used for all medication reviews
- Individuals can be identified using the Scottish Therapeutics Utility (STU) in GP practices.

Notes:

1. Formulations excluded from NTI: injectables, suppositories, enemas
2. For tools (NTI) using more than eight weeks avoids 56-day prescribing
3. BNF section 4.3 includes tricyclic and related antidepressants, monoamine-oxidase inhibitors, SSRIs, other antidepressant medication
4. This indicator may trigger individuals prescribed low dose amitriptyline which may be indicated for pain. However these individuals should still be reviewed due to the duration of the B-Z prescribing, especially if prescribed to manage symptoms associated with back pain

NTI: All people prescribed two or more antidepressant medications (excluding low dose nortriptyline 10mg/ amitriptyline 10mg and 25mg) per 1,000 list size

Using more than one antidepressant is not recommended.

- Combining an SSRI or serotonin and noradrenaline re-uptake inhibitor (SNRI) (e.g. venlafaxine) with mirtazapine is sometimes used by specialist services.
    - Non-specialist psychiatry prescribers should not initiate such antidepressant combinations, unless on the advice of specialists.
    - The potential benefits of such combinations are small and may be of questionable clinical value due to the variable response rates.
- Combining an SSRI/SNRI with low dose mirtazapine 15mg daily:
    - Is sometimes undertaken for its short-term sedating antihistamine effects (also seen with trazodone)
    - These additional antidepressants are possibly being used to treat SSRI/SNRI induced insomnia, agitation etc., and as alternative to B-Z.
    - This combination is of questionable benefit, and it may be more appropriate to reduce the dose of the SSRI/SNRI to minimise potential adverse effects and drug-related harms rather than adding extra psychotropics, especially as tolerance can quickly develop to the sedating effect of mirtazapine and trazodone.
- Neuropathic pain plus depression/anxiety treatment may require treatment with two antidepressants:
    - For example, a TCA (e.g. low dose amitriptyline 10mg/25mg or nortriptyline 10mg) for neuropathic pain and another antidepressant for depression, but not two TCAs.
    - Use should be reviewed regularly, considering interactions, adverse and synergistic effects, e.g. TCA dose related QTc interval prolongation, sedating effects.

Prescribing by specialist services can and does influence general practitioners prescribing.

This indicator should have a low percentage, indicating alignment with current best practice prescribing guidance.

Actions:

- Health boards and prescribers to ensure appropriate use of antidepressants, considering licensed indications, duration of therapy and combinations
- The 'What matters to you' approach should assist the individual to achieve goals which have been identified and developed in partnership with clinicians.
- Non-pharmacological options, including psychosocial and/or psychological interventions, should be encouraged and pursued where appropriate

- Review effectiveness, tolerability and compliance on an ongoing basis
- Any reduction/stop should be gradual to minimise discontinuation effects.
- In managing pain, it may be more appropriate to optimise the dose of one antidepressant or change to duloxetine to manage mood and pain. However the TCA or duloxetine may only be effective for one condition, and not the other. Individuals may not tolerate higher doses of TCAs, or duloxetine which can be more effective for treating depression
- Where mirtazapine was initiated to manage SSRI/SNRI induced insomnia or agitation, review dose of SSRI/SNRI with aim to reduce and then reduce and stop mirtazapine
- The 7-Steps review process should be used for all medication reviews.
- Individuals can be identified using the Scottish Therapeutics Utility (STU) in GP practices.

