

# The anticholinergic burden: from research to practice

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## SUMMARY

Drugs with anticholinergic effects are known to cause adverse effects such as dry mouth, constipation and urinary retention. In older people drugs with anticholinergic effects may contribute to cognitive decline and a loss of functional capacity.

Many drugs that are not in the anticholinergic drug class also have anticholinergic effects. They include antidepressants, antipsychotics and antihistamines.

Taking multiple drugs with anticholinergic effects creates an anticholinergic burden. It is important that clinicians identify which patients are at risk. There are several tools to assess the anticholinergic burden.

Clinicians can use these tools to make a pharmacological risk assessment when reviewing a patient's medicines. This can assist decisions about continuing or stopping drugs with anticholinergic effects.

Deprescribing drugs with anticholinergic effects has several potential benefits in older people. In addition to reversing adverse effects, deprescribing may prevent problems such as falls.

## Introduction

Drugs that have anticholinergic effects block acetylcholine receptors in central or peripheral tissues. This cholinergic antagonism can either be an intended therapeutic effect or an unwanted adverse effect. In addition to drugs classified as anticholinergics,<sup>1</sup> many other drugs have some anticholinergic effects.<sup>2</sup> These include antidepressants, antipsychotics and antihistamines. Drugs with anticholinergic properties are commonly taken by older adults to treat conditions such as Parkinson's disease, depression, pain, urinary incontinence and allergy.<sup>3</sup> Evidence suggests that 20–50% of older adults are prescribed drugs with anticholinergic effects.<sup>4</sup> Multiple drugs acting to block acetylcholine receptors will have cumulative effects, which can be described as the person's anticholinergic burden.

The anticholinergic burden appears to be increasing. A recent UK study reported up to a ninefold increase in the anticholinergic burden over 25 years with increases in prescribing of most anticholinergic drug classes and in polypharmacy.<sup>5</sup>

## Adverse effects

Drugs with anticholinergic effects have a significant adverse-effect profile. Common anticholinergic adverse effects include dry mouth, urinary retention, constipation, cognitive decline and loss of the functional capacity to perform activities of daily living. Adverse

anticholinergic effects are particularly problematic in older adults due to age-related changes in pharmacokinetic and pharmacodynamic processes, and the presence of multi-morbidity, polypharmacy and geriatric syndromes such as frailty.<sup>6</sup>

In older adults, the anticholinergic burden is linked with serious adverse effects including falls, functional decline, delirium and death.<sup>7</sup> A recent Cochrane review suggests that older adults without cognitive impairment who are exposed to drugs with anticholinergic effects may be at an increased risk of cognitive decline and dementia.<sup>8</sup> Furthermore, many drugs with anticholinergic effects may cause significant deterioration in the oral health of older adults.<sup>9</sup>

## Assessing the anticholinergic burden

At present, there is no universal way to assess the anticholinergic burden to inform clinical practice. Several tools have been developed to estimate the cumulative effects of drugs with anticholinergic effects in individuals. They are based on either expert consensus, serum anticholinergic activity or pharmacological principles.

Examples of tools to measure the anticholinergic burden include the Anticholinergic Drug Scale, Anticholinergic Cognitive Burden Scale and the Anticholinergic Risk Scale. The Drug Burden Index (DBI) is a measure of exposure to drugs with anticholinergic and sedative effects.<sup>10,11</sup> However,

many of the drugs classified as sedative for calculation of the DBI are also included in other anticholinergic burden scales. The agreement between the various measures of anticholinergic burden is poor, with tools identifying different drugs as anticholinergic and giving them different weightings using different criteria. A barrier to the use of the tools for clinical risk assessment is the difficulty of calculating the anticholinergic burden during a consultation.

### Quality use of drugs with anticholinergic effects

Measures of anticholinergic burden and the DBI can inform clinicians of the cumulative risk of adverse drug effects, including global effects on functional independence. The clinician can weigh up the risk of adverse events against the benefits of continuing the drug for an individual patient. This pharmacological risk assessment score differs conceptually from long expert consensus lists of 'potentially inappropriate medications', and the Screening Tool of Older Persons' Prescriptions (STOPP) or the Screening Tool to Alert to Right Treatment (START), which consider evidence of both safety and efficacy in older populations.

