Cardiovascular disease in older people living with frailty: Optimising medicines in multimorbidity and polypharmacy

The first stop for professional medicines advice
**Audience**
Pharmacists and other clinicians in primary and secondary care settings undertaking medication reviews for older people with cardiovascular conditions living with frailty, multimorbidity and polypharmacy.

**Purpose**
To provide a pragmatic framework and highlight resources to optimise medicines use when managing common cardiovascular long-term conditions (LTC) in older people living with frailty, multimorbidity and polypharmacy.

It is not intended to provide specific answers but a process for weighing up the evidence base, to facilitate shared decision-making between the patient (and/or their carers) and the clinicians involved in delivering care for the patient. Case studies are included to allow readers to consider the evidence and apply this to everyday scenarios in clinical practice. Many of the recommendations in this document follow good practice principles of prescribing and deprescribing and will either assume these or emphasise them.

**Summary**
Cardiovascular medicines are the most frequently prescribed class in older people. Heterogeneity of function and resilience of older people, frailty, multimorbidity, inapplicability of research evidence, frequency of adverse drug events, limited life expectancy and changing therapeutic goals present challenges to the clinician. An individualised and holistic approach to the management of cardiovascular disease (CVD) in older people is required to optimise outcomes.

This document outlines the principles for managing CVD in older people which include:

- **H**olistic, patient centred goal setting – establishing what matters most to the patient
- **E**vidence and guideline limitations in this population
- **A**dverse drug events – identify actual ADEs and consider the risks of potential ADEs when prescribing
- **R**eview medication regularly recognising co-morbidities and changing patient priorities
- **T**herapy modification in line with the principles of good prescribing practice and appropriate deprescribing

The document outlines a range of clinical tools to support decision making to optimise outcomes and discusses key issues for managing common cardiovascular LTCs in older people with multimorbidity including the management of hypertension, heart failure, atrial fibrillation and coronary heart disease with illustrative case studies and ‘top tips’

Ultimately the practitioner’s judgement is required to make prescribing and deprescribing decisions balancing the evidence, the risk and benefits of each medication and the patient’s goals.
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Disclaimer: Whilst reasonable endeavours have been made to ensure the accuracy of the information contained in this document, SPS cannot accept responsibility for any errors or omissions.
1. Background

1.1 Issues facing older people with cardiovascular disease or cardiovascular LTCs
The risk of cardiovascular disease increases with age\(^1\). Therefore, older people have a higher prevalence of cardiovascular long-term conditions (like hypertension, coronary heart disease (CHD), heart failure, atrial fibrillation (AF)) and associated adverse events (stroke, myocardial infarction, revascularisation and hospitalisation) compared to younger adults.

Cardiovascular medicines are the most frequently prescribed class in older people\(^2\) and are associated with a high incidence of adverse drug events (ADEs). The risk of multimorbidity (the presence of two or more diseases) and frailty also increase with age, with 75% of 75year olds in the UK having more than one long-term condition rising to 82% of 85year olds\(^3\). Studies have shown that 20-50% of older people with CVD also live with frailty\(^4\).

Therefore, the management of CVD in older people requires a holistic approach that takes into account frailty and multimorbidity. Frailty is a distinct health state where a minor event can trigger major changes in health from which the person may fail to return to their previous level of health\(^5\). Older people with frailty often present in clinical settings with one or more frailty syndrome (falls, immobility, incontinence, delirium or acute confusion and increased sensitivity to medicines), all of which can be exacerbated by cardiovascular conditions themselves and the medicines used in their management. This makes therapeutic management complex and presents challenges to both generalist practitioners as well as specialists in geriatrics and CVD\(^6\). Table 1 highlights some of the reasons for these challenges.

### Table 1. Challenges in the therapeutic management of CVD in older people

- Heterogeneity of older people: In relation to health, functioning, resilience to stressors, there is a wide variation between older people of a similar age therefore assessing their cardiovascular risks and benefits from therapy needs an individualised approach.
- Limitations of current research evidence and the application to frailty
- Increased risk of ADEs due to age-related physiological (pharmacokinetic and pharmacodynamic) changes that alter drug handling
- Presence of frailty syndromes that increase vulnerability to ADEs
- Various health, functional and psychosocial circumstances that impact on the patient’s willingness and capability to take/use medicines as prescribed
- Limited life expectancy in frailty alters the risk: benefit ratio for patient outcomes.
- Shift in care goals from preventative to mainly palliative in later years. Outcomes set in clinical trials for younger people often differ from the outcomes important to older people.

