A GUIDE TO
deprescribing

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CPS Experts in Medicines
CONSULTANT PHARMACY SERVICES

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 (e.g. antipsychotics, benzodiazepines) has not been shown to cause any harm, and indeed, in some situations has improved outcomes.

Triggers for deprescribing may include patients with an increased frequency of falls, with delirium and/or cognitive impairment and in end-of-life situations.

Engaging and educating the patient regarding the rationale for deprescribing improves success rates 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. The priority will be based on individual case considerations.

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, implementing recommendations in guidelines may result in a significant medication load, without clear evidence of net health benefits. The use of prescribed and over the counter products has increased. In the United Kingdom, the number of over 65year old people who self report taking 5 or more items has quadrupled from 12% (over 7000 people in 1991-1993) to 49% (over 7000 people in 2001 to 2004). Over the same two surveys, the number of people not taking any medication has decreased from 1 in 5 to 1 in 13.[1]

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.[2] In addition, patients with low resilience (typically older, frailer patients) may have undesirable outcomes from the indiscriminate implementation of guideline recommendations.[3,4] 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.[5,6] The term can also be considered more broadly, taking in the concept of minimisation and reduction of medication burden in terms of dose and/or number of tablets/administration times.

Deprescribing medication may be an appropriate action in certain clinical situations. Triggers for deprescribing may include:

- patients taking a large number of medications (polypharmacy)
- patients with an increased frequency of falls,
- patients with delirium and/or recent onset cognitive impairment
- patients where a change in treatment strategy or goals of care has occurred (e.g. after admission to hospital or residential care, end-of-life or limited prognosis situations).[7,8]

Many medicines are intended to be prescribed for an intermediate duration and these can be inadvertently continued indefinitely. Such "legacy prescribing" is often seen with proton pump inhibitors, benzodiazepines and antidepressants.

In some situations, a sign or symptom due to an adverse effect of a medication can be interpreted as a new medical condition, leading to a "prescribing cascade". In this situation, an additional medication is often added to treat the new condition. Common examples include prescribing of diuretics after development of peripheral oedema associated with calcium channel blockers, the prescribing of prochlorperazine for dizziness associated with addition or increase of antihypertensive agents and the prescribing of levodopa for tremors associated with antidepressants or antipsychotics.

Deprescribing 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. The various methods have been reviewed by Scott et al.[9] 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.

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
	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: Heirarchy of Utility of Medications (from Reference 2)

