Title

Impact of a comprehensive intervention bundle including the Drug Burden Index on deprescribing anticholinergic and sedative drugs in older acute inpatients: a non-randomised controlled before and after pilot study

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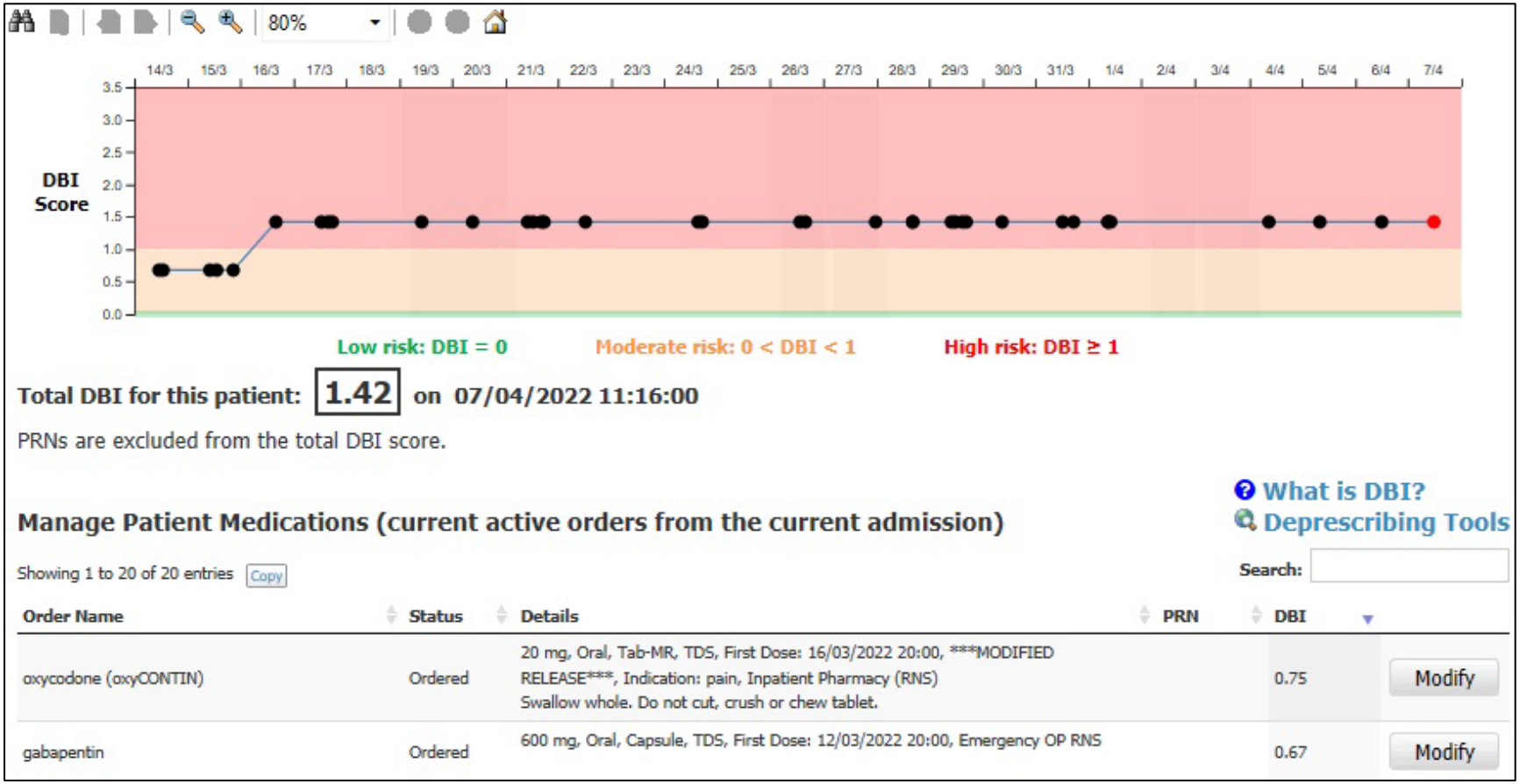
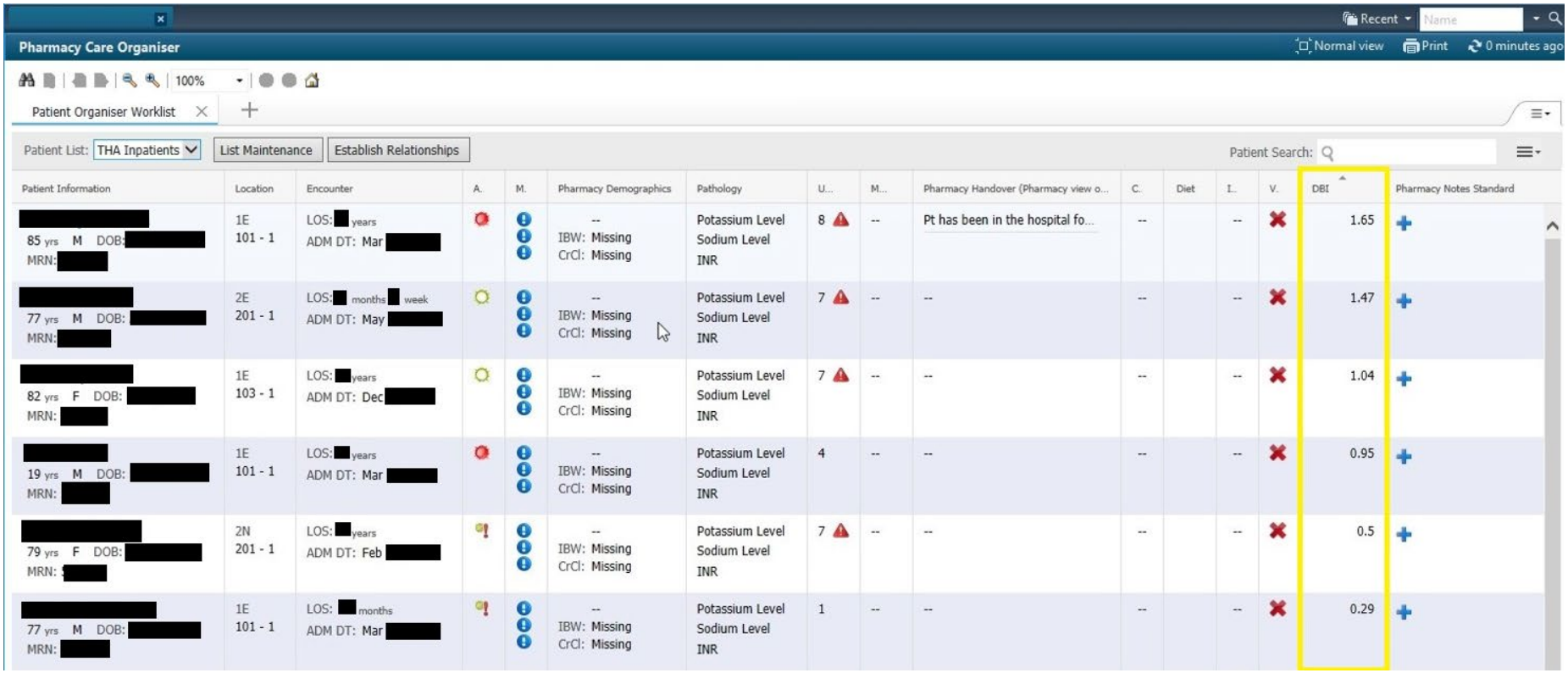
Appendix 1. Snapshot of the Drug Burden Index clinician interface in Electronic Medical Records



