**Benefits of deprescribing for older people with frailty and polypharmacy: part one**

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**Abstract**

The UK population is ageing rapidly, a trend that is likely to continue due to improvements in chronic disease management and increased life expectancy. Comorbidities, including frailty, become increasingly common with age and as a result it is likely that multiple medicines will be prescribed for older people, leading to polypharmacy. This is a concern because polypharmacy is associated with various adverse effects and an increased medicine burden in this population, as well as a financial burden for the healthcare system. This article, the first of two parts, explains the physiology of ageing and frailty, and considers the adverse effects of polypharmacy on older people with frailty, using a fictional case study to illustrate this. Part two will use the case study to explore the use of medication reviews and deprescribing benefits as part of medicines optimisation.

**Introduction**

The number of older people in the UK is increasing and it has been projected that one in four people will be aged 65 years or over by 2050 (Office for National Statistics 2019). Life expectancy is also increasing; it is estimated that 434 million people globally will be aged 80 years and over by 2050 (United Nations 2015).

Many people aged over 65 years are taking five or more medicines (polypharmacy) and are living with multiple comorbidities, including frailty. In England, more than one in ten people aged over 65 years take at least eight different medicines each week (Age UK 2019).

It is likely that this situation will be challenging for healthcare services due to the associated costs and resources associated with polypharmacy and comorbidities (Age UK 2019).
Physiology of ageing and frailty

Around 10% of people aged over 65 years are living with frailty, rising to between one quarter and one half of those aged over 85 years (Clegg et al 2013). While ageing itself is not a disease, frailty is a distinctive health state related to the ageing process in which multiple body systems gradually lose their physiological reserves and their ability to function as effectively (Harrison et al 2015, World Health Organization 2022). Due to this progressive loss of reserves and function, frailty can result in a disproportionate response from these body systems to what are typically considered minor stressors, such as sustaining a minor injury or taking a new medicine (Clegg et al 2013).

Due to the physiological changes associated with ageing, older people have a greater sensitivity to medicines and are more susceptible to adverse effects than younger people. Some major organs, such as the liver and kidneys, are significantly affected by the ageing process, resulting in changes to pharmacokinetic and pharmacodynamic processes (Midlöv 2013).

Pharmacokinetics

Pharmacokinetics is defined as the movement of a drug into, through and out of the body – that is, its absorption, bioavailability, distribution, metabolism and excretion. It is affected to varying degrees by the ageing process itself and by diseases commonly associated with ageing (Drenth-van Maanen et al 2020).

Renal impairment is one significant physiological change associated with ageing. The kidneys reduce in mass between the ages of 30 years and 80 years, and fat and fibrosis (scarring) may replace the remaining tissue. This decline occurs primarily in the renal cortex, where nephrosclerosis (hardening of the kidneys) is associated with older age (Denic et al 2016). Renal impairment affects drug pharmacokinetics and has subsequent adverse effects. Patients with renal impairment are increasingly susceptible to drug-induced nephrotoxicity and have an increased risk of developing hyperkalaemia (high potassium levels) when taking certain prescribed medicines, including renin-angiotensin-aldosterone system inhibitors (Elbeddini et al 2021). When prescribing medicines for patients with renal impairment, it is important to use the appropriate measure to assess renal function. In most cases, estimated glomerular filtration rate will be appropriate, but in some circumstances creatinine clearance should be calculated (Medicines and Healthcare products Regulatory Agency 2019) – for example when introducing a new medicine or adjusting a dose in people over the age of 75 years. This is because estimated glomerular filtration rate can overestimate renal function in such situations (Medicines and Healthcare products Regulatory Agency 2019).

The liver is also affected by the ageing process. With age, the liver decreases significantly in volume by 20-40% and there is an associated reduction in blood flow by 35%, which has an adverse effect on drug clearance (Kim et al 2015). Age is a major risk factor for drug-induced liver injury (Rochon 2022), and patients aged 75 years and over require significantly longer hospital stays to recover from it (Pedraza et al 2021). Polypharmacy may also be a contributing factor, as several pharmacokinetic and pharmacodynamic mechanisms may predispose a patient with polypharmacy to an increased risk of drug-induced liver injury (Rochon 2022).