If a clinician and a patient decide to continue a treatment with a drug with anticholinergic or sedative effects, there are several principles to consider.

1. Minimise the use of the anticholinergic or sedative drug.
  - a. Optimise non-pharmacological management strategies for the condition being treated.
  - b. Optimise treatment of the condition using drugs without anticholinergic or sedative effects.
  - c. Use the minimum dose of the anticholinergic or sedative drug that is required to manage the condition for the shortest duration.
2. Proactively address the adverse effects of the anticholinergic or sedative drug, for example refer for exercise training to reduce falls and frailty.
3. Minimise exposure to other drugs that are contributing to the anticholinergic and sedative load. Review all of the person's other drugs, including over-the-counter medicines, such as antihistamines.
4. Monitor the patient closely (and teach them to self-monitor) for efficacy and safety. Look for alternative treatments without anticholinergic or sedative effects. Review all drugs frequently.
5. If another drug with anticholinergic or sedative effects is needed subsequently, then revisit steps 1-4, with the aim of minimising the person's total exposure to drugs with these effects.

### Deprescribing

Tools like the DBI help identify the functional burden of drugs and provide a framework for shared decision making in prescribing and deprescribing.<sup>12-14</sup> To calculate the DBI, registered Australian healthcare professionals can enter the patient's drugs into G-MEDSS software. This will provide the patient's total DBI score and the contribution of each of their drugs to that score.

The priorities for deprescribing depend on the treatment options, harms, benefits, patient preference and the complexity of drug withdrawal. Applying these criteria, it is often a priority to deprescribe antipsychotic drugs if possible, when they are being used to manage behavioural and psychological symptoms of dementia.<sup>15</sup>

In practice, anticholinergic drug effects are difficult to differentiate from the effects of ageing and disease. However, it is important to differentiate adverse drug effects because they are often reversible with deprescribing. While studies aiming to reduce overall anticholinergic burden have only been powered to assess changes in drug use,<sup>16</sup> there is evidence of clinical benefit from deprescribing some drug classes with anticholinergic or sedative effects. For example, falls can be reduced by withdrawing psychotropic drugs.<sup>17</sup>

Considering the anticholinergic and sedative burden and the possibility of deprescribing are important parts of a comprehensive medication review of frail older people. Deprescribing anticholinergic and sedative drugs is feasible but often requires slow tapering to prevent withdrawal reactions.<sup>3</sup> The discontinuation syndrome seen after abruptly stopping drugs with anticholinergic effects can include nausea, sweating, urinary urgency, orthostatic hypotension, tachycardia, anxiety and sleep disruption. Detailed guides on deprescribing drugs with anticholinergic and sedative effects are freely available to clinicians (see Box).

When discussing a trial of deprescribing sedative and anticholinergic drugs with a patient, it is helpful to consider the impact of adverse effects on what matters the most to that person. Most adverse

#### Box Examples of deprescribing guides

- [NSW Therapeutic Advisory Group - Deprescribing tools](#)
- [Primary Health Tasmania - Deprescribing resources](#)
- [Canadian Deprescribing Network - Deprescribing guidelines and algorithms](#)

effects of anticholinergic and sedative drugs are multifactorial syndromes, such as falls, functional impairment, confusion, constipation, dry mouth or urinary retention. Drugs are the most reversible factors contributing to these syndromes. Reversing even one factor contributing to a geriatric syndrome can be enough to alleviate it. A medication review and trial of deprescribing may therefore improve successful ageing.

## Conclusion

Many commonly prescribed drugs have anticholinergic effects. When a patient is taking several of these drugs, they may have a high anticholinergic burden. In older people this can lead to a loss of function and problems such as falls.

Several tools are available to assess the anticholinergic burden. These may assist clinicians when deciding if a patient's treatment should be changed. There may be benefits from reducing the anticholinergic burden by deprescribing. ◀

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*Conflicts of interest: Sarah Hilmer developed and continues to lead an active research program on the Drug Burden Index. The Goal-directed Medication review Electronic Decision Support System (G-MEDSS), which includes a Drug Burden Index calculator, was developed by Lisa Kouladjian O'Donnell under the supervision of Sarah Hilmer, and is under consideration for commercialisation.*

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