Appendix 2. Snapshot of the pharmacy patient list in Electronic Medical Records



Appendix 3. Hypothetical case demonstrating the stewardship process to identify and recommend deprescribing opportunities

Background

Mrs AB, who is a 78-year-old female living with daughter, presents with a fall and confusion.

Past Medical History	**Medications on admission**
Cardiac Ischaemic heart disease Hypertension Hypercholesterolaemia	 Ramipril 10mg night Amlodipine 10mg morning Rosuvastatin 20mg night Aspirin 100mg morning
Musculoskeletal Osteoporosis	Alendronate/ colecalciferol 70mg/ 70 microg weekly on Friday
Osteoarthritis- total knee replacement	Paracetamol SR 1330mg three times daily
Gastrointestinal Gastro-oesophageal reflux disease	Pantoprazole 40mg morning
Psychological Depression	Sertraline 100mg morning Temazepam 10mg night
Geriatric syndromes 10 falls in the last year	Oxycodone 5mg every 4-6 hourly as needed, with maximum 20mg per day (newly commenced in hospital for pain)

Drug allergies or intolerances

Penicillin- rash

DBI on admission

Sertraline 0.67
Temazepam 0.50
Oxycodone as needed > 0
Total DBI> 1.17

Management and progress

The patient is admitted under Geriatric Medicine. Upon questioning, the patient and daughter state that Mrs AB lost her balance and fell forwards, hitting her elbow. She is in pain and an elbow X-ray shows a right distal humerus fracture. The Orthopaedics team is consulted, with decision made to undertake Open Reduction and Internal Fixation surgery, whilst withholding the aspirin.

When screening for potential contributors to her presenting complaint, causes such as infections were ruled out. The blood test results show mild hyponatraemia.

Stewardship process

1. ***Identifying patients eligible for stewardship pharmacist review***

The Pharmacy Patient List flags Mrs AB as having a DBI score greater than zero on admission, warranting medication review by the stewardship pharmacist.

2. ***Identifying opportunities for deprescribing in eligible patients***

The stewardship pharmacist looks at the DBI Clinician Interface in the electronic Medical Records (eMR), which shows DBI-contributing medicines and their contributions to the DBI score. The stewardship pharmacist assesses current indication/ benefit for each of these drugs against any potential adverse effects they are causing. Of the three DBI-contributing medicines, the patient was taking sertraline and temazepam pre-admission. When assessing any potential adverse effects or outcomes from these medicines, sertraline may be contributing to falls, hyponatraemia and confusion, which are listed as triggers for deprescribing in the 'Deprescribing Guide for Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Noradrenaline Reuptake Inhibitors (SNRIs)' as shown in Figure 1.