\(^1\) Naganathan V. Cardiovascular drugs in older people. Aust Prescr 2013; 36:190-4. doi.org/10.18773/austprescr.2013.077
\(^5\) Introduction to Frailty, Fit for Frailty Part 1 British Geriatric Society https://www.bgs.org.uk/resources/introduction-to-frailty
1.2 Principles for medicines optimisation in older people with CVD

In older people CVD should not be managed in isolation, but in the context of frailty, multimorbidity and other vulnerabilities. NICE CG56 guidance and British Geriatric Society Fit for Frailty part 1 recommend general principles for managing multimorbidity. Also geriatrics and cardiology experts in the US provide useful strategies specifically for managing CVD in frailty and multimorbidity. Both emphasise the need to:

- Identify and prioritise those most vulnerable to ADEs;
- Screen for and assess frailty as part of overall care
- Apply a biopsychosocial approach that is patient centred and individualised. This takes into account biological, psychological, and social aspects
- Align each older person’s individual preferences with the care offered
- Coordinate care between multiple health and social practitioners, providers and systems
- Pay attention to polypharmacy, pill burden and treatment burden such as multiple appointments
- Pay attention to non-adherence as up to 60% of patients with cardiovascular LTCs are non-adherent to therapy within 3 years
- Undertake regular medication reviews particularly after initial prescribing and use a structured evidence based patient centred framework.
- Use clinical judgment and personalised goals when applying disease-based clinical guidelines to drug management decisions
- Generate a personalised shared care and support plan which includes the treatment goals, interventions, follow up reviews, a crisis plan, with sustained support over a long time, continued through intervening crises and adverse events.

CASE 1

A 95-year-old lady living in a warden controlled flat with no support with taking medicines. She was living with moderately frailty, multi-morbidities and polypharmacy (7 medicines, 12 units).

Her repeat medicines were:

1. Digoxin tablets 125 micrograms daily
2. Simvastatin tablets 20mg daily
3. Dipyridamole tablets 100mg 2 twice daily
4. Furosemide tablets 80mg daily
5. Perindopril erbumine tablets 8mg daily
6. Allopurinol tablets 100mg twice daily
7. Ferrous fumarate tablets 210mg three times daily

She had started to forget whether she had taken her medicines and was taking them less regularly. She had poor renal function (CrCl~10ml/min)

During the medication review with the pharmacist they agreed to reduce her pill burden and simply her medicines regimen in order to increase the likelihood of adherence to the essential medicines.

Ferrous fumarate was stopped due to high ferritin levels.

Allopurinol was reduced to once daily due to renal impairment.

Dipyridamole was changed to clopidogrel once daily in line with the current stroke guidelines.

Simvastatin was discontinued due to the patient’s advanced frailty and increased risk of myopathy in view of renal impairment.

The indication for digoxin was unclear in the GP records so the elderly care specialist was contacted to review the ongoing need for digoxin in the context of frailty, poor renal function and increased risk of toxicity, falls and confusion.

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1.3 Evidence based practice for initiating or deprescribing CVD medicines as part of medicines optimisation in frail older people

Guidance and tools are available to support a holistic and individualised approach to medicines review and optimisation in older people. They use a patient centred approach that aims to address some of the challenges in Table 1. They incorporate shared decision making throughout the process to consider the best available research, alongside the patient’s perspectives as well as the clinical expertise and judgment of the practitioner. There is not a single ‘preferred’ tool. Examples of UK tools include:

- NHS Scotland realistic prescribing 7 steps tool (App)
- NICE Multimorbidity guidance NG56 (Section 1.6)
- NHS Specialist Pharmacy Service Patient centred approach to managing polypharmacy.
- Resources to support local delivery

As part of the medication review process there is the opportunity to apply current research evidence for cardiovascular medicines by using a range of tools for identifying potentially inappropriate medicines (PIMs) that should be considered for deprescribing as well as appropriate medicines that should be considered for prescribing. Examples of such tools include:

- NHS Scotland Cumulative Toxicity tool (1.8) and adverse drug reactions pages in the Polypharmacy Guidance Realistic Prescribing 2018
- NICE guidance NG56: database of treatment effects and multimorbidity
- STOPP/START tool vs 2 2015 (O’Mahony et al)
- STOPPFrail tool 2017 (O’Mahony et al)
- CRIME (Criteria to assess appropriate Medication use among complex Elderly patients). Paper from Italian group 2014
- Beers Criteria (Updated 2019). American Geriatric Society
- PRESQIPP Improving Medicines and Polypharmacy Appropriateness Clinical Tool (IMPACT) 2016

1.4 Principles for initiating or deprescribing medicines in older people

**PRINCIPLE ONE:** Establish the Holistic goals of treatment and what matters most to the patient including extending life, disease management and improving function. Generally, therapeutic management in CVD is aimed at controlling symptoms, preventing adverse cardiovascular events and reducing mortality. Because of the heterogeneity among older people, these goals must be individualised and prioritised through shared decision making, to guide prescribing or deprescribing. A discussion with the patient (or suitable person if the patient cannot engage) to explore and establish the goals of care at the outset is crucial before a drug is prescribed or deprescribed1 (NHS Scotland, SPS guidance). It is in this context that a drug should be prescribed if it aligns with the overall goals or deprescribed if it does not.

It is important to remember that many of the medicines used in the management of CVD are licensed for a number of indications. Always establish why the medicine was prescribed when reviewing whether this should be continued or can be deprescribed.
PRINCIPLE TWO: Consider the limitations of current research Evidence. Multimorbid frail older people are usually not included in clinical studies for CVD (or other) conditions and there is limited information on the benefits of medicines in people over 75 years, female, functionally impaired, frail (includes dementia) and minority ethnic groups.