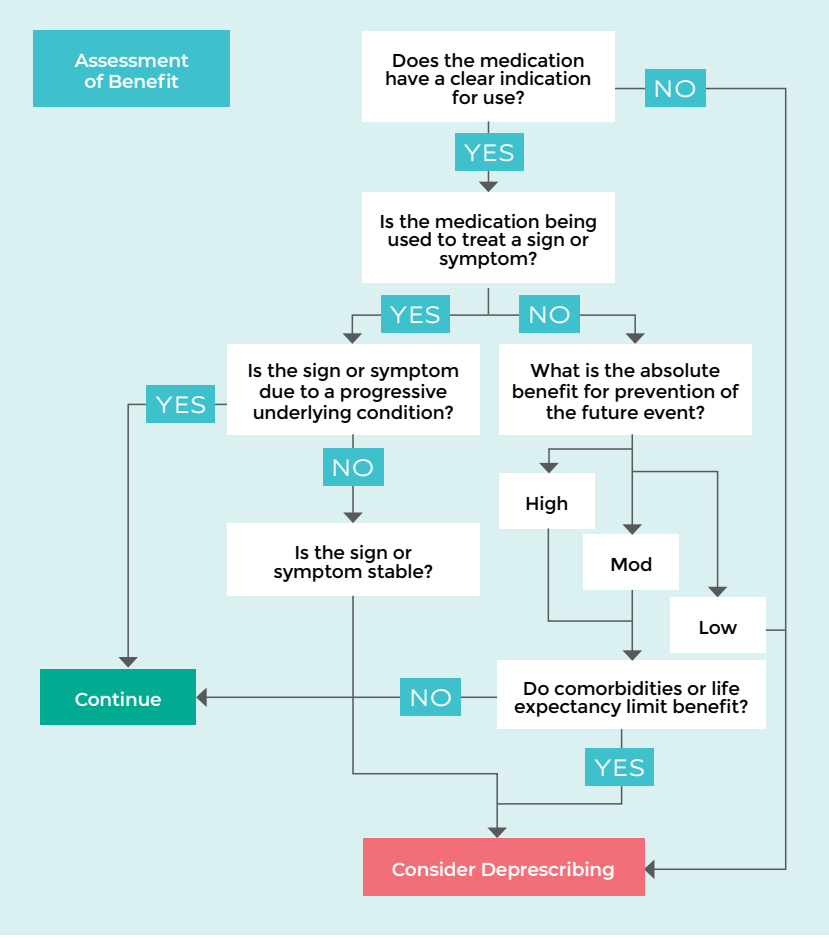


Figure 2: Considering deprescribing in terms of benefit of a medication

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) 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 achievable.

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 is likely to be achieved. In the presence of significant comorbidities (for example moderate to advanced dementia or end-stage COPD) consideration of cessation of preventative therapy would seem appropriate.[10]

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 where this is present, consideration of deprescribing.

Even medications that are not commonly associated with causing harm may do so if contraindications are present (for example metformin 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.

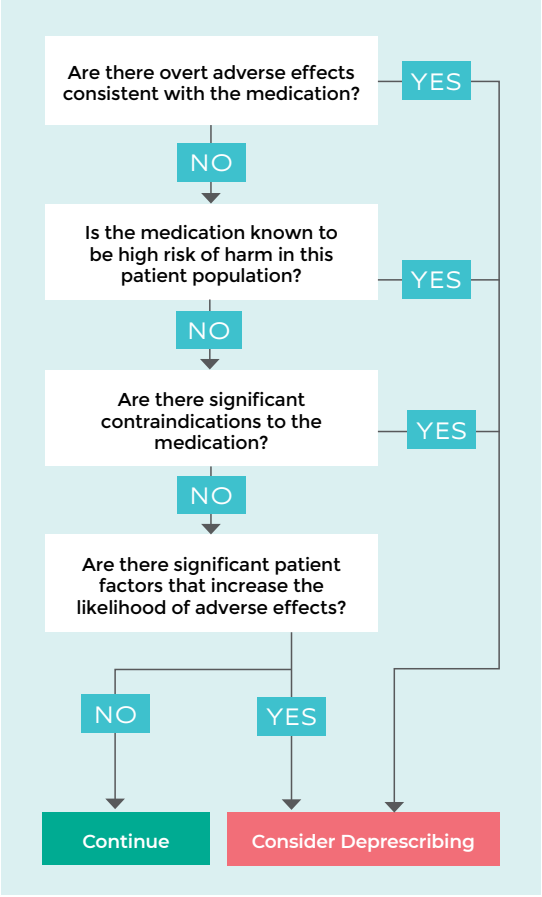


Figure 3: Considering Deprescribing in terms of Potential for Harm of a Medication

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

Table 1: Examples of Different Benefit/Harm Medication Situations

CLINICAL 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 have been undertaken and some of these are discussed below.

In 2016, Page et al.[11] reviewed 132 studies where older adults had at least one medication deprescribed. 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, oral benzodiazepines, antipsychotics or antidepressants.[11]

More recent systematic and narrative reviews have focussed on deprescribing in older adults near the end of life,[12] in older adults with dementia,[13] in nursing homes,[14] and in hospitalised patients.[15]

These authors of these reviews came to similar conclusions, i.e. that there is some evidence for the benefits of deprescribing, but also highlighted the need for good-quality studies focussing on outcomes such as mortality, quality of life and physical or cognitive functioning.

It can be said, however, that **over a range of different practice settings (e.g. community, hospital, aged care), deprescribing of a range of different medications (e.g. antipsychotics, benzodiazepines) has not been shown to cause any harm, and indeed, in some situations has improved outcomes.**

WITHDRAWAL AND RECURRENCE ISSUES

If cessation of an agent is undertaken it is important to monitor the patient afterwards for any potentially negative outcomes.[16] Some medications carry a risk of 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 medications, 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 effect). 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 abrupt cessation of proton pump inhibitors).[16]

PATIENT PERCEPTIONS

Patient attitudes to deprescribing have been examined by Qi et al.[17] They 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,[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. a 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 an antiplatelet dose of aspirin for primary prevention 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.