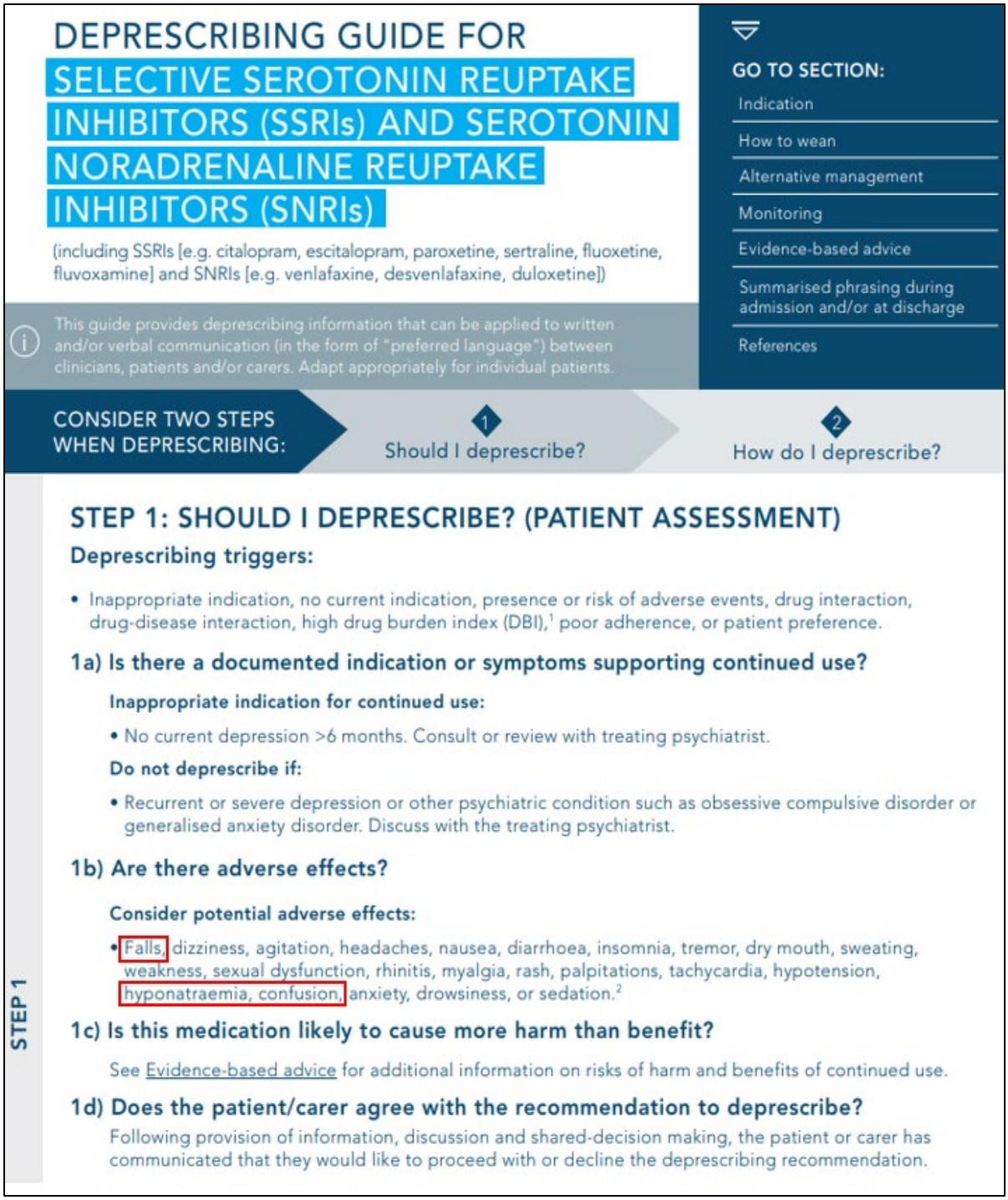
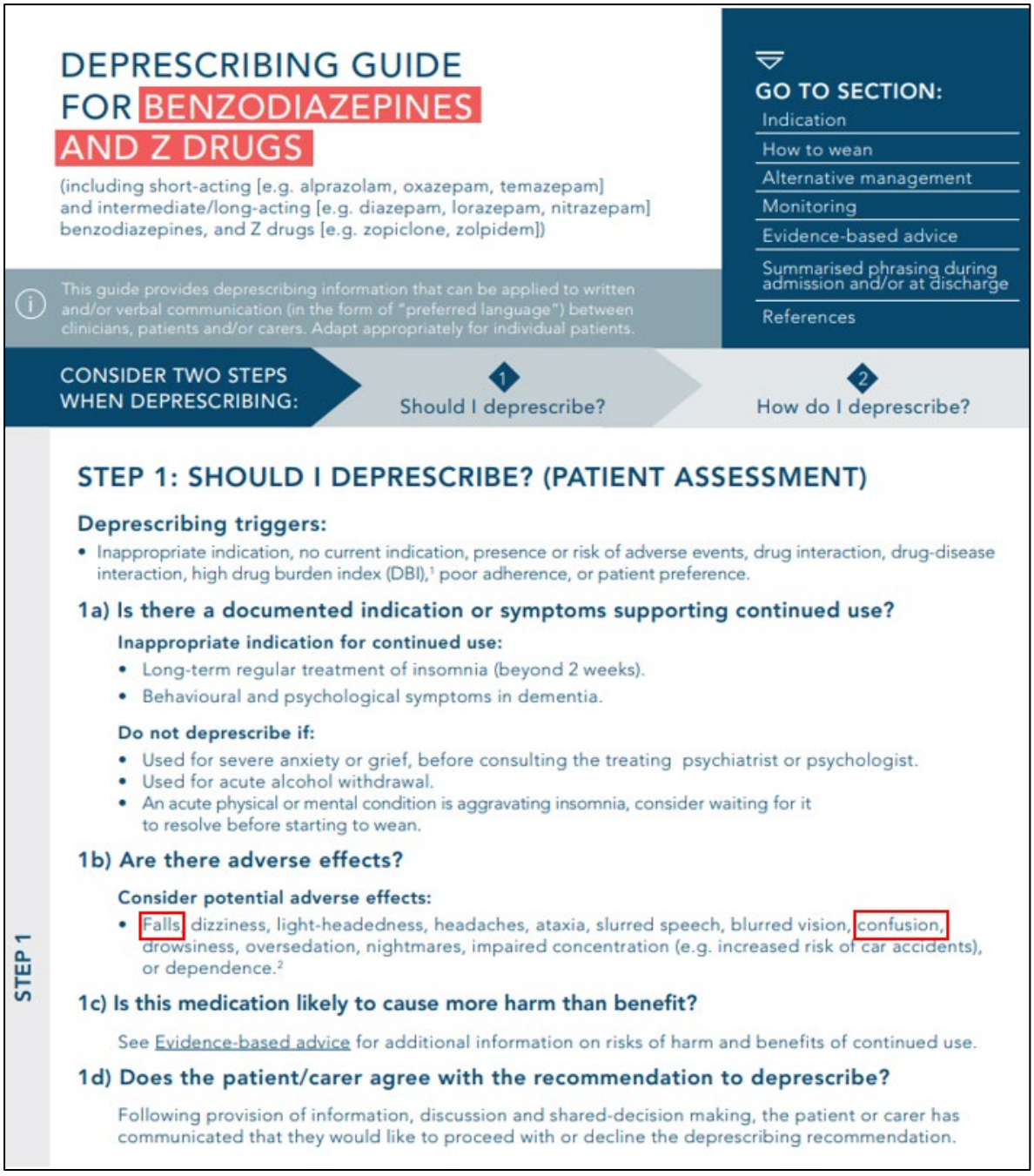


