

# **Drugs that may worsen cognitive decline**

Dementia is defined by the WHO as a condition where there is a deterioration in cognitive function that adversely affects many aspects of life including memory, understanding, learning capacity, language, behaviour and judgement. Certain classes of drugs, including anticholinergics, have been shown to be associated with an increased risk of dementia in clinical trials and they appear to have more extreme effects in older adults.

Anticholinergics are used to treat a range of conditions including psychosis, depression, urinary incontinence, allergies and COPD. Anticholinergics work by blocking the action of acetylcholine in the nervous system, preventing signal transmission between nerve cells in the brain or nerve cells and muscles in the body. Other side effects include dry mouth, drowsiness, blurred vision, urinary retention and constipation. The mechanism by which anticholinergics could act to increase the risk of dementia remains unclear.

Dementia is usually progressive and chronic with few potentially modifiable risk factors, however, it is possible to alter the level of anticholinergics prescribed to people with dementia and this may improve their cognitive functioning to some extent. The cumulative effect of taking several medicines containing anticholinergics, known as the anticholinergic burden, also increases the risk of cognitive decline and thus it is essential to carefully monitor the use of anticholinergics in older people and those with dementia.

This chapter focuses on identifying which anticholinergics are commonly used for people with dementia with the aim of reducing the level of prescription of these drugs where possible. In addition, it seeks to address whether there are tools which would allow the identification of specific drugs that may be causing cognitive decline.

## **12.1. Drugs that may cause cognitive decline**

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## Review questions

- What drugs that may worsen cognitive decline are commonly prescribed in people diagnosed with dementia?
- What are the most effective tools to identify drugs that may be causing cognitive decline?

### 12.1.1. Introduction

The aim of the first specified review question was to identify drugs that may cause cognitive decline that are commonly prescribed in people living with dementia. It was agreed that the main class of drugs that is a cause of concern (anticholinergics) was clear, and the harms of these drugs were well established. Therefore, the key question to answer was not what the harms of these drugs are, but rather which of these drugs are commonly in use, as this may help to focus efforts to reduce levels of inappropriate prescribing.

The aim of the second review question was to identify whether there are appropriate tools available to identify medicines that may be the cause of cognitive decline in a person suspected of having dementia, and therefore prevent false positive diagnoses. The review identified studies that fulfilled the conditions specified in [Table 57](#). The full review protocol is available in [Appendix C](#).

| Table 57 Review summary: drugs that may cause cognitive decline |   |
|---|---|
| Population  | People (aged 40 years and over) with a suspected diagnosis of dementia  |
| Diagnostic variables  | <ul style="list-style-type: none"><li>• Standardised tools assessments, instruments - cognitive decline</li><li>• Anticholinergic burden scale</li><li>• Clinical history</li></ul> |
| Outcomes  | <ul style="list-style-type: none"><li>• Incidence of accurately identified dementia</li><li>• Pharmaceutical adverse reactions</li></ul>  |

**Table 57**

Review summary: drugs that may cause cognitive decline.

## 12.1.2. Evidence review

No literature review was undertaken to identify commonly prescribed drugs that may cause cognitive decline in people with dementia, as it was decided that such a review would only be able to provide data on the well-established harms of certain medicines, rather than identify which of these medicines are currently commonly used in the UK. Therefore, this question was instead supported by evidence provided from an expert witness, the UK Prescribing Observatory for Mental Health. Data were provided on current prescribing patterns in mental health trusts, with the evidence presented to the committee summarised in [Appendix N](#).

A systematic literature search was carried out to identify diagnostic accuracy studies, or systematic reviews of diagnostic accuracy studies for the question considering the tools used to identify drugs that may cause cognitive decline. A total of 6,337 references were screened at the title and abstract level, with 37 potentially relevant references being ordered for full text review. No evidence was identified in a population of people living with dementia, but 1 systematic review of anticholinergic scales in older people (Salahudeen 2015) was included. The excluded studies, with reasons for their exclusion, are listed in [Appendix F](#). Evidence tables for Salahudeen (2015) and the 7 studies included in that review are presented in [Appendix E](#).

### 12.1.2.1. Description of included studies

The characteristics of the studies included in Salahudeen (2015) are summarised in [Table 58](#). References for the included studies are given in [appendix I](#).

| Table 58 Summary of studies included in Salahudeen (2015) |  |   |                                  |
|---|--|---|----------------------------------|
| Study details   | Study population                                       | Assessment scales                           | Method devices                   |
| Ancelin (2006)  | 372 people aged >60 years living in the community      | Anticholinergic Burden Classification (ABC) | Based on Anticho (SAA) i opinion |
| Bontani (2008)  | 87 nursing home residents with dementia aged ≥65 years | Anticholinergic Cognitive Burden Score      | Based on data and                |

**Table 58**

Summary of studies included in Salahudeen (2015).

### **12.1.3. Health economic evidence**

Standard health economic filters were applied to the clinical search for these questions, and a total of 1,062 citations was returned. Following review of titles and abstracts, no full text studies were retrieved for detailed consideration. Therefore, no relevant cost–utility analyses were identified for these questions.

### **12.1.4. Evidence statements**

Moderate-quality evidence from 1 systematic review of 7 observational studies with 2,325 people (including 297 people diagnosed with dementia) found 7 validated anticholinergic scales developed by expert opinion detected an association between higher scores on anticholinergic scales and harms caused by anticholinergic medicines in older aged populations.

#### **12.1.4.1. Health economic evidence**

No health economic evidence was identified for this review question.