Proportions of lean and fat body mass can affect the volume of distribution (the movement of a drug between the intravascular and extravascular compartments of the body). For example, body fat increases with age, so lipophilic (fat-soluble) drugs such as diazepam, propranolol hydrochloride and vitamin D have an increased volume of distribution (Rodrigues et al 2020). In contrast, hydrophilic (water-soluble) drugs such as gentamicin, lithium, digoxin, ethanol and atenolol have a decreased volume of distribution with age. Additionally, larger drug storage reservoirs and decreased drug clearance can prolong the half-life of medicines and lead to increased plasma drug concentrations in older people (Rochon 2022). The overall effect of this is an increased risk of drug toxicity when these medicines are prescribed to older patients compared with when they are prescribed to younger patients (Rodrigues et al 2020).

Pharmacodynamics

Pharmacodynamics refers to the biochemical and physiological effects of drugs on the body and their mechanisms of action (Drenth-van Maanen et al 2020). Pharmacodynamics...
Aims to describe the potential adverse effects of polypharmacy for patients and the nurses' role in optimising medicines for older people. Evidenced based on recent research and initiatives.

**Polypharmacy**

Polypharmacy is typically defined as taking more than five medications (Masnoon et al. 2017) and hyperpolypharmacy as taking ten or more medicines (Bhagavathula et al. 2022). Polypharmacy is associated with suboptimal prescribing (Royal Australian College of General Practitioners 2019) and can be further described as ‘problematic polypharmacy’; that is, the prescribing of multiple medicines inappropriately or where the intended benefit is not realised (Duerden et al. 2013). Around one in five prescriptions for older people living at home may be inappropriate (Age UK 2019), which can contribute to adverse effects for patients and increased costs for healthcare organisations.

Box 1 shows some of the risk factors associated with polypharmacy.

One risk factor associated with polypharmacy is prescribing cascades, whereby an adverse drug reaction (ADR) is misinterpreted as a new condition and an additional medicine is then prescribed to treat it (Cesari 2020, Rochon 2022). An example is the initiation of anti-Parkinson pharmacological treatment for symptoms arising from medicines such as antipsychotics. The anti-Parkinson drugs can lead to new symptoms, such as orthostatic (postural) hypotension (Rochon 2022), which is then treated as a new condition.

**TIME OUT 2**

It is important that nurses are aware of the potential adverse effects that polypharmacy can have for older people. Note down five adverse effects of polypharmacy that you think older people might experience

Adverse effects of polypharmacy for patients

Polypharmacy can lead to a medicine burden for patients and subsequently to non-adherence to treatment. It can also cause various drug-related problems, including ADRs and drug-to-drug interactions (Kojima 2018, Rochon 2022), especially when a single-disease focus is adopted rather than considering the whole person and the presence of any comorbidities. This may subsequently increase the risk of hospitalisation; Kojima (2018) found that older people are seven times more likely than younger people to have an emergency hospital admission due to ADRs.

One example of a drug-related problem associated with polypharmacy is the increased risk of bleeding from warfarin sodium that occurs with the co-administration of omeprazole, amiodarone hydrochloride and non-steroidal anti-inflammatory drugs (Joint Formulary Committee 2023). Another example is the use of diuretics for oedema in patients who have been prescribed calcium channel blockers (Savage et al. 2020); oedema can be a common side effect of calcium channel blockers, so alternative medicines should be considered instead.

