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The importance of reducing anticholinergic burden

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What are ‘anticholinergics’?

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- Anticholinergic medicines block the action of **acetylcholine**.
- Acetylcholine is a **neurotransmitter** – a chemical that enables nerves to communicate with organs and with other nerves. It's particularly important in the parasympathetic nervous system, the arm of the autonomic nervous system concerned with body maintenance and baseline functioning. So acetylcholine mediates activities such as bladder emptying, slowing of the heart, saliva production, control of body temperature, focusing of the eye, and peristalsis. Acetylcholine is also found in the brain where, amongst other actions, it helps alertness, concentration, and learning.

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- Anticholinergic drugs are sometimes called antimuscarinic drugs because the site where acetylcholine mediates many of its actions is known as the muscarinic receptor. (The other type of cholinergic receptor is the nicotinic receptor.)
- Anticholinergic drugs are prescribed for a wide range of conditions, including:
    - Parkinson’s disease
    - overactive bladder
    - COPD
    - nausea and vomiting
    - depression and psychosis

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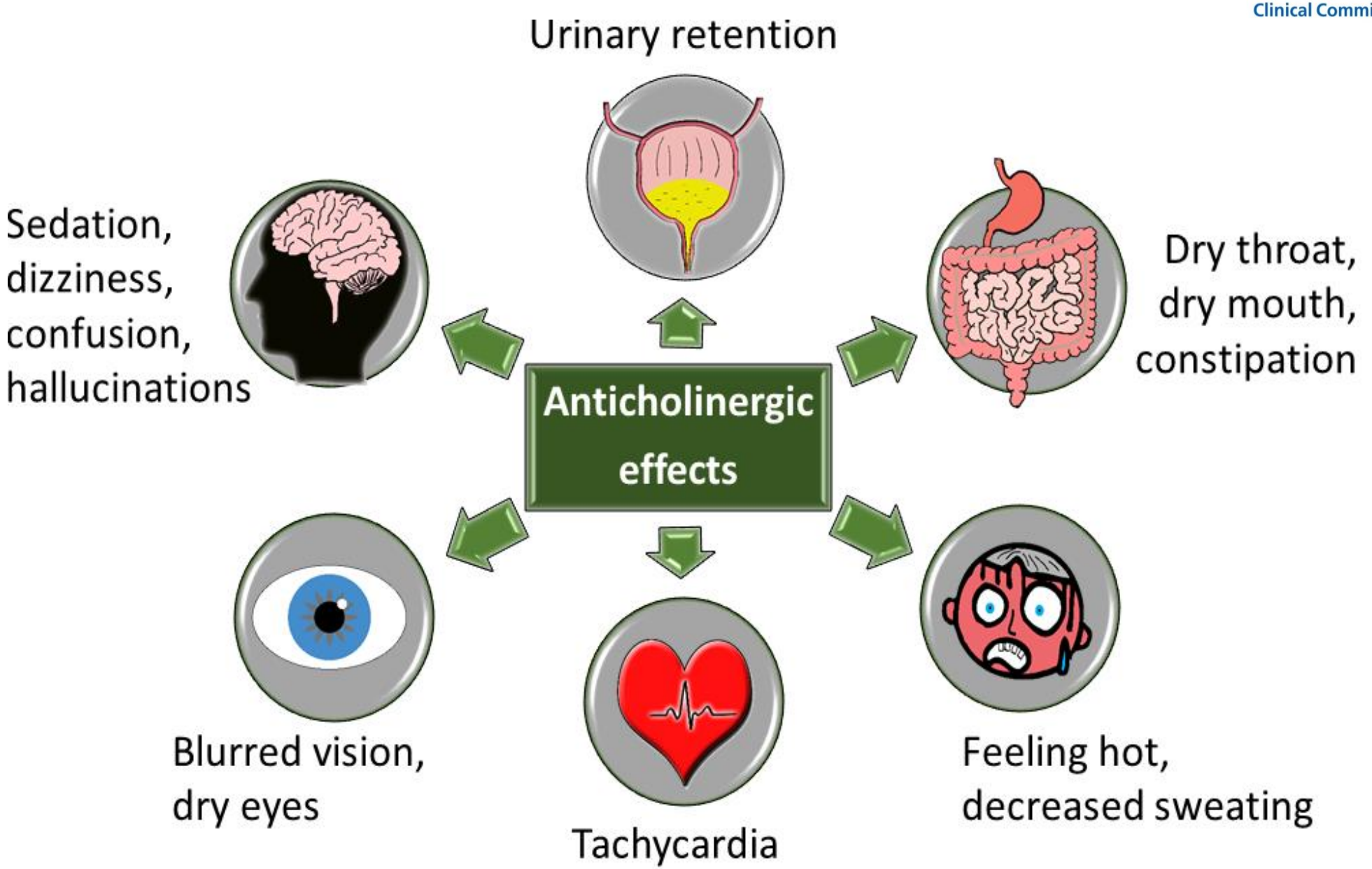