Notes:

1. Age limited to 18 years and over due to licensing, however there may be some individuals under 18 years who are prescribed off-licence and should have regular follow-up by specialists.
2. In NTIs, count of people dispensed at least two approved names from BNF section 4.3 in the first three months and at least two of the same approved names in the last three months of a six-month period. Note that there may be different strengths prescribed within the same approved (drug) name

Antidepressants included are those in BNF section 4.3, including tricyclic and related antidepressants, monoamine-oxidase inhibitors, SSRIs, other antidepressant drugs. Exclusions: injectables

NTI: Mental Health Triple Whammy – All people in receipt of three or more of benzo/ Z-drug, strong opioid (including tramadol), gabapentinoid, antidepressant, antipsychotics (excluding levomepromazine 6mg tabs or injections) per 1,000 list size

The combination of three or more of these medications increases the risks of medicine-related harm. Prescribers should consider the ‘benzo-burden’ – the total benzodiazepine-type drug load prescribed per day – as benzodiazepines, z-drugs and gabapentinoids have similar synergistic effects: sedation, respiratory depression, etc. These may interact with an individual’s conditions to cause more adverse effects and avoidable medicine-related harms e.g. increased breathlessness, fatigue, respiratory depression which can be potentially fatal.

- Opioids: the effects of B-Z and the ‘benzo-burden’ can be further be exacerbated by the addition of a range of opioids, and even reduce the protective ceiling

effects of buprenorphine. MHRA advice is only prescribe B-Z and opioids together if there is no alternative and closely monitor individuals for signs of respiratory depression.
- B-Z use with antipsychotics is associated with a higher mortality risk for people with schizophrenia.
- B-Z use with antidepressants: the use of SSRIs, and particularly high dose SSRIs for the treatment of depression. This may cause more avoidable adverse effects and harms such as anxiety, agitation and insomnia. However, B-Z are also associated with an increased incidence of depressive symptoms, so reviewing and reducing B-Z use may help to optimise care and recovery.

People who report/present with street/non-prescribed B-Z use, often set within the context of polysubstance use, are arguably at greatest risk of combination effects.

This indicator should have a high percentage, indicating alignment with current best practice prescribing guidance.

Actions:

- Health boards and prescribers to ensure appropriate use of B-Z in conjunction with other medication; promoting person-centred reviews, and appropriate continuation, reduction and stopping
- The 'What matters to you' approach should assist the individual to achieve goals which have been identified and developed in partnership with clinicians
- The long-term B-Z should be reviewed.
    - where appropriate gradually withdraw using an agreed structured and planned reduction schedule
    - a small minority of individuals may require longer-term B-Z treatment with regular review to optimise care and minimise street/illicit B-Z use
- Consider pain management and ensure valid indication for analgesia, e.g. neuropathic pain, nociceptive pain. If no ongoing indication for opioid or gabapentinoids, reduce gradually to prevent withdrawal
- Review duration of treatment for depression, and if ongoing need. If none, reduce gradually to prevent discontinuation effects
- Non-pharmacological options, including psychosocial and/or psychological interventions, should be encouraged and pursued where appropriate, e.g. regular physical activity, cognitive behavioural therapy
- Review effectiveness, tolerability and compliance on an ongoing basis
- The 7-Steps review process should be used for all medication reviews
- The Scottish Drug Deaths Taskforce and Public Health Scotland's: Medication Assisted Treatment (MAT) standards informed response for benzodiazepine harm reduction guidance:
    - highlights that everyone has a responsibility to respond to B-Z related harms and to have supportive, collaborative conversations regarding B-Z

    - supports a comprehensive, holistic assessment of need to develop a psychological formulation of the presenting issues to inform highly intensive, flexible and individualised care plans
    - supports addition of psychological components of care, to support harm reduction and stabilisation
- Individuals can be identified using the Scottish Therapeutics Utility (STU) in GP practices

Notes

1. Levomepromazine not included as generally used in palliative care.
2. Opioids include: buprenorphine, fentanyl, morphine, oxycodone (with/without naloxone), pentazocine, tapentadol, hydromorphone, pethidine, methadone, tramadol (with/without paracetamol)
3. Benzodiazepines and z-drugs include: Diazepam, Chlordiazepoxide, clonazepam, loprazolam, lorazepam, lormetazepam, oxazepam, nitrazepam, temazepam, alprazolam, clobazam, flurazepam, zolpidem, zopiclone, zaleplon

Formulations excluded: injectables (B-Z and opiate pain medicines), suppositories and enemas (benzodiazepines).

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