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INTEGRATING ON-SITE PHARMACISTS INTO RESIDENTIAL AGED CARE FACILITIES

ON-SITE PHARMACIST'S **TOOLKIT**

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The University of Canberra acknowledges the Ngunnawal people, traditional custodians of the lands where Bruce Campus is situated. We wish to acknowledge and respect their continuing culture and the contribution they make to the life of Canberra and the region. We also acknowledge all other First Nations Peoples on whose lands we gather.

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CONTENTS

USING THE ON-SITE PHARMACIST'S **TOOLKIT**

This Toolkit provides practical information and guidance for on-site pharmacists working in residential aged care facilities (RACFs) which aim to improve the quality use of medicines. It contains:

- core activities of the on-site pharmacist, along with recommended targets
- suggestions for building collaborative relationships between the on-site pharmacist, RACF residents, families and carers, staff, GPs and health care professionals and integration of the role into the RACF
- an orientation checklist to support the implementation the on-site pharmacist role
- resources including lists of Potentially Inappropriate Medications, deprescribing guides for psychotropics, and an anticholinergic burden therapeutic brief.

ON-SITE PHARMACIST'S CLINICAL NOTES

(see separate resource)

Contains forms and templates to assist with workflow management and record-keeping while performing the role as an on-site pharmacist. Use them in conjunction with this Toolkit.

RESIDENTIAL AGED CARE FACILITY'S HANDBOOK

(see separate resource)

Provides practical information and guidance for residential aged care facilities (RACFs) to integrate an on-site pharmacist into their facility.

SECTION 1. ABOUT THE ON-SITE PHARMACIST MODEL OF CARE

The on-site pharmacist in residential aged care model is a new model of care where a qualified pharmacist, employed by the RACF, works with residents, families, carers, facility staff, GPs and other health care professionals to improve medication management. The pharmacist's expertise in medication management, pharmacotherapy, monitoring, and care coordination complements the skills of other health care professionals, and their integration into the interdisciplinary care teams in RACFs assists to achieve resident-specific and facility-level goals across the care continuum.

The model was developed by the University of Canberra (UC) and tested in a pilot study in 2017, followed by a cluster Randomised Controlled Trial and an implementation study the *Pharmacist in Residential Aged Care Facilities (PiRACF) study* conducted from 2020–23.[1] The aim is to improve outcomes for residents and facilities by enhancing medication management and the quality use of medicines.

1 Kosari S, Naunton M, Koerner J, Lancsar E, Munira L, Haider I, Batten M, Dale M, Davey, R and the Study Team. (2022) Pharmacists in Residential Aged Care Facilities (PiRACF) Study — Final Evaluation Report. University of Canberra, Canberra.

The on-site pharmacist's role and activities

The on-site pharmacists conduct activities that are within their scope of practice as an Australian health care professional registered with Australian Health Professional Registered Agency.

On-site pharmacist's activities include, but are not limited to:

- conducting clinical audits of resident's medication charts to identify residents at high-risk of medication related harms. Examples include Potentially Inappropriate Medications (PIMs) and other high-risk medications, such as psychotropic medicines, opioids, and antibiotics
- conducting medication reviews, where an on-site pharmacist reviews resident's medications at any time required, including following a clinical audit or at transitions of care, such as when a resident enters the facility, returns from hospital, is diagnosed with a new condition or is referred to palliative care
- providing ad-hoc and regular education to RACF staff about medication management through individual and group education sessions, including training and assessment of medication administration competencies
- discussing resident's medication management with residents, families, carers and RACF staff
- reconciling resident's medications at transition of care, to ensure new medication regimes are correctly updated and that the resident and staff are aware of changes
- optimising the process of administering medicines during medication rounds to improve efficiencies and reduce time spent
- improving residents' clinical documentation to ensure allergies and diagnoses are up to date
- participating in residents' case conferences (multidisciplinary case conferences with GPs, residents, families, RACF staff, and other health care professionals)
- liaising with GPs and prescribers and other health care professionals including community and hospital pharmacists, occupational and speech therapists, dietitians, nurse practitioners, geriatricians, and specialists to improve resident's medication management
- reviewing medication incidents and taking appropriate quality improvement actions
- developing and updating RACF medication management policies and procedures in RACFs such as medication storage, disposal of medicines, and psychotropic medicines reporting
- vaccination and coordinating vaccinations of residents and staff against influenza and COVID-19 (as per state and territory legislation)
- undertaking professional development.

The benefits of the on-site pharmacist model of care

The on-site pharmacist model of care, evaluated in the PiRACF study, has been found to improve medication management in RACF settings including reduction in the proportion of residents prescribed PIMs, anti-cholinergic burden of medicines prescribed, and dose of antipsychotic medicines prescribed. The study is supported by funding from the ACT Primary Health Network through the Australian Government's Primary Health Network Program. The model also established positive collaborative relationships between on-site pharmacists, RACF staff and GPs and was shown to potentially became a part of routine practice and normalised in RACFs.[2]

2 Kosari S, Naunton M, Koerner J, Lancsar E, Munira L, Haider I, Batten M, Dale M, Davey, R and the Study Team. (2022) Pharmacists in Residential Aged Care Facilities (PiRACF) Study — Final Evaluation Report. University of Canberra, Canberra.

SECTION 2. ENSURING QUALITY MEDICATION MANAGEMENT

The primary objective of the on-site pharmacist model of care is to support the quality use of medicine through reduction of PIMs and improvements in medication management.

2.1 THE REDUCTION OF PIMS

PIMs are medications with risk of adverse health outcomes. The use of PIMs among residents in aged care facilities is widespread, with a systematic review estimating a median prevalence of 46.5% to 61.1% of all residents.[3] Another study in an Australian RACF reported an exceptionally high 81.4% of all residents being on at least one PIM.[4]

The use of PIMs has been associated with significant adverse drug events for older individuals including hospitalisations, falls, fractures, cognitive decline, delirium, stroke, cardiovascular events and death, as well as higher medical costs.[5]

2.1.1 Detecting PIMs using the Beers Criteria

The Beers Criteria is a validated tool used to assess PIMs among adults aged 65 years or over. The Beers Criteria were developed by the American Geriatrics Society, based on systematic reviews of evidence and expertise consensus, and modified for the purpose of the on-site pharmacist model of care to fit the Australian setting (i.e. including medications that are only available in Australia and excluding those that are not).

The Beers Criteria consist of three main tables to determine the appropriateness of medications used in older people under certain conditions.[6] A summary of these, modified for the Australian context, appears in **Table 6.1** to **Table 6.3** (in **Section 6** at the end of this Toolkit) and may be used as a quick reference when undertaking medication reviews.

2.2 INAPPROPRIATE USE OF PSYCHOTROPIC MEDICATIONS

Inappropriate use of psychotropic drugs in aged care has been highlighted by the Aged Care Quality and Safety Commission.[7] Psychotropic drugs are classified as any drug capable of affecting a person's mind, emotion or behaviour. The common types of psychotropic drugs include antidepressants, anxiolytics/hypnotics, antipsychotics and in some cases, anticonvulsants and stimulants. These drugs can be used appropriately when they are prescribed based on a confirmed diagnosis, used at the right dose, for the right duration of time and with proper monitoring and assessment. If at least one element (of indication, dose, duration, monitoring and assessment) is missing, the medication could be defined as a potentially inappropriate psychotropic. Examples include high doses of sedative antidepressants, antihistamines or anticonvulsants without an appropriate related diagnosis.

Table 6.4 (in **Section 6** at the end of this Toolkit) lists psychotropics that could potentially be prescribed inappropriately (excluding for residents who have psychiatric conditions such as bipolar disorder or schizophrenia). **Section 6** also contains general information about deprescribing psychotropic medications.

3 Storms H, Marquet K, Aertgeerts B, Claes N. Prevalence of inappropriate medication use in residential long-term care facilities for the elderly: A systematic review. European Journal of General Practice. 2017;23:69e77. doi: 10.1080/13814788.2017.1288211

4 Harrison SL, Kouladjian O'Donnell L, Milte R, Dyer SM, Gnanamanickam ES, Bradley C, Liu E, Hilmer SN, Crotty M. Costs of potentially inappropriate medication use in residential aged care facilities. *BMC geriatrics*. 2018;18(1): 9. doi: 10.1186/s12877-018-0704-8

5 Harrison SL, Kouladjian O'Donnell L, Milte R, Dyer SM, Gnanamanickam ES, Bradley C, Liu E, Hilmer SN, Crotty M. Costs of potentially inappropriate medication use in residential aged care facilities. *BMC geriatrics*. 2018;18(1): 9. doi: 10.1186/s12877-018-0704-8

6 By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *Journal of the American Geriatrics Society*. 2019;67: 674-694. doi: **https://doi.org/10.1111/jgs.15767**

7 For example: Royal Commission into Aged Care Quality and Safety Final Report: Care, dignity and respect, Volume 2: The current system, Chapter 3. Commonwealth of Australia: Canberra, Australia, 2021. Available from: https://www.royalcommission.gov.au/aged-care/final-report

2.2.1 The use of antipsychotics

Residents living in RAFCs have considerably higher rates of insomnia, anxiety, and behavioural and psychological symptoms of dementia (BPSD).[8] Guidelines recommend non-pharmacological management as first line treatment, and the use of antipsychotics should be restricted for short term use only after other therapies have been sought. Some antipsychotics may have limited evidence of efficacy with significant adverse effects such as falls, stroke, cardiovascular events and death.[9]

2.2.2 The use of benzodiazepines

Benzodiazepines including non-benzodiazepines (i.e., z-drugs) are prescribed to manage sleep disturbances, anxiety and agitation. Their use in people with dementia has been linked to negative adverse outcomes such as falls, pneumonia, hospitalization and dementia.[10] **Section 6** at the end of this Toolkit contains a guide to deprescribing benzodiazepines, as well as a benzodiazepine deprescribing algorithm.

2.3 ANTICHOLINERGIC BURDEN

Many medicines have anticholinergic effects such as causing dry mouth, blurred vision, and dizziness. These effects are more pronounced in older people as metabolism slows with age. Medicines with anticholinergic properties have been linked to adverse effects including cognitive impairment, falls and death.[11,12]

A person's anticholinergic burden increases as medications with anticholinergic activity are combined.

2.3.1 The Anticholinergic Cognitive Burden (ACB) Scale

The Anticholinergic Cognitive Burden (ACB) scale is a validated tool used for measuring medications with anticholinergic effects.[13] The combined ACB score should be measured for all medications with anticholinergic activity that a resident is taking to give an indication of the ACB burden.

Table 6.5 (in **Section 6** at the end of this Toolkit) contains a summary of medications with possible anticholinergic effects, modified for the Australian context. Refer to this table for a full list of medications included and relevant scores to assess ACB using the ACB scorecard (scores from 1–3). You may also choose to use an electronic version of the ACB score calculator that allows you to enter the names of medications to calculate the ACB score, which is available here: **http://www.acbcalc.com/**.

If a resident has scored an ACB score of three or more, they are at a higher risk of confusion, falls and death.

8 Chen L, Bell JS, Visvanathan R, Hilmer SN, Emery T, Robson L, Hughes JM, Tan EC. The association between benzodiazepine use and sleep quality in residential aged care facilities: a cross-sectional study. BMC geriatrics. 2016;16:196. **doi:10.1186/s12877-016-0363-6**

9 Maher AR, Maglione M, Bagley S, Suttorp M, Hu JH, Ewing B, Wang Z, Timmer M, Sultzer D, Shekelle PG. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: a systematic review and meta-analysis. *Journal of the American Medical Association*. 2011;306(12): 1359–1369. **doi:10.1001/jama.2011.1360**

10 Islam MM, Iqbal U, Walther B, Atique S, Dubey NK, Nguyen PA, Poly TN, Masud JH, Li YJ, Shabbir SA. Benzodiazepine Use and Risk of Dementia in the Elderly Population: A Systematic Review and Meta-Analysis. *Neuroepidemiology*. 2016;47(3-4):181–191. **doi: 10.1159/000454881**

11 Fox C, Richardson K, Maidment ID, Savva GM, Matthews FE, Smithard D, Coulton S, Katona C, Boustani MA, Brayne C. Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study. Journal of the American Geriatric Society. 2011 Aug;59(8):1477–83. **doi: 10.1111/j.1532-5415.2011.03491.x**

12 Boustani M, Campbell N, Munger S, Maidment I, Fox C. Impact of anticholinergics on the aging brain: A review and practical application. *Aging Health*. 2008 Jun 1;4(3):311–320. **doi: 10.2217/1745509X.4.3.311**

13 Campbell N, Boustani M, Limbil T, Ott C, Fox C, Maidment I, Schubert CC, Munger S, Fick D, Miller D, Gulati R. The cognitive impact of anticholinergics: a clinical review. Clinical Interventions in Aging. 2009;4:225–33. **doi: 10.2147/cia.s5358**

SECTION 3. ON-SITE PHARMACIST'S ACTIVITIES

This section outlines activities and ways in which on-site pharmacists can contribute to medication management in RACFs:

- 3.1 Clinical audits
- 3.2 Medication reviews, including at transition of care
- 3.3 Vaccination
- 3.4 Medication round optimisation
- 3.5 Contribution to policies and procedures
- 3.6 Education.

On-site pharmacists' activities in RACFs are summarised in Figure 1.

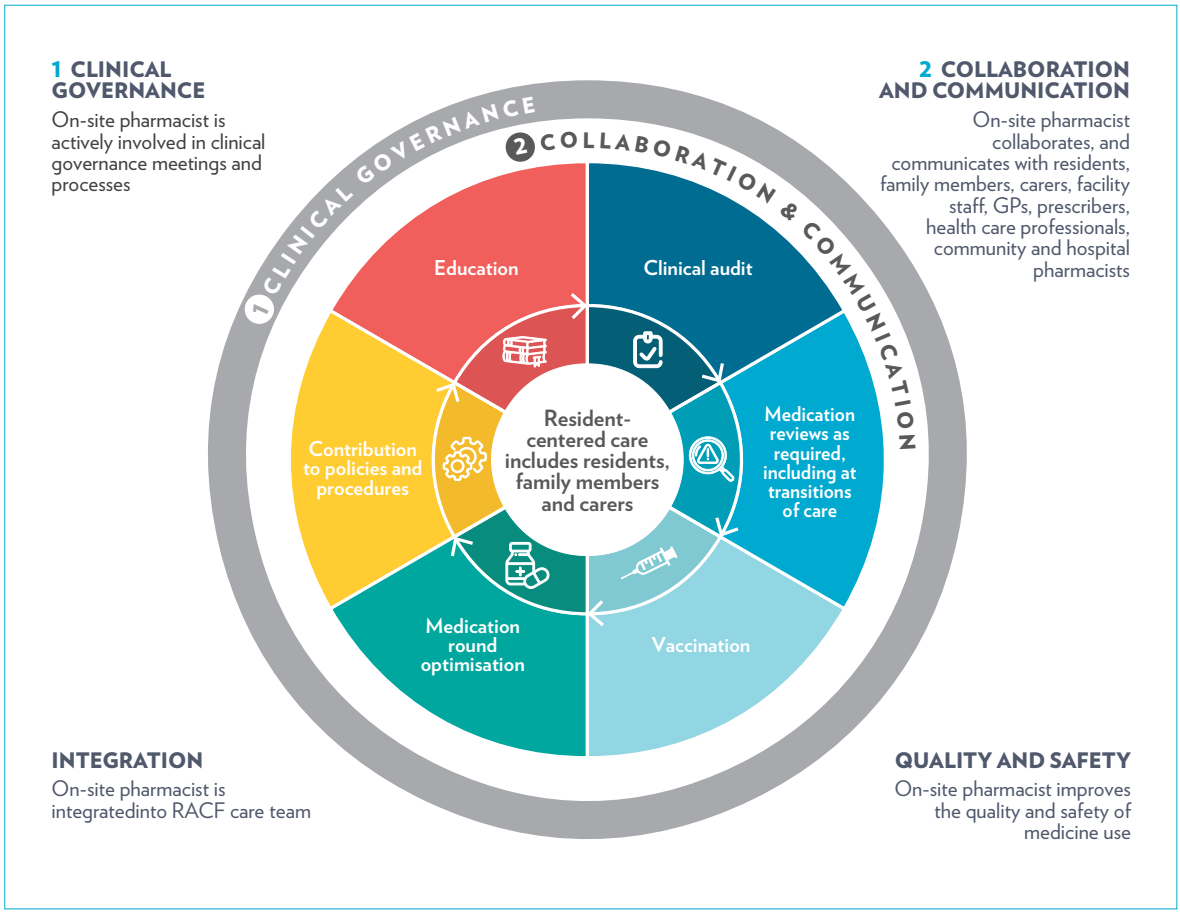


FIGURE 1. On-site pharmacists' activities in RACFs

3.1 CLINICAL AUDITS

KEY POINTS

- Clinical audits are a key activity of on-site pharmacists
- Clinical audits aim to identify residents at high risk of medication related misadventure
- Document the outcomes and keep records using Form 1 in the On-site Pharmacist's Clinical Notes

TARGETS

- Minimum of 6 clinical audits per year

Clinical audits in the on-site pharmacist model of care aim to improve residents' medication management and outcomes through systematic review of residents' medications and conditions against explicit criteria, and can be followed by medication reviews to resolve issues identified.

Conducting regular clinical audits of residents on high-risk medications can improve medication safety. A clinical audit involves reviewing all residents' charts to identify specific high-risk medications, reviewing the risks and benefits of medicine use, and conducting a medication review that recommends lower risk alternatives to the prescriber. The first step of a clinical audit is to identify and list all residents that meet the criteria of the clinical audit topic. This will allow the on-site pharmacist to shortlist residents that require a medication review so that at the next step, pharmacist can plan and conduct medication review for those residents. Clinical audits should be conducted regularly (for example, every 2 to 3 months).

The **three essential clinical audits** that must be conducted by the on-site pharmacist are:

- **PIMs** (section **2.1** of this Toolkit)
- **antipsychotics** (section **2.2** of this Toolkit), and
- **benzodiazepines** audits (also section **2.2** of this Toolkit).

It is also highly recommended that pharmacists conduct additional clinical audits, for example high dose proton pump inhibitors (PPI), opioids, long-term antibiotics, psychotropics indication and dosage. Please refer to **Form 1** in the **On-site Pharmacist's Clinical Notes** when conducting and recording clinical audits.

3.2 MEDICATION REVIEWS, INCLUDING AT TRANSITIONS OF CARE

KEY POINTS

- Medication reviews are another key activity of on-site pharmacists
- Prioritise residents at high risk of medication misadventure
- Follow up recommendations with GPs by arranging case conferences or other methods to ensure take-up
- Document the outcomes and keep records using Form 2 in the On-site Pharmacist's Clinical Notes

TARGETS

- Minimum of 1 medication review per resident, per year

Medication reviews are a core activity that on-site pharmacists (and other health care professionals) in clinical settings can use to reduce medication related risks and improve medication safety. In RACFs, on-site pharmacists are expected to conduct ongoing medication reviews for all permanent residents and additional medication reviews at transitions of care including upon admission to the facility, post hospital discharge, upon diagnosis of new conditions and when referred to palliative care. In addition, on-site pharmacists can influence RACF workflow and procedures so that nursing and care staff refer residents at high risk of medication misadventure to you. Evidence from international studies has shown that medications such as antipsychotics, benzodiazepines, anticoagulants, opioids, and PPIs increase the risk of hospitalisation and adverse health outcomes for RACF residents.

Considering the high rate of polypharmacy in RACF residents, particular attention should be paid to deprescribing when appropriate (refer to section **2.2** above). Deprescribing requires a comprehensive review of risk and benefits of a medication treatment in the context of the quality of remaining life, goals of care, and resident and family priorities and preferences.[14] It is recommended that deprescribing be conducted as part of a shared decision-making process between the resident and their families, on-site pharmacist and GP or prescriber. One of the goals of the on-site pharmacist model of care is to promote resident-centred care and to involve residents and families in the decision-making process around their medication management. Having on-site pharmacists present in RACFs provides an opportunity for pharmacists to involve residents and families in their medication and care. Working on-site allows the on-site pharmacist to monitor the progress on care and follow up as required.

Please refer to **Form 2** in the **On-site Pharmacist's Clinical Notes** when conducting and recording medication reviews.