Most studies measure cardiovascular events and mortality as outcomes rather than function. Also many do not consider non-therapeutic (e.g. exercise) or ‘no drug’ as alternative options. So while single LTC CVD research evidence or guidance provides a helpful starting point tools like STOPP/START, STOPPFrail, Beers criteria etc (see section 1.3) that are specifically designed for use in older people or frailty are a truer reflection of the risks and benefits in real practice and should be used as part of the shared decision making process.

Unlike patients enrolled in research studies who are relatively stable patients, with adequate disease control, frailty is dynamic, so the patient’s risks and treatment benefits may change with time. Few guidelines discuss duration of therapy and when they do, most clinical trials for CVD medicines monitor long-term benefits for not more than 10 years (average of 3 years). Therefore, the ongoing need for medicines should be reviewed in the context of the patient’s changing circumstances or need, instead of an indefinite prescribing ‘for life’.

PRINCIPLE THREE: Consider the risks of potential and actual Adverse Drug Events. CVD medicines are implicated in about 20% of ADEs. Even at recommended doses, well tolerated CVD medicines can result in harmful effects in frail older people.

Age-related pharmacokinetic effects such as impaired renal function (ACE inhibitors, direct acting oral anticoagulants (DOACs), increased body fat (digoxin), reduced muscle mass (statins) and plasma proteins (digoxin) can lead to accumulation or redistribution of medicines in the body leading to ADEs.

Similarly, pharmacodynamic changes alter drug response at receptor and organ/system levels. For example impaired orthostatic response (antihypertensive medicines), increased receptor sensitivity (warfarin, aspirin), impaired visceral smooth muscle function (thiazide diuretics), impaired blood brain barrier (beta blockers) can exaggerate drug effects at normal adult doses resulting in falls, GI bleeds, incontinence and nightmares respectively. Therefore, drug doses, formulations, frequency and class may have to be changed or adjusted to suit the individual patient to reduce ADEs.

Unlike in younger or robust older people, ADEs can be non-specific and vague in the frail older people and may be missed if not proactively sought out or monitored. Also the consequences of ADEs can be more exaggerated and severe. For example: a fall can result in a fracture, hospitalisation and reduced self-confidence with regards to mobility, leading to being housebound; muscle pain with statins may hinder independence and functioning such as doing housework or enjoyable activities. Many cardiovascular medicines can trigger or worsen the five frailty syndromes, dehydration, loss of appetite and lead to hospital admission or institutionalisation in a care home.

The balance between ADEs and beneficial effects of medicines should be considered not only in relation to extending life but also preserving quality of life (QoL), maintaining daily function and independence. Studies have identified that older people may prioritise function over disease-based outcomes.

For example, half of older patients prioritised preventing a fall over CVD risk and only 3% were willing to take medicines for primary prevention of a myocardial infarction (MI) if ADEs

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impact on functioning. This further highlights the need to ask and involve patients in shared decision making about prescribing or deprescribing.

**PRINCIPLE FOUR: Consider and Review co-morbidities.** Older people with CVD often have other CVD or non-CVD related LTCs. They all interact with each other and inevitably require medicines to be prescribed as part of their management. The resulting polypharmacy leads to drug:drug and/or drug: disease interactions which complicate therapeutic management, lead to prescribing cascades (where a new drug is started because of side effects produced by another drug with subsequent drugs increasing the risk of further side effects, drug interactions, and patient harm) which may limit the use of the preferred evidence-based medicines doses or choices. For example: simvastatin and donepezil can both cause nightmares; the risk of GI bleed is increased in patients taking antiplatelets or anticoagulants concurrently with NSAIDs for arthritis, SSRIs for depression, or corticosteroids for polymyalgia or COPD. Diuretics needed for symptomatic relief of congestion in heart failure may cause incontinence and nocturnal diuresis and preventative beta-blockers may cause bradycardia, all of which can lead to falls. Like most disease based guidance, NICE CVD guidance address the individual conditions and the evidence is drawn mainly from studies in younger, fitter and more robust populations that may not apply to frail older people with multimorbidity.

**PRINCIPLE FIVE: Prescribing or deprescribing Therapy.** Once it has been agreed to prescribe or deprescribe a drug, the rule of thumb to ‘start low, go slow and monitor closely’ is important to ensure that the risks of ADEs are minimised and the benefits are realised.

### 1.5 General principles for deprescribing

Comorbidity and frailty syndromes are not usually addressed in single CVD guidance, so patients no longer benefitting from cardiovascular medicines but experiencing harm may not be easily identified and the problems may not, therefore be addressed. Clinicians should actively seek opportunities to review CVD drug management and deprescribe medicines that have been inappropriately continued.