A shared decision-making tool is available that is designed to support discussions with patients about their goals and preferences in relation to a number of factors including: [20]

- general understanding of their health
- preferences for decision making
- priorities relating to medications

Key aspects of this conversation guide are shown in **Table 2**.

Patients may be more likely to participate in trials of deprescribing their medications if:

- they have or fear adverse effects or habituation from their medications
- they lack symptoms that the medication is treating
- they "dislike" medications and have concerns about cost, inconvenience or compatibility
- they have a good relationship and open communication with their supportive health professionals.

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

Medicines Conversation Guide	
Set up the Conversation	Introduce purpose
	Expectations
	Information preferences
Explore Key Topics	Goals
	Activities and function
	Fears and worries
	Side effects
Make Trade-offs	Making changes
	Side effects/burden
Close the Conversation	Summarise goals, priorities and medicines

Table 2: Medicines Conversation Guide (Modified from Ref 20)

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 above). A number of authors have examined attitudes of health professionals and medical practitioners to deprescribing.[21,22,23,24,25,26]

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 SPECIALIST/HOSPITAL PRESCRIBING OR TREATMENT GUIDELINES

While there are disease specific guidelines available for a wide range of chronic conditions, many people with 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, including both in- and out- patient hospital visits.

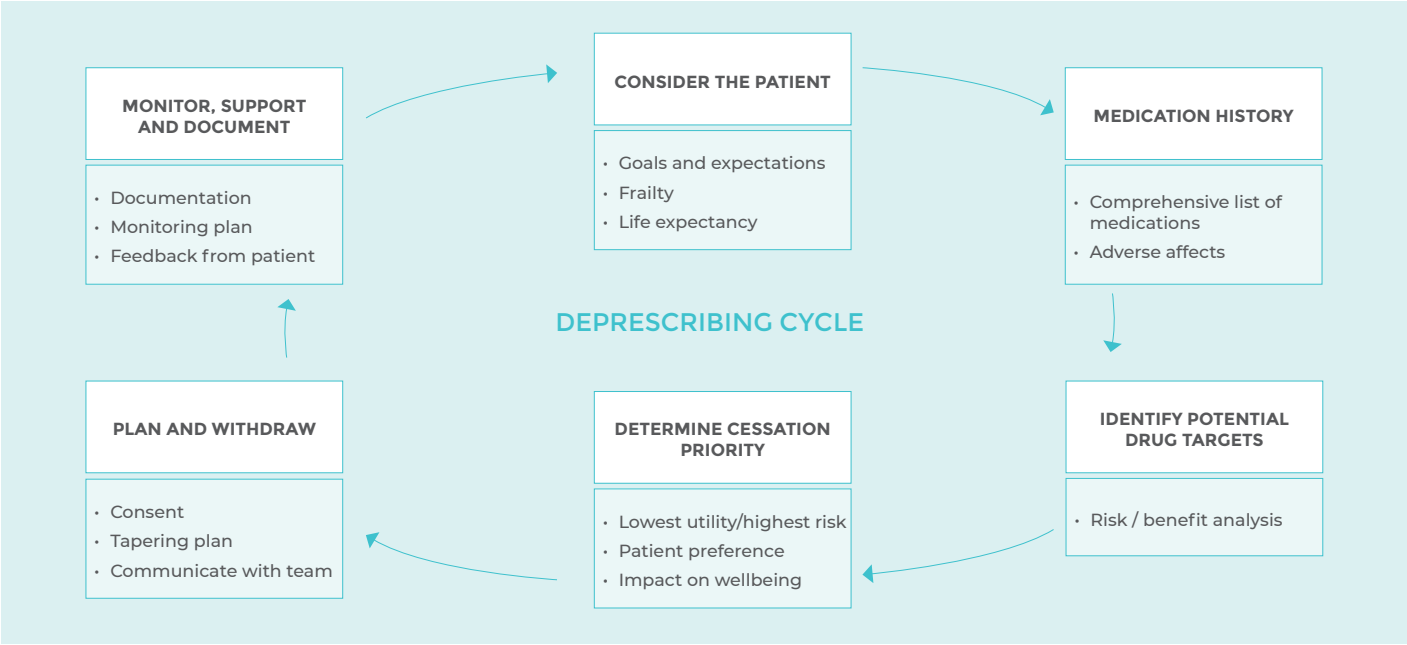
Recommendations from disease-specific guidelines may be inappropriate as the trials underpinning the recommendations often exclude people with multimorbidity.