14 Naughton C, Hayes N. Deprescribing in older adults: a new concept for nurses in administering medicines and as prescribers of medicine. *European Journal of Hospital Pharmacy: Science and Practice*. 2017;24(1):47–50. doi: 10.1136/ejhpharm-2016-000908

3.3 VACCINATION

KEY POINTS

- On-site pharmacists play an important role in increasing vaccination rates, including conducting and coordinating vaccinations
- Follow state and territory legislation regulating pharmacist's involvement in flu and COVID-19 vaccination
- Liaise with the Facility Manager to develop ways to increase vaccination coverage
- Register your RACF as a vaccination provider with the Australian Immunisation Register
- Obtain informed consent using Form 5 in the On-site Pharmacist's Clinical Notes

TARGET

- Staff: 100% vaccination rate (unless contra-indicated)
- Residents: 100% vaccination rate (unless contra-indicated) noting that residents' COVID and flu vaccinations should be coordinated with residents' GPs

Influenza vaccination: There is high quality evidence that influenza vaccination reduces the rate of hospitalisation in RACF residents.[15] A report by the Australian Aged Care Quality Agency showed that about 43% of RACFs in Australia have less than half of their staff vaccinated against influenza,[16] indicating scope for improvement. In Australia, 91% of influenza-related deaths were in those aged over 65 years.[17]

RACF residents are at greater risk of influenza-related hospitalisation and other adverse health outcomes due to the greater degree of frailty and presence of multiple co-morbidities.[18] Additionally, RACF nursing and care staff are in close contact with residents and sometimes work in multiple facilities, increasing the risk of influenza transmission if not vaccinated.[19] The study supporting the roll-out of the on-site pharmacist model of care showed that pharmacist-led influenza vaccination increased the rate of staff vaccination and was well received by the staff (the study was conducted in the ACT which does not restrict pharmacists from administering influenza vaccines in community pharmacy locations[20]). While RACFs may have contracts for staff vaccination programs, **on-site pharmacists can liaise with Facility Managers to develop processes to assist RACFs in increasing their annual influenza vaccination**. These can include providing education to staff about the benefits of vaccination to themselves and residents, convening vaccination sessions, inviting and reminding staff, and highlighting to staff mandatory vaccination requirements.

COVID vaccination: In some RACFs, the pharmacist may assist with conducting and coordination of COVID vaccinations, in discussion with GPs and Facility/Clinical Managers.

Please refer to **Form 5** in the **On-site Pharmacist's Clinical Notes** when seeking consent for vaccinations.

15 Australian Aged Care Quality Agency. Review of infection control practices in residential aged care in Australia [online]. Available at: https://www.agedcarequality.gov.au/sites/default/files/media/report_on_review_of_infection_control_in_residential_aged_care_in_australia_april_2018.pdf

16 Wang KN, Bell JS, Chen EYH, Gilmartin-Thomas JFM, Ilomäki J. Medications and Prescribing Patterns as Factors Associated with Hospitalizations from Long-Term Care Facilities: A Systematic Review. *Drugs & Aging*. 2018;35(5):423–457. doi:10.1007/s40266-018-0537-3

17 National Influenza Surveillance Committee. 2017 Influenza season in Australia. A summary from the National Influenza Surveillance Committee [online]. Australian Department of Health; 2017. http://www.health.gov.au/internet/main/publishing.nsf/Content/ozflu-surveil-2017-final.htm. Accessed May 24, 2018.

18 Raina MacIntyre C, Menzies R, Kpozehouen E, Chapman M, Travaglia J, Woodward M, Jackson Pulver L, Poulos CJ, Gronow D, Adair T. Equity in disease prevention: Vaccines for the older adults — a national workshop, Australia 2014. *Vaccine*. 2016;34(46):5463–5469. doi: 10.1016/j.vaccine.2016.09.039

19 Wendelboe AM, Grafe C, McCumber M, Anderson MP. Inducing Herd Immunity against Seasonal Influenza in Long-Term Care Facilities through Employee Vaccination Coverage: A Transmission Dynamics Model. *Computational and Mathematical Methods in Medicine*. 2015;2015:178247. doi:10.1155/2015/178247

20 McDerby NC, Kosari S, Bail KS, Shield AJ, MacLeod T, Peterson GM, Naunton M. Pharmacist-led influenza vaccination services in residential aged care homes: A pilot study. *Australasian Journal on Ageing*. 2019;38(2):132–135. doi:10.1111/ajag.12611

3.4 MEDICATION ROUND OPTIMISATION

KEY POINTS

- Medication administration rounds are a common source of medication errors and often present opportunities for improvement
- On-site pharmacists can identify and recommend policies and practices to reduce medication errors and improve efficiencies

TARGET

- On commencement and on an on-going basis

Medication rounds in aged care settings are time consuming activities that have high levels of medication administration risks to residents. On-site pharmacists' involvement in medication rounds can minimise medication errors and maximise efficiencies.[21] Collaborate with nursing staff to identify inappropriate dosage form modification (crushing and cutting), recommend alternatives, and improve the organisation of the medication trolley (such as developing checklists, removing expired items, separating and grouping unpacked medications per residents or adding appropriate tools). A study conducted in the UK found that pharmacists' involvement in medication rounds resulted in a saving of 56.7 minutes per day for nursing staff.[22] Similarly, the pilot study showed that on-site pharmacist involvement reduced medication round time from 4.8 min to 3.2 min per resident per round.[23]

21 Relihan E, O'Brien V, O'Hara S, Silke, B. The impact of a set of interventions to reduce interruptions and distractions to nurses during medication administration. *Quality and Safety in Health Care*. 2010;19(5):e52. doi: 10.1136/qshc.2009.036871

22 Baqir W, Barrett S, Desai N, et al. A clinico-ethical framework for multidisciplinary review of medication in nursing homes. *BMJ Open Quality*. 2014;3(1):1-5. doi:10.1136/bmjquality.u203261.w2538

23 McDerby NC, Kosari S, Bail KS, Shield AJ, Peterson GM, Naunton M. The effect of a residential care pharmacist on medication administration practices in aged care: a controlled trial. *Journal of Clinical Pharmacy and Therapeutics*. 2019; 44(4):595-602. doi: 10.1111/jcpt.12822

3.5 CONTRIBUTION TO POLICIES AND PROCEDURES

KEY POINTS

- Review and identify ways to enhance facility policies and procedures to prevent errors and improve efficiencies in medications management
- Prioritise processes that facilities can put in place to identify residents on high-risk medications or who are at risk of hospitalisations or falls
- Communicate with relevant staff to get understanding and agreement

TARGET

- When the on-site pharmacist commences and on an on-going basis

On-site pharmacists working in RACFs can improve RACF medication management policies and procedures and identify particular needs that are not addressed by existing policies. For example, consider:

- reviewing and updating medication management policies relating to high-risk medications or conditions such as warfarin management, diabetes management, and prescribing and using chemical restraints, cognisant of the limitations of your knowledge and the need to consult with relevant senior staff members if the policy being updated falls outside your area of expertise
- participating in and developing policies for the Medication Advisory Committee (MAC), clinical governance meetings, Antimicrobial Stewardship policies, and Aged Care Quality Standards policies and activities
- attending (or chairing, if appropriate) MAC and other committee meetings relevant to medication management
- reviewing medication incidents and putting into place appropriate policies and procedures to address recurring issues.

3.5.1 Identify and address policy priorities

Take the opportunity to observe facility practices while undertaking the clinical aspects of your role, and take part in clinical rounds, clinical handovers, interact with residents and families, and participate in medication administration rounds. On-site pharmacists are in a prime position to identify policies and procedures that require improvement. This may be facilitated through the quality improvement team, or through formal committees such as the MAC or clinical governance structures.

For example:

- it may be appropriate to include in the RACF Medication Management Policy that nursing staff refer to the on-site pharmacist when a resident consistently refuses medication
- you could provide expert opinion on the safe modification of dosage forms such as whether it is safe to crush a tablet prior to administration, which may in turn, assist to reduce the refusal of doses.

3.5.2 Identify and take action for residents using high-risk medications

On-site pharmacists are well placed to implement systems to identify residents with polypharmacy, and those taking high-risk medications, including antipsychotics, benzodiazepines antibiotics, opioids, cytotoxic medications and medications with a narrow therapeutic index. The Quality and Safety Commission requires consent and charting of chemical restraints to be up to date. Consider conducting clinical audits and medication reviews, as well as reviews of dispensing reports from the supply pharmacy.

- Regularly review high-risk medications with the GP or prescriber and resident, family member and carer
- Communicate with the GP or prescriber, RACF staff, health care professional, and the resident, family member and carer. This can be done as part of a case conference, to ensure everyone agrees with and understands why changes have been made to the resident's regimen
- Alternative methods for reviewing high-risk medications may include written or verbal communication with the GP or prescriber, or referring residents to the pharmacist conducting Residential Medication Management Reviews (RMMRs) in the facility
- Reviews should be as frequent as is practical and clinically appropriate. If medication charts are renewed every 3 months this may act as a prompt for review, particularly for *Pro Re Nata* (PRN) medications that are charted but not being administered
- Formal review of all chemical restraints every 3 months is mandatory.

3.5.3 Implementing policies to reduce hospitalisation of residents

Identify residents at high risk of hospitalisation by being present at clinical handovers and clinical care meetings. Review pathology reports, progress notes, discharge summaries, GP or prescriber notes and charts on an on-going basis for vital signs, weight, blood glucose levels, bowel patterns, behaviours and neurological symptoms.

- Use this information to discuss with GPs or prescribers, nurses, residents, family and identify the need for intervention
- When there is a deterioration in health, undertake a medication review and follow up with the GP or prescriber to provide information on the resident's medication related needs.

3.5.4 Improving medication management policies and procedures

Upon commencing in a facility, the on-site pharmacist should review medication management policies and procedures. The on-site pharmacist can develop policies and procedures to support the improvement of medication management. These may include, but are not limited to:

- Appropriate storage of medication
- Recording medication storage refrigerator temperatures and restricting the use of refrigerators to store medicines
- Recording room temperatures where medications are stored
- Accepting pharmacy deliveries, particularly in relation to the correct identification and storage of Schedule 8 and Schedule 4 (Appendix D) medication, and medications that should be stored in a refrigerator
- Ensuring the appropriate monitoring of expiry dates and labelling of all medications
- Destruction of unwanted or expired medication
- Adherence to state and territory policies for appropriate destruction of Schedule 8 medicines
- Managing medications that have been inappropriately stored
- Reordering stock to ensure continuous supply to residents
- Responding to medication incidents — identifying problems and developing policies and procedures to address issues in the longer term.

3.5.5 Policies and procedures for appropriate administration of medications

The on-site pharmacist can develop policies and procedures to support the appropriate administration of medication. These include:

- Education and assessment of staff responsible for medication administration
- Highlighting the correct methods for administration of non-packed medications, correct storage of medications, and appropriate documentation of refusal of doses and "missed" doses such as when stock is not available
- Policies to identify medications that should only be administered by RNs
- Providing information on safe dosage administration and developing procedures for identifying medications which should not be crushed prior to administration, as well as appropriate crushing methods
- Updating dosing instructions for each resident which should be readily available at each medication round
- Recording and updating allergies and adverse reactions to resident's records.

3.6 EDUCATION

KEY POINTS

- On-site pharmacists can play an important role in educating nurses and care staff about medicines and medication use, including through ad hoc and regular sessions
- On-site pharmacists should discuss the priorities for education with the clinical and facility managers
- Facility Managers should encourage staff participation

TARGET

- At least once a month

The on-site pharmacist can provide education sessions to new and current nursing and care staff, as well as residents, families and carers on a regular and as needed basis. Discuss needs and priorities with the clinical and facility managers. Regular attendance at handover and clinical meetings with nursing and care staff will allow you to identify priority education topics and ensure that staff receive updates on key medication related issues and policies, which could include:

- the use of antipsychotics for BPSD
- PRN antipsychotics and benzodiazepines
- opioid medications and PRN analgesics
- psychotropics
- high risk medications
- what medicines to crush and not crush
- anticoagulants and monitoring
- referral pathways
- cytotoxic medications and handling issues for RACF staff.

You will also have an opportunity to provide ad hoc education sessions at handover and daily clinical meetings. One-off face to face encounters allow the on-site pharmacist and staff to discuss medication related issues as they arise. This can include, for example, recent developments in the use of non-invasive blood glucose monitors, use and storage of medicinal cannabis for newly admitted residents, implications of changes made to PBS, and other medication related regulations and the impact these may have on residents.

Consider ways to make information available to staff who are unable to attend facetoface meetings, such as through written resources, email updates, and verbal hand overs will ensure the greatest reach.

Regular attendance at residents and family meetings will also allow you to share information about infection control and the importance of correct hand washing, the benefits of vaccination, side effects of medications and polypharmacy.

SECTION 4. MAKING IT WORK: COLLABORATION, COMMUNICATION AND INTEGRATION

4.1 COLLABORATION AND COMMUNICATION

KEY POINTS

- The success of the on-site pharmacist's role will depend on effective communication with GPs, prescribers and facility staff, as well as residents, families and carers
- Conducting case conferences with GPs, prescribers, health care professionals, nurses, residents and families has been shown to be an effective communication method
- Rapport is a key factor for facilitating a collaborative working environment
- Establishing agreed upon methods of communication will support the development and maintenance of successful relationships

TARGET

- On commencement and on an on-going basis

Building collaborative relationships is crucial to improving medication management for residents. Awareness of individual roles, accessibility, preferred communication channels, and mutual trust and respect are important in enabling collaboration.

The on-site pharmacist should strive to develop and maintain effective communication with staff to embed themselves as part of the care team and support an open and trusting relationship. Ensure a people centred care approach that puts residents at the centre of health care delivery and involve residents, families and carers in decision-making processes to develop and action care plans and goals of care.

Consider using a combination of these strategies to develop an effective collaborative environment:

- **the on-site pharmacist should introduce** themself and outline their role and what they can do to assist residents, families and carers, and to help other health care professionals (RNs and care staff, GPs/prescribers, other health care professionals). Proforma letters introducing the on-site pharmacist to residents, families and carers, facility staff and GPs, prescribers and health care professionals are available in the **Residential Aged Care Facility's Handbook** to aid in this initial process
- **Find out from RACF staff what their preference is for communication** such as phoning, emailing, face-to-face discussion, or creating notes in the resident's files so staff and medical professionals can access them
- **The on-site pharmacist should facilitate face-to-face** contact with residents, families and carers and with facility nursing and care staff, and GPs, prescribers and health care professionals, including nurse practitioners, dietitians and speech and occupational therapists, to support the development of collaborative, effective and satisfying relationships
- **Discuss with GPs and prescribers their preferred ways to communicate** your recommendations resulting from medication reviews and other discussions about residents and medication management. You can use the GP and Prescriber's Communication Notes (Form 3) in the Clinical Notes for On-site Pharmacists to assist with this
- **Follow-up** to communicate recommendations and understand that building trust is key to working together effectively.

Collaboration between pharmacists and nursing staff in RACFs is essential to ensure medicines are administered appropriately and that RACF staff are aware of potential adverse effects of medicines and other medication-related issues. Findings from the PiRACF study showed that it takes between 2 to 4 months for these relationships to be fully developed, mediated by:

- the process of establishing relationships (face-to-face, informal and incidental interactions)
- the characteristics of the on-site pharmacist support the establishment and maintenance of these relationships (friendly, adaptable and approachable, proactive and engaged)
- the perceived or potential benefit of the on-site pharmacist role.

Promoting a culture of openness will support residents and their families and carers, and nursing and care staff to feel empowered to discuss issues and concerns regarding medication management.

4.2 INTEGRATION OF THE ON-SITE PHARMACIST INTO THE RACF

KEY POINTS

- Integration is key to the success of the on-site pharmacist's role
- Integration will, to a large extent, rely on good communication and collaboration
- At commencement, the facility manager and pharmacist should go through the Orientation Checklist in **Section 5** of this Toolkit.

TARGETS

- On commencement and on an on-going basis

To encourage and support integration of the on-site pharmacist in RACFS, we suggest that:

- the on-site pharmacist is introduced to residents, families and carers, RACF nursing and care staff, GPs, prescribers and health care professionals
- the on-site pharmacist is provided full access to RACF information systems including resident records, medication charts, and medication incidents and falls records
- the on-site pharmacist develops ways to be involved in reviewing resident's medications at transition of care such as when residents enter the facility, post Emergency Department or hospital admission, or after a new diagnosis or change in medication regimen
- the on-site pharmacist and facility manager organises monthly or regular pharmacist-led education sessions around medication management for RACF staff
- the on-site pharmacist is involved in organising medication administration education and assessment for staff
- the on-site pharmacist is involved in managing ward stock and Schedule 8 medications
- the on-site pharmacist is involved in observing medication rounds and suggesting ways to improve efficiency
- the on-site pharmacist is involved in coordinating and conducting vaccination programs for residents and staff
- the on-site pharmacist reviews medications of residents at high risk of falls or hospitalisation
- the on-site pharmacist acts as a liaison between the nursing staff, hospital, community and supply pharmacies, RMMR pharmacists and GPs and prescribers in dealing with medication management issues
- the on-site pharmacist provides input into facility policies and procedures and that they have an active role on relevant policy committees such as:
  - Medication Advisory Committee
  - Falls Committee
  - Quality and Safety Committee

SECTION 5. STARTING OUT: YOUR ORIENTATION CHECKLIST

Ways in which the RACF can support integration of the on-site pharmacist are outlined in the orientation checklist below. It includes ways to orientate the pharmacist to the facility and identify priority activities. We suggest the facility manager and clinical manager work through this and then shares a copy with the on-site pharmacist.

5.1 ORIENTATION CHECKLIST

In the first 1 to 2 weeks		
Checked	**Item**	**Comments**
☐	Ensure the on-site pharmacist completes the facility's induction processes	
☐	Identify the on-site pharmacist's line manager and discuss preferred communication processes e.g. weekly face to face meeting, emails	
☐	Ensure the on-site pharmacist has access to facility information systems, including: • resident records • medication charts • My Health Records • Email • access to a computer • eMIMS or similar resources	
☐	Go through the position description and on-site pharmacist's activities (see pages 3–4) and identify priority activities for the facility	
☐	Introduce the on-site pharmacist to residents, families and carers: • Send the Introduction letter to residents, families and carers (see Template Letter at the end of the RACF Handbook) • Invite the on-site pharmacist to attend residents and families meetings • Invite the on-site pharmacist to contribute an article to the residents and families newsletter	
☐	Introduce the on-site pharmacist to facility staff, including care managers, RNs, ENs, and care staff: • Introduce the on-site pharmacist to facility staff at clinical and staff meetings • Discuss the activities the on-site pharmacist will be conducting in the facility • Send the Introduction letter to RACF managers and facility staff (see Template Letter at the end of the RACF Handbook)	

ORIENTATION CHECKLIST *(continued)*

Checked	Item	Comments
	In the first 1 to 2 weeks	
☐	Introduce the on-site pharmacist to health care staff who visit the facility and discuss how the on-site pharmacist can collaborate with them, including: — GPs — Geriatricians and specialists — Community/supply pharmacist — Nurse practitioners — Specialist palliative care team — Other relevant health care professionals such as dietitians, occupational therapists, speech pathologists. • Provide the on-site pharmacist with a list of GPs and their contact details for GPs • Introduce the on-site pharmacist to GPs, prescribers and other health care professionals when they visit the facility • Invite the on-site pharmacist to attend resident's case conferences • Send the Introduction letter to GPs, prescribers and health care professionals (see Template Letter at the end of the RACF Handbook)	
	Ongoing	
☐	Invite the on-site pharmacist to attend and actively contribute to clinical governance at the facility, including participating in the relevant committees and meetings: • Medication Advisory Committee • Committees assessing falls, medication incidents, quality and safety, and Anti-Microbial Stewardship • Attend hand over and clinical meetings	
☐	Involve the on-site pharmacist in reviewing and improving medication management policies and procedures including: • Reviewing and updating medication management policies and procedures • Updating resident's clinical documentation including allergies, adverse drug reactions and diagnoses • Ensuring S8 medicines are used, stored and disposed of according to legislation	
☐	• Invite the on-site pharmacist to develop systems to review resident's medications at transitions of care such as when residents enter the facility, after an Emergency Department or hospital admission, when a resident has declining health, or admission to palliative care	
☐	• Identify priorities for regular individual and group education sessions around medication management for new and existing staff and encourage staff to attend these • Involve the on-site pharmacist in assessing staff medication administration competencies	
☐	• Invite the on-site pharmacist to observe medication administration rounds and advise on ways to improve efficiencies	
☐	• Discuss vaccination processes and how the on-site pharmacist can conduct or contribute to improving staff and resident's vaccination uptake	
	3 months after commencement	
☐	Review on-site pharmacist activities and this checklist with on-site pharmacist	