Adverse effects can be serious and may include falls, cognitive impairment and hospitalisation (Ibrahim et al. 2021). A strong and bidirectional relationship (Gutiérrez-Valencia et al. 2018) or associative relationship

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**Box 1. Risk factors associated with polypharmacy**

- Advancements in medicines and the evidence base for medicines
- Multiple comorbidities, particularly when a single-disease approach to prescribing is taken
- Patients' expectations regarding treatment, for example if they expect to be prescribed certain medicines
- Older age and increased longevity
- Iatrogenic effects such as prescribing cascades
- Absence of a primary care coordinator
- Lack of medication reviews and deprescribing
- Miscommunication, especially when several healthcare professionals are involved in care
- Multiple transfers across inpatient settings

(Pazan and Wehling 2021) has been identified between polypharmacy and frailty, suggesting that polypharmacy could contribute significantly to the development of frailty. Furthermore, a study by Veronese et al (2017) found that each added medicine was associated with an 11% increase in older people's risk of frailty.

In a randomised controlled trial, Pfister et al (2017) examined drug-related problems in older patients with dementia. They cited an example of a patient who had been treated for bursitis with fluconazole. However, fluconazole had been added as a repeat prescription rather than the intended seven-day treatment. The patient was also taking citalopram for depression. Once admitted to hospital, he experienced increasing hallucinations and agitation, for which he was prescribed haloperidol. It was considered likely the patient's symptoms may have been a result of the interaction between fluconazole and citalopram increasing his blood concentration of citalopram. Therefore, the fluconazole was stopped and the haloperidol was prescribed as required, and as a result the patient no longer experienced hallucinations.

Polypharmacy is the main risk for potentially inappropriate medications (Rankin et al 2018). In the context of the care of people aged 65 years or older, a potentially inappropriate medication is one that could lead to a significant risk of ADRs and arises from prescribing practices such as continuing therapy for longer than necessary or than recommended in prescribing guidelines (Rankin et al 2018). Around 29% of older people are prescribed at least one potentially inappropriate medication (Bradley et al 2014), and Muhlack et al (2017) found that the use of these was associated with a 1.6-fold increase in mortality rate among older adults. To avoid prescribing potentially inappropriate medications, it is essential to consider the risks and benefits of each medicine.

In the author's clinical experience, there is often a ‘legacy’ of prescribing, where a medicine has been prescribed for an intermediate duration but has continued indefinitely. Examples in clinical practice may include proton pump inhibitors and antihypertensives. When prescribing for older adults with frailty, consideration should be given to maintaining quality of life and reducing the treatment burden, rather than solely focusing on reducing disease risk and prolonging life.

**TIME OUT 3**
Read the fictional case study (Case study 1) and identify Simon’s risk factors for polypharmacy. How might you support Simon to address these risk factors and optimise his medicines?

**Conclusion**
Various comorbidities, including frailty, become increasingly common with age. As a result, it is likely that multiple medicines will be prescribed to older people, leading to polypharmacy. Polypharmacy is associated with various adverse effects and can increase the medicine burden for older people with frailty, so it is important to optimise medicines use in this population. Using the case study introduced in this article, part two will focus on medicines optimisation for older people with frailty and polypharmacy through medication reviews and deprescribing.

**TIME OUT 4**
Identify how deprescribing for older people with frailty and polypharmacy applies to your practice and the requirements of your regulatory body

**TIME OUT 5**
Now that you have completed the article, reflect on your practice in this area and consider writing a reflective account: rcni.com/reflective-account
Case study 1. Frailty and polypharmacy

Simon is a 90-year-old man who lives alone in his own home. Over the past few months, he has developed increasing frailty and, following a recent fall at home, he was admitted to hospital for several days for treatment of a urinary tract infection.

His son and daughter are supportive, staying with Simon on a regular basis. However, Simon has decided to move into a residential home because he feels ‘lonely and isolated’ and believes it is unfair for his family to sustain their current level of support.