**CASE 2**

An 87-year-old lady with mild frailty, multi morbidity, polypharmacy (17 medicines) and uncontrolled hypertension (BP 198/103mmHg) despite being prescribed six antihypertensive agents, including:
- Candesartan tablets 32mg daily
- Amlodipine tablets 10mg daily
- Atenolol/Chlorthalidone tablet 100/25mg daily
- Doxazosin 8mg tablets twice daily
- Moxonidine tablets 300mg daily

Due to her high blood pressure, she had been unable to receive zoledronic acid infusion which was indicated for low bone mineral density and osteoporosis. This was impacting negatively on her quality of life. During the medication review visit the pharmacist found out that she disliked her medicines dispensed into a multi-compartment compliance aid (MCA). She was concerned about the frequent changes in appearance of her tablets that were due to brand substitutions by her community pharmacy. She did not trust that she was being given the right medicines in the MCA, and so decided not to take the tablets.

They both agreed a plan and with her consent the pharmacist arranged for medicines to be supplied in their original packaging and provided a Medicine Record Card with details of the medicines prescribed, including what for, how often to take them and other useful information. The pharmacist also discussed with her consultant from the Hypertension Clinic and it was agreed to stop all antihypertensives except candesartan and amlodipine. Her blood pressure was monitored twice weekly. By the next clinic appointment her blood pressure had reduced to 122/68mmHg and the dose of amlodipine was further reduced to 5mg daily. Subsequently she was able to get an appointment for the Zoledronic injection.
The following should trigger the need for a review with a view to deprescribe where appropriate:

- Actual or potential ADEs. Seven or more medicines are associated with an 80% risk of ADEs which could be symptomatic, asymptomatic, CVD or non-CVD related
- Inappropriate polypharmacy and prescribing cascades
- Non-adherence behaviours in relation to their willingness (motivation) and capabilities to take medicines.
- Uncontrolled symptoms or evidence of poorly managed LTC
- Need to realign drug treatment with overall goals of care especially in reduced life expectancy e.g. ≤1-2 years life expectancy, palliative care and end of life (EoL) care

In order to get the right balance of risks and benefits for the individual patient, a needs assessment that covers non-health areas such as patient values, goals of care, cognitive and physical function, and pill burden must be incorporated into treatment decisions.

Some people may find the following acronym helpful in relation to the principles:

**H**olistic, patient centred goal setting – establishing what matters most to the patient

**E**vidence and guideline limitations in this population

**A**dverse drug events – identify actual ADEs and consider the risks of potential ADEs when prescribing

**R**eview medication regularly recognising co-morbidities and changing patient priorities

**T**herapy modification in line with the principles of good prescribing practice and appropriate deprescribing

### 2. Key issues and challenges with managing common cardiovascular LTCs in frail older people with multimorbidity

#### 2.1 Hypertension

Hypertension is one of the most important preventable causes of premature morbidity and mortality and it is estimated that at least 25% of adults (increasing with age) will have high blood pressure. It is a cause of premature mortality and a major risk factor for ischaemic and haemorrhagic strokes, myocardial infarction, heart failure, chronic kidney disease and cognitive decline. The risk associated with increasing blood pressure (BP) is continuous as blood pressure increases. There is debate over the optimal blood pressure target in different patient groups with international guidelines producing differing recommendations.

In the recently updated guidelines for hypertension [NICE recommended BP targets](https://www.nice.org.uk/guidance/ng129) are dependent on age and co-morbidities. **Blood pressure targets and choice of drug therapy are not given for frailty** but there is advice to ‘use clinical judgement for people with frailty or multimorbidity’. The [European Society of Cardiology/European Society of Hypertension guidelines for the Management of Arterial Hypertension](https://www.escardio.org/Guidelines/Hypertension) (section 8.8) outlines the data available from clinical trials to date whilst acknowledging the gaps in the evidence around the value of lowering blood pressure in the very frail population.
Most clinical trials in hypertension have not included the very old population. The Treatment of Hypertension in Patients Aged 80 Years or Older (The HYVET) study (2008) provides the main evidence for managing hypertension in people over 80 years. The results of HYVET indicate that antihypertensive treatment aiming to achieve a target blood pressure of 150/80 mmHg based on a regimen of indapamide (sustained release 1.5 mg once a day), with or without 2 to 4 mg of perindopril, significantly reduced the risks of death from stroke and death from any cause and incidence of heart failure in very elderly patients. In addition, a subgroup analysis of the HYVET trial reported that in patients aged >80 years CV risk reduction was greatest in those who continued treatment rather than in those whose treatment was discontinued. However, the recruited cohort were healthier and more robust than the normal population of frail older people seen in practice. Also, patients with postural hypotension where excluded, which is significant in real practice as observational studies have shown a prevalence of 79% in women between 60-80 years.

The SHEP study showed that benefits of very low BP in older people disappear in those with limited function. Similarly, Olgiveri et al found in the MILAN 75+ study that for older people with impaired function and cognition lower is not always better and BP readings lower than 140 mmHg were associated with increased mortality. They found the optimum BP in this group to be 165/90 mmHg. Approximately 45% of older people with hypertension also have dementia. Hypertensive dementia patients are particularly vulnerable to cardiovascular ADEs and have a higher prevalence of orthostatic hypotension, polypharmacy, and lesser ability to engage in shared decision-making about therapy.