SECTION 6. GUIDELINES

This section contains the following resources:

- **Table 6.1** Beers criteria for PIMs in older adults
- **Table 6.2** Beers criteria for PIMs in older adults due to drug-disease or drug syndrome interactions that may exacerbate the disease or syndrome
- **Table 6.3** Beers criteria for potentially clinically important drug-drug interactions that should be avoided in older adults
- **Table 6.4** Psychotropics that could potentially be prescribed inappropriately
- **Table 6.5** List of medications with anticholinergic properties (with ACB scores)

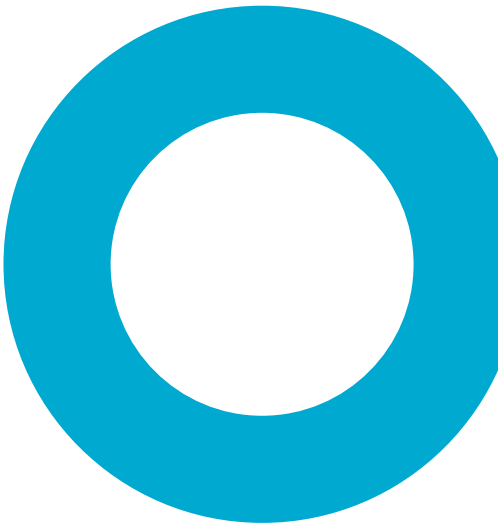


TABLE 6.1: Beers criteria for PIMs in older adults[24]

Potentially inappropriate medications according to Beers criteria 2019 — for all older adults	
Generic name	**Brands available in Australia**
First generation antihistamines	
Brompheniramine	*Demazin, Dimetapp*
Chlorpheniramine	*Codral*
Cyproheptadine	*Periactin*
Dexchlorpheniramine	*Polaramine, Polaramine Syrup*
Dimenhydramine (oral)	*Travacalm*
Doxylamine	*Dozile, Restamine, Restavit*
Promethazine	*Allersoothe, Fenezal, Phenergan, avomine*
Triprolidine	*Sudafed sinus*
Antiparkinsonian agents	
Benzatropine	*Benztrop*
Biperiden	*Akineton*
Trihexyphenidyl	*Benzhexol, Artane*
Antispasmodics	
Atropine (excludes phthalmic)	
Belladonna alkaloids, Hyoscine	*Buscopan, Gastro-Soothe Forte, Stomach Ease Forte*
Hyoscyamine	*Donnatab*
Propantheline	*Pro-Banthine*
Antithrombotics	
Dipyridamole, oral short-acting	*Persantin*
Ticlopidine	
Anti-infective	
Nitrofurantoin	*Macrodantin*
Peripheral alpha-1 blockers	
Prazosin	*Minipress*
Central alpha blockers	
Clonidine	*Catapres*
Disopyramide	*Rythmodan*
Methyldopa	*Aldomet, Hydopa*
Moxonidine	*Physiotens*
Other cardiovascular medications	
Amiodarone	*Aratac, Cordarone X, Rithmik*
Digoxin	*Lanoxin, Sigmaxin*
Nifedipine, immediate release	*Adefin*

24 Adapted Beers Criteria from the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. Journal of the American Geriatrics Society. 2019;67: 674–694. doi:https://doi.org/10.1111/jgs.15767

Potentially inappropriate medications according to Beers criteria 2019 — for all older adults	
Generic name	**Brands available in Australia**
Antidepressants, alone or in combination	
Amitriptyline	*Endep, Entrip*
Clomipramine	*Anafranil, Placil*
Doxepin	*Deptran, Sinequan*
Imipramine	*Tofranil*
Nortriptyline	*Allegron, NortriTABS*
Paroxetine	*Aropax, Extine, Roxet*
Antipsychotics (first and second generation)	
Amisulpride	*Amipride, Solian, Sulprix*
Aripiprazole	*Abilify, Abyraz, Tevaripiprazole*
Asenapine	*Saphris*
Chlorpromazine	*Largactil*
Clozapine	*Clopine, Clozaril*
Droperidol	*Droleptan*
Flupentixol	*Fluanxol Depot*
Fluphenazine	
Haloperidol	*Serenace, Haldol*
Lurasidone	*Latuda*
Olanzapine	*Ozin, Pryzex, Zypine, Zyprexa, Zypine ODT, Zyprexa Zydis*
Paliperidone	*Invega, Invega Sustenna*
Periciazine	*Neulactil*
Quetiapine	*Kaptan, Quetia, Seroquel, Syquet, Quepine XR, Seroquel XR, Tevatiapine XR*
Risperidone	*Ozidal, Rispa, Risperdal, Rispericor, Rispernia, Rixadone*
Trifluoperazine	
Ziprasidone	*Zeldox, Ziprox*
Zuclopenthixol	*Clopixol*
Barbituates	
Phenobarbital	*Phenobarb, Phenobarbitone*
Primidone	*Mysoline*

TABLE 6.1: Beers criteria for PIMs in older adults *(continued)*

Potentially inappropriate medications according to Beers criteria 2019 — for all older adults	
Generic name	**Brands available in Australia**
Benzodiazepines (short and immediate acting)	
Alprazolam	*Alprax, Kalma*
Bromazepam	*Lexotan*
Clobazam	*Frisium*
Flunitrazepam	*Hypnodorm*
Lorazepam	*Ativan*
Midazolam	*Hypnovel*
Nitrazepam	*Alodorm, Mogadon*
Oxazepam	*Alepam, Serepax*
Temazepam	*Normison, Temaze, Temtabs*
Clonazepam	*Paxam, Rivotril*
Diazepam	*Antenex, Valium, Valpam*
Zolpidem	*Stildem, Stilnox, Dormizol, Zolpibell, Somidem*
Zopiclone	*Imoclone, Imrest, Imovane*
Endocrine	
Testosterone	*AndroForte, Testogel, Androderm*
Estrogens with or without progestins (not vaginal creams)	*Premarin, Estrofem, Progynova, Zumenon, Sandrena,Climara, Estraderm, Estradot, Kliogest, Kliovance, Femoston-Conti, Estalis Continuous*
Progestogens and estrogens, fixed combinations (not vaginal creams)	*Provera, Ralovera*
Glibenclamide	*Daonil, Glimel*
Gliclazide	*Glyade, Nidem, Diamicron MR*
Glimepiride	*Amaryl, Aylide, Diapride, Dimirel*
Glipizide	*Minidiab*
Growth hormone	
Insulin, sliding scale short or ultra	
Insulin aspart	*NovoRapid*
Insulin lispro	*Humalog*
Insulin glulisine	*Apidra*
Neutral insulin	*Actrapid, Humulin R*
Megestrol	
Gastrointestinal	
Metoclopramide	*Pramin, Emexlon, Maxolon*
Mineral oil, given orally	

Potentially inappropriate medications according to Beers criteria 2019 — for all older adults	
Generic name	**Brands available in Australia**
Proton-pump inhibitors *(For over 8 weeks use)*	
Esomeprazole	*Nexazole, Nexium, Nexole, Mepreze, Noxicid*
Lansoprazole	*Lanzopran, Zopral, Zoton Fas Tabs*
Omeprazole	*Acimax, Losec, Omepral, Ozmep, Maxor, Pemzo, Probitor*
Pantoprazole	*Ozpan, Panthron, Panto, Pantofast, Salpraz, Sozol, Somac, Gastenz, Salpraz Heartburn Relief*
Rabeprazole	*Parbezol, Pariet, Zabep*
Pain medications	
Aspirin >325mg/day	*Solprin*
Celecoxib	*Celaxib, Celebrex, Celexi*
Etoricoxib	*Arcoxia*
Ibuprofen	*Nurofen, Brufen, Advil, Bugesic, Maxigesic, Combigesic, Fenmol, Ibupane, Nuromol, Mersynofen*
Indomethacin	*Arthrexin, Indocid*
Ketoprofen	*Orudis SR, Oruvail SR*
Ketorolac, includes parenteral	*Ketoral, Toradol*
Mefenamic acid	*Ponstan*
Meloxicam	*Meloxiauro, Meloxibell, Mobic, Movalis, Moxicam*
Naproxen	*Inza, Naprosyn, Proxen SR, Naprogesic, Anaprox, Crysanal*
Parecoxib	*Dynastat*
Pentazocine	
Pethidine	
Piroxicam	*Feldene, Mobilis*
Sulindac	*Aclin*
Diclofenac	*Clonac, Fenac, Voltaren, Viclofen, Difenac*
Skeletal muscle relaxants	
Orphenadrine	*Norflex*
Genitourinary	
Desmopressin	*Minirin, Octostim*

TABLE 6.2: Beers criteria for PIMs in older adults due to drug-disease or drug syndrome interactions that may exacerbate the disease or syndrome[25]

6.2.1 Additional PIMs for adults with cognitive impairment or dementia	
Generic name	**Brands available in Australia**
Antimuscarinics (urinary incontinence)	
Darifenacin	*Enablex*
Oxybutynin	*Ditropan, oxytrol*
Solifenacin	*Vesicare*
Tolterodine	*Detrusitol*
6.2.2 Additional PIMs for adults with heart failure	
Generic name	**Brands available in Australia**
Diltiazem	*Cardizem, Vasocardol*
Verapamil	*Anpec, Isoptin, cordilox*
Pioglitazone	*Acpio, Actaze, Actos, Vexazone*
Cilostazol	*Pletal*
6.2.3 Additional PIMs for adults with Parkinson's disease	
Generic name	**Brands available in Australia**
Antiemetics	
Metocloperamide	*Pramin, Emexlon, Maxolon*
prochlorperazine	*Procalm, Stemetil, Stemzine, Nausetil, Nausrelief*
Droperidol	*Droleptan*
Domperidone	*Motilium*
6.2.4 Additional PIMs for adults with delirium	
Generic name	**Brands available in Australia**
Corticosteroids	
Betamethasone	*Chronodose*
Cortisone	*Cortate*
Dexamethasone	*Dexmethsone*
Hydrocortisone	*Solu-Cortef*
Methylprednisolone	*Methylpred, Depo-Medrol, Depo-Nisolone, Solu-Medrol*
Prednisolone/prednisone	*Panafcortelone, Solone, Predsolone, Predmix, Redipred, Panafcort, Predsone, Sone*
Triamcinolone	*Kenacort*
Fludrocortisone	*Florinef*
H2 antagonists	
Cimetidine	*Magicul*
Famotidine	*Ausfam*
Nizatidine	*Nizac, Tacidine, Tazac*
Ranitidine	*Ausran, Rani, Zantac, Zantac, Ranital*

25 Adapted Beers Criteria from the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. Journal of the American Geriatrics Society. 2019;67: 674–694. doi:https://doi.org/10.1111/jgs.15767

6.2.5 Additional PIMs for adults with history of falls/fractures	
Generic name	**Brands available in Australia**
Antiepileptics	
Acetazolamide (neurology)	*Diamox*
Brivaracetam	*Briviact*
Carbamazepine	*Tegretol*
Ethosuximide	*Zarontin*
Gabapentin	*Gapentin, Neurontin, Nupentin*
Lacosamide	*Vimpat*
Lamotrigine	*Lamictal, Lamitan, Logem, Reedos*
Levetiracetam	*Keppra, Kerron, Levactam, Levi*
Oxcarbazepine	*Trileptal*
Perampanel	*Fycompa*
Phenytoin	*Dilantin*
Pregabalin	*Lypralin, Lyrica, Lyzalon, Neuroccord*
Rufinamide	
Sulthiame	*Ospolot*
Tiagabine	*Gabitril*
Topiramate	*Epiramax, Tamate, Topamax*
Valproate	*Epilim, Valprease, Valpro*
Vigabatrin	*Sabril*
Zonisamide	*Zonegran*
Opioids	
Alfentanil	*Rapifen*
Buprenorphine	*Bupredermal, Norspan, Temgesic*
Codeine	*Aspalgin, Nurofen Plus, Panafen Plus, Ibudeine, Panamax Co, Panadeine, Codalgin Forte, Codapane Forte, Comfarol Forte, Prodeine Forte*
Fentanyl	*Denpax, Durogesic, Dutran, Fenpatch, Abstral, Fentora, Actiq, Sublimaze*
Hydromorphone	*Dilaudid, Jurnista,*
Methadone	*Physeptone, Biodone*
Morphine	*Sevredol, Anamorph, Ordine, Momex SR, MS Contin, MS Contin, Kapanol, MS Mono*
Oxycodone	*Endone, Novacodone, OxyContin, OxyNorm, Proladone,*
Oxycodone with naloxone	*Targin*
Pethidine	
Remifentanil	*Ultiva*
Tapentadol	*Palexia*
Tramadol	*Tramal, Tramedo, Zydol*

TABLE 6.2: Beers criteria for PIMs in older adults due to drug-disease or drug syndrome interactions that may exacerbate the disease or syndrome *(continued)*

6.2.5 Additional PIMs for adults with history of falls/fractures *(continued)*	
Generic name	**Brands available in Australia**
Antidepressants	
Moclobemide	*Amira, Aurorix, Clobemix*
Phenelzine	*Nardil*
Tranylcypromine	*Parnate, Parpromine*
Mirtazapine	*Axit, Mirtanza, Mirtazon, Milivin, Avanza*
Desvenlafaxine	*Desfax, Desven, Pristiq*
Duloxetine	*Andepra, Cymbalta, Duloxecor, Dytrex, Tixol*
Reboxetine	*Edronax*
Venlafaxine	*Efexor-XR, Elaxine-SR, Enlafax-XR*
Citalopram	*Celapram, Cipramil, Talam*
Escitalopram	*Cilopam-S, Esitalo, Lexam, Loxalate, Esipram, Lexapro*
Fluoxetine	*Lovan, Prozac, Zactin, Fluotex*
Fluvoxamine	*Faverin, Luvox, Movox, Voxam*
Sertraline	*Sertra, Setrona, Eleva, Zoloft*
Dothiepin	*Dothep, Dosulepin*
Mianserin	*Lumin*
Agomelatine	*Valdoxan*
Vortioxetine	*Brintellix*
Milnacipran	*Joncia*
6.2.6 Additional PIMs for adults with syncope	
Generic name	**Brands available in Australia**
AchEIs	
Donepezil	*Aricept, Aridon, Aridon, Arazil*
Galantamine	*Galantyl, Gamine XR, Reminyl*
Rivastigmine	*Exelon, Rivastigmelon*

TABLE 6.3: Beers criteria for potentially clinically important drug-drug interactions that should be avoided in older adults[26]

6.3.1 INTERACTION TYPE 1: Any RAS inhibitor (ACEIs, sartans, aliskiren) or potassium-sparing diuretics (amiloride, triamterene) with another RAS inhibitor (ACEIs, ARBs, aliskiren) or potassium-sparing diuretics (refer to table below for specific medications)			
Object drug and class		**Interacting drug and class**	
Generic name	**Brands**	**Generic name**	**Brands**
ACE inhibitors		**ACE inhibitors**	
Captopril	*Capoten, Zedace*	Captopril	*Capoten, Zedace*
Enalapril	*Acetec, Malean, Renitec, Zan-Extra*	Enalapril	*Acetec, Malean, Renitec, Zan-Extra*
Fosinopril	*Fosipril, Monace, Monopril*	Fosinopril	*Fosipril, Monace, Monopril*
Lisinopril	*Fibsol, Zestril, Zinopril*	Lisinopril	*Fibsol, Zestril, Zinopril*
Perindopril	*Coveram, Reaptan, Coversyl, Prexum, Idaprex, Indosyl Mono, Perindo*	Perindopril	*Coveram, Reaptan, Coversyl, Prexum, Idaprex, Indosyl Mono, Perindo*
Quinapril	*Accupril, Acquin, Qpril, Accuretic*	Quinapril	*Accupril, Acquin, Qpril, Accuretic*
Ramipril	*Ramace, Tritace, Tryzan, Triasyn*	Ramipril	*Ramace, Tritace, Tryzan, Triasyn*
Trandolapril	*Dolapril, Gopten, Tranalpha*	Trandolapril	*Dolapril, Gopten, Tranalpha*
Sartans		**Sartans**	
Candesartan	*Adesan, Atacand, Candesan, Asartan*	Candesartan	*Adesan, Atacand, Candesan, Asartan,*
Eprosartan	*Teveten*	Eprosartan	*Teveten*
Irbesartan	*Abisart, Avapro, Avsartan, Irprestan, Karvea, Karvezide, KSART,*	Irbesartan	*Abisart, Avapro, Avsartan, Irprestan, Karvea, Karvezide, KSART*
Losartan	Cozavan, Cozaar	Losartan	*Cozavan, Cozaar*
Olmesartan	*Olmertan, Olmetec, Sevikar*	Olmesartan	*Olmertan, Olmetec, Sevikar*
Telmisartan	*Micardis, Mizart, Teltartan, Pritor, Twynsta*	Telmisartan	*Micardis, Mizart, Teltartan, Pritor, Twynsta*
Valsartan	*Diovan, Exforge, Co-Diovan*	Valsartan	Diovan, Exforge, Co-Diovan
Potassium-sparing diuretics		**Potassium-sparing diuretics**	
Eplerenone	*Espler, Inpler, Inspra*	Eplerenone	*Espler, Inpler, Inspra*
Spironolactone	*Aldactone, Spiractin*	Spironolactone	*Aldactone, Spiractin*
Amiloride	*Kaluril, Moduretic*	Amiloride	*Kaluril, Moduretic*

26 Adapted Beers Criteria from the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. Journal of the American Geriatrics Society. 2019;67: 674–694. doi:https://doi.org/10.1111/jgs.15767

TABLE 6.3: Beers criteria for potentially clinically important drug-drug interactions that should be avoided in older adults *(continued)*

6.3.2 INTERACTION TYPE 2: any opioids with any benzodiazepines, gabapentin or pregabalin would be counted as PIM (refer to table below for specific medications)			
Object drug and class		**Interacting drug and class**	
Opioids		**Benzodiazapines**	
Alfentanil	*Rapifen*	Alprazolam	*Alprax, Kalma*
Buprenorphine	*Bupredermal, Norspan, Temgesic*	Bromazepam	*Lexotan*
Codeine	*Aspalgin, Nurofen Plus, Panafen Plus, Ibudeine, Panamax Co, Panadeine, Codalgin Forte, Codapane Forte, Comfarol Forte, Prodeine Forte*	Clobazam	*Frisium*
Fentanyl	*Denpax, Durogesic, Dutran, Fenpatch, Abstral, Fentora, Actiq, Sublimaze*	Flunitrazepam	*Hypnodorm*
Hydromorphone	*Dilaudid, Jurnista*	Lorazepam	*Ativan*
Methadone	*Physeptone, Biodone*	Midazolam	*Hypnovel*
Morphine	*Sevredol, Anamorph, Ordine, Momex SR, MS Contin, MS Contin, Kapanol, MS Mono*	Nitrazepam	*Alodorm, Mogadon*
Oxycodone	*Endone, Novacodone, OxyContin, OxyNorm, Proladone*	Oxazepam	*Alepam, Serepax*
Oxycodone with naloxone	*Targin*	Temazepam	*Normison, Temaze, Temtabs*
Pethidine		Clonazepam	*Paxam, Rivotril*
Remifentanil	*Ultiva*	Diazepam	*Antenex, Valium, Valpam*
Tapentadol	*Palexia*	Zolpidem	*Stildem, Stilnox, Dormizol, Zolpibell, Somidem*
Tramadol	*Tramal, Tramedo, Zydol*	Zopiclone	*Imoclone, Imrest, Imovane*
		Pregabalin	*Lypralin, Lyrica, Lyzalon, Neuroccord*
		Gabapentin	*Gapentin, Neurontin, Nupentin*

6.3.3 INTERACTION TYPE 3: Any combination of 2 anticholinergics (refer to table below for specific medications)	
Object drug and class	**Interacting drug and class**
Antiarrhythmic	**Promethazine**
Disopyramide	Pyrilamine
	Triprolidine
Antidepressants	**Antimuscarinics (urinary incontinence)**
Amitriptyline	Darifenacin
Amoxapine	Fesoterodine
Clomipramine	Flavoxate
Desipramine	Oxybutynin
Doxepin (>6 mg)	Solifenacin
Imipramine	Tolterodine
Nortriptyline	Trospium
Paroxetine	Propantheline
Protriptyline	
Trimipramine	
Antiemetics	**Antiparkinsonian agents**
Prochlorperazine	Benztropine
Promethazine	Trihexyphenidyl
Antihistamines (first generation)	**Antipsychotics**
Brompheniramine	Antipsychotics
Carbinoxamine	Chlorpromazine
Chlorpheniramine	Clozapine
Clemastine	Loxapine
Cyproheptadine	Olanzapine
Dexbrompheniramine	Perphenazine
Dexchlorpheniramine	Thioridazine
Dimenhydrinate	Trifluoperazine
Diphenhydramine (oral)	**Antispasmodics**
Doxylamine	Atropine (excludes ophthalmic)
Hydroxyzine	Belladonna alkaloids
Meclizine	Scopolamine (excludes ophthalmic)
Clidinium chlordiazepoxide	**Skeletal muscle relaxants**
Dicyclomine	Cyclobenzaprine
Homatropine (excludes ophthalmic)	Orphenadrine
Hyoscyamine	
Methscopolamine	