Figure 1. Triggers for deprescribing Selective Serotonin Reuptake Inhibitors and Serotonin Noradrenaline Reuptake Inhibitors as per the deprescribing guide

Temazepam may also be contributing to falls and confusion, which are listed as triggers for deprescribing in the 'Deprescribing Guide for Benzodiazepines and Z Drugs' as shown in Figure 2.



DEPRESCRIBING GUIDE FOR BENZODIAZEPINES AND Z DRUGS

(including short-acting [e.g. alprazolam, oxazepam, temazepam] and intermediate/long-acting [e.g. diazepam, lorazepam, nitrazepam] benzodiazepines, and Z drugs [e.g. zopiclone, zolpidem])

GO TO SECTION:
Indication
How to wean
Alternative management
Monitoring
Evidence-based advice
Summarised phrasing during admission and/or at discharge
References

This guide provides deprescribing information that can be applied to written and/or verbal communication (in the form of "preferred language") between clinicians, patients and/or carers. Adapt appropriately for individual patients.

CONSIDER TWO STEPS WHEN DEPRESCRIBING:
1 Should I deprescribe?
2 How do I deprescribe?

STEP 1

STEP 1: SHOULD I DEPRESCRIBE? (PATIENT ASSESSMENT)

Deprescribing triggers:
- Inappropriate indication, no current indication, presence or risk of adverse events, drug interaction, drug-disease interaction, high drug burden index (DBI),[1] poor adherence, or patient preference.

1a) Is there a documented indication or symptoms supporting continued use?

Inappropriate indication for continued use:
- Long-term regular treatment of insomnia (beyond 2 weeks).
- Behavioural and psychological symptoms in dementia.

Do not deprescribe if:
- Used for severe anxiety or grief, before consulting the treating psychiatrist or psychologist.
- Used for acute alcohol withdrawal.
- An acute physical or mental condition is aggravating insomnia, consider waiting for it to resolve before starting to wean.

1b) Are there adverse effects?

Consider potential adverse effects:
- Falls dizziness, light-headedness, headaches, ataxia, slurred speech, blurred vision, confusion, drowsiness, oversedation, nightmares, impaired concentration (e.g. increased risk of car accidents), or dependence.[2]

1c) Is this medication likely to cause more harm than benefit?

See Evidence-based advice for additional information on risks of harm and benefits of continued use.

1d) Does the patient/carer agree with the recommendation to deprescribe?

Following provision of information, discussion and shared-decision making, the patient or carer has communicated that they would like to proceed with or decline the deprescribing recommendation.

Figure 2. Triggers for deprescribing Benzodiazepines and Z Drugs as per the deprescribing guide

Upon searching the eMR, there is no additional history documented regarding these medicines, including any prior attempts to deprescribe.

Given oxycodone has a current indication, it is not shortlisted as a potential opportunity for deprescribing at the time but a deprescribing target for the future, once pain settles.