One of the main adverse drug effects of managing hypertension in older people is the increased risk of falls. Medicines that cause hypotension, postural hypotension, vasovagal syncope, bradycardia and postural orthostatic tachycardia syncope (POTS) increase the risks of falls. Older people with BP < 110 mmHg are at risk of falling but even those with normal BP could be at risk of syncope. The risk of falls and fractures are further worsened by impaired balance, polypharmacy and visual impairment in frailty.

Parekh et al10 offer a pragmatic approach to managing hypertension in older people in the context of multimorbidity, frailty, orthostatic hypotension, falls and cognitive impairment. They suggest that hypertension in this cohort should not be managed in isolation but to use clinical expertise and judgement to prevent a fragmented care plan. They recommend the use of the BEGIN algorithm10 to initiate antihypertensives and also offer suggestions for deprescribing. They conclude that a BP of <150/90 is beneficial in reducing CVS morbidity and mortality in robust people. For those over 60 years and frail, one size does not fit all and hypertension should be managed using an individualised approach that takes into consideration their functional and cognitive impairment.

The Tasmanian Deprescribing network gives detailed guidance on deprescribing antihypertensive agents and Parekh et al10 recommend tapering doses slowly. Antihypertensives can be deprescribed safely in frail older people without increase in mortality or adverse outcomes11. The DANTE study found that stopping antihypertensives in older people with mild cognitive impairment and postural hypotension increased SBP by 7.4 mmHg and DBP by 2.6 mmHg with higher recovery from postural hypotension. Similarly, Potter et al12 found no increase in mortality as a result of stopping antihypertensives. Older people who were normotensive with therapy and on monotherapy were more likely to remain normotensive after stopping. The risk of an elevated blood pressure was highest in the first month and within 12 months.

2.2 Postural hypotension

Postural hypotension (orthostatic hypotension) is common in older people. It is defined as a sustained reduction in the systolic BP by at least 20 mmHg or the diastolic BP of at least 10 mmHg within 3 minutes of standing or a 60° head tilt.\textsuperscript{13}

People with postural hypotension may be asymptomatic but typical symptoms include dizziness within a few seconds of standing; light headedness, syncope and falls; dim, blurred or tunnel vision; or a dull pain in the back of the neck/shoulders (coat hanger distribution).

To assess for postural hypotension, measure the BP with the person either seated or supine and repeat this measurement after the patient has been standing for at least one minute. Asking the patient or carer to keep a blood pressure diary over a few days can be useful in assessment of postural hypotension. Early morning measurements tend to most consistent. It is useful to also measure the heart rate which will increase as the blood pressure drops. An exaggerated increase in heart rate (>15 beats/minute) may suggest dehydration/volume depletion.

If the systolic blood pressure falls by 20 mmHg or more when the person is standing:

- Review medication.
- Measure subsequent blood pressures with the person standing.
- Consider referral to specialist care if symptoms of postural hypotension persist.

Causes of postural hypotension may be medication related or due to co-existing medical conditions with autonomic dysfunction (e.g. diabetes, Parkinson’s disease), anaemia, dehydration, infection or physical deconditioning.

Examples of medicines that may cause postural hypotension are shown in the table 2

\begin{table}
\centering
\begin{tabular}{|l|l|}
\hline
\textbf{Antihypertensives} & Diuretics, alpha-blockers, beta blockers \\
\hline
\textbf{Opioids} & Morphine, oxycodone, fentanyl, buprenorphine \\
\hline
\textbf{Analgesics} & Gabapentin, pregabalin \\
\hline
\textbf{Antidepressants} & Tricyclics, trazadone, MAOIs, SSRIs \\
\hline
\end{tabular}
\end{table}

\textsuperscript{13} Arnold A, Raj S Orthostatic hypotension – a practical approach to investigation and management Can J Cardiol. 2017; 33 (12):1725-1728. doi.org/10.1016/j.cjca.2017.05.007

CASE 3
An 85 year old lady has just been discharged from hospital after an admission with a urinary tract infection. She has a past medical history of diabetes and hypertension and is moderately frail.

Her medication is listed as: amlodipine 5mg once a day, atorvastatin 20mg once a day, doxazosin 2mg once a day, lansoprazole 15mg once a day, losartan 100mg once a day and metformin 1g twice a day.

The hospital discharge summary lists the amlodipine and doxazosin as ‘new medicines’

What factors would you consider in a post discharge medication review with the patient?
<table>
<thead>
<tr>
<th>Parkinson’s medications</th>
<th>Levodopa, dopamine agonists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasodilators</td>
<td>Nitrates, calcium channel blockers, Phosphodiesterase 5 inhibitors (e.g. sildenafil)</td>
</tr>
</tbody>
</table>

**Tips for managing postural hypotension:**
- Identify and stop the causative drug if possible
- Switch to a drug class that has less effect on postural hypotension e.g. calcium channel blockers
- Split doses or give a single night-time dose

[Parkinson’s UK](https://www.parkinson.org.uk) gives useful patient advice on managing low blood pressure

2.3 Heart Failure

The most common symptoms of heart failure are:
- Breathlessness – this may be after activity or at rest. It may be worse when lying down and may cause night time waking needing to catch the breath or a persistent cough
- Swollen ankles and legs caused by a build-up of fluid (oedema)
- Fatigue – feeling tired most of the time and finding exercise exhausting

Diagnosis is not always straightforward as many of these patients have co-morbidities including hypertension, diabetes, chronic kidney disease, ischaemic heart disease, airways disease or cognitive impairment. It is not unusual for patients to attribute their symptoms to ‘getting older’ and adapt their activity levels accordingly.