TABLE 6.3: Beers criteria for potentially clinically important drug-drug interactions that should be avoided in older adults *(continued)*

6.3.4 INTERACTION TYPE 4: Any combination of three or more CNS-active drugs medications (Antidepressants (TCAs, SSRIs, and SNRIs) Antipsychotics Antiepileptics Benzodiazepines and nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (ie, "Z-drugs") Opioids

6.3.5 INTERACTIONS TYPE 5: Any corticosteroids with any NSAIDs

Object drug and class		Interacting drug and class	
Corticosteroids		**NSAIDs**	
Betamethasone	*Chronodose*	Aspirin >325mg/day	*Solprin*
Cortisone	*Cortate*	Celecoxib	*Celaxib, Celebrex, Celexi*
Dexamethasone	*Dexmethsone*	Etoricoxib	*Arcoxia*
Hydrocortisone	*Solu-Cortef*	Ibuprofen	*Nurofen, Brufen, Advil, Bugesic, Maxigesic, Combigesic, Fenmol, Ibupane, Nuromol, Mersynofen*
Methylprednisolone	*Methylpred, Depo-Medrol,* Depo-Nisolone, *Solu-Medrol*	Indomethacin	*Arthrexin, Indocid*
Prednisolone/ prednisone	*Panafcortelone, Solone, Predsolone, Predmix, Redipred, Panafcort, Predsone, Sone*	Ketoprofen	*Orudis SR, Oruvail SR*
Triamcinolone	*Kenacort*	Ketorolac, includes parenteral	*Ketoral, Toradol*
Fludrocortisone	*Florinef*	Mefenamic acid	*Ponstan*
Hydrocortisone (endocrine)	*Hysone, Solu-cortef*	Meloxicam	*Meloxiauro, Meloxibell, Mobic, Movalis, Moxicam*
		Naproxen	*Inza, Naprosyn, Proxen SR, Naprogesic, Anaprox, Crysanal*
		Parecoxib	*Dynastat*
		Pentazocine	
		Pethidine	
		Piroxicam	*Feldene, Mobilis*
		Sulindac	*Aclin*
		Diclofenac	*Clonac, Fenac, Voltaren, Viclofen, Difenac*

6.3.6 INTERACTION TYPE 6: All other drug to drug interactions		
Object drug and class	**Interacting drug and class**	
Lithium	**Loop diuretics**	
Lithicarb, Quilonum SR	Bumetanide	*Burinex*
	Etacrynic acid	*Edecrin*
	Furosemide (frusemide)	*Lasix, Urex, Uremide*
	ACEIs	All ace inhibitors as shown above
Peripheral alpha blockers	**Loop diuretics**	
Prazosin	Bumetanide	*Burinex*
Tamsulozin	Etacrynic acid	*Edecrin*
	Furosemide (frusemide)	*Lasix, Urex, Uremide*
Warfarin	**Loop diuretics**	
	Amiodarone	*Aratac, Cordarone X, Rithmik*
	Ciprofloxacin	*C-Flox, Ciproxin, Loxip, Ciprol*
	Macrolides	
	Azithromycin	*Zithro, Zithromax, Zedd*
	Clarithromycin	*Clarithro, Kalixocin, Klacid*
	Erythromycin	*E-Mycin, Eryc*
	Roxithromycin	*Biaxsig, Roxar, Roximycin, Rulide*
	Trimethoprim-sulfamethaxazole	*Resprim Forte, Septrin Forte*
	NSAIDs	
	Pain medications	
	Aspirin >325mg/day	*Solprin*
	Celecoxib*	*Celaxib, Celebrex, Celexi*
	Etoricoxib	*Arcoxia*
	Ibuprofen	*Nurofen, Brufen, Advil, Bugesic, Maxigesic, Combigesic, Fenmol, Ibupane, Nuromol, Mersynofen*
	Indomethacin	*Arthrexin, Indocid*
	Ketoprofen	*Orudis SR, Oruvail SR*
	Ketorolac, includes parenteral	*Ketoral, Toradol*
	Mefenamic acid	*Ponstan*
	Meloxicam	*Meloxiauro, Meloxibell, Mobic, Movalis, Moxicam*
	Naproxen	*Inza, Naprosyn, Proxen SR, Naprogesic, Anaprox, Crysanal*
	Parecoxib	*Dynastat*
	Piroxicam	*Feldene, Mobilis*
	Sulindac	*Aclin*
	Diclofenac	*Clonac, Fenac, Voltaren, Viclofen, Difenac*

TABLE 6.4: Psychotropics that could potentially be prescribed inappropriately[27]

6.4.1 Anxiolytic/hypnotics	
Generic name	**Brands available in Australia**
Alprazolam	*Alprax, Kalma*
Bromazepam	*Lexotan*
Clobazam	*Frisium*
Flunitrazepam	*Hypnodorm*
Lorazepam	*Ativan*
Midazolam	*Hypnovel*
Nitrazepam	*Alodorm, Mogadon*
Oxazepam	*Alepam, Serepax*
Temazepam	*Normison, Temaze, Temtabs*
Clonazepam	*Paxam, Rivotril*
Diazepam	*Antenex, Valium, Valpam*
Zolpidem	*Stildem, Stilnox, Dormizol, Zolpibell, Somidem*
Zopiclone	*Imoclone, Imrest, Imovane*
Buspirone	
Diphenhydramine	
Doxylamine	*Dozile, Restamine, Restavit*
6.4.2 Antipsychotics	
Generic name	**Brands available in Australia**
Amisulpride	*Amipride, Solian, Sulprix*
Aripiprazole	*Abilify, Abyraz, Tevaripiprazole*
Asenapine	*Saphris*
Chlorpromazine	*Largactil*
Clozapine	*Clopine, Clozaril*
Droperidol	*Droleptan*
Flupentixol	*Fluanxol Depot*
Fluphenazine	
Haloperidol	*Serenace, Haldol*
Lurasidone	*Latuda*
Olanzapine	*Ozin, Pryzex, Zypine, Zyprexa, Zypine ODT, Zyprexa Zydis*
Paliperidone	*Invega, Invega Sustenna*
Periciazine	*Neulactil*
Quetiapine	*Kaptan, Quetia, Seroquel, Syquet, Quepine XR, Seroquel XR, Tevatiapine XR*
Risperidone	*Ozidal, Rispa, Risperdal, Rispericor, Rispernia, Rixadone*
Trifluoperazine	
Ziprasidone	*Zeldox, Ziprox*
Zuclopenthixol	*Clopixol*

27 Australian Medicines Handbook. Australian Medicines Handbook Pty Ltd: Adelaide, Australia, 2022.

TABLE 6.5: List of medications with anticholinergic properties (with ACB scores)[28]

6.5.1 Medicines with ACB Score of 1	
Generic name	**Brands available in Australia**
alprazolam	*Kalma; Alprax*
atenolol	*Noten, Tenolten, Tenormin, Tensig*
brompheniramine maleate	
bupropion hydrochloride	*Zyban, contrave*
captopril	*Capoten, Zedace*
chlorthalidone	*Hygroton*
cimetidine hydrochloride (Tagamet)	*Magicul*
codeine	*Aspalgin, Nurofen Plus, Panafen Plus, Ibudeine, Panamax Co, Panadeine, Codalgin Forte, Codapane Forte, Comfarol Forte, Prodeine Forte*
colchicine (Colcrys)	*Colgout, Lengout*
diazepam (Valium)	*Antenex, Valium, Valpam*
digoxin (Lanoxin)	*Lanoxin, Sigmaxin*
dipyridamole (Persantine)	*Persantin*
disopyramide phosphate	*Rythmodan*
fentanyl	*Denpax, Durogesic, Dutran, Fenpatch, Abstral, Fentora, Actiq, Sublimaze*
isosorbide (Ismotic)	*Isordil, Sorbidin, Duride, Imdur, Isobide MR, Isomonit, Monodur*
loperamide (Imodium)	*Harmonise, Diareze, Imodium, Stop-It, Gastrex, Gastro-Stop, GastroStop*
metoprolol (Lopressor, Toprol-X)	*Betaloc, Lopresor, Metrol, Minax, Mistrom, Metrol-XL, Minax XL, Toprol-XL*
morphine	*Sevredol, Anamorph, Ordine, Momex SR, MS Contin, MS Contin, Kapanol, MS Mono*
nifedipine (Adalat, Procardia)	*Adalat Oros, Addos XR, Adefin XL*
rednisolone/prednisone	*Panafcortelone, Solone, Predsolone, Predmix, Redipred, Panafcort, Predsone, Sone*
quinidine	*Quinbisul, Quinate, quinine*
risperidone	*Ozidal, Rispa, Risperdal, Rispericor, Rispernia, Rixadone*
theophylline	*Nuelin*
triamterene (Dyrenium)	*Hydrene*
Warfarin	*Coumadin, Marevan*

6.5.2 Medicines with ACB Score of 2	
Generic name	**Brands available in Australia**
amantadine	*Symmetrel*
Belladonna alkaloids, Hyoscine	*Buscopan, Gastro-Soothe Forte, Stomach Ease Forte*
carbamazepine	*Tegretol*
cyproheptadine	*Periactin*
oxcarbazepine (Trileptal)	*Trileptal*

28 Boustani M, Campbell N, Munger S, Maidment I, Fox C. Impact of Anticholinergics on the Ageing Brain; a review and practical application. *Ageing Health*. 2008;4(3):311–320. doi: 10.2217/1745509X.4.3.311

TABLE 6.5: List of medications with anticholinergic properties (with ACB scores) *(continued)*

6.5.3 Medicines with ACB Score of 3	
Generic name	**Brands available in Australia**
amitriptyline	*Endep, Entrip*
benztropine	*Benztrop*
chlorpheniramine (an ingredient in many cough and cold medicines)	*Codral, sinus*
clomipramine	*Anafranil, Placil*
clozapine	*Clopine, Clozaril*
darifenacin	*Enablex*
dimenhydrinate	
diphenhydramine (an ingredient in cough and cold medicines)	
doxepin	*Deptran, Sinequan*
imipramine	
nortriptyline	*Allegron, NortriTABS*
olanzapine	*Ozin, Pryzex, Zypine, Zyprexa, Zypine ODT, Zyprexa Zydis*
orphenadrine	*Norflex*
oxybutynin	*Ditropan, oxytrol*
paroxetine	*Aropax, Extine, Roxet*
promethazine	*Allersoothe, Fenezal, Phenergan, avomine*
quetiapine	*Kaptan, Quetia, Seroquel, Syquet, Quepine XR, Seroquel XR, Tevatiapine XR*
tolterodine (Detrol)	*Detrusitol*
trihexyphenidyl (Artane, Tremin)	*Benzhexol, Artane*

SECTION 7. RESOURCES

You can also find resources here:

- A guide to deprescribing — general information
- A guide to deprescribing — antipsychotics
- A guide to deprescribing — benzodiazepines

These deprescribing guides are reproduced with permission from Primary Health Tasmania (Tasmania PHN). They are part of a broader range of medication management resources developed by Primary Health Tasmania under the Australian Government's Primary Health Networks Program. The guides reproduced in this toolkit are the versions used by pharmacists during the PiRACF study. For the latest version of the full suite of deprescribing resources, go to **primaryhealthtas.com.au/deprescribing**.

- Antipsychotic deprescribing algorithm[29]
- Benzodiazepines deprescribing algorithm[30]
- Thinking about anticholinergic burden[31]

29 Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L, Raman-Wilms L, Rojas-Fernandez C, Sinha S, Thompson W, Welch V, Wiens A. Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia: Evidence-based clinical practice guideline. Canadian Family Physician. 2018;64:17–27 (Eng), e1-e12 (Fr). PMID: 29358245

30 Pottie K, Thompson W, Davies S, Grenier J, Sadowski CA, Welch V, Holbrook A, Boyd C, Swenson R, Ma A, Farrell B. Deprescribing benzodiazepine receptor agonists: Evidence-based clinical practice guideline. Canadian Family Physician. 2018;64(5):339–351. PMID: 29760253

31 Provided by University of South Australia — Quality Use of Medicines and Pharmacy Research Centre, in association with: Discipline of General Practice, The University of Adelaide | School of Public Health, The University of Adelaide, NPS MedicineWise, Australian Medicines Handbook, Drug and Therapeutics Information Service. Available from: **https://www.veteransmates.net.au**

A GUIDE TO

deprescribing

GENERAL INFORMATION

KEY POINTS

- **Indications for use of many medications may change with time, and medication that was clearly appropriate in the past, may no longer be so (e.g. peptic ulcer treatment, analgesia, preventative strategies).**
- **Over a range of different practice settings (community, hospital, aged care), deprescribing of a range of different medications (antipsychotics, benzodiazepines, general deprescribing) has not been shown to cause any harm, and indeed, in some situations has improved outcomes.**
- **Cessation of medication may be an appropriate action in certain clinical situations amongst older adults. Triggers could include patients with an increased frequency of falls, with delirium and/or cognitive impairment and in end-of-life situations.**
- **Patients should be informed that deprescribing is intended to improve their quality of life by ensuring they do not receive unnecessary medicines with either no or minimal benefit and/or some potential for harm.**
- **Informing the patient of the rationale for deprescribing improves success rates in deprescribing and empowers the patient to take better control of their medications.**
- **Although many medications may be targeted for deprescribing, it may be prudent to initiate a trial of withdrawal of one medication at a time. Choosing priority will be based on individual case considerations.**

FOR BETTER HEALTH OUTCOMES

INTRODUCTION

Modern medications have had a major impact on survival and symptom reduction from a range of medical conditions, and clinical guidelines for the management of the majority of common medical conditions are available. In patients with multiple morbidities, however, applying the relevant guidelines may result in a significant medication load.[1,2] The use of prescribed and over the counter products has increased in the last 2 decades. The number of people taking 5 or more items has quadrupled from 12% to 49% and the number of people not taking any medication has decreased from 1 in 5 to 1 in 13.[3]

The higher the medication load, the more likely that an adverse effect will occur as a result of interactions between the medications and multiple conditions. Over a 5 year period, one in four older people are hospitalised for medication related problems. In addition, patients with low resilience (typically older, frailer patients) may have undesirable outcomes from the indiscriminate use of clinical guidelines.[4] In particular, patients who are frail are more likely to have adverse effects from medication.

DEPRESCRIBING PRINCIPLES

Deprescribing has been described as the systematic process of identifying and discontinuing potentially inappropriate drugs (including those with minimal efficacy) with the aim of minimising polypharmacy and improving patient outcomes.[4,5] The term can also be considered more broadly, taking in the concept of minimisation and reduction of medication "load" in terms of dose and/or number of tablets/administration times.

Cessation of medication may be an appropriate action in certain clinical situations amongst older adults. Triggers for deprescribing could include patients with an increased frequency of falls, with delirium and/or cognitive impairment and in end-of-life or limited prognosis situations.

Drug cessation should also be considered in all patients as a part of regular medication review.

A number of structured guides for deprescribing have been recommended and trialled.[7,8,9] The various methods have recently been reviewed by Scott et al and comprise explicit screening tools/criteria or a range of risk scores/scales to determine the "appropriateness" of an agent in a particular circumstance.

Fundamentally, these tools assess whether the benefit of the agent is sufficient to outweigh any potential harm.

DEPRESCRIBING PRINCIPLES

UTILITY	MEDICATIONS THAT:	EXAMPLES:
More Useful	**Provide immediate relief** for distressing symptoms	analgesics, antiemetics
	Modify an acute condition that is life-threatening, or will soon result in distressing symptoms if not treated	antibiotics for severe pneumonia or sepsis, diuretics for acute heart failure
	Modify a chronic condition that may progress to become life-threatening or cause significant symptoms if not treated	methotrexate for rheumatoid conditions, ACE Inhibitors for heart failure
	Have the potential to **prevent a serious disease**, without symptomatic benefit	antiplatelet agents, antihypertensives, statins
Less Useful	Are **unlikely to be useful** in either short or long term	fish oils, vitamins, glucosamine
	Are used **for indications where non-pharmacological therapy is equally or more effective**	physiotherapy for back pain, sleep hygiene vs long term benzodiazepines

Figure 1 Hierarchy of utility of medications

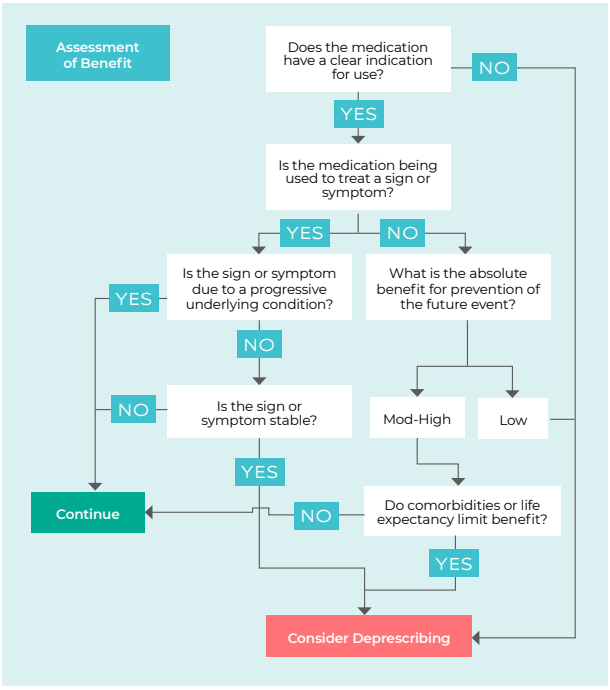


Figure 2 Considering deprescribing in terms of benefit of a medication

ASSESSMENT OF BENEFIT

Medications may have symptomatic and/or disease modifying benefits. Quantifying the benefit of symptom relieving medications can sometimes be easier than for preventative medications.

Scott et al identified a hierarchy of utility of medications that assists in determining the strength of the current indication of a medication (See **Figure 1**).[2]

Identifying whether the medication has a clear indication, and that the indication is not to treat a symptom or sign that may be related to another medication being taken, is the first step in assessing the possible benefit of the medication. If a clear indication cannot be found consideration of a dose reduction with appropriate monitoring and potentially ceasing the agent altogether should be considered. A summary of this process can be found in **Figure 2**.

For those medications where the indication is clear, determining whether it is primarily for symptom management or prevention of a future event assists in determining its ongoing benefit. If the sign or symptom that is being treated is due to an underlying progressive condition (for example Parkinson's disease or heart failure) then ongoing use of the medication at the minimum effective dose remains appropriate. When the symptom is, however, intermittent (for example gastro-oesophageal reflux disease or pain) and the situation is stable, a dose reduction is frequently possible and cessation may also be achieved.

For those medications which are preventative in nature, consideration of the absolute benefit and the time required to achieve that benefit in terms of the life expectancy and comorbidities of the patient should be considered. If the medication has low absolute benefit (for example vitamin D and calcium supplementation for fracture risk reduction or a statin for primary prevention) then consideration for cessation would be reasonable. In situations where the absolute benefit is higher, consideration of the patient's life expectancy (taking into account both age and significant comorbidities) assists in determining whether the benefit will be achieved. In the presence of significant comorbidities (for example moderate to advanced dementia, end-stage COPD or moderate to advanced heart failure) consideration of cessation of preventative therapy maybe appropriate.

ASSESSMENT OF HARM

While harm from some medications may be obvious, many medications may cause subtle, insidious harm (e.g. long term benzodiazepines) that can be difficult to distinguish from changes in underlying disease states. As such, medications that are known to be associated with high risk of harm should be closely monitored for evidence of such harm and considered for deprescribing.

Even medications that are not commonly associated with causing harm may do so if contraindications are present (for example allopurinol in severe renal dysfunction) or in particular patient circumstances (e.g. antihypertensives in the frail elderly). If contraindications or other factors are present that increase the likelihood of harm, then this would favour consideration of deprescribing (see **Figure 3**).