Adverse effects on:

Peripheral nervous system (blurred vision, constipation, urinary retention, dry mouth)

Central nervous system (sedation, learning, cognition, memory, confusion, delirium, dementia)

- The CNS side effects caused by anticholinergic drugs may vary depending on the ability of the drugs to penetrate the blood-brain barrier (BBB). The elderly are more susceptible to these effects, especially as there is increased permeability of the BBB.

Why should we be concerned?

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- An increasing number of systematic reviews and meta-analyses report that medicines with anticholinergic effects are associated with an increased risk of cognitive impairment, falls and all-cause mortality in older people.

(PrescQipp bulletin 253 Sept 2020)

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- A study of 13,004 patients over 65 found that 20% of participants who had an ACB score of four or more had died by the end of the two year study period compared with 7% of patients with a score of zero.
- For every additional ACB point scored, the risk of dying increased by 26%.

Anticholinergic Medication Use and Cognitive Impairment in the Older Population: The Medical Research Council Cognitive Function and Ageing Study - Fox - 2011 - Journal of the American Geriatrics Society

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- A study has found that if people aged 55 years old and above take certain anticholinergic medicines for the equivalent of three years or more, it may increase their risk of developing dementia. These findings highlight the importance of reducing exposure to anticholinergic drugs in middle-aged and older people.

Anticholinergic Drug Exposure and the Risk of Dementia: A Nested Case-Control Study | Dementia and Cognitive Impairment | JAMA Internal Medicine | JAMA Network 2019

BITE_78 – Do anticholinergic drugs cause dementia.pdf (nihr.ac.uk)

What is anticholinergic burden (ACB) score?

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- The term "**anticholinergic burden**" refers to the cumulative effect of using multiple medications with anticholinergic properties concomitantly.
- Not all medicines with anticholinergic properties may individually put patients at risk of severe adverse effects, however when used in combination, effects may accumulate. Reducing the anticholinergic burden may result in improvements in short term memory, confusion, behaviours and delirium. Polypharmacy-Guidance-2018.pdf (scot.nhs.uk)
- Medicines with anticholinergic effects are assigned a number - the higher the ACB number, the stronger the effect

(ACB 0 = no anticholinergic activity)

ACB 1 = low/possible anticholinergic activity

ACB 2 or 3 = definite anticholinergic activity

Highly anticholinergic medicines:

ACB = 3

- Tricyclic antidepressants e.g. amitriptyline, nortriptyline
- 1st generation antihistamines e.g. chlorphenamine (Piriton®), diphenhydramine (Nytol®)
- Antimuscarinic bladder drugs e.g. oxybutynin, tolterodine, solifenacin

Many clinicians will be aware of these highly anticholinergic medicines but may be less aware of those with a lower anticholinergic burden, such as opioids, loratadine, cetirizine, ranitidine and loperamide for example and the effects may be additive.

ACB Score Tools

- There are a number of validated tools for assessing ACB including the Anticholinergic Cognitive Burden (ACB) Scale, ACB Calculator and Medichec.
- Different drugs may be rated differently in each scale with some drugs scoring higher for ACh activity than others – this is likely to result from the different methodologies by which each scale was constructed.
- NICE states that there is insufficient evidence to recommend one over the others.

ACB calculator

Home | About ACB | Medicines Scorecard | Admin login

Oxybutynin

Score: 3
Medicine: Oxybutynin
Brands: Ditropan™

Codeine

Score: 1
Medicine: Codeine
Brands: Contin™

Ranitidine

Score: 1
Medicine: Ranitidine
Brands: Zantac™

+ Add new medicine | Reset

Total ACB Score: 5 **High Risk**

Your patient has scored ≥3 and is therefore at a higher risk of confusion, falls and death.