### **12.1.5. Evidence to recommendations**

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| <b>Relative value of different outcomes</b> | <p>The committee agreed there was a need to raise awareness that there are certain groups of drugs that may influence cognitive function and that any recommendations should acknowledge both the minimisation of drugs causing anticholinergic activity and raise awareness of the scales that may be used to detect anticholinergic activity or burden. The committee recognised that there was a clinical issue that older aged populations include a substantial proportion of people with multimorbidities, where more than one condition may be treated with a medicine that has an anticholinergic effect, and the use of multiple medications with anticholinergic burden has a cumulative effect.</p> <p>Two separate settings were identified where anticholinergic burden may be an important factor to consider. The first is when considering a diagnosis of dementia, where the presence of a substantial anticholinergic burden may mimic the symptoms of dementia and therefore lead to false diagnoses. The second, in people with a known diagnosis of dementia, is that the use of anticholinergics may exacerbate the symptoms of cognitive decline, and therefore their use should be carefully monitored.</p> |
|---|---|

**Trade-off  
between  
benefits and  
harms**

**At the time of diagnosis**

The committee agreed that although the evidence they had seen was in relation to a generally older aged population, there should be little difference for people living with dementia. Although the effects of anticholinergic burden may differ by population, the specific drugs that cause the largest anticholinergic burden are likely to remain the same. It noted that there may be implications for community prescribers to assess cognition before prescribing medications, in order to recognise that some drugs may affect anticholinergic burden.

The committee agreed that, at the time of considering a diagnosis of dementia, it would be appropriate to reduce the level of anticholinergic drugs being used, if possible alternatives were available, in order to rule out potential false diagnoses, and a ‘consider’ recommendation was made on this point.

The committee agreed that, whilst many of the classes of drugs with high anticholinergic activity were understood widely by clinicians, there were other individual drugs where the high level of anticholinergic activity was not well known, particularly when these come from a class of drugs not usually associated with it. Therefore, it agreed that validated, structured tools to assess anticholinergic burden would be useful, as they would make clinicians undertaking reviews aware of drugs they might not otherwise have considered.

The committee considered the types and classes of drugs listed in each scale. It noted that different drugs may be rated differently in each scale, with some drugs scoring higher for anticholinergic activity than others (this is likely to result from the different methodologies by which the scales were constructed). It agreed that there was currently no evidence to recommend the use of one scale in preference to another, so agreed that it was appropriate only to make clinicians aware of the existence of these scales, rather than make a specific recommendation that one should be

used. However, the committee agreed it would be helpful to provide a link to an example of one of these scales, to ensure that non-specialist clinicians could understand the sorts of tools that exist. The Anticholinergic Cognitive Burden Scale was chosen as the most appropriate to reference because it uses standard UK names for drugs, and because it has been updated more recently (2012) than some of the scales identified. It did however, want the recommendation to re-emphasise that this was simply one tool available for determining the anticholinergic activity of specified drugs and not the only tool available for consideration.

The committee recognised that awareness of anticholinergic burden should form part of the full patient pathway and acknowledged there were other areas of the guideline (for example when undertaking diagnostic assessments) where this issue would be revisited.

### **After diagnosis**

The committee agreed it remained important to continuously assess the level of anticholinergic burden in people living with dementia, and that an assessment should be made of anticholinergic burden as part of medication reviews. The committee agreed that, again, possible alternatives should be sought for drugs with a high anticholinergic burden, if these are available. It noted that the audit data presented showed that high levels of anticholinergic medicines were still prescribed in people living with dementia, and that while much of this prescribing is likely to be appropriate and necessary, it is likely that there is still inappropriate prescribing of medications with an anticholinergic effect when alternatives without this effect are available.

No evidence was identified about how reviews should be conducted and what tools should be used, and therefore the committee agreed the most appropriate action was to cross-reference the NICE guideline on medicines optimisation, which provides guidance on how to undertake medication reviews.

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|---|--|
| <b>Trade-off between net health benefits and resource use</b> | <p>The committee agreed that there was potentially a high cost associated with the inappropriate prescription of drugs causing a high level of anticholinergic burden, both due to the side effects they can cause and the costs associated with inaccurate diagnoses. Therefore, appropriate reviews of anticholinergic medicines, both at diagnosis and reviews, would be likely to be cost-saving if it reduced levels of inappropriate prescribing.</p>  |
| <b>Quality of evidence</b>                                    | <p>The committee agreed that the most appropriate method of validating the scales would have been to consider measures of diagnostic accuracy, such as sensitivity and specificity, but they noted the evidence they had seen did not report validity in this way. This meant it was difficult to assess the overall utility of each scale. After considering the methodologies in each scale, the committee agreed there was an absence of evidence to identify one single well-validated tool over another.</p> <p>The committee noted that the audit data presented on commonly prescribed anticholinergic medicines came from mental health trusts, and therefore there was still a gap in the evidence for which are the most commonly prescribed anticholinergic medicines in primary care. However, the committee agreed the recommendations made for medication reviews would still be appropriate in a primary care setting, as the adverse effects to the person treated will be the same.</p> |
| <b>Other considerations</b>                                   | <p>The committee acknowledged there is a gap in the current evidence base for considering whether reducing anticholinergic burden can improve the cognitive outcomes for people who have cognitive impairment, as the currently available studies are either cross-sectional or look at populations with a stable or increasing anticholinergic burden overtime. It was therefore agreed that randomised control trials comparing a strategy of</p>  |

actively lowering anticholinergic burden, versus usual care, would be useful to fill this gap in the evidence.