The term heart failure is a broad term and it is important to ensure that you ascertain whether the patient has heart failure with reduced ejection fraction or heart failure with preserved ejection fraction as the treatment pathway depends on the classification of heart failure as illustrated in the NICE Guideline for chronic heart failure

2.3.1 Management of congestive symptoms and fluid retention

Diuretics are commonly prescribed to manage fluid overload. A loop diuretic such as furosemide or bumetanide is typically used with the dose titrated to the minimum dose required to control symptoms with careful monitoring of renal function and electrolytes. In resistant cases, more specialist management may involve adding a thiazide diuretic such as bendroflumethiazide 2.5mg every day or perhaps on alternate days for a short period. Failure to respond to combinations of loop and thiazide diuretics, or hyponatraemia with accompanying fluid gain, would warrant specialist input and may require admission to hospital or a day-case unit for intravenous diuretics.

As the prevalence of heart failure increases with age this is a common problem in the frail older people population.

Balancing diuretic requirements for management of fluid congestion with the electrolyte disturbances and renal impairment, blood pressure and patient acceptance is often challenging. It is important to identify those patients with fluid retention, over-diuresis or unstable renal function or electrolytes. Although management may be outside of the scope for practice for many pharmacists they should be aware of the heart failure services within their locality and how to refer people for more specialist advice and support.
2.3.2 Heart failure with preserved ejection fraction (HFpEF)
Clinical trials in HFpEF have not identified any specific treatments to reduce mortality. The aim is to control the symptoms of heart failure and ensure good management of co-morbidities that may co-exist such as hypertension, atrial fibrillation, diabetes and chronic kidney disease in line with current guidelines.

2.3.3 Heart failure with reduced ejection fraction (HFrEF)
There is a substantial evidence base to support the use of medicines to reduce both mortality and symptoms. In the absence of contra-indications, all patients should be considered for a combination of:

- an angiotensin converting enzyme inhibitor or alternatively an angiotensin receptor blocker if side effects such as cough occur PLUS
- A beta-blocker licensed for heart failure (bisoprolol, carvedilol or nebivolol) AND
- If still symptomatic a mineralocorticoid receptor antagonist (spironolactone or eplerenone) can be added.

These medicines are introduced at low doses and up titrated to the maximum dose or the maximum tolerated dose with careful monitoring of renal function, electrolytes, blood pressure, heart rate and symptoms. Many frail older people will not make it to the recommended evidence based ‘target dose’ to reduce mortality and it is more likely their renal function will decline, so improving symptoms is the priority. Wherever possible these medicines should be continued even if doses need to be reduced due to co-morbidities or frailty as they effect both mortality and symptoms even in the later stages of life expectancy.

Useful resources on managing renal function in these patients can be found on the ‘Think Kidneys’ website and in: ‘Change in renal function associated with drug treatment in heart failure: national guidance’ (2019).

Specialist options in HFrEF
If despite the above measure patients are still symptomatic, specialist advice should be sought.

Tips for managing CHF in older people with frailty
- Establish the diagnosis – is this HFpEF or HFrEF?
- Take a comprehensive history to establish what specific symptoms the patient is experiencing
- Take a comprehensive medication history – in particular in relation to diuretic therapy as patients may find the diuresis difficult to manage and omit doses or discontinue altogether
- Monitor for adverse effects such as symptomatic hypotension or postural hypotension or bradycardia
- Review other medication – is this adding to the effects on blood pressure and heart rate? Could it be causing fluid retention? Is it affecting renal function or heart failure symptoms (e.g. NSAIDs)
- During goal setting, establish the impact of these symptoms on the patients daily functioning so that drug therapy can align with the patient’s goals
- Consider how you might carry out a face-to-face or virtual review of a patient with heart failure

www.sps.nhs.uk | Cardiovascular disease in older people living with frailty LO and AW November 2020 (version 1) 13
Further information can be found in recent review papers on heart failure\textsuperscript{14,15}

2.4 Atrial Fibrillation

Atrial fibrillation (AF) is the most common cardiac arrhythmia. Prevalence increases significantly with age to more than 10% in those over the age of 80 years. The mortality and morbidity from AF is due to the increased risk of stroke. Patients with AF have, on average, a five-fold increase in their risk of a stroke compared to patients in sinus rhythm (the normal heart rhythm) and AF related strokes are associated with increased mortality or higher levels of on-going disability. Anticoagulation of the appropriate patients is a highly effective intervention, which will reduce an individual’s stroke risk from an AF related stroke by around two-thirds.