3. ***Exploring possible deprescribing opportunities with different medication management stakeholders***

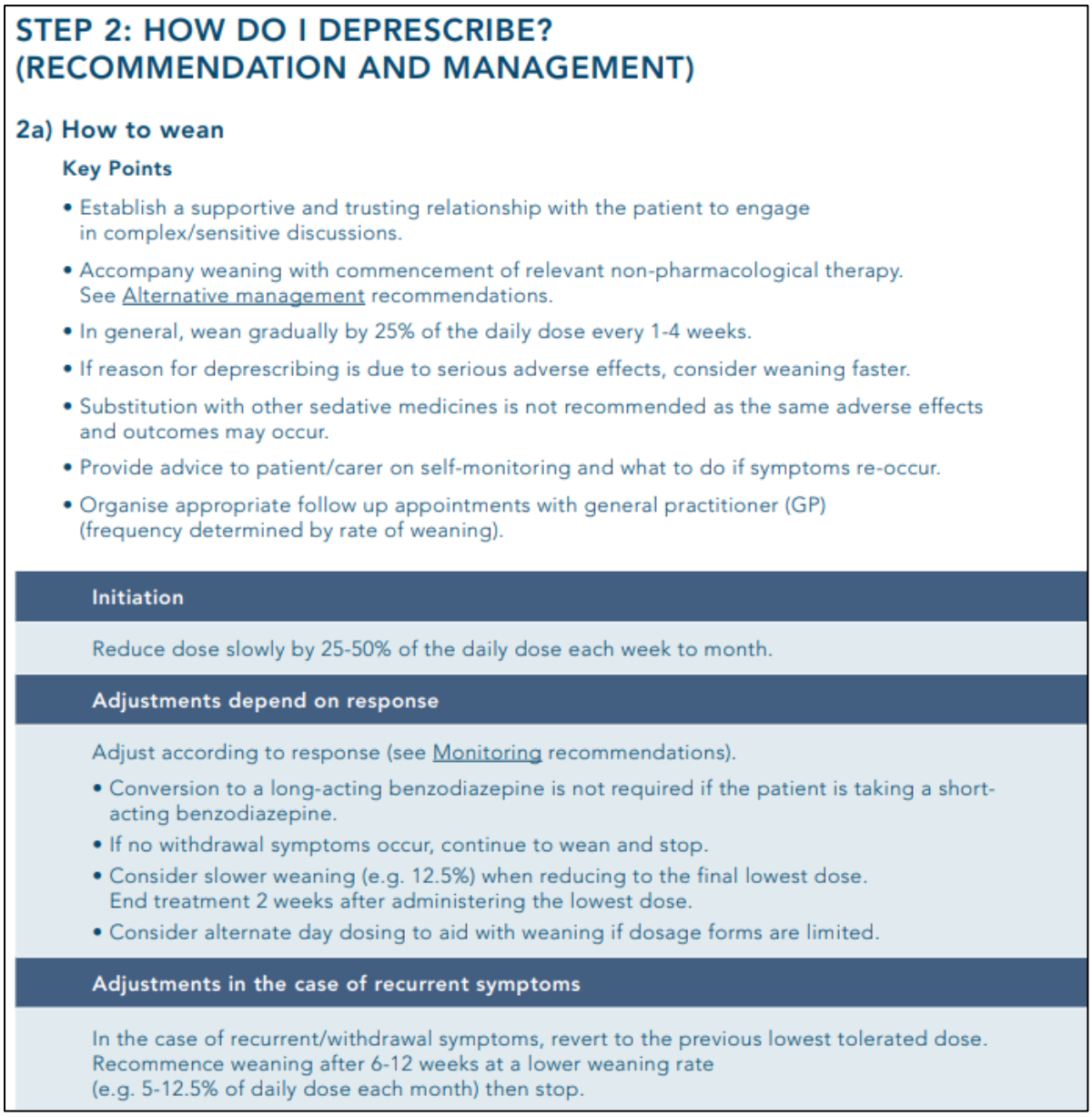
Given sertraline and temazepam may be causing adverse effects and outcomes, the stewardship pharmacist flags these as potential deprescribing opportunities to the hospital medical team, supporting these recommendations using the deprescribing guides. The medical team agrees to explore these deprescribing opportunities by firstly contacting the usual prescriber, who in this case, is the General

Practitioner (GP). The GP states that the patient was started on these six years ago, when there were significant stressors in her life, including the death of her husband, leading to depression and difficulty sleeping. However, depression and difficulty sleeping have not been active issues since then and in the context of falls and confusion, the GP agrees to trial deprescribing, with the consensus that there should be one deprescribing change at a time. Upon further discussion with the patient and her daughter, they agree to deprescribing of both these drugs, expressing preference to start deprescribing temazepam in hospital and sertraline post-discharge, once the patient is home.

With regards to the oxycodone, the medical team agrees to include a recommendation in the Discharge Summary for the GP to wean, once pain settles.

4. ***Actioning deprescribing opportunities and communication at discharge***

The stewardship pharmacist advises the medical team to reduce the dose of temazepam, monitor for any withdrawal effects and trial non-pharmacological measures, as per the deprescribing guide. A snapshot of the section on how to deprescribe in shown as an example in Figure 3.



STEP 2: HOW DO I DEPRESCRIBE? (RECOMMENDATION AND MANAGEMENT)