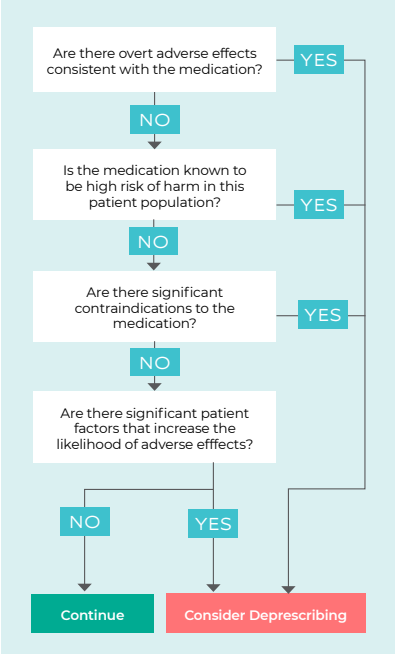


Figure 3 Considering Deprescribing in terms of Potential for Harm of a Medication

BENEFIT VERSUS HARM

While a simple assessment of benefit vs harm can be undertaken for a particular medication, the appropriateness and harm of a medication may vary in different situations. As such, it may be useful to consider medications according to both their degree of benefit and their degree of harm in particular situations
(see examples in **Table 1**). Situations where there is low benefit or high risk of harm (or both) would favour consideration of deprescribing and vice-versa.

High Benefit, Low Risk of Harm	Statins/Antiplatelet agents for secondary prevention of vascular events
	Antihypertensive management in hypertensive people with high cardiovascular risk
	Proton pump inhibitors for acute oesophagitis
High Benefit, High Risk of Harm	Opioid analgesics for recurrent or acute pain
	Benzodiazepines for short term treatment of anxiety
Low Benefit, High Risk of Harm	Antipsychotics for behavioural management in patients with dementia
	Opioid analgesics for chronic non-cancer pain
	Antihypertensives in frail elderly patients with postural hypotension
	Benzodiazepines for long term treatment of insomnia
Low Benefit, Low Risk of Harm	Vitamin D/Calcium supplementation for fracture risk reduction
	Statins/Antiplatelet agents for primary prevention of vascular events
	Proton pump inhibitors for long term treatment of reflux

GENERAL INFORMATION

TRIALS OF DEPRESCRIBING

The focus of clinical trials of deprescribing has been in older people as they are more likely to be taking multiple medications and are more likely to be at risk of harm from medication. Several reviews of these trials and studies have been undertaken (some of these are discussed below). Over a range of different practice settings (community, hospital, aged care), deprescribing of a range of different medications (antipsychotics, benzodiazepines, general deprescribing) has not been shown to cause any harm, and indeed, in some situations has improved outcomes.

In 2008, Iyer et al reviewed 31 published studies of drug withdrawal in a range of clinical settings (general practice, nursing home and hospital). Studies that were reviewed followed discontinuation of diuretics, antihypertensives and psychotropics (benzodiazepines and antipsychotics). [9] They concluded that there was a lack of significant harm when medication withdrawal was undertaken for these drug groups in older people.

More recently, Page et al reviewed 132 papers where older adults had at least one medication deprescribed. [10] There were no significant changes in mortality in the randomised studies that they reviewed despite an overall reduction in the total number of medications. They found that the health outcomes from deprescribing varied with the target medication. Slight increases in blood pressure were identified in patients ceasing antihypertensive agents but there was no statistical difference in exacerbation of underlying conditions after deprescribing glucosamine, carbamazepine, corticosteroids, benzodiazepines, antipsychotics or antidepressants. [10]

In Australia, Scott and others completed a pilot study of deprescribing for older patients receiving multiple medications hospitalised in Queensland.[11] Among 50 patients (Mean age 82.5), it was possible to cease 186 of 542 regular medications (34.3%). The list of regular medications was reduced by at least one medication in 47 patients (94%), at least two medications in 42 patients (84%) and by 4 or more in 25 (50%) of patients.

Highest rates of discontinuation (more than 50%) occurred for

- nitrates [8/11(73%)],
- inhaled bronchodilators [14/20(70%)],
- oral hypoglycaemics [9/15(60%)],
- antihypertensives other than ACEIs/ARBs [10/17(59%)],
- statins [21/37(57%)] and
- benzodiazepines [8/15(53%)].

The authors were able to follow up 39 of the patients (median follow-up was 78 days) and only 5 of the 149 ceased medications were recommenced (in three patients), all due to symptom relapse (amitriptyline and fentanyl for refractory pain, frusemide for pedal oedema and carbamazepine for recurrent trigeminal neuralgia).[11]

A study in nursing homes in Western Australia has also recently been completed.[12] Ninety-five people aged over 65 years living in four RACF in rural mid-west Western Australia were randomised in an open study. The intervention group (n = 47) received a deprescribing intervention, the planned cessation of non-beneficial medicines. The control group (n = 48) received usual care. Participants were monitored for twelve months from randomisation. Study participants had a mean age of 84.3±6.9 years and 52% were female. Intervention group participants consumed 9.6±5.0 and control group participants consumed 9.5±3.6 unique regular medicines at baseline. Of the 348 medicines targeted for deprescribing (7.4 ±3.8 per person, 78% of regular medicines), 207 medicines (4.4±3.4 per person, 59% of targeted medicines) were successfully discontinued. The mean change in number of regular medicines at 12 months was -1.9±4.1 in intervention group participants and +0.1±3.5 in control group participants (estimated difference 2.0±0.9, 95%CI 0.08, 3.8, p = 0.04). See **Figure 4**. [12]

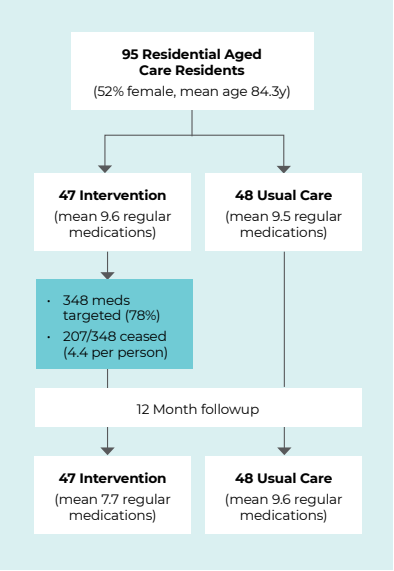


Figure 4 Western Australian deprescribing randomised controlled trial[12]

Authors in Israel had undertaken a similar study using similar principles to in 70 patients (average age 82.8 years).[13] They followed patients for an average of 19 months and were able to cease 311 different medications in 64 of the patients. At 19 month followup, 81% of the medications had not been recommenced and 88% of patients reported an improvement in global improvement in health. Cessation was most commonly attempted with benzodiazepines, statins, antihypertensives and frusemide. The same group extended their study and examined deprescribing for 122 participants compared to 55 non participants in a deprescribing intervention.[14] All participants were followed for at least 3 years. At the last followup, the median drug count was 4 (IQR 2-5) for the deprescribing group, compared to 11 (IQR 8-12) for the non-participants. They found no differences in survival rate or hospitalisations but improvements in a number of self-reported parameters including mental/ cognitive state, continence and appetite.[14]

WITHDRAWAL AND RECURRENCE ISSUES

If cessation of an agent is undertaken it is important to monitor the patient after the cessation for any potentially negative outcomes.[15] Some medications may cause withdrawal reactions which may require that cessation be undertaken by tapering the dose. Some medications may be having an impact on the patient's metabolism or elimination of other agents, and cessation may result in a changed effect from remaining medications (e.g. ceasing amiodarone in a patient taking digoxin will result in a gradual reduction in the digoxin level). Finally, and most commonly, the underlying condition for which the medication was prescribed may return. In some cases, true rebound may occur and the condition is worse than when the medication was originally commenced (e.g. rebound hyperacidity from ceasing proton pump inhibitors).[12]

PATIENT PERCEPTIONS

Patient attitudes to deprescribing have been examined by Qi et al.[16] It was found that of 180 patients (median age 78), 161 (89%) reported that they would be willing to stop one or more of their regular medications if their doctor said it was possible.

Similar patient attitude surveys have been published,[17,18,19] and a summary of key barriers are shown below:

- previous negative experiences with drug withdrawal (e.g. previous rebound insomnia after ceasing temazepam)
- anxiety and fear of consequences of stopping a medicine that has been prescribed for a long period (e.g. previous doctors' instructions to take "for the rest of their lives")
- reluctance to stop a drug when a patient believes it may prolong life or improve function (e.g. Statins in the elderly many years after a primary event)
- perception that deprescribing suggests that the patient is 'not worth treating' (e.g. cessation of aspirin interpreted as "giving up")

Ideally, the doctor and the patient/carer need to be engaged in the process, as without cooperation, deprescribing is less likely to succeed.

Patients should be informed that deprescribing is intended to improve their quality of life by ensuring they do not receive unnecessary medicines with either no or minimal benefit and/or some potential for harm.

Often, explaining that cessation/reduction is for a trial period, so that they are aware that drugs may be restarted if needed, enhances the likelihood of participation. Following up to determine the success or otherwise (ie development of any withdrawal symptoms etc) of any reduction/ cessation is also an important part of the process.

GENERAL PRACTITIONER PERCEPTIONS OF DEPRESCRIBING

In routine clinical practice, deprescribing can be challenging. Surveys of patient attitudes consistently identify the opinion of the General Practitioner as highly influencing whether the patient undertakes a trial of deprescribing (see section on patient perceptions). A number of authors have examined attitudes of health professionals and medical practitioners to deprescribing. [20-24]

Key perceptions of why deprescribing was difficult included:

- A lack of "evidence" for deprescribing outcomes;
- Patients' perceived expectation of continuation of medication;
- Pressure to conform to disease specific treatment guidelines;
- Pressure to conform to prescribing undertaken by system-specific specialists; and
- Limited time for discussion with/education of the patient.

EVIDENCE FOR DEPRESCRIBING OUTCOMES

Multiple studies in a variety of clinical settings, including primary care have not shown harm from deprescribing (see section on Clinical Trials). Indeed, many authors show that deprescribing of inappropriate agents has benefit.

PATIENTS' PERCEIVED EXPECTATIONS

Many patients can be anxious at the suggestion of ceasing or reducing a medication, particularly if it has been in place for some time (see section on Patient Perceptions). The perceptions outlined above are frequently enhanced by an unrealistic estimation of the benefit of the medication. Provision of information regarding the absolute benefit (for preventative agents) and the possible resolution of underlying symptoms (for symptom-relieving medications) may assist with patients' willingness to trial dose reduction or cessation.

CONFORMING TO TREATMENT GUIDELINES/ SPECIALIST PRESCRIBING

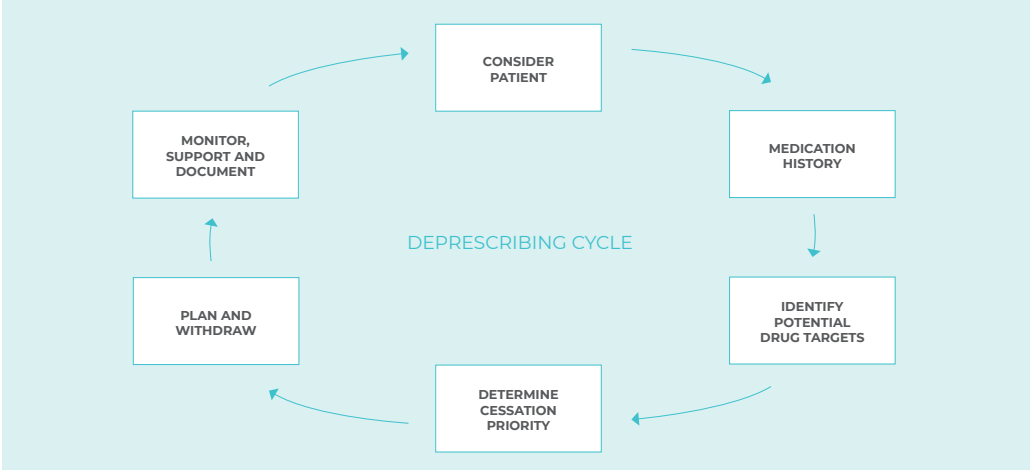
While there are disease specific guidelines available for a wide range of chronic conditions, many people with chronic conditions have one or more other chronic conditions and multimorbidity is common in older people. Such patients often receive care from general practitioners and multiple specialists. Recommendations from disease-specific guidelines may be inappropriate as trials underpinning the recommendations often exclude people with multimorbidity. [25] The National Institute for Health and Care Excellence (NICE) have developed guidance for the clinical assessment and management of multimorbidity. Their assessment recommendations include identifying patients who would benefit from such an approach, establishing what is important to them and then establishing their personal disease and treatment burden. Management recommendations are based around careful review of medication and other treatments with benefits and harms assessed in light of their personal goals and priorities. General practitioners are ideally placed to provide this wholistic approach.

LIMITED TIME FOR DISCUSSION/EDUCATION

Deprescribing can be undertaken over multiple steps (see below in the personalised approach to deprescribing), and not all of these steps need to directly involve the General Practitioner. Judicious use of practice nurses and appropriate referral for medication reviews (with specific instructions to target deprescribing) may be useful to reduce the time required.

GENERAL INFORMATION

DEPRESCRIBING: A PERSONALISED APPROACH



CONSIDER THE PERSON

1

- What are their goals and expectations?
- What is most important to the person?
- What is their degree of frailty?
- Can you assess their reasonable life-expectancy?

Estimating life expectancy is problematic in an individual. Often asking the question "would I be surprised if this patient died in the next 6-12 months?" is as effective as other techniques. Some formal life expectancy resources are available, all of which take into account the level of comorbidity, specific high mortality disease states, functional status and age.[26,27]

Independent of any specific disease processes, frailty is a vulnerable state known to be more likely to be associated with adverse outcomes. Frailty has been defined as three or more of: unintentional weight loss, exhaustion, weakness, slow walking, low physical activity and accumulation of medical, functional or social deficits.[28]

Quantification of frailty is possible using a number of available techniques.[29] Frailty scales incorporate number of measures including cognitive state, weight loss, social supports as well as some measures of muscle strength (e.g. a "timed get up and go" test). The Edmonton Frail Scale is available as an application. Walking speed is also a useful clinical measure (taking longer than 5 seconds to walk 4 metres).

Listening carefully to the person regarding aspects of their quality and duration of life and expectations of treatment (including efficacy) will assist with determining priorities for deprescribing. Deprescribing should be viewed as an individualised process allowing that individual patients attach different importance to particular outcomes depending on a range of factors, including life experience.

CONSIDER THE MEDICATIONS

2

- What are they taking?
- How long and how much have they been taking? (including dose, frequency and duration)
- Why are they taking them?
- Any adverse effects or possible interactions? (drug-drug or drug-disease)

Determine what prescription and OTC medication is being taken, including prescriptions from other practitioners along with any vitamins and herbal medicines. This can be done by asking the patient to bring all medications to an appointment or via a home visit either by a pharmacist (i.e. a Home Medicines Review) or a nurse visit (Comprehensive Health Assessment or similar).

Indications for use of many medications may change with time, and medication that was clearly appropriate in the past, may no longer be so (e.g. peptic ulcer treatment, analgesia, preventative strategies).

Although many adverse effects are predictable, uncommon adverse effects still occur and the role of medication should be considered in all patients who develop new symptoms. In particular, medication interactions with underlying diseases should be evaluated (e.g. anticholinergic drugs and cognitive impairment, NSAIDs/ACE inhibitors and renal impairment)

IDENTIFY POTENTIAL DRUGS TO BE CEASED/MODIFIED	
3	■ Risk/benefit analysis for individual drugs with particular attention to high risk drugs and those originally prescribed for disease prevention which may no longer be relevant or needed. In addition to determining the usefulness of a medication, attempting to determine the likelihood of any harm (incorporating the concept of medication load) also assists in identifying potential agents for deprescribing. Scott at al. suggested the following: ■ Medications known to have a poor risk : benefit ratio in the elderly (e.g. Beer's criteria,[30], STOPP/START criteria,[31] or other inappropriate prescribing lists) Alternatives to many of these high risk agents have been recently published.[32] ■ Medications that duplicate indications and/or classes of agents (e.g. mirtazapine at night with temazepam at night). ■ Medications to treat a sign or symptom that may be an adverse drug event from another medication (e.g. oxybutynin for urinary incontinence associated with cholinesterase inhibitors). ■ Medications used at a dose that is likely to cause toxicity in the elderly (e.g. 20mg rivaroxaban in elderly patients, 4g paracetamol in lightweight elderly women) should have doses reduced. ■ Medications that are associated with multiple drug-drug or drug-disease interactions (e.g. diltiazem) may be substituted. ■ Medications that are taken more than once daily (e.g. three times daily metformin) could be converted to once daily. ■ Multiple medications that are available in combination forms may reduce medication burden (e.g. amlodipine/ atorvastatin). ■ Medications where adherence is an issue (e.g. metered dose aerosols, night-time statins).
PRIORITISE MEDICATIONS TO BE DEPRESCRIBED	
4	■ Drugs with least utility or highest risk. ■ Drugs adversely impacting on wellbeing. ■ Patient preference. ■ Drugs with complicated administration regimens. Although many medications may be targeted for deprescribing, it may be prudent to initiate a trial of withdrawal of one medication at a time. Choosing priority will be based on individual case considerations. In some cases, deprescribing may be a case of simplifying or reducing the dose regimen prescribed rather than ceasing an agent.
PLAN AND INITIATE WITHDRAWAL TRIAL	
5	■ Seek consent from patient/carer explaining rationale and steps to take if symptoms recur. ■ Prepare withdrawal plan with appropriate tapering of one medication at a time. ■ Inform other health professionals involved of rationale and tapering plan. Explaining the rationale to the person improves success rates in deprescribing and empowers the patient to take control of their medications. The National Prescribing Service has prepared a number of specific and general patient resources with regard to deprescribing of medications.[35] It is important to provide the patient and carer with information on what they should do if symptoms recur and about alternative non-drug strategies that may used to control symptoms. A written tapering plan is desirable, especially for the classes of medication that require slow tapering to avoid either return of disease symptoms or withdrawal symptoms (e.g. corticosteroids, opioids, PPIs).
MONITOR AND SUPPORT	
6	■ Set up a follow-up plan to monitor for any withdrawal/adverse effects or return of symptoms. ■ Review plan with person and ask for feedback. ■ Document result of withdrawal process and move on to next medication if appropriate. As with prescribing, deprescribing should involve a review/monitoring plan for efficacy and adverse outcomes. The required frequency of this will depend on the medication/disease process involved and the duration of the tapering regimen.

RESOURCES

- GENERAL INFORMATION
- ALLOPURINOL
- ANTIHYPERGLYCAEMICS
- ANTIHYPERTENSIVES
- ANTIPSYCHOTICS
- ASPIRIN
- BENZODIAZEPINES
- BISPHOSPHONATES
- CHOLINESTERASE INHIBITORS
- GLAUCOMA EYE DROPS
- NSAIDS
- OPIOIDS
- PROTON PUMP INHIBITORS
- STATINS
- VITAMIN D AND CALCIUM

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A GUIDE TO

deprescribing

ANTIPSYCHOTICS

KEY POINTS

- **Non-pharmacological therapy, particularly person-centred interventions that address the precipitants of the symptoms, is often equally or more effective than antipsychotics in the majority of people with BPSD.**
- **Antipsychotics are effective in approximately one in five people with dementia for short term management of significant agitation, aggression and psychosis.**
- **Antipsychotics are considerably less effective for some types of behavioural problems than others (e.g. wandering, calling out, sexual disinhibition, urinating in inappropriate places).**
- **Serious adverse effects of antipsychotic agents may include falls, increased mortality and increased risk of stroke. The risk of several of these is evident within weeks of commencing treatment.**
- **Antipsychotics may precipitate a number of adverse effects, particularly akathisia, some of which may mimic BPSD.**
- **Certain groups of people are more sensitive to the adverse effects of antipsychotic agents (e.g. those with Parkinson's disease, Lewy body dementia, or cardiac disease).**
- **Most people on long term antipsychotics for behavioural and psychological symptoms of dementia can have their antipsychotics ceased, often without any decline in BPSD.**
- **Discontinuation of antipsychotics should be gradual, particularly if use has been long term.**

FOR BETTER HEALTH OUTCOMES

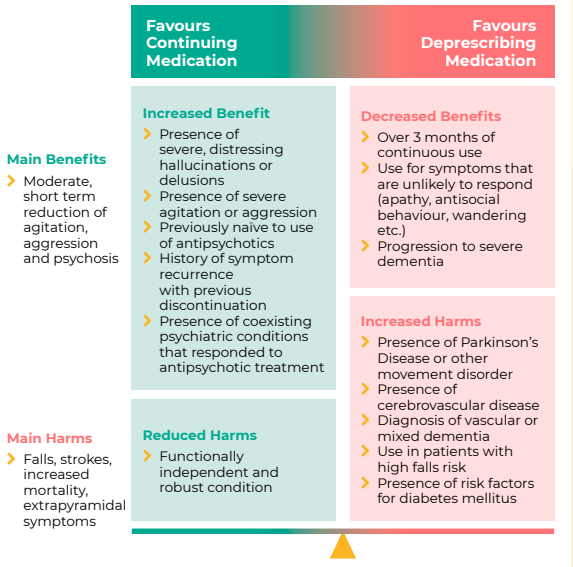
CONTEXT

This guide considers the use of antipsychotic agents in the context of the behavioural and psychological symptoms of dementia (BPSD).