2.4.1 Assessing the risk of stroke and bleeding

A stroke risk assessment should be undertaken using the CHA\textsubscript{2}DS\textsubscript{2}-VASc score. If the score is two or more the patient should be offered anticoagulation (anticoagulation may also be considered in a male patient with a score of 1). As age and female gender feature in the score it is likely that older people will fulfil the criteria to consider anticoagulation regardless of any co-morbidity. Clinical data and guidelines support the offer of anticoagulation in elderly and very elderly people\textsuperscript{16,17,18}

Any offer of anticoagulation should take into account bleeding risk. The use of a scoring system such as HAS-BLED or ORBIT can help to identify modifiable bleeding risk factors. These include uncontrolled hypertension, previous bleeds, labile INR in patients taking warfarin, alcohol intake and co-prescription of other medicines that may increase bleeding risk such as NSAIDs, aspirin or other antiplatelet agents, SSRI antidepressants or oral corticosteroids.

The combination of anticoagulation and antiplatelet therapy significantly increases bleeding risk. In many cases, the antiplatelet can be stopped when anticoagulation is introduced so this combination should always be clarified to ensure it is intentional and/or required. Always seek specialist advice if there is any uncertainty of the intended combination or duration of combined therapy.

Risk of falls should not be used as the sole criteria for not offering anticoagulation to a patient although this may be taken into account as part of that overall assessment of suitability and/or frailty.

\textsuperscript{14} Beezer J, O'Neil H Heart failure, older people and frailty. Clinical Pharmacist 2019; 11 (7) \texttt{doi.org/10.1211/CP.2019.20206426}
\textsuperscript{15} Pandey A, Kitzman D, Reeves G Frailty Is Intertwined With Heart Failure: Mechanisms, Prevalence, Prognosis, Assessment, and Management JACC: Heart Failure 2019; 7(12): 1001-1011 \texttt{doi.org/10.1016/j.jchf.2019.10.005}
\textsuperscript{18} Chao T, Lui C, Lin Y et al Oral anticoagulation in very elderly patients with atrial fibrillation: A nationwide cohort study Circulation 2018; 138: 37-47 \texttt{doi.org/10.1161/CIRCULATIONAHA.117.031658}
This information should provide a framework to help with shared decision-making for individual patients on the prescription of anticoagulation, the choice of anticoagulant and the frequency of follow up required. Provision of written and verbal patient and/or carer information is important to support adherence to treatment and to ensure that any adverse effects are identified and acted upon.

2.4.2 Rate or rhythm control?
Patients with AF may be symptomatic with typical symptoms being awareness of an irregular heartbeat, palpitations, dizziness or syncope (fainting or blackouts), shortness of breath and chest tightness. However, many patients are asymptomatic and unaware that they have this cardiac arrhythmia.

A rate control strategy:
A normal resting heart rate for adults in sinus rhythm is 60-100 beats per minute. Studies in AF have not shown a benefit of strict heart rate control (less than 80 beats/minute) versus more lenient heart rate control (less than 110 beats/minute). The first choice of medication is usually a beta-blocker. Alternatively, or in addition, a rate limiting calcium channel blocker (not verapamil + beta-blocker) or digoxin may be added. In sedentary, frail patients digoxin monotherapy can be a good option as digoxin does not lower blood pressure and can be used in patients with heart failure. However digoxin has a narrow therapeutic index and needs to be dosed carefully with respect to renal function and electrolyte disturbances such as hypokalaemia, hypomagnesaemia or hypercalcaemia which can be triggered by the use of diuretics or dehydration which can increase digoxin toxicity. Proactively monitor for signs of digoxin toxicity, which include nausea, vomiting, confusion, anorexia, visual disturbances and depression.

A rhythm control strategy
In frail older people attempting to convert the heart back to its normal rhythm would only be undertaken if the patient was not tolerating the arrhythmia. Medication that may be used includes beta-blockers or anti-arrhythmic medicines such as flecainide, sotalol or amiodarone.

CASE 4
You have been asked to see a 76-year old man with a new diagnosis of AF

PMH: STEMI with stent to the coronary artery 4 years ago
Hypertension for 10 years
GI bleed 9 months ago
Fractured neck of femur following a fall 1 year ago

Would you offer this patient anticoagulation?
What factors would you need to consider?
How would you discuss this with the patient?
Do you have a check list of points to cover when starting a patient on anticoagulation?

Useful resources:
NICE patient decision aid for AF
AF association: Preventing AF related stroke
Wessex AHSN video: Starting anticoagulation with Jack
The use of flecainide and sotalol in older people is limited by the presence of heart failure or coronary heart disease (where these medicines are contra-indicated). Although amiodarone can be a useful drug, long-term use should ideally be avoided because of its adverse drug effect profile. If the patient remains in atrial fibrillation or has been prescribed amiodarone and is no longer under specialist (cardiology) review primary care may need seek advice from the cardiology specialist regarding stopping or continuing treatment.

