Polypharmacy: Guidance for Prescribing

Figure 1: Key Considerations for Prescribing in Frail Adults

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CONTENTS

Figure 1. Key Considerations for Prescribing in Frail Adults ................................................. 2

Why is reviewing polypharmacy important? ............................................................... 2

Medicines adherence .................................................................................................... 4

Start with the basics – Can the patient manage their medicines? ............................. 5

Medication review process .......................................................................................... 6

High-risk medication ................................................................................................. 7

Other factors to consider when conducting a review .................................................. 8

Polypharmacy in the frail elderly ................................................................................. 9

Specific considerations for patients with dementia ................................................... 10

Patients with renal dysfunction ................................................................................. 11

Anticholinergic effects ............................................................................................... 11

Indications of shortened life expectancy ................................................................... 12

REFERENCES ..................................................................................................................... 13

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Figure 1. Key Considerations for Prescribing in Frail Adults

Why is reviewing polypharmacy important?

Medication is by far the most common form of medical intervention. Four out of five people aged over 75 years take a prescription medicine and 36% are taking four or more. However, it is suggested that up to 50% of medicines are not taken as prescribed. Many medicines in common use can cause problems, and adverse reactions to medicines are implicated in 6.5% hospital admissions.

Patients on multiple medications are at increased risk of suffering side effects. This is more likely to be related to the co-morbidities a patient has, rather than to their age. Patients are often prescribed (and may remain on) medication that causes ADRs and prescribers should consider if the harm of each medicine outweighs the benefits.

These guidelines aim to provide guidance on how to make a safe and sensible decision in situations where extra thought and consideration are needed.

Patient groups include:

1. **Patients who are taking a large number of medications (polypharmacy)** – this may include over the counter remedies.
   - **Medication review process** – A review should be conducted holistically by considering each medication and its impact on the individual clinical circumstances of the patient. As part of this it is important to consider the additive effects of each medication. It is essential to ensure that the patient is capable of taking the medicine and that compliance is satisfactory. The “NO TEARS” tool can be used to simplify and aid the review process.
   - **High-risk medication** – Medications that are most likely to cause significant harm to the patient should be prioritised and reviewed.

2. **Patients with indications of shortened life expectancy** (where life expectancy is shorter than the time that medication would take to give significant effect).
   - It is important to identify these patients and to consider the expected benefits of the medication prescribed. Should they be included on the palliative care register?

3. **‘Frail’ and elderly patients** – Frail elderly patients appear to be particularly at risk of ADRs and patients in this group are also likely to be receiving several medicines.

4. Situations where guidelines suggest ‘medication review’ but are not specific as to what is to be done, e.g. comprehensive assessment of falls risk, anticipatory care plan, care home medication reviews.
Never assume the patient is taking what you think they are taking. Review regularly and consider brown bag reviews (where patients are asked to bring all of the medicines they are taking to clinic) or reviews at the patient’s home.

Keep medication regimens as simple as possible – ideally once or twice daily dosing. Keep the number of pills or ‘pill burden’ to the minimum necessary to provide effective treatment.

Provide clear written instructions and a dosing schedule. Avoid use of ‘as directed’ and put specific dosage instructions on the prescription.

Ensure that directions on