RECOMMENDED DEPRESCRIBING STRATEGY

- Consensus-based deprescribing guidelines that address antipsychotic use for BPSD were published by a Canadian group in 2018 (see **Figure 1, Page 2**).
- Consideration may be given to a trial of cessation of antipsychotics if a person has been symptom/target behaviour free for three months or more.
- People whose BPSD are unchanged or improving over several weeks or months may benefit from a trial of dose reduction and/or cessation of antipsychotics.
- The provision of person-centred interventions that address the precipitants of BPSD should be maintained throughout the provision of care.

BENEFIT VERSUS HARM



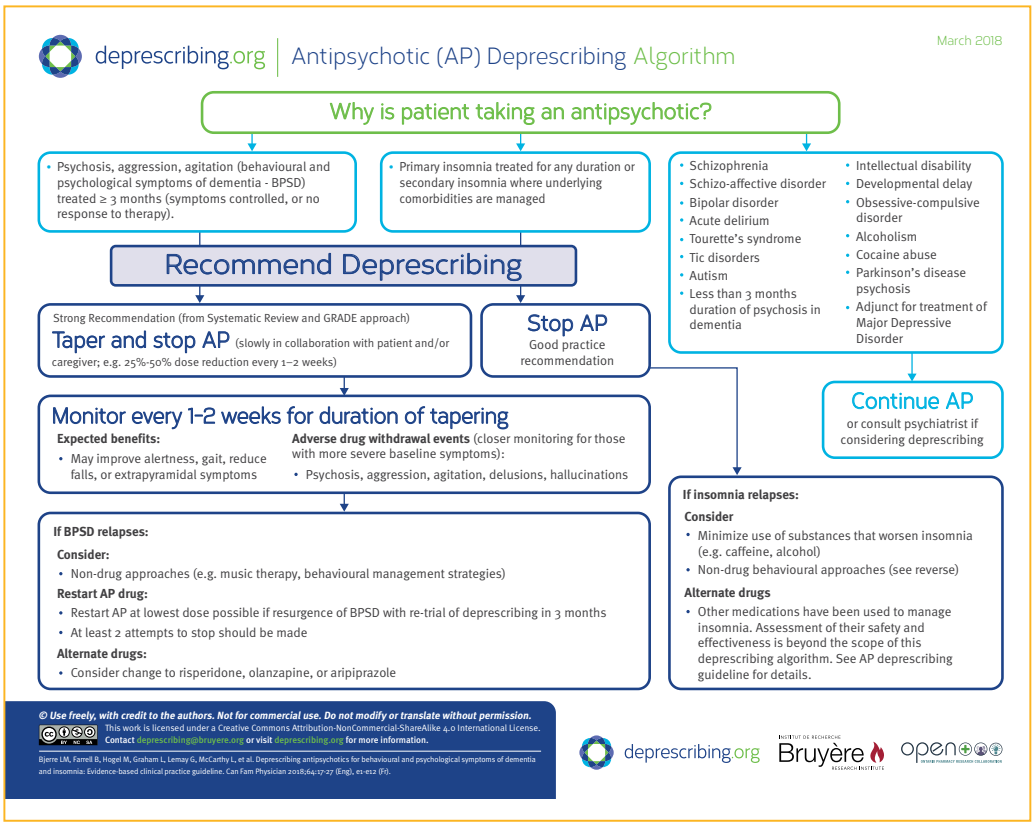


Figure 1: Antipsychotic (AP) deprescribing algorithm [38]

BACKGROUND

The term "behavioural and psychological symptoms of dementia" (BPSD) describes a constellation of non-cognitive phenomena frequently observed in people with dementia, particularly in the latter stages of the disease. Behavioural symptoms include agitation, aggression, walking without purpose and vocalisation; psychological symptoms include hallucinations, delusions, depression and psychosis.

BPSD are presumed to occur due to multiple interacting factors, including pathological changes in the brain, the person's lived experience, unmet needs, environment, emotions, and altered clinical circumstances (e.g. pain, constipation or infection). Consequently, the most appropriate strategy to support a person with dementia who has BPSD is to identify and address as many precipitants as possible. Such measures frequently mitigate the need to use pharmacological measures, and avoids the risk of adverse effects associated with medication use. Nonetheless, the use of antipsychotic agents for BPSD is particularly common.

Dementia Support Australia (DSA) provides a comprehensive guide to non-pharmacological and pharmacological management of specific behaviours commonly encountered in dementia. The guide is available in several formats at https://www.dementia.com.au/resources/library.

ANTIPSYCHOTICS AGENTS

EFFICACY

Many randomised trials have evaluated the efficacy of antipsychotic agents for BPSD. As most of these studies had small sample sizes, monitored participants for a maximum of 12 weeks, and a number had methodological limitations, the applicability of their findings to practice is somewhat limited.[1] Furthermore, the rate of response to treatment with placebo in several studies was around 30%.

The evidence regarding older agents (conventional or "typical" antipsychotics) is particularly limited. These medications were evaluated in a systematic review and meta-analysis that involved two previous meta-analyses of 12 trials, and two additional studies. [2] This review reported that there was no clear evidence for efficacy for alleviating BPSD in any of the conventional antipsychotics included in the analysis (such as haloperidol, trifluoperazine and thioridazine). A 2002 Cochrane review of haloperidol for agitation in dementia found some benefit for aggression, but not for other BPSD including agitation. [3]

Newer, "atypical" antipsychotics have been evaluated somewhat more thoroughly. The CATIE-AD was a 42 site, double blind, placebo controlled trial of 421 people with BPSD. BPSD symptoms included psychosis, aggression, and agitation; participants were randomised to a flexible dose regimen of risperidone, quetiapine, olanzapine or placebo for up to 36 weeks.[4] The main outcome was time to discontinuation. No significant differences were found in overall time to discontinuation or in clinical improvement between treatment with antipsychotics and placebo.[4] The study allowed for a change between treatments at the physician's discretion after a 12 week period (termed end of Phase one). An analysis of the Phase one results indicated that antipsychotic agents may be more effective for particular symptoms such as anger, aggression and paranoid ideas.[5]

A 2006 Cochrane review of the use of atypical antipsychotic agents found that risperidone and olanzapine had a beneficial effect on aggression in approximately 20% of people.[6] A 2016 systematic review of 10 meta-analyses involving atypical antipsychotics for BPSD concluded that risperidone, olanzapine and aripiprazole modestly improve BPSD, with psychosis, aggression, agitation and more severe symptoms the most responsive to atypical antipsychotic treatment.[7] The same review reported that there is no evidence that quetiapine is of benefit for BPSD.

Whilst improvement in some behaviours may occur during the initial phases of treatment with antipsychotics, there is minimal evidence of fficacy in the long term (i.e. more than 3 months). Some behaviours are not improved by antipsychotics in the intermediate to long term, such as wandering, undressing, urinating inappropriately, shadowing staff or calling out (see **Table 1**).

A study of withdrawal of antipsychotic agents in 102 people with dementia who had been taking antipsychotics (at least 10mg chlorpromazine equivalent or 0.5mg risperidone daily) for BPSD for 3 months or more found that cessation did not significantly affect symptom severity, as measured by the Neuropsychiatric Inventory (NPI).[8]

A Cochrane review that assessed ten studies that investigated withdrawal versus continuation of chronic antipsychotic drugs for BPSD was published in 2018.[9] Whilst it was not possible to meta-analyse data from all ten trials due to a high level of heterogeneity, the review found that, in general, **antipsychotic discontinuation appeared to make minimal to no difference in overall BPSD** as measured by the NPI. In fact, there was some evidence that antipsychotic discontinuation reduced agitation in people with less severe BPSD at baseline. Conversely, those with more severe BPSD (as indicated by a NPI score >14) may have benefited from continuing antipsychotic treatment, particularly people who previously had psychotic features or severe agitation.[9] Similarly, Patel et al reported that people with severe hallucinations at baseline were significantly more likely to relapse with the cessation of risperidone, compared to those with mild or no hallucinations (HR 2.96, 95% CI 1.52 to 5.76). [10]

ANTIPSYCHOTICS MAY HELP TO MANAGE SYMPTOMS OR BEHAVIOURS LIKE:	ANTIPSYCHOTICS DO NOT HELP TO MANAGE SYMPTOMS OR BEHAVIOURS LIKE:
✓ Hallucinations (hearing voices, seeing things/people)	✗ Apathy or not being social with others
✓ Delusions (paranoia or severe suspicion)	✗ Inappropriate behaviour (urinating inappropriately, sexual advances, removing clothes)
✓ Severe Agitation (screaming, severe irritability, sleep disturbances)	✗ Perseveration (repeating actions or words over and over)
✓ Aggression (shouting, kicking/biting/hitting)	✗ Wandering or restlessness
	✗ Hoarding/hiding items

Table 1: Symptoms likely or unlikely to respond to antipsychotics

ADVERSE EFFECTS

Antipsychotics have a range of metabolic, cardiac, movement and CNS adverse effects. Metabolic adverse effects include weight gain, diabetes and the development of metabolic syndrome. Many antipsychotic agents also prolong the QT interval and can exacerbate or precipitate arrhythmias and syncope. Movement disorders that can result from, or be exacerbated by, antipsychotics include a range of extrapyramidal symptoms from acute dystonic reactions, akathisia, parkinsonism and tardive dyskinesia. CNS adverse effects can be variable, with somnolence, cognitive worsening and occasionally abnormal gait and seizures.

Akathisia is an extrapyramidal syndrome that may be induced by antipsychotic and other anti dopaminergic agents. It is characterised by an "inner restlessness" that makes the patient feel anxious, agitated and is often associated with and urge to move, manifesting as pacing, leg movements or leg rubbing. This adverse effects typically commences 3-8 weeks after initiation or dose increase of an antipsychotic agent.

In addition to these adverse effects, there are serious concerns regarding the use of antipsychotics in patients with dementia in terms of increased mortality, strokes and falls.

INCREASED MORTALITY

In 2005, the United States Food and Drug Administration (FDA) analysed 17 trials of atypical antipsychotic use in dementia (some of which were unpublished) and showed an increased relative risk of death between approximately 54 and 70% (an absolute increased risk of 1-2% per year; NNH 50-100) [11]. The increased mortality was mainly due to vascular or infectious causes. A boxed warning was issued at this time.

The FDA warning was subsequently extended in 2008 to cover all antipsychotics (including the older agents) following retrospective population-based studies that demonstrated that typical antipsychotics also showed a similar increased risk of death. [12,13]

A retrospective cohort study examined mortality using national data from the US Department of Veterans Affairs for people ≥65 years old with dementia, beginning outpatient treatment with an antipsychotic (risperidone, olanzapine, quetiapine, or haloperidol) or valproic acid. [14] They associated the commencement of antipsychotic treatment with the following absolute increases in mortality risk and numbers needed to harm after 180 days:

- Haloperidol: 3.8% (95%CI 1.0 to 6.6%); NNH 26 (95%CI 15 to 99)
- Olanzapine: 2.5% (95%CI 0.3 to 4.7%); NNH 40 (95%CI 21 to 312)
- Quetiapine: 2.0% (95%CI 0.7 to 3.3%); NNH 50 (95%CI 30 to 150)
- Risperidone: 3.7% (95%CI 2.2 to 5.3%); NNH 27 (95%CI 19 to 46)

Mittal et al reviewed the evidence relating to antipsychotic associated cerebrovascular events and mortality risk. [15] The increase in mortality was 1.2 to 1.6 fold higher when antipsychotics were used. Older age, male gender, severe dementia and functional impairment were all associated with a higher risk of death. [15]

Long-term mortality follow-up data from the DART-AD study indicated that discontinuation of antipsychotics was associated with reduced mortality at 12, 24, and 36 months. [16]

CEREBROVASCULAR EVENTS

There is evidence that antipsychotic use in people with dementia is associated with an increased risk of stroke, however, this has not been reported consistently in trials. While several studies have reported such a link,[17,18,19] others have not. [20,21,22]

A Cochrane review of five studies of risperidone use in people with dementia found a rate of stroke of 3.1% for risperidone after 13 weeks of treatment, compared to 1% for placebo (OR 3.64 [95%CI 1.72-7.69]: NNH 47). [23]

Mittal et al also reviewed the evidence relating to antipsychotic associated cerebrovascular events and mortality risk in people with dementia.[15] They concluded that the risk of cardiovascular events was between 1.3 and 2 times higher in people treated with antipsychotics. No one antipsychotic drug was found to be safer than any other in terms of the cerebrovascular risk. They also concluded that higher doses, older age of patient, presence of vascular dementia and presence of atrial fibrillation all increased the risk of strokes in this group.[15]

In 2015 the Australian Therapeutic Goods Administration (TGA) increased restrictions on the indication for risperidone use in people with dementia to the following:

treatment (up to 12 weeks) of psychotic symptoms, or persistent agitation or aggression unresponsive to non-pharmacological approaches in patients with moderate to severe dementia of the Alzheimer type.

This change was based on the increased risk of stroke being more prominent in people with vascular or mixed dementia, compared to Alzheimer's type dementia. The data presented by the TGA in justification of the changed approval was an odds ratio for any cerebrovascular adverse event in people with vascular or mixed dementia being 5.26 (95% confidence interval [CI] 1.18-48.11) in those taking risperidone. The comparative odds ratio for people with Alzheimer's dementia was 2.23 (95% CI 0.85-6.88).[24]

FALLS

Antipsychotic use in people with dementia has been associated with an increased risk of falls in numerous studies. Multiple meta-analyses of the impact of drugs on falls found increased relative risk of falls associated with antipsychotic/neuroleptic use. In studies that reported an increased risk of falls, the overall increase in risk of at least one fall during trial periods (often 12 weeks or less) ranged between 25 and 79%. [25-29]

There is also evidence associating an increased risk of hip fracture with the use of antipsychotics in people with dementia.

For example, a population based cohort study from the United Kingdom identified a prior event rate ratio of 1.62 (95% CI 1.59 to 1.65) in people using antipsychotics.[30]

ANTIPSYCHOTICS AGENTS

DISCONTINUATION SYNDROMES

Most studies have found that many individuals can have antipsychotics safely discontinued without worsening of behavioural symptoms.[8,16] A 2018 Cochrane review reported that antipsychotic discontinuation may have little or no effect on overall cognitive function, and may not adversely affect quality of life.[9] Predictors of successful discontinuation antipsychotics include lower daily doses of antipsychotics and lower baseline severity of behavioural and psychological symptoms of dementia.

There is little evidence to guide the most appropriate dose reduction strategy. Withdrawal schedules from randomised controlled studies have varied from abrupt cessation to dose tapering over a number of weeks.

A number of withdrawal effects are possible, such as the following:

- autonomic symptoms such as nausea, vomiting, anorexia, rhinorrhoea, diarrhoea, diaphoresis, myalgia and paraesthesia
- anxiety, agitation, insomnia and restlessness (although these may also be BPSD not directly related to the initial symptom for which the antipsychotic was originally prescribed)
- neuroleptic malignant syndrome, which is very rare but extremely severe

It is possible that tapering withdrawal schedules reduce the likelihood of these effects occurring. Canadian deprescribing guidelines recommend a 25-50% dose reduction every 1-2 weeks to cessation.[38] Australian guidelines recommend that the longer the medication has been prescribed, no matter at what dose, and the less the concern over current adverse drug reactions, the slower the withdrawal can be.[39]

During withdrawal, it is important to monitor for recurrence of target symptoms or behaviours, or emergence of new ones.

FACTORS TO CONSIDER

Most Australian and international guidelines recommend that antipsychotics should only be used short-term for BPSD, if at all. The severity of most BPSD can be effectively reduced with appropriate person-centred interventions that address the precipitants of such symptoms. Whenever an antipsychotic is commenced for BPSD, there should be an intention of eventual dose reduction and cessation.

The natural history of most BPSD is a waxing and waning of severity in response to precipitants (clinical and environmental factors), and disease progression.[31] A 2017 antipsychotic deprescribing study by Brodaty et al reported that 76% of participants remained off antipsychotic treatment 12 months after cessation, with minimal change in measures of BPSD severity 6 months after cessation.[32]

IN FAVOUR OF DEPRESCRIBING

- Any person with overt or suspected adverse effects will be more likely to benefit from dose reduction or cessation of the antipsychotic agent. Some people may be at higher risk of adverse effects from antipsychotics and these agents should be reconsidered regularly in such people. These include people:
  - three months of ongoing antipsychotic use
  - with Parkinson's disease
  - with Lewy body or vascular dementia[33]
  - with previous stroke or TIA history
  - with existing prolonged QT syndromes
  - taking agents that prolong QT syndrome (in particular, tricyclic antidepressants and macrolide antibiotics)
  - with risk factors for arrhythmias, including existing cardiac pathology and/or electrolyte disorders (esp. hypokalaemia, hypomagnesaemia).[34]
- People whose dementia has progressed and whose previous BPSD have ceased or lessened are less likely to relapse if the antipsychotic is ceased.
- For many people with dementia, any benefit from antipsychotic treatment occurs shortly after its commencement. A post-hoc analysis of the CATIE-AD study reported that a lack of response 2 weeks after the commencement of an antipsychotic was associated with a lack of response at 8 weeks.[35]
- There is some evidence that cessation of antipsychotic agents is associated with a reduction in risk of falls.[36]
- Stopping antipsychotics may also reduce the risk of death (NNT = 4 at 2 years), with minimal effect on BPSD.[37]

AGAINST DEPRESCRIBING

- People with more severe BPSD, for example severe hallucinations, physically violent aggression or distressing agitation may be more likely to relapse or experience worsening of symptoms if dose reduction or cessation is attempted.
- People with a history of psychosis or other psychiatric disorders requiring antipsychotics prior to them developing dementia may experience worsening of their underlying psychiatric condition by reducing or ceasing antipsychotics.

A GUIDE TO

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BENZODIAZEPINES

KEY POINTS

- **Benzodiazepines are generally regarded by clinical practice guidelines as only a short-term therapeutic option for anxiety and insomnia.**
- **Treating 13 patients with benzodiazepines for insomnia will improve sleep quality in one and there will likely be two patients with adverse effects.**
- **Non-pharmacological methods for insomnia (e.g. sleep hygiene, relaxation techniques) are often as effective as benzodiazepines.**
- **Abrupt discontinuation of benzodiazepines used for insomnia often results in short-term reduction of sleep quality.**
- **There is strong evidence that improvement in a range of neuropsychiatric functions occurs after discontinuation of benzodiazepines.**
- **Deprescribing of long term benzodiazepines for insomnia may take at least 6-8 weeks.**
- **Some patients reducing benzodiazepines may develop withdrawal symptoms and will require more gradual dose reduction.**
- **Providing patients with information regarding the risks of benzodiazepines in a structured format increases the efficacy of deprescribing.**

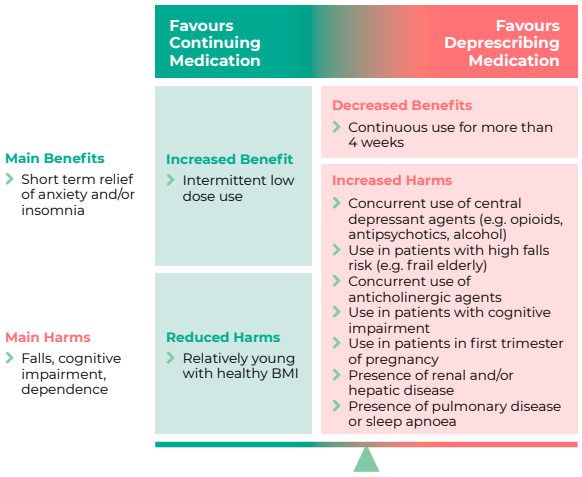
CONTEXT

This guide considers the use of benzodiazepines for insomnia and anxiety.