Simon has a history of:
- Moderate frailty on the Clinical Frailty Scale (Rockwood et al 2005).
- Folate deficiency.
- Acquired hypothyroidism.
- Essential hypertension.
- Angina.
- Ischaemic heart disease.
- Non-ST-elevation myocardial infarction.
- Chronic kidney disease stage 3.
- Shoulder injury.
- Vitamin D deficiency.
- Chronic obstructive pulmonary disease.
- Cerebrovascular accident.
- Vitamin B12 deficiency.

Simon has been prescribed 15 medicines, so he is experiencing polypharmacy – specifically hyperpolypharmacy. Table 1 details the medicines prescribed for Simon.

Having been discharged home, Simon remains under the care of a respiratory specialist and a consultant endocrinologist. He receives visits from the community nursing team for his vitamin B12 injections. Part two of this article will detail Simon’s medication review and the deprescribing process that was undertaken with him to reduce the risks associated with hyperpolypharmacy.

### Table 1. Medicines prescribed for Simon

<table>
<thead>
<tr>
<th>Indication</th>
<th>Medicine</th>
<th>Dose, formulation and frequency*</th>
</tr>
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<tbody>
<tr>
<td>Folate deficiency</td>
<td>Folic acid</td>
<td>5mg tablet, once daily</td>
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<tr>
<td>Acquired hypothyroidism</td>
<td>Levothyroxine sodium</td>
<td>25 micrograms tablet, once daily</td>
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<td></td>
<td></td>
<td>on alternate mornings</td>
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<td></td>
<td></td>
<td>30-60 minutes before breakfast for</td>
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<td></td>
<td>maintenance</td>
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<td></td>
<td></td>
<td>100 micrograms tablet, once daily</td>
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<td></td>
<td></td>
<td>30-60 minutes before breakfast for</td>
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<tr>
<td></td>
<td></td>
<td>maintenance</td>
</tr>
<tr>
<td>Secondary prevention of myocardial infarction and stroke</td>
<td>Simvastatin</td>
<td>40mg tablet, once daily at bedtime</td>
</tr>
<tr>
<td>Nocturnal leg cramps</td>
<td>Quinine</td>
<td>300mg tablet, once daily at bedtime</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>Clopidogrel</td>
<td>75mg tablet, once daily</td>
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<tr>
<td>Prevention of gastrointestinal issues associated with clopidogrel such</td>
<td>Esomeprazole</td>
<td>20mg tablet, once daily</td>
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<tr>
<td>as bleeding, dyspepsia and ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate non-malignant pain resulting from a previous shoulder injury</td>
<td>Buprenorphine</td>
<td>5 micrograms per hour transdermal</td>
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<tr>
<td>which is unresponsive to non-opioid analgesics</td>
<td></td>
<td>patch, applied weekly</td>
</tr>
<tr>
<td>Dependent lower limb oedema</td>
<td>Furosemide</td>
<td>20mg tablet, once daily in the morning</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Lorazepam</td>
<td>0.5mg tablet, twice daily</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>Salbutamol</td>
<td>100 micrograms, inhalation of aerosol, twice daily as</td>
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<td></td>
<td></td>
<td>required</td>
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<td></td>
<td></td>
<td>2.5mg, inhalation of nebulised solution, four times per</td>
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<td></td>
<td></td>
<td>day</td>
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<tr>
<td></td>
<td>Tiotropium</td>
<td>2.5 micrograms, inhalation of powder, once daily</td>
</tr>
<tr>
<td>Vitamin D deficiency</td>
<td>Colecalciferol</td>
<td>800 units capsule, once daily</td>
</tr>
<tr>
<td>Vitamin B12 deficiency</td>
<td>Hydroxocobalamin</td>
<td>1mg intramuscular injection, three times per week for two</td>
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<td></td>
<td></td>
<td>weeks, then 1mg every three months</td>
</tr>
</tbody>
</table>