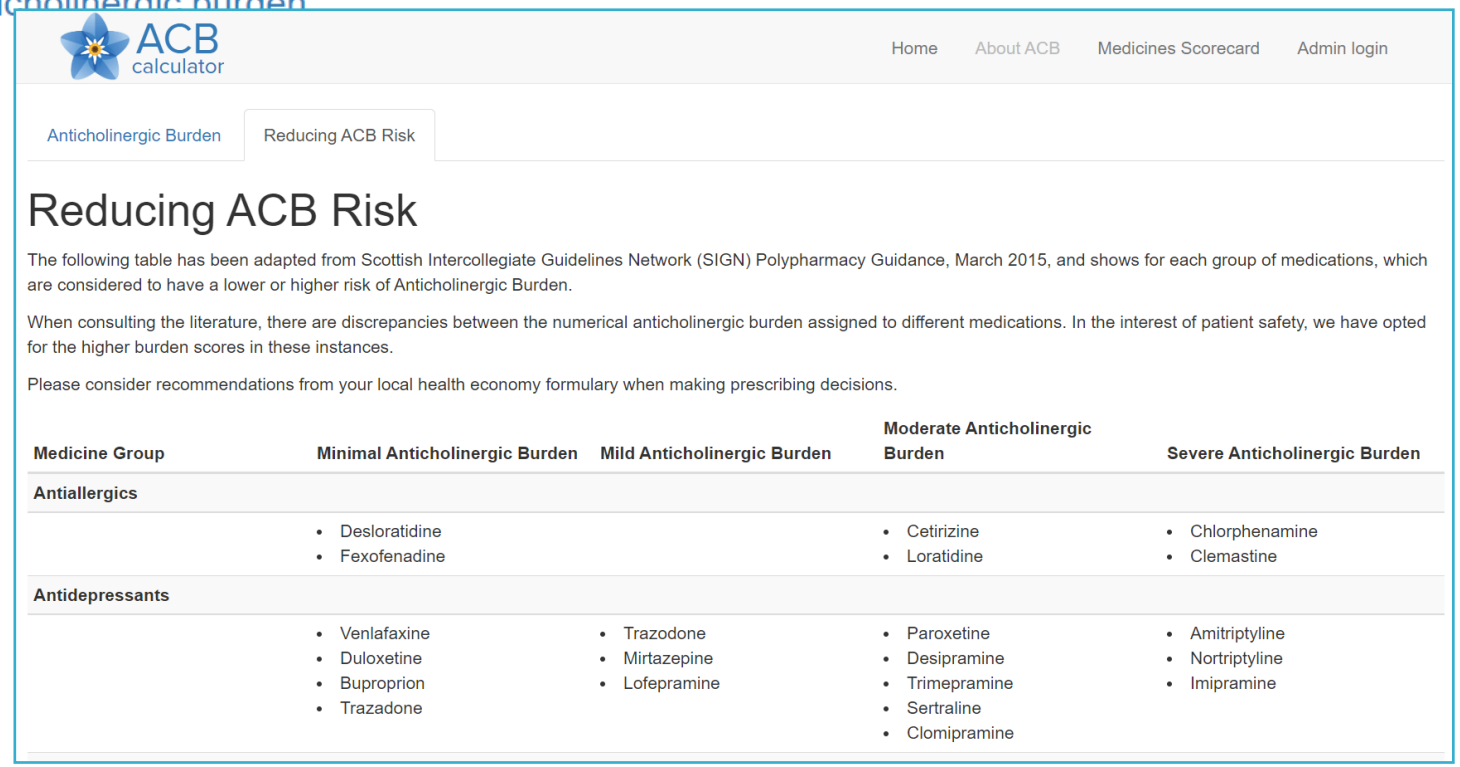
Many of the medications that we commonly prescribe have anticholinergic properties.

In patients over 65 years of age these can cause adverse events, such as confusion, dizziness and falls. These have been shown to increase patient mortality.

You can use this calculator to work out the Anticholinergic Burden for your patients.

A score of 3+ is associated with an increased cognitive impairment and mortality.