RECOMMENDED DEPRESCRIBING STRATEGY

- Any patients taking benzodiazepines with overt adverse effects (daytime sedation, cognitive impairment, falls or dependence) may benefit from dose reduction and/or cessation.
- Many patients taking long-term benzodiazepines will gain benefits from cessation even though they do not have overt adverse effects.
- A tapering strategy should be used for all patients, but the duration and amount of tapering is variable.
  - The majority of patients will tolerate tapering by 15-20% per step over 6-8 weeks. One option (for patients using benzodiazepines for insomnia) is to advise not taking the agent one night a week for a week (or two), two nights the next week or two, three nights the next, etc. In most patients, this strategy will enable cessation.
  - If patients develop significant intolerant withdrawal or discontinuation symptoms, a return to the previous tapering step for a longer period of time (e.g. a month) often allows for a reattempt of dose reduction.

BENEFIT VERSUS HARM



BENZODIAZEPINES

EFFICACY

Benzodiazepines are widely used (and often misused) in Australia for a number of psychiatric conditions. These medications are generally effective, particularly when used short term, and are well tolerated by most people (in the short term). However, prolonged use is common and of concern due to a risk of dependence and an increased likelihood of other adverse effects, particularly sedation, falls, depression and cognitive impairment. Benzodiazepines were involved in approximately one third of drug induced deaths in Australia in 2016, commonly in combination with opioids.[1]

Long term use should therefore be frequently re-evaluated with a view to dose minimisation or cessation if possible.

Benzodiazepines have anxiolytic, hypnotic, muscle relaxant and anticonvulsant properties. In terms of the use of benzodiazepines for psychiatric conditions, there is only demonstrated efficacy in four conditions: insomnia, panic disorder (PD), generalised anxiety disorder (GAD) and social anxiety disorder (SAD).[2]

The most common indications for the prescribing of benzodiazepines are insomnia and anxiety. As tolerance to the beneficial effects of benzodiazepines often develops, usually within weeks of commencement, short term use is recommended for these indications.

INSOMNIA

While hypnotics have been used for decades for insomnia, the studies that support this practice are limited to short term treatment and overall impact on sleep is moderate at best. Meta-analyses of sedative hypnotic use published in 2005 and 2007 identified that:[3,4]

- The number of patients that would need to be treated with a sedative for one to have an improvement in sleep quality was 13 (95% CI 6.7-62.9).
- The increase in total sleep time with any sedative compared with placebo was 25.2 minutes (95%CI 12.8-37.8 minutes).
- There was a decrease in sleep latency (time trying to get to sleep) by approximately 10 minutes.
- The mean number of awakenings decreased by 0.63 (95%CI -0.48 - -0.77).

Tolerance to the hypnotic effects occurs rapidly and guidelines for pharmacological management of insomnia consistently recommend short term use only after attempts to use non-pharmacological methods (which have comparable efficacy to benzodiazepines).[5] Suggested non-pharmacological therapies that have been shown to be effective for insomnia of different causes are shown in **Table 1** below.[6]

In people living with dementia, a Cochrane review found "a distinct lack" of evidence to help guide drug treatment of sleep problems in dementia patients. In particular, they found no trials of drugs that are widely prescribed for sleep problems, including the benzodiazepine and non-benzodiazepine hypnotics.[7]

ANXIETY

Anxiety disorders are a commonly occurring spectrum of conditions that vary from mild situational responses to stressors, to severe chronic anxiety with comorbid psychiatric illness. First-line therapy for GAD, PD, and panic attacks should include cognitive behaviour therapy (CBT) due to its effectiveness at reducing the symptoms of anxiety in the short and long term.[8]

Selective serotonin reuptake inhibitor (SSRI) and serotonin-norepinephrine reuptake inhibitor (SNRI) medications are effective across the range of anxiety disorders and are generally suitable for first-line pharmacological treatment of anxiety, particularly when there are elements of comorbid depression.

Short-term benzodiazepine use as occasional adjunctive therapy may be effective at reducing exacerbations of anxiety symptoms that can occur in the first few days to weeks of initiating antidepressant medication.[9] Benzodiazepines are regarded by most clinical practice guidelines as a short-term therapeutic option.[8] Use beyond four weeks is not recommended for most patients, as the risks of adverse effects associated with benzodiazepines outweighs the benefits in a number of patient groups (see adverse effect over).

WHAT IS THE CAUSE?	WHICH THERAPY AND WHAT APPROACH CAN I USE?
Lifestyle habits and environment not conducive to sleep	**Advice on good sleep practices** Practical tips on how to modify diet, exercise patterns, substance use, sleep-wake schedule, daytime napping, and sleep environment.
Negative thoughts or unrealistic expectations about sleep and the consequences of sleep loss	**Cognitive therapy** Techniques that replace distorted beliefs and attitudes with positive ones (e.g. reassure that <8 hours sleep a night is not necessarily detrimental).
Learned association between going to bed and being unable to sleep	**Stimulus control** Go to bed only when tired (and only use the bed for sleep or sex), get out of bed if not asleep within a perceived 20 minutes (do not watch the clock); repeat each night until a stable sleep-wake schedule is established.
Poor sleep drive results in broken sleep or excessive time spent in bed awake	**Sleep restriction** Restrict time in bed to actual sleep duration and have a set wake-up time; increase gradually as total sleep duration improves, and until the target sleep time is reached (not <5 hours).
Unable to mentally and/or physically wind down each night	**Relaxation techniques** Progressively focus on and relax each muscle group; taking deep breaths, relax and imagine something pleasant for as long as possible.

Table 1: Educational, behavioural and cognitive therapies for insomnia.[11]

ADVERSE EFFECTS

The adverse effects of benzodiazepines have been only adequately studied in the short term. Few studies have specifically addressed adverse effects associated with long term usage. Epidemiologic and experimental data has demonstrated a causal association between benzodiazepine use and motor vehicle accidents, falls and bone fractures.[10]

Some adverse effects may subside due to tolerance, in a similar way that tolerance develops to the desired effect of the medication. Most often, subjective feelings of dysphoria, heaviness, and sedation rapidly subside with continuous treatment.[11]

This is because GABA receptors become less responsive with prolonged use of benzodiazepines, making the inhibitory effects of GABA less effective. In addition, negative feedback mechanisms cause a reduction in production of GABA, resulting in tolerance to its sedating and anxiolytic effects. However, enhancement of GABA's inhibitory activity also results in reduced production of excitatory neurotransmitters, which results in some of the long term side effects of benzodiazepines including ataxia, memory loss, confusion and possibly depression.

The impact of these adverse effects is greater in certain subgroups as outlined in **Table 2** below.

SUBGROUP AT HIGHER RISK	Reason for higher risk
PREGNANCY	there is increased risk of foetal abnormalities in the first trimester.
ALCOHOL CONSUMPTION	increased risk of excessive sedation and respiratory depression
RENAL AND/OR HEPATIC DISEASE	metabolic clearance of the agents will be compromised.
PULMONARY DISEASE/SLEEP APNOEA	benzodiazepines are respiratory suppressants
OLDER ADULTS	As a consequence of multiple comorbidities and CNS changes associated with aging, the risk of adverse effects is increased in older adults, especially those over 75 years of age

Table 2: Subgroups of people at high risk of benzodiazepine adverse effects

The use of benzodiazepines in older people is particularly problematic. A meta-analysis of sedative-hypnotic use in this population identified that:

- the most common adverse effects recorded were drowsiness or fatigue, headache, nightmares, nausea and other gastrointestinal disturbances
- the number needed to harm for sedative hypnotics compared to placebo was 6 (95%CI 4.7-7.1)
- adverse cognitive effects were significantly more common with sedative use than placebo.[3]

IMPAIRED COGNITION

Benzodiazepine use is frequently implicated in impairing cognition. Whilst this is most common in people using high doses long term, it may also occur with low doses over the short term, particularly in older adults. Whilst these effects typically resolve with discontinuation, there is concern that benzodiazepine use may contribute to dementia, with a number of observational studies associating an increased incidence of dementia with benzodiazepine use.[10] Meta-analyses of several of these studies reported an increased odds of developing dementia of between 49% and 78% in users of benzodiazepines.[12,13] However, it should be acknowledged that these studies have not definitively demonstrated that benzodiazepine use causes dementia, and the potential for reverse causality (e.g. benzodiazepine use was treating symptoms associated with preclinical dementia) cannot be excluded.

FALLS

Benzodiazepines are associated with an increased risk of falls. Multiple meta-analyses have found an increased relative risk of falls associated with sedative/hypnotic use. For example, a 2013 meta-analysis reported an overall increase in risk of at least one fall during the reported trial periods (often 6 months or less) of between 35% and 60%.[14]

DEPENDENCE

In addition to the above range of adverse effects, regular benzodiazepine use commonly results in the development of psychological and physical dependence. The likelihood of this occurring increases with duration of use and is also higher in elderly patients and those with multiple medical conditions.

FACTORS TO CONSIDER

The discontinuation of benzodiazepines has been a focus of improved medication use for decades. A number of discontinuation strategies have been employed for adult long-term users. A recent review of the clinical evidence and guidelines for benzodiazepine discontinuation found that most studies utilised dose tapering either alone or as part of other interventions (usually psychotherapy).[15-19]

Relatively simple interventions may effectively reduce many patients' use of benzodiazepines. For example, studies that utilised patient-directed letters from their prescriber (with or without a follow-up consultation) reported significant reductions in benzodiazepine use. In these studies, cessation of benzodiazepines occurred in 20 to 35% of subjects in the intervention groups, compared to 10 to 15% of the "usual care" groups at six month follow-up, with a number needed to treat (NNT) of 12.[20]

Tannebaum et al utilised a more intensive strategy involving a "deprescribing patient empowerment intervention" to reduce benzodiazepine use. This consisted of an education package for patients that described the risks associated with benzodiazepines and a stepwise tapering protocol.[21] At 6 months, 37.8% of the intervention group had either discontinued benzodiazepine use or reduced the dose of benzodiazepine (of 148 participants, [40] [27%] ceased and 16 [10.8%] reduced doses). The NNT for this study was 3.7. Of interest, in multivariate sub-analyses, age >80 years, sex, duration of use, indication for use, dose, previous attempt to taper, and concomitant polypharmacy (defined as ≥10 drugs per day) did not have a significant interaction effect with benzodiazepine therapy discontinuation. [21]

A similar study utilised a structured interview to provide patients with:

- information regarding benzodiazepine dependence and withdrawal symptoms
- information regarding the risks of long term use on memory, cognition, falls and accidents
- reassurance about reducing medication
- a patient self-help leaflet to assist with sleep quality (for those taking benzodiazepines for insomnia).

At 12 months, 162 of 369 patients (45%) that received the education (some with further followup) had ceased their benzodiazepine(s), compared with 26 of 173 (15%) in the control group (ARR 30%; NNT 3.3).[22]

A 2017 systematic review assessed seven studies that reported on interventions to deprescribe benzodiazepines and other hypnotics amongst older people.[23] Mixed interventions, such as patient education and tapering, pharmacological substitution with psychological support, and tapering with psychological support, were associated with discontinuation rates between 27 and 80%.

Based on these data, **it is apparent that patient education regarding the long-term use of benzodiazepines has a significant impact on successful deprescribing**. Such interventions are of low cost, easily integrated into regular care and involve patients in therapeutic decision-making. The Royal Australian College of General Practitioners (RACGP) has developed patient fact sheets on both the use and cessation of benzodiazepines, along with sample letters for patient mailouts and sample dose reduction strategies for particular agents.[8]

IN FAVOUR OF DEPRESCRIBING

- Patient willingness to change has been positively associated with successful cessation of benzodiazepines.[30]
- Some patients may be aware of being dependent on benzodiazepines and may be amenable to a weaning regimen.
- There is evidence that informing patients of the potential harms of benzodiazepine use increases the likelihood of long term discontinuation.
- Lower baseline benzodiazepine doses and shorter durations of use are associated with greater rates of successful cessation and lower risks of resumption.

AGAINST DEPRESCRIBING

- Short term benzodiazepine use may be appropriate for patients with a self-limiting stressor.
- Patients receiving benzodiazepines for other significant indications (muscle spasm) may require continuation of the agents.

DISCONTINUATION SYNDROMES

Sudden cessation of benzodiazepines in tolerant patients result in them being exposed to hypoactive GABA and hyperactive glutamatergic excitation, which causes discontinuation symptoms.[24] This may even occur in patients who have only used low doses for a few weeks. Discontinuation symptoms include recurrence, rebound and withdrawal.

Recurrence involves the person experiencing symptoms identical to those for which the benzodiazepine was initially prescribed. **Rebound** symptoms reflect the inverse of the therapeutic effect of benzodiazepines, such as increased anxiety, insomnia and restlessness. For example, insomnia can return in an exaggerated form with changes to sleep patterns. Sleep latency is increased, sleep is more disturbed, and overall sleep is shorter in duration.[25] Although these changes are of short duration (usually less than a week), the recommencement of benzodiazepines is a common patient response to these symptoms.

WITHDRAWAL

There is limited data regarding pharmacological management of benzodiazepine cessation. A 2018 Cochrane review evaluated the benefits and harms of pharmacological interventions to facilitate discontinuation of benzodiazepines in chronic users.[26] The interventions assessed included valproate, tricyclic antidepressants, pregabalin, carbamazepine, paroxetine and flumazenil. Whilst over 30 studies involving over 2000 participants were evaluated in this review, most studies were of low quality and small sample sizes, and the review was unable to draw firm conclusions as to the appropriateness or effectiveness of these interventions in reducing benzodiazepine use.

About 20% of long term users of benzodiazepines become physically addicted and attempts to withdraw the drug are associated with frank withdrawal symptoms.[25] While it is difficult to predict which patients are more likely to become dependent, those who take higher doses, use high potency compounds (e.g. alprazolam) and have used the agents for prolonged periods of time are more likely to become dependent.

Withdrawal symptoms include anxiety, insomnia, nightmares, changes to memory and concentration as well as muscle spasms (see **Table 3**). Patients often experience an increase in sensory acuity, often with photophobia and increased sensitivity to everyday sounds.[8]

The duration of withdrawal symptoms is often dependent upon the agent. Withdrawal from benzodiazepines with short half-lives (e.g. oxazepam, alprazolam) usually improves significantly within four to five days; withdrawal from long half-life benzodiazepines (e.g. diazepam) usually subsides after two to four weeks, but can be prolonged. An appropriate tapering schedule can minimise and sometimes avoid these withdrawal effects. Whilst there is no evidence regarding the most suitable benzodiazepine tapering regimen, factors that may indicate a slower tapering regimen will be required include high dose, high potency and prolonged duration of benzodiazepine use.

ANXIETY SYMPTOMS			
PSYCHOLOGICAL	PHYSICAL	DISTORTED PERCEPTIONS	MAJOR INCIDENTS (MAINLY WHEN HIGH DOSES ARE STOPPED ABRUPTLY)
■ Anxiety ■ Panic attacks ■ Insomnia ■ Poor memory ■ Depression ■ Paranoia ■ Intrusive memories ■ Cravings ■ Nightmares ■ Excitability ■ Agoraphobia ■ Social phobia ■ Obsessions ■ Rage, aggression ■ Irritability	■ Agitiation ■ Tremor ■ Headache ■ Weakness ■ Dizziness ■ Nausea ■ Vomiting ■ Diarrhoea ■ Constipation ■ Palpitations ■ Rashes ■ Tingling, numbness, altered sensation ■ Fatigue ■ Flu-like symptoms	■ Hypersensitivity to sound, light, touch, taste ■ Abnormal body sensation e.g. itching, pain, stiffness, blurred vision, paraesthesia, muscle twitching, tinnitus, burning sensations ■ Feeling self or world to be abnormal (depersonalisation or derealisation)	■ Fits (1-2% of patients) ■ Delirium (rare) ■ Transient hallucinations (visual, tactile, auditory) or illusions (rare) ■ Psychosis (very rare)

Table 3: Acute withdrawal effects after ceasing benzodiazepines[8]

BENZODIAZEPINES

RESOURCES

- GENERAL INFORMATION
- ALLOPURINOL
- ANTIHYPERGLYCAEMICS
- ANTIHYPERTENSIVES
- ANTIPSYCHOTICS
- ASPIRIN
- BENZODIAZEPINES
- BISPHOSPHONATES
- CHOLINESTERASE INHIBITORS
- GLAUCOMA EYE DROPS
- NSAIDS
- OPIOIDS
- PROTON PUMP INHIBITORS
- STATINS
- VITAMIN D AND CALCIUM

AUTHORSHIP

This guide was updated by Dr Andrew Stafford, Dr David Dunbabin and Dr Peter Tenni from a document developed in consultation with the Deprescribing Reference Group.

MAY 2019

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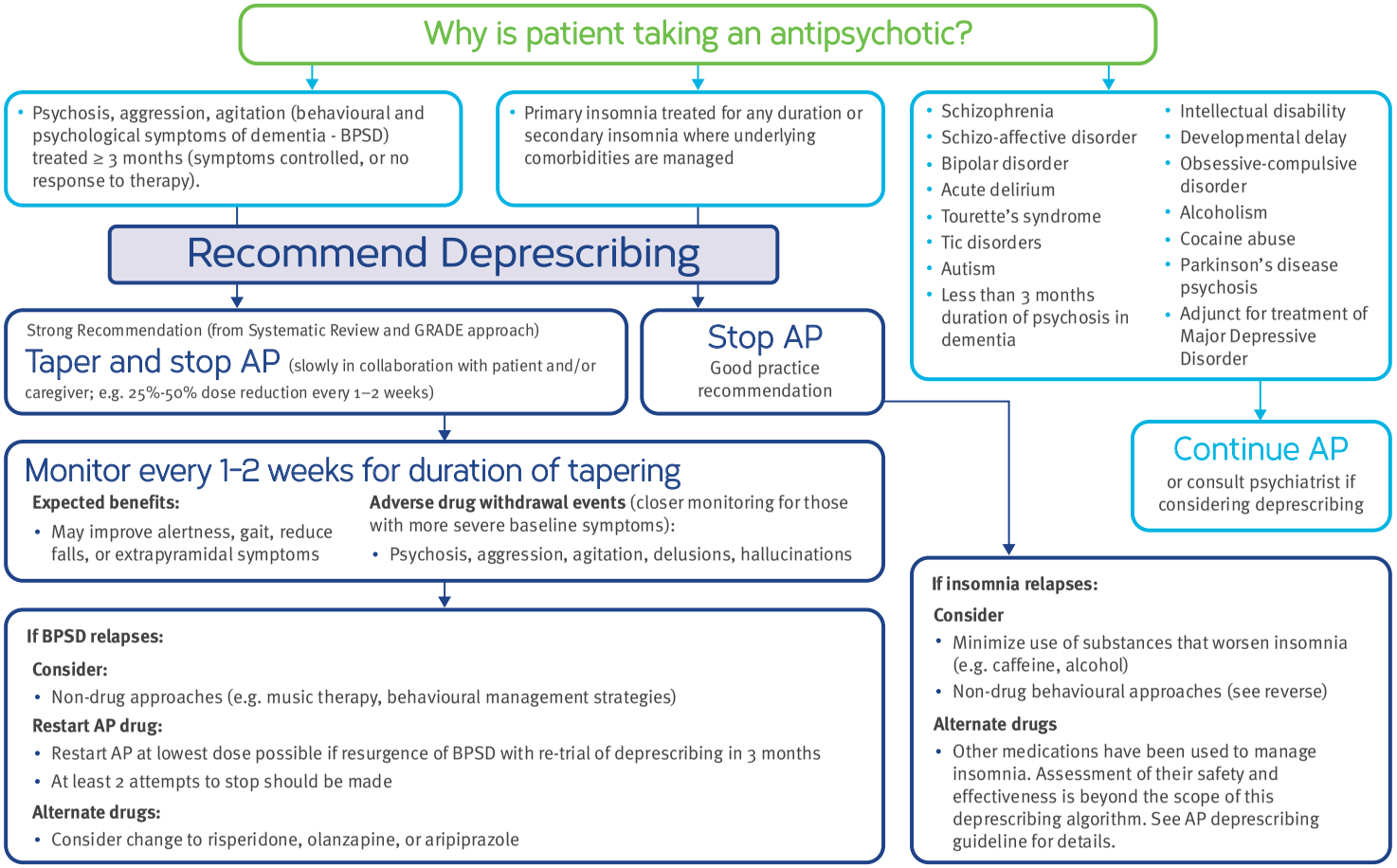
March 2018