2.5 Coronary Heart Disease (CHD) and Cardiovascular Risk

The burden of coronary heart disease increases with age. Reducing cardiovascular risk through lifestyle measures can be recommended regardless of age or frailty but should be considered in line with patient preferences and life expectancy. Publications from bodies such as the British Heart Foundation are an excellent source of patient friendly documents which are available, often in a choice of languages.

When thinking about prescribing medication to reduce cardiovascular risk it is important to determine whether you are considering primary prevention or secondary prevention (i.e. patients with established cardiovascular disease such as coronary heart disease, stroke or TIA or peripheral arterial disease).

2.5.1 Aspirin for primary prevention

Over the last 10 years the role of aspirin in primary prevention has been the subject of much debate. In 2018 three clinical trials were published looking at the risks and benefits of prescribing aspirin for primary prevention. A useful summary of the data and an algorithm for the place of aspirin was published in Circulation in 2019.

If aspirin is currently prescribed for older people and/or frail patients for primary prevention of atherosclerotic cardiovascular disease this should be reviewed in discussion with the patient. The same principles apply if an alternative antiplatelet has been prescribed in cases of aspirin intolerance.

2.5.2 Stable angina

Stable angina should be managed medically with the aim to reduce symptoms. This may involve the use of beta-blockers, calcium channel blockers, nitrates or other anti-anginals. The same caveats apply with respect to blood pressure and heart rate. In frailty as mobility decreases medication should be reviewed as these may no longer be required. Patients should be supplied with GTN tablets/spray and they or their carer be confident in their use.

2.5.3 Acute coronary syndromes

Many older people with acute coronary syndrome will undergo coronary intervention (angioplasty and stents) and this can be a lifesaving treatment. This will require a period of dual antiplatelets (DAPT) — the duration of which should be advised by secondary care.

With increasing frailty medical management (prescription of medication rather than an

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interventional procedure) may be more appropriate – this would be decided with the patient by the attending medical team. If DAPT is prescribed a clear plan on duration should be advised. Gastro-protection with a proton pump inhibitor is recommended with DAPT in this high risk cohort - avoiding omeprazole/esomeprazole if the DAPT regimen includes clopidogrel due to the potential drug interaction.

2.5.4 Lipid modification
Compared to younger adults the heterogeneity between frail and fit older people with regards to physical and functional status results in a wider variation in CVS risk and life expectancy. A recent study in the Netherlands has called for a shift from the strict 10-year CVS risk to a patient centred approach that is based on lifetime benefit. Current tools overestimate the risk of CVD in frail older people and they propose a new tool (UPrevent) that is specifically tailored to older people. In assessing benefits, the pre-treatment risk (e.g. primary or secondary prevention), and the burden of treatable risk factors and competing risks of mortality from other causes should be taken into account. The authors propose a benefit-based over a risk-based approach to management. Therefore, before initiating lipid lowering therapy, there should be a discussion about estimated lifetime risk of CVS, risks of ADEs and patient preferences. Generally in patients with a lifetime expectancy of below 1-2 years, medicines should not be initiated. Deprescribing should be considered in those currently on a drug, but remember the patient may have taken for a long enough period to accrue benefits and deprescribing should be considered on a case-by-case basis.

Adverse effects of statins
The most widely quoted adverse effects of statins are muscular aches and pains and although this can result in serious muscle toxicity and rhabdomyolysis this is in fact extremely rare. The adverse effects are dose related so a reduction in dose or switching to an alternative statin can often overcome these effects. Frail older people with multimorbidity are more likely to be at risk from muscle ADEs (8-11% in real life compared to 1-5% in clinical studies), polypharmacy and drug interactions with statins.

The decision to discontinue a statin for primary prevention in older people and/or frailty should be made taking into account the patient preferences. It is useful to refer to the NICE resource for treatment effects for multimorbidity.

The Australian Deprescribing Network has a useful document for deprescribing statins and a recent paper on statins for primary prevention in older people provides an overview.

CASE 5
84-year old man living with moderate to severe frailty, multiple morbidities and polypharmacy (21 medicines).
He was prescribed seven different cardiovascular medicines including Simvastatin tablets 20mg.

He suffered with shortness of breath and severe intermittent claudication which limited mobility and activities of daily living.

During the medication review it was discovered that he was experiencing myalgia and nightmares (adverse effects of simvastatin) both of which were causing significant distress. Through shared decision-making discussions with patient and the STOPPFrail criteria, it was agreed to stop the simvastatin as he prioritised his mobility and sleep over the potential long-term benefits.)

Both the nightmares and pain in the leg reduced considerably within a few weeks.

Conclusions

Managing patients with CVD who are living with frailty and multiple morbidities is complex. There is limited clinical trial evidence in this population which gives uncertainty in the overall benefits and the potential harm that medicines may have for these patients. There a number of clinical tools that can help in the decision-making process to achieve the best outcomes. However, these must be balanced with the patient’s perspective and the clinical judgment of the practitioner.
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Appendix

Further reading on deprescribing


- RPS polypharmacy Guidance 2018. Getting our medicines right
NHS Specialist Pharmacy Service

www.sps.nhs.uk