Find more information on Anticholinergic Burden or help choosing medicines to reduce anticholinergic burden



NICE guidance on dementia (NG97):

- Be aware that some commonly prescribed medicines are associated with increased anticholinergic burden, and therefore cognitive impairment. Consider minimising the use of medicines associated with increased anticholinergic burden, and if possible look for alternatives:

- when assessing whether to refer a person with suspected dementia for diagnosis

The presence of a substantial ACB may mimic the symptoms of dementia and therefore lead to a false diagnosis of dementia

- during medication reviews with people living with dementia

Anticholinergics may exacerbate the symptoms of cognitive decline therefore their use should be carefully monitored

NICE guidance on falls in older people (CG161)

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- recommends that people who have had a fall or are at increased risk of falling should have their medication reviewed as part of a multifactorial risk assessment; psychotropic medications (including neuroleptics, sedatives, hypnotics and antidepressants) should be reviewed and if possible discontinued to reduce their risk of falling.

NICE guidance on urinary incontinence in women (2019)

- cautions about the uncertainty of long-term effects of anticholinergic medicines on cognitive function and recommends taking this into account when prescribing anticholinergic medicines to treat overactive bladder.

Reviewing ACB score

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- ACB reduction should be carried out as part of a full polypharmacy & holistic review.
- Highly anticholinergic medicines with an ACB score of 3 should be avoided where possible
- Be aware of the cumulative effects of drugs with a lower ACB score
- Patients may not link drugs to anticholinergic side effects - when drugs with a high ACB are stopped, polypharmacy can be further reduced as medicines will no longer be needed to manage side-effects.
- Some highly specialised therapeutic areas (e.g. Parkinson's disease) will require expert advice before considering a change
- Anticholinergics are commonly associated with adverse effects (inc. anxiety, nausea, vomiting, dizziness & headache) if discontinued suddenly and may require slow withdrawal
- Reducing the ACB may result in improvements in short term memory, confusion, behaviours and delirium.

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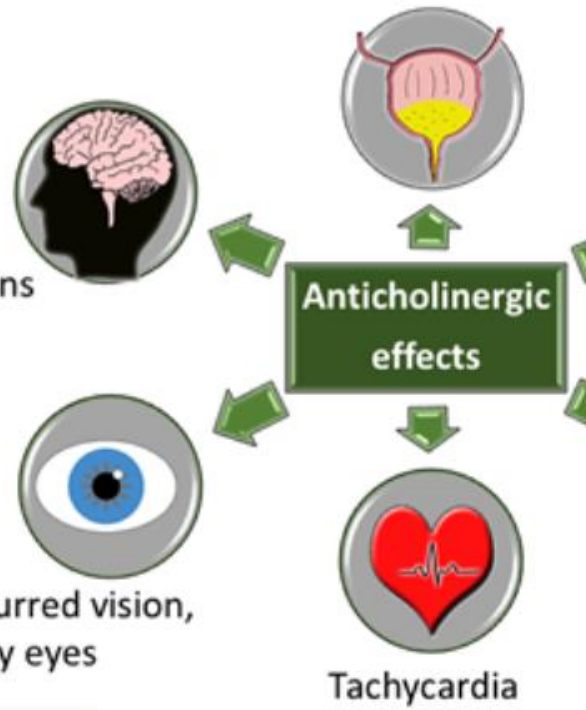
Managing Anticholinergic Side Effects

from www.medicinesafety.co.uk

General approach is to review patients regularly and:

- **Awareness**. Know your anticholinergic effects.
- **Alternatives**. Use lower risk medicines or non-drugs.
- **Additive effects**. Don't co-prescribe anticholinergics.
- **Amounts**. Keep doses low, especially in elderly.



Signs could include:

- Decreased cognition, or ability to take care of self.
- Falls.
- Daytime sleep.

Signs could include:

- Difficulty swallowing.
- Dental caries.
- Eating less.
- Gut ache.

Signs could include:

- Difficulty reading/ using glasses.
- Eye infections.

Signs could include:

- Dehydration.
- Decreased exercise.

Signs could include:

- Worsening angina or heart condition.
- Palpitations, dizziness.