*See Joint Formulary Committee 2023 for further prescribing information
Bhagavathula AS, Tedeyae W, Vidyasagar K et al (2022) Polypharmacy and hyperpolypharmacy in older individuals with Parkinson’s disease: a systematic review and meta-analysis. Gerontology. 68, 10. 10.1093/geront/gnaa239
Pflüger B, Jonsson J, Gustafsson M (2017) Drug-related problems and medication reviews among old people with dementia. BMC Pharmacology and Toxicology. 18, 52. doi: 10.1186/s40706-017-0075-2

References
Deprescribing for older people with frailty and polypharmacy: part one

TEST YOUR KNOWLEDGE BY COMPLETING THIS MULTIPLE-CHOICE QUIZ

1. Frailty:
   a) is a distinctive health state that is not related to the ageing process □
   b) Can result in a disproportionate response from body systems to what are typically considered minor stressors □
   c) Involves multiple body systems increasing their physiological reserves and their ability to function □
   d) Typically occurs in those aged under 65 years □

2. Which of these is a physiological change associated with ageing?
   a) The liver significantly increases in volume □
   b) Renal impairment □
   c) The kidneys increase in mass □
   d) Normoglycaemia □

3. Which statement is false?
   a) Pharmacodynamics refers to the biochemical and physiological effects of drugs on the body and their mechanisms of action □
   b) Pharmacodynamics depends on the concentration of a drug at the receptors □
   c) Pharmacodynamics does not affect the adverse and toxic effects of drugs □
   d) Pharmacodynamics depends on changes in binding sites, receptors, post-receptor events within cells and homeostatic mechanisms □

4. Hyperpolypharmacy has been defined as:
   a) Taking five or more medicines □
   b) Taking fewer than five medicines □
   c) Taking ten or more medicines □
   d) Taking fewer than ten medicines □

5. Which of the following is not considered a risk factor for polypharmacy?
   a) Presence of a primary care coordinator □
   b) Older age □
   c) Multiple comorbidities □
   d) Miscommunication □

6. Adverse effects associated with polypharmacy may include:
   a) Falls □
   b) Cognitive impairment □
   c) Hospitalisation □
   d) All of the above □

7. Which statement is false?
   a) Polypharmacy is the main risk for potentially inappropriate medications □
   b) Polypharmacy could contribute significantly to the development of frailty □
   c) Polypharmacy is less likely to occur when a single-disease focus is adopted □
   d) Polypharmacy can lead to adverse drug reactions and drug-to-drug interactions □

8. What is a prescribing cascade?
   a) When increasingly strong analgesics are prescribed to treat pain □
   b) When an adverse drug reaction is misinterpreted as a new condition and an additional medicine is prescribed to treat it □
   c) When a patient wishes to receive a medicine because they have seen other people benefit from it □
   d) When there is a sudden increase in the prescription of a medicine □

9. When prescribing for older adults with frailty:
   a) Consideration should be given to maintaining quality of life and reducing the treatment burden □
   b) Medicines should always be continued indefinitely □
   c) The sole focus should be on reducing disease risk and prolonging life □
   d) Healthcare professionals should assume that the person does not have mental capacity □

10. All primary care networks in England are required to identify and prioritise patients who would benefit from a structured medication review, including:
    a) Those with severe frailty □
    b) Those who are particularly isolated □
    c) Those with recent hospital admissions and/or falls □
    d) All of the above □

This activity has taken me ____ minutes/hours to complete. Now that I have read this article and completed this assessment, I think my knowledge is:

Excellent □ Good □ Satisfactory □ Unsatisfactory □ Poor □

As a result of this I intend to: ____________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

How to complete this assessment

This multiple-choice quiz will help you test your knowledge. It comprises ten multiple choice questions broadly linked to the previous article. There is one correct answer to each question.

You can read the article before answering the questions or attempt the questions first, then read the article and see if you would answer them differently.

You may want to write a reflective account. Visit rcni.com/reflective-account

Go online to complete this multiple-choice quiz and you can save it to your RCNi portfolio to help meet your revalidation requirements.

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This multiple-choice quiz was compiled by Alex Bainbridge

The answers to this quiz are:

bADCDBDCDCD

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