2a) How to wean

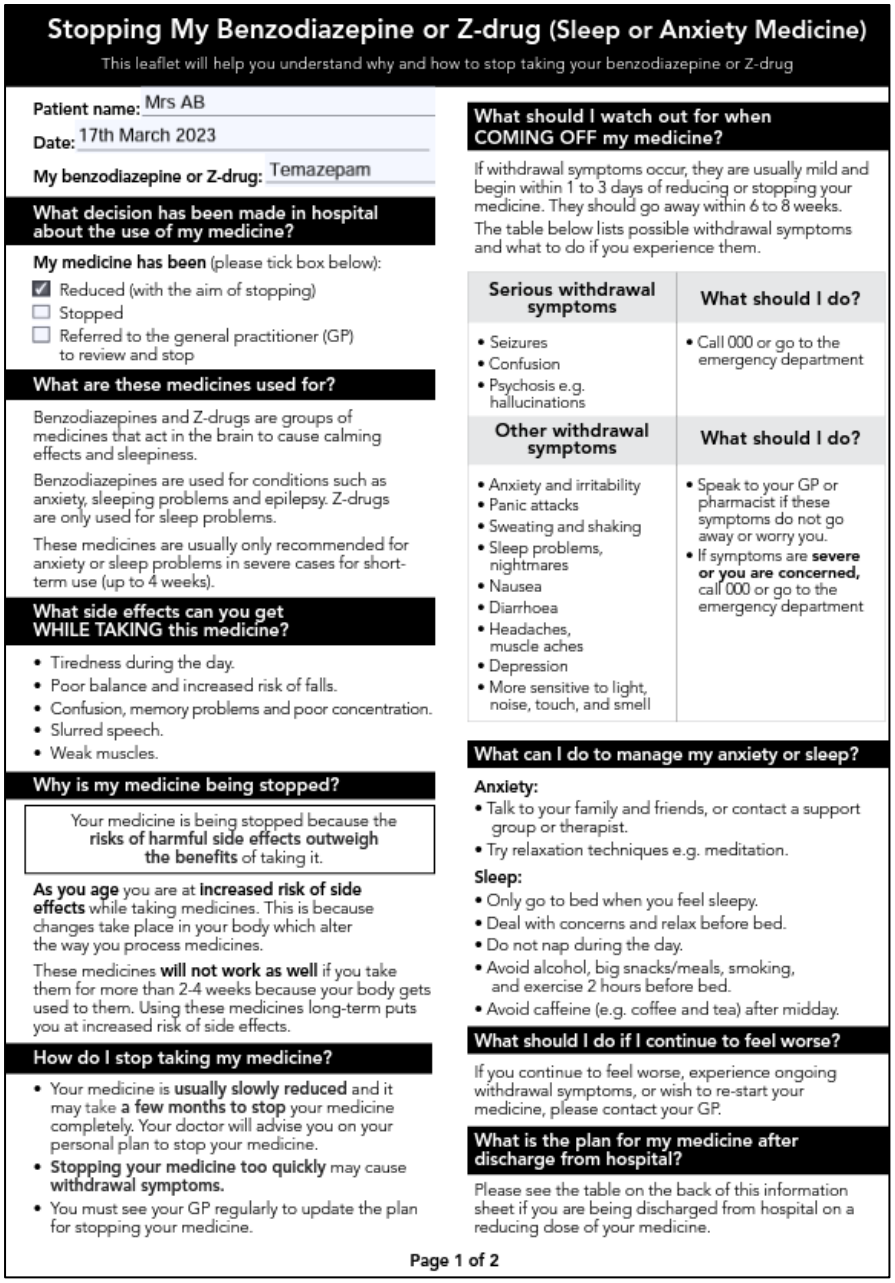
Key Points

- Establish a supportive and trusting relationship with the patient to engage in complex/sensitive discussions.
- Accompany weaning with commencement of relevant non-pharmacological therapy. See Alternative management recommendations.
- In general, wean gradually by 25% of the daily dose every 1-4 weeks.
- If reason for deprescribing is due to serious adverse effects, consider weaning faster.
- Substitution with other sedative medicines is not recommended as the same adverse effects and outcomes may occur.
- Provide advice to patient/carer on self-monitoring and what to do if symptoms re-occur.
- Organise appropriate follow up appointments with general practitioner (GP) (frequency determined by rate of weaning).

Initiation
Reduce dose slowly by 25-50% of the daily dose each week to month.
Adjustments depend on response
Adjust according to response (see Monitoring recommendations). • Conversion to a long-acting benzodiazepine is not required if the patient is taking a short-acting benzodiazepine. • If no withdrawal symptoms occur, continue to wean and stop. • Consider slower weaning (e.g. 12.5%) when reducing to the final lowest dose. End treatment 2 weeks after administering the lowest dose. • Consider alternate day dosing to aid with weaning if dosage forms are limited.
Adjustments in the case of recurrent symptoms
In the case of recurrent/withdrawal symptoms, revert to the previous lowest tolerated dose. Recommence weaning after 6-12 weeks at a lower weaning rate (e.g. 5-12.5% of daily dose each month) then stop.

Figure 3. How to deprescribe a Benzodiazepine and Z Drug as per the deprescribing guide

The stewardship pharmacist also advises the medical team and ward pharmacist to go through the Consumer Information Leaflet called 'Stopping My Benzodiazepine or Z drug (Sleep or Anxiety Medicine)' with the patient and daughter, including discussion of potential withdrawal symptoms. The first page of this leaflet is as shown as an example in Figure 4.



Stopping My Benzodiazepine or Z-drug (Sleep or Anxiety Medicine)

This leaflet will help you understand why and how to stop taking your benzodiazepine or Z-drug

Patient name: Mrs AB
Date: 17th March 2023
My benzodiazepine or Z-drug: Temazepam

What decision has been made in hospital about the use of my medicine?

My medicine has been (please tick box below):

- [x] Reduced (with the aim of stopping)
- [ ] Stopped
- [ ] Referred to the general practitioner (GP) to review and stop

What are these medicines used for?

Benzodiazepines and Z-drugs are groups of medicines that act in the brain to cause calming effects and sleepiness.

Benzodiazepines are used for conditions such as anxiety, sleeping problems and epilepsy. Z-drugs are only used for sleep problems.