Identifying patients with high ACB

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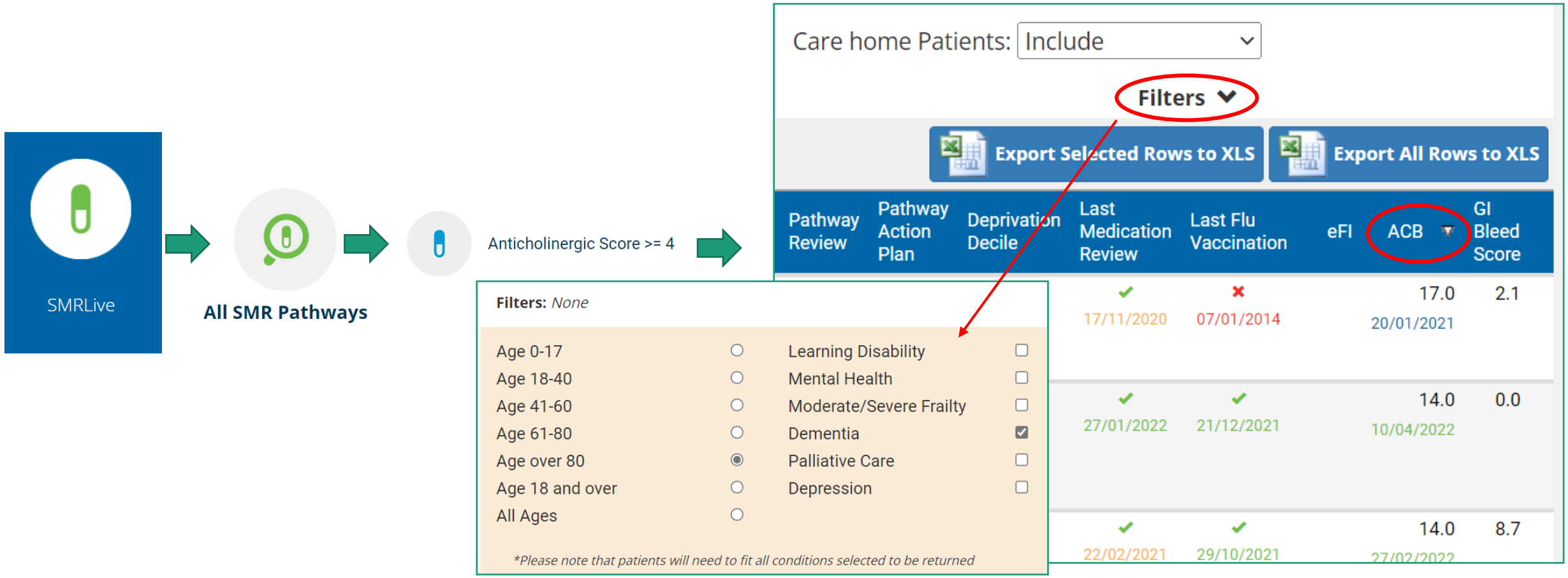
1. Eclipse Live - alert has been set up to identify dementia patients with an ACB >/= 6
2. https://www.nhspathways.org/NHSpathways/login.aspx



Solifenacin scorecard indicator

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- It is now nearly 3 years since solifenacin lost its patent and it is now the most cost effective anticholinergic incontinence drug alongside immediate release oxybutynin.
- All patients should be regularly reviewed for any anticholingeric side effects which may mean they have better outcomes with no prescribing, but if they have minimal side effects and the benefits which warrant continued prescribing of an anti-cholinergic incontinence drug, we now recommend a switch to solifenacin.
- Pts with incontinence pads – do they need bladder drugs??
- Restricting fluid -> conc. urine -> bladder irritation -> incontinence worse
- Hydration-leaflet.pdf (somersetccg.nhs.uk)

Key messages:

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- Be aware of the anticholinergic burden of drugs and cumulative anticholinergic effects of multiple drugs.
- Identify older or frail people or people with complex multimorbidities on anticholinergic drugs. Minimise the use of anticholinergic drugs where possible.
- Review patient's treatment at regular intervals for efficacy or tolerance. Review medication in older people that have had a fall or are at increased risk of falling as part of a multifactorial risk assessment.
- Dementia: identify and minimise use of drugs that may adversely affect cognitive function. Avoid prescribing anticholinergics with acetylcholinesterase inhibitors (donepezil, galantamine & rivastigmine).

Useful info:

- ACB Calculator http://www.acbcalc.com/
- Medichec https://www.medichec.com/
- Anticholinergic Cognitive Burden (ACB) Scale https://www.uea.ac.uk/documents/746480/2855738/Anticholinergics.pdf
- Bulletin 253: Anticholinergic burden | PrescQIPP C.I.C

https://www.prescqipp.info/our-resources/bulletins/bulletin-253-anticholinergic-burden/

- Anticholinergic burden indicator available on the ePACT2 polypharmacy dashboard: '**Percentage of patients with an anticholinergic burden score of 6 or more' (All ages)**