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 referral for residential medication management and home medicines reviews (RMMRs/HMRs), with specific instructions to target deprescribing may help support general practitioners who are considering deprescribing.

DEPRESCRIBING: A PERSONALISED APPROACH



STEP 1: CONSIDER THE PATIENT

1

PATIENT GOALS AND EXPECTATIONS

A discussion with the patient regarding aspects of their quality and duration of life and expectations of treatment (including efficacy and potential harms) will assist with determining priorities for deprescribing. Involving patients and their carers in shared decision making is important to reducing overuse of medications as individual patients may attach different importance to particular outcomes depending on their life experience. It is important that patients are aware that reducing overuse does not mean withholding the care that they require.

FRAILTY

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. 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 and the Clinical Frailty Scale are both available as applications for phone or other devices. The Walking speed is also a useful clinical measure e.g. taking longer than 5 seconds to walk 4 metres is an indicator of frailty.

LIFE EXPECTANCY

Estimating life expectancy is problematic in an individual. Use of the question "would I be surprised if this patient died in the next 6-12 months?" by an experienced clinician can be 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.[29,30] The presence of a life-limiting illness may prompt a review of medications that are being used for prophylaxis of unrelated, unlikely events.

STEP 2: MEDICATION HISTORY

2

Determine all medicines that the patient is taking and the reasons for each one. This should include prescription and OTC medication, including prescriptions from other practitioners along with any vitamins and complementary and alternative 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 (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

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,[31] STOPP/START criteria,[32,33] or other inappropriate prescribing lists) There are safer alternative agents for many of these high risk medications.[34]
- 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. rivaroxaban 20 mg/day in those someone with renal impairment, paracetamol 4 g/day in lightweight elderly) should have doses reduced
- Medications that are associated with multiple drug-drug or drug-disease interactions (e.g. diltiazem) may be replaced with safer alternatives
- Medications that are taken more than once daily could be converted to once daily. (e.g. twice daily metformin changed to once daily metformin MR)
- Medications that are prescribed separately, but are available in combination products could be converted to these to reduce medication burden and cost (e.g. amlodipine/atorvastatin)
- Medications where device management or 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 are obvious first targets. Consideration of the relative risk of benefit and harm in the individual patient needs to be made rather than applying arbitrary guidelines. Drugs may also be targeted on the basis of impact on the patient's wellbeing, patient preference or those 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. The priority will be based on individual case considerations. In some cases, deprescribing may involve reducing the dose or simplifying the regimen rather than ceasing an agent.

PLAN AND INITIATE WITHDRAWAL TRIAL

5

A shared decision making process should be used to obtain consent from patient/carer explaining rationale and steps to take if symptoms recur. A withdrawal plan with appropriate tapering of one medication at a time may be prepared.

Informing the patient of the rationale for deprescribing improves success rates in deprescribing and empowers the patient to take better control of their medications. The National Prescribing Service has prepared a number of specific and general patient resources with regard to deprescribing of medications.

Provide the patient/carer with information on what they should do if symptoms recur and alternative non-drug strategies that they may use to control symptoms. It is important to inform other health professionals involved of the rationale for the deprescribing and the details of any tapering plan.

A written tapering plan is desirable, bearing in mind that some classes of medication require slow tapering to avoid either return of disease symptoms or withdrawal symptoms (e.g. corticosteroids, opioids, PPIs).

MONITOR AND SUPPORT

6

- Follow up withdrawal plan to look for any adverse effects or return of symptoms.
- Review plan with patient 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. How frequently this is required will depend on the medication/disease process involved and the duration of the tapering regimen. Progress should be regularly reviewed with the patient, with feedback determining any changes to the deprescribing schedule.

Documentation of the outcome of the deprescribing attempt should be undertaken, ensuring that medications ceased are not recommenced unnecessarily.

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