These medicines are usually only recommended for anxiety or sleep problems in severe cases for short-term use (up to 4 weeks).

What side effects can you get WHILE TAKING this medicine?

- Tiredness during the day.
- Poor balance and increased risk of falls.
- Confusion, memory problems and poor concentration.
- Slurred speech.
- Weak muscles.

Why is my medicine being stopped?

Your medicine is being stopped because the **risks of harmful side effects outweigh the benefits** of taking it.

As you age you are at **increased risk of side effects** while taking medicines. This is because changes take place in your body which alter the way you process medicines.

These medicines **will not work as well** if you take them for more than 2-4 weeks because your body gets used to them. Using these medicines long-term puts you at increased risk of side effects.

How do I stop taking my medicine?

- Your medicine is **usually slowly reduced** and it may take **a few months to stop** your medicine completely. Your doctor will advise you on your personal plan to stop your medicine.
- **Stopping your medicine too quickly** may cause **withdrawal symptoms.**
- You must see your GP regularly to update the plan for stopping your medicine.

What should I watch out for when COMING OFF my medicine?

If withdrawal symptoms occur, they are usually mild and begin within 1 to 3 days of reducing or stopping your medicine. They should go away within 6 to 8 weeks.

The table below lists possible withdrawal symptoms and what to do if you experience them.

Serious withdrawal symptoms	What should I do?
• Seizures • Confusion • Psychosis e.g. hallucinations	• Call 000 or go to the emergency department
Other withdrawal symptoms	**What should I do?**
• Anxiety and irritability • Panic attacks • Sweating and shaking • Sleep problems, nightmares • Nausea • Diarrhoea • Headaches, muscle aches • Depression • More sensitive to light, noise, touch, and smell	• Speak to your GP or pharmacist if these symptoms do not go away or worry you. • If symptoms are **severe or you are concerned,** call 000 or go to the emergency department

What can I do to manage my anxiety or sleep?

Anxiety:

- Talk to your family and friends, or contact a support group or therapist.
- Try relaxation techniques e.g. meditation.

Sleep:

- Only go to bed when you feel sleepy.
- Deal with concerns and relax before bed.
- Do not nap during the day.
- Avoid alcohol, big snacks/meals, smoking, and exercise 2 hours before bed.
- Avoid caffeine (e.g. coffee and tea) after midday.

What should I do if I continue to feel worse?

If you continue to feel worse, experience ongoing withdrawal symptoms, or wish to re-start your medicine, please contact your GP.

What is the plan for my medicine after discharge from hospital?

Please see the table on the back of this information sheet if you are being discharged from hospital on a reducing dose of your medicine.

Figure 4. Consumer Information Leaflet on deprescribing a Benzodiazepine or Z Drug

The deprescribing change in hospital (temazepam) and further recommendations for deprescribing (temazepam, sertraline and oxycodone) are summarised by the medical team in the Discharge Summary using the deprescribing communication templates included in the deprescribing guides. The communication template for benzodiazepines is shown as an example in Figure 5.

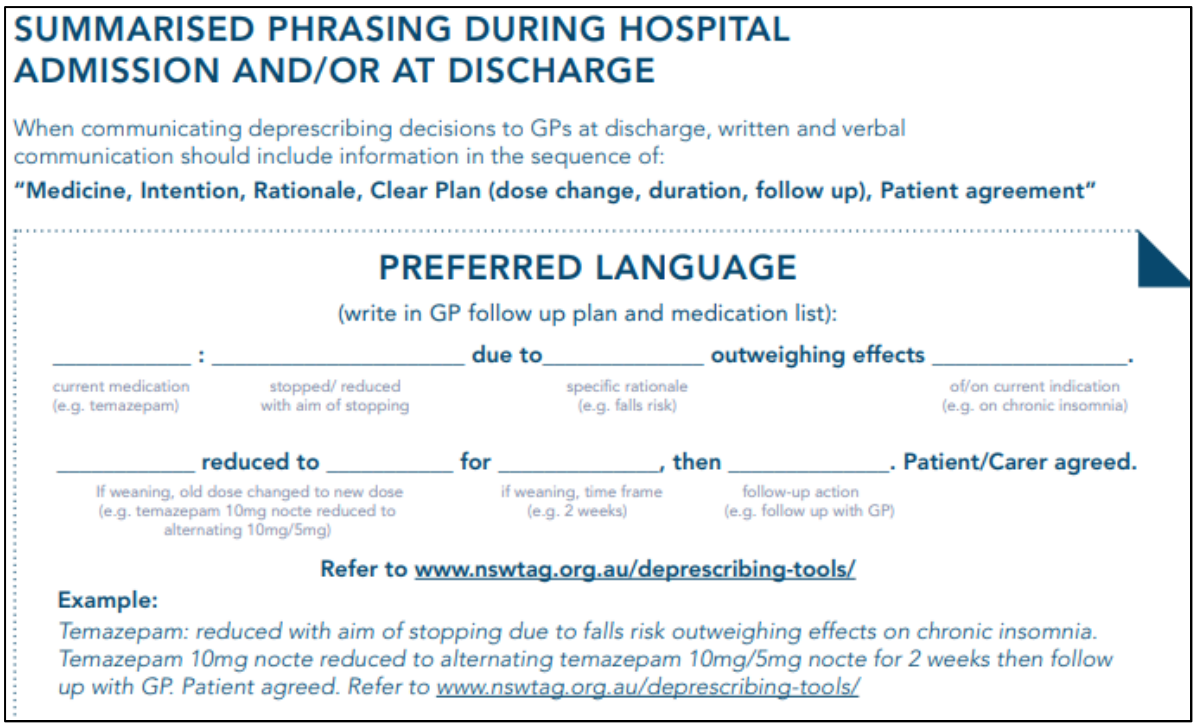


Figure 5. Communicating Benzodiazepine and Z Drug deprescribing with the General Practitioner at discharge

The links to the relevant deprescribing guides are additionally included in the Discharge Summary for the GP.