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deprescribing.org | Antipsychotic (AP) Deprescribing Notes

October 2016

Commonly Prescribed Antipsychotics

Antipsychotic	Form	Strength
Chlorpromazine	T IM, IV	25, 50, 100 mg l25 mg/mL
Haloperidol (Haldol®)	T L IR, IM, IV LA IM	0.5, 1, 2, 5, 10, 20 mg 2 mg/mL 5 mg/mL 50, 100 mg/mL
Loxapine (Xylac®, Loxapac®)	T L IM	2.5, 5, 10, 25, 50 mg 25 mg/L 25, 50 mg/mL
Aripiprazole (Abilify®)	T IM	2, 5, 10, 15, 20, 30 mg 300, 400 mg
Clozapine (Clozaril®)	T	25, 100 mg
Olanzapine (Zyprexa®)	T D IM	2.5, 5, 7.5, 10, 15, 20 mg 5, 10, 15, 20 mg 10mg per vial
Paliperidone (Invega®)	ER T PR IM	3, 6, 9 mg 50mg/0.5mL, 75mg/0.75mL, 100mg/1mL, 150mg/1.5mL
Quetiapine (Seroquel®)	IR T ER T	25, 100, 200, 300 mg 50, 150, 200, 300, 400 mg
Risperidone (Risperdal®)	T S D PR IM	0.25, 0.5, 1, 2, 3, 4 mg 1 mg/mL 0.5, 1, 2, 3, 4 mg 12.5, 25, 37.5, 50 mg

IM = intramuscular, IV = intravenous, L = liquid, S = suppository, SL = sublingual, T = tablet, D = disintegrating tablet, ER = extended release, IR = immediate release, LA = long-acting, PR = prolonged release

Antipsychotic side effects

- **APs associated with increased risk of:**
  - Metabolic disturbances, weight gain, dry mouth, dizziness
  - Somnolence, drowsiness, injury or falls, hip fractures, EPS, abnormal gait, urinary tract infections, cardiovascular adverse events, death
- **Risk factors**: higher dose, older age, Parkinsons', Lewy Body Dementia

Engaging patients and caregivers

Patients and caregivers should understand:
- The rationale for deprescribing (risk of side effects of continued AP use)
- Withdrawal symptoms, including BPSD symptom relapse, may occur
- They are part of the tapering plan, and can control tapering rate and duration

Tapering doses

- No evidence that one tapering approach is better than another
- Consider:
  - Reduce to 75%, 50%, 25% of original dose on a weekly or bi-weekly basis and then stop; **or**
- Consider slower tapering and frequent monitoring in those with severe baseline BPSD
- Tapering may not be needed if low dose for insomnia only

Sleep management

Primary care:
1. Go to bed only when sleepy
2. Do not use your bed or bedroom for anything but sleep (or intimacy)
3. If you do not fall asleep within about 20-30 min at the beginning of the night or after an awakening, exit the bedroom
4. If you do not fall asleep within 20-30 min on returning to bed, repeat #3
5. Use your alarm to awaken at the same time every morning
6. Do not nap
7. Avoid caffeine after noon
8. Avoid exercise, nicotine, alcohol, and big meals within 2 hrs of bedtime

Institutional care:
1. Pull up curtains during the day to obtain bright light exposure
2. Keep alarm noises to a minimum
3. Increase daytime activity and discourage daytime sleeping
4. Reduce number of naps (no more than 30 mins and no naps after 2pm)
5. Offer warm decaf drink, warm milk at night
6. Restrict food, caffeine, smoking before bedtime
7. Have the resident toilet before going to bed
8. Encourage regular bedtime and rising times
9. Avoid waking at night to provide direct care
10. Offer backrub, gentle massage

BPSD management

- Consider interventions such as: relaxation, social contact, sensory (music or aroma-therapy), structured activities and behavioural therapy
- Address physical and other disease factors: e.g. pain, infection, constipation, depression
- Consider environment: e.g. light, noise
- Review medications that might be worsening symptoms

Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L, et al. Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia: Evidence-based clinical practice guideline. Can Fam Physician 2018;64:17-27 (Eng), e1-e12 (Fr).

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deprescribing.org | Benzodiazepine & Z-Drug (BZRA) Deprescribing Algorithm

February 2019

Why is patient taking a BZRA?

If unsure, find out if history of anxiety, past psychiatrist consult, whether may have been started in hospital for sleep, or for grief reaction.

- Insomnia on its own OR insomnia where underlying comorbidities managed
  For those ≥ 65 years of age: taking BZRA regardless of duration (avoid as first line therapy in older people)
  For those 18-64 years of age: taking BZRA > 4 weeks

- Other sleeping disorders (e.g. restless legs)
- Unmanaged anxiety, depression, physical or mental condition that may be causing or aggravating insomnia
- Benzodiazepine effective specifically for anxiety
- Alcohol withdrawal

Engage patients (discuss potential risks, benefits, withdrawal plan, symptoms and duration)

Recommend Deprescribing

Continue BZRA

- Minimize use of drugs that worsen insomnia (e.g. caffeine, alcohol etc.)
- Treat underlying condition
- Consider consulting psychologist or psychiatrist or sleep specialist

Taper and then stop BZRA

(taper slowly in collaboration with patient, for example ~25% every two weeks, and if possible, 12.5% reductions near end and/or planned drug-free days)

- For those ≥ 65 years of age (strong recommendation from systematic review and GRADE approach)
- For those 18-64 years of age (weak recommendation from systematic review and GRADE approach)
- Offer behavioural sleeping advice; consider CBT if available (see reverse)

Monitor every 1-2 weeks for duration of tapering

Expected benefits:

- May improve alertness, cognition, daytime sedation and reduce falls

Withdrawal symptoms:

- Insomnia, anxiety, irritability, sweating, gastrointestinal symptoms (all usually mild and last for days to a few weeks)

Use non-drug approaches to manage insomnia

Use behavioral approaches and/or CBT (see reverse)

If symptoms relapse:

Consider

- Maintaining current BZRA dose for 1-2 weeks, then continue to taper at slow rate

Alternate drugs

- Other medications have been used to manage insomnia. Assessment of their safety and effectiveness is beyond the scope of this algorithm. See BZRA deprescribing guideline for details.

Pottie K, Thompson W, Davies S, Grenier J, Sadowski C, Welch V, Holbrook A, Boyd C, Swenson JR, Ma A, Farrell B. Evidence-based clinical practice guideline for deprescribing benzodiazepine receptor agonists. Can Fam Physician 2018;64:339-51 (Eng), e209-24 (Fr)

This algorithm and accompanying advice support recommendations in the NICE guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia, and medicines optimisation. National Institute for Health and Care Excellence, February 2019

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deprescribing.org | Benzodiazepine & Z-Drug (BZRA) Deprescribing Notes

February 2019

BZRA Availability

BZRA	Strength
Alprazolam (Xanax®) T	0.25 mg, 0.5 mg, 1 mg, 2 mg
Bromazepam (Lectopam®) T	1.5 mg, 3 mg, 6 mg
Chlordiazepoxide C	5 mg, 10 mg, 25 mg
Clonazepam (Rivotril®) T	0.25 mg, 0.5 mg, 1 mg, 2 mg
Clorazepate (Tranxene®) C	3.75 mg, 7.5 mg, 15 mg
Diazepam (Valium®) T	2 mg, 5 mg, 10 mg
Flurazepam (Dalmane®) C	15 mg, 30 mg
Lorazepam (Ativan®) T, S	0.5 mg, 1 mg, 2 mg
Nitrazepam (Mogadon®) T	5 mg, 10 mg
Oxazepam (Serax®) T	10 mg, 15 mg, 30 mg
Temazepam (Restoril®) C	15 mg, 30 mg
Triazolam (Halcion®) T	0.125 mg, 0.25 mg
Zopiclone (Imovane®, Rhovane®) T	5mg, 7.5mg
Zolpidem (Sublinox®) S	5mg, 10mg

T = tablet, C = capsule, S = sublingual tablet

BZRA Side Effects

- **BZRAs have been associated with:**
  - physical dependence, falls, memory disorder, dementia, functional impairment, daytime sedation and motor vehicle accidents
- **Risks increase in older persons**

Engaging patients and caregivers

Patients should understand:
- The rationale for deprescribing (associated risks of continued BZRA use, reduced long-term efficacy)
- Withdrawal symptoms (insomnia, anxiety) may occur but are usually mild, transient and short-term (days to a few weeks)
- They are part of the tapering plan, and can control tapering rate and duration

Tapering doses

- No published evidence exists to suggest switching to long-acting BZRAs reduces incidence of withdrawal symptoms or is more effective than tapering shorter-acting BZRAs
- If dosage forms do not allow 25% reduction, consider 50% reduction initially using drug-free days during latter part of tapering, or switch to lorazepam or oxazepam for final taper steps

Behavioural management

Primary care:
1. Go to bed only when sleepy
2. Do not use bed or bedroom for anything but sleep (or intimacy)
3. If not asleep within about 20-30 min at the beginning of the night or after an awakening, exit the bedroom
4. If not asleep within 20-30 min on returning to bed, repeat #3
5. Use alarm to awaken at the same time every morning
6. Do not nap
7. Avoid caffeine after noon
8. Avoid exercise, nicotine, alcohol, and big meals within 2 hrs of bedtime

Institutional care:
1. Pull up curtains during the day to obtain bright light exposure
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6. Restrict food, caffeine, smoking before bedtime
7. Have the resident toilet before going to bed
8. Encourage regular bedtime and rising times
9. Avoid waking at night to provide direct care
10. Offer backrub, gentle massage

Using CBT

What is cognitive behavioural therapy (CBT)?
- CBT includes 5-6 educational sessions about sleep/insomnia, stimulus control, sleep restriction, sleep hygiene, relaxation training and support

Does it work?
- CBT has been shown in trials to improve sleep outcomes with sustained long-term benefits

Who can provide it?
- Clinical psychologists usually deliver CBT, however, others can be trained or can provide aspects of CBT education; self-help programs are available

How can providers and patients find out about it?
- Some resources can be found here: https://mysleepwell.ca/

Pottie K, Thompson W, Davies S, Grenier J, Sadowski C, Welch V, Holbrook A, Boyd C, Swenson JR, Ma A, Farrell B. Evidence-based clinical practice guideline for deprescribing benzodiazepine receptor agonists. Can Fam Physician 2018;64:339-51 (Eng), e209-24 (Fr)

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Veterans' MATES

Therapeutic Brief 39

www.veteransmates.net.au

Topic 39: Thinking clearly about the anticholinergic burden

Older people can be particularly sensitive to the anticholinergic effects of medicines.[1] Adverse effects may arise from an individual anticholinergic medicine, and from the cumulative effects of multiple medicines with varying degrees of anticholinergic properties.[2-4]

The anticholinergic burden may be unintentionally increased by medicines prescribed with other mechanisms of action intended, but also having anticholinergic effects, such as antihistamines, tricyclic antidepressants and antipsychotics.[2] In addition, medicines not typically thought of as having anticholinergic effects, such as citalopram, mirtazapine and metoclopramide, when added to other strongly anticholinergic medicines, may tip the balance of the cumulative anticholinergic burden and result in significant adverse effects.[2, 4, 5]

Older Australians commonly use medicines with anticholinergic effects; at any point in time 21-33% of Australians aged over 60 years use at least one medicine with anticholinergic effects.[6-8] A cumulative anticholinergic burden in older people with co-morbidities who are taking multiple medicines is associated with an increased risk of confusion, cognitive and physical decline, delirium, hospitalisation and death.[2, 3, 9-11]

This therapeutic brief provides information on anticholinergic adverse effects and outlines steps to take to reduce the anticholinergic burden.

Inside

Key points

- Medicines that contribute to an anticholinergic burden are medicines:
  - prescribed for their anticholinergic effects
  - prescribed with other mechanisms of action intended but also having anticholinergic effects, and
  - not typically thought of as having anticholinergic effects.
- A high anticholinergic burden in older people is associated with an increased risk of cognitive decline.
- Be alert to anticholinergic adverse effects in your older patient.
- Consider reducing the anticholinergic burden where possible.

Ask yourself and your patient: What are the adverse effects and potential outcomes?

Anticholinergic adverse effects may be subtle or severe (see Figure 1). In older people, the effects may be overlooked and considered part of the natural ageing process or attributed to the progression of underlying disease.[1, 5] Consequences of blurred vision, dizziness or memory loss from an anticholinergic burden may include loss of independence, falls or motor vehicle accidents.[1, 12] Acute confusion or delirium may result in hospitalisation, functional and cognitive decline or aged care facility placement.[13, 14]

Be alert to possible anticholinergic adverse effects in your older patient, as the anticholinergic load differs between medicines, and individuals differ in their ability to tolerate them.[4]

Consider that any worsening of chronic conditions, new symptoms or adverse events may be the result of medicines with anticholinergic effects, especially if they occur after changes in the medicine regimen.[4, 13]

Avoid treating adverse effects with medicines.[13]

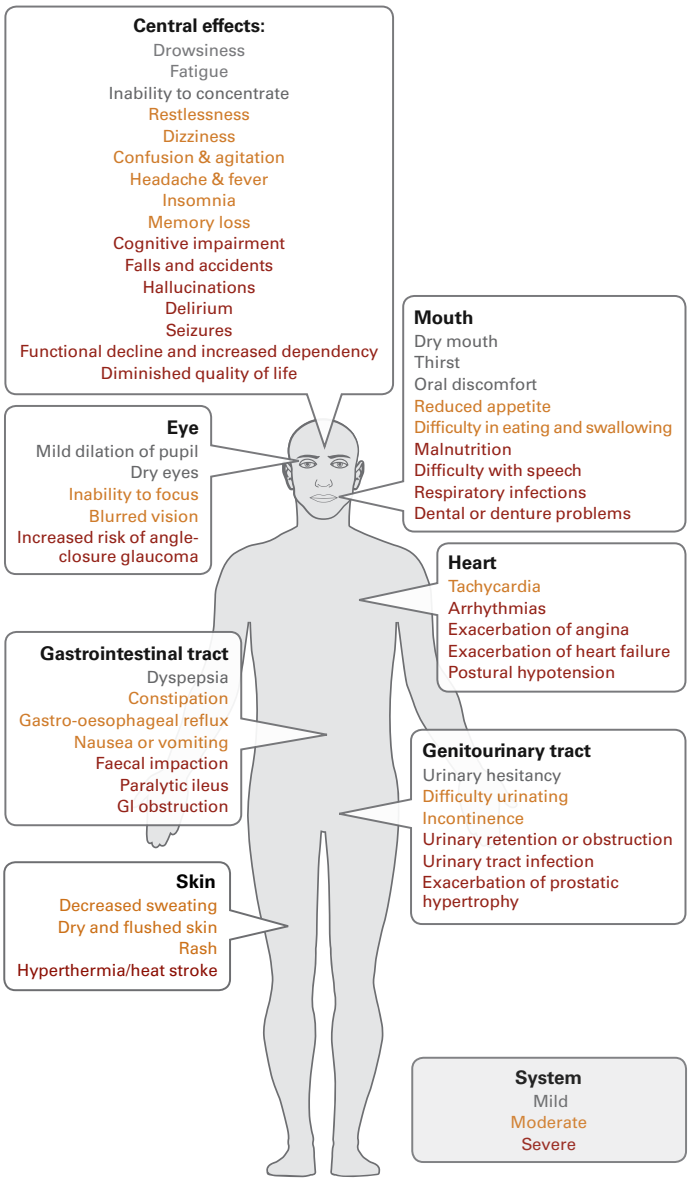

Figure 1: Anticholinergic adverse effects and potential outcomes[2, 12, 13, 15]

Ask: What is the burden?

While exact quantification of a medicine's anticholinergic effect is difficult,[16] it is estimated one medicine with strong anticholinergic effects is likely to cause two or more anticholinergic adverse effects in more than 70% of older patients.[17] Additionally, older patients prescribed two or more anticholinergic medicines are at a significantly increased risk of hospitalisation for confusion or dementia.[10] Table 1 lists some of the commonly used medicines with anticholinergic effects in older veterans.

Individual pharmacokinetic and pharmacodynamic variability, the number of medicines, dosages prescribed, drug interactions, and prevalence and severity of co-morbidities may also influence cumulative anticholinergic burden and severity of adverse effects.[4, 18]

The increase in the number of medicines, including prescribed and self-prescribed over the counter medicines used by many older people, may contribute to an unintended high anticholinergic burden.[2, 3, 11] Herbal preparations such as knotweed (*polygonum aviculare*) as well as over the counter medicines for coughs and colds, antihistamines, travel sickness products and antidiarrhoeals may have anticholinergic properties.[4]

Ask your patient specific questions about self-prescribed medicines they may be taking.

Anticholinesterases and anticholinergic medicines

Where possible avoid using anticholinesterases, such as:

- donepezil
- galantamine
- rivastigmine
- pyridostigmine

with anticholinergic medicines; anticholinergic medicines antagonise the therapeutic effect of anticholinesterases.[4]

Be alert to the cholinergic effects of anticholinesterases. Avoid prescribing anticholinergic medicines to compensate for the cholinergic effects of anticholinesterases. If an anticholinergic medicine is prescribed, and you stop the anticholinesterase, the effects of the anticholinergic medicine may be magnified.[12]

Table 1: Commonly used medicines with anticholinergic effects in older veterans[12, 16]

	Antipsychotics	Antidepressants	Bladder antispasmodics	Antihistamines	Opioids	Inhaled medicines	Other medicines
Higher anticholinergic effects	chlorpromazine clozapine trifluoperazine	amitriptyline clomipramine dothiepin doxepin imipramine nortriptyline	darifenacin* oxybutynin propantheline solifenacin* tolterodine*	cyproheptadine promethazine	tapentadol	aclidinium glycopyrronium ipratropium tiotropium	benztropine homatropine
Lower anticholinergic effects	haloperidol lithium carbonate olanzapine prochlorperazine quetiapine risperidone	citalopram fluoxetine fluvoxamine mirtazapine paroxetine		cetirizine fexofenadine loratadine	codeine fentanyl methadone morphine oxycodone tramadol		alprazolam amantadine baclofen carbamazepine clonazepam colchicine diazepam digoxin disopyramide domperidone entacapone frusemide loperamide metoclopramide ranitidine temazepam theophylline

Note: The list of medicines is based on Duran et al.'s 2013 Systematic review of anticholinergic risk scales in older adults (reviewing 7 studies, one of which was Australian), the Australian Medicines Handbook, Martindale: The Complete Drug Reference and expert opinion.

Note: *these medicines are not available on the PBS/RPBS

Ask: Can the burden be reduced?

Step 1: Assess your patient for adverse effects

Assess your patient for anticholinergic symptoms including dry mouth, constipation, blurred vision, increased heart rate, heat intolerance, sedation and mild confusion or memory loss. In your older patient, these symptoms can develop into serious problems (see Figure 1).[1]

Step 2: Review your patient's medicines

Identify medicines to consider ceasing or substituting: target medicines of lesser benefit to your patient.[19] Assess whether your patient is taking their medicines as prescribed, potential adverse effects, such as risk of falls and cognitive decline, indications, time of benefit and interactions.[20] Consider recommending a Medicines Review (HMR or RMMR) by an accredited pharmacist. Ask the pharmacist to specifically consider the anticholinergic burden. Consider consulting the opinion of a geriatrician in difficult cases.

Step 3: If problematic, ask the question: is a medicine essential?

If a medicine is not essential, can it be ceased? Ceasing a medicine with anticholinergic effects may not always be possible. Consider, in consultation with your patient, their goals and expectations, co-morbidities and individual preferences when making a decision.[4, 19]

Once you have confirmed the medicines to be ceased and a plan has been developed with your patient, begin by ceasing one medicine at a time. Monitor your patient closely and gradually taper the medicine.[19] Talk to your patient about possible withdrawal effects, such as anxiety, nausea, vomiting, headache and dizziness. Advise your patient to talk to you if any of these symptoms worry them.[21]

If a medicine is essential, ask these questions:

- **Is there a safer alternative treatment option? (see Insert)**
- **If not, can the dose, frequency or duration of the medicine be reduced?**

When a medicine with anticholinergic effects is essential and the dose, frequency or duration cannot be reduced, advise your patient of non-pharmacological measures to minimise the impact of adverse effects. Examples include artificial tears for dry eyes and increased water intake and a high fibre diet for constipation.[5]

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