Discharge Plan

1. Discharge home from hospital, with subsequent follow-up with the GP
2. Temazepam dose has been reduced due to falls and confusion, outweighing effects on difficulty sleeping, which is no longer an active issue. Upon discussion with the GP, patient and her daughter, temazepam 10mg was reduced to 7.5mg for 2 weeks and then for follow-up with the GP. If appropriate, to continue weaning as per the deprescribing guide below: https://www.nswtag.org.au/wp-content/uploads/2018/06/1.1-Deprescribing-Guide-for-Benzodiazepines-and-Z-Drugs.pdf
3. Sertraline is recommended for weaning due to the adverse effects of falls, hyponatraemia and confusion, outweighing effects on depression, which is no longer an active issue. Upon discussion with the GP, patient and her daughter, suggest GP to initially reduce dose post-discharge from 100mg to 75mg for 2 weeks and then for follow-up. If appropriate, to continue weaning as per the deprescribing guide below: https://www.nswtag.org.au/wp-content/uploads/2018/06/1.3-Deprescribing-Guide-for-Selective-Serotonin-Reuptake-Inhibitors-SSRIs-and-Serotonin-Noradrenaline-Reuptake-Inhibitors-SNRIs.pdf
4. Oxycodone has been commenced newly in hospital for acute pain. Due to falls and confusion and the potential for other adverse effects, suggest GP to review ongoing use, monitor pain and consider weaning once pain settles.

Medications at discharge

Ramipril 10mg night
Amlodipine 10mg morning
Rosuvastatin 20mg night
Aspirin 100mg morning

Alendronate/ colecalciferol 70mg/ 70 microg weekly on Friday
Calcium 500mg midday (NEW)
Sertraline 100mg morning (RECOMMENDED TO WEAN)
Temazepam 7.5mg night (RECOMMENDED TO FURTHER WEAN)
Pantoprazole 40mg morning
Paracetamol SR 1330mg three times daily
Oxycodone 5mg every 4-6 hourly as needed, with maximum 20mg per day (NEW, RECOMMENDED TO WEAN)

DBI at discharge

Sertraline 0.67
Temazepam 0.43
Oxycodone as needed > 0
Total DBI> 1.10

Appendix 4. Sensitivity analysis that included patients in the transition periods as separate categories

Analysis	Control	Transition (from Control to Intervention)	Intervention	Transition (from Intervention to Stewardship)	Stewardship
Crude DBI reduction	29.9% (43/144)	22.7% (5/22)	37.5% (66/176)	50.0% (9/18)	43.1% (59/137)
Adjusted DBI reduction†	31.4% [24.6, 38.4]	17.2% [5.1, 32.2]	37.8% [30.7, 45.0]	41.3% [20.5, 67.3]	43.3% [35.0, 51.5]
Adjusted risk difference†	Reference	-14.2% [-28.1, 1.9]	6.5% [-3.7, 16.8]	9.9% [-11.9, 35.3]	11.9% [1.2, 22.2]
NNT	Reference	NS	NS	NS	9

Abbreviation: DBI, Drug Burden Index; NNT, number needed to treat, NS: adjusted risk difference not statistically significant, †: age, sex, length of stay and the number of DBI-contributing medications at admission were adjusted.

Appendix 5. Sensitivity analysis that included patients in the transition periods into the precedent period

Analysis	Control + Transition (from Control to Intervention)	Intervention + Transition (from Intervention to Stewardship)	Stewardship
Crude DBI reduction	28.9% (48/166)	38.7% (75/194)	43.1% (59/137)
Adjusted DBI reduction†	29.2% [22.4, 36.1]	38.2% [31.4, 45.3]	43.3% [35.4, 51.1]
Adjusted risk difference†	Reference	9.0% [-0.7, 18.5]	14.0% [3.7, 25.0]
NNT	Reference	NS	8

Abbreviation: DBI, Drug Burden Index; NNT, number needed to treat, NS: adjusted risk difference not statistically significant, †: age, sex, length of stay and the number of DBI-contributing medications at admission were adjusted.

Appendix 6. Sensitivity analysis that included patients in the transition periods into the antecedent period

Analysis	Control	Transition (from Control to Intervention) + Intervention	Transition (from Intervention to Stewardship) + Stewardship
Crude DBI reduction	29.9% (43/144)	35.9% (71/198)	43.9 (68/155)
Adjusted DBI reduction†	31.3% [24.0, 39.0]	35.3% [29.1, 42.0]	43.1% [35.4, 50.4]
Adjusted risk difference†	Reference	4.1% [-6.6, 13.3]	11.9% [0.6, 22.6]
NNT	Reference	NS	9

Abbreviation: DBI, Drug Burden Index; NNT, number needed to treat, NS: adjusted risk difference not statistically significant, †: age, sex, length of stay and the number of DBI-contributing medications at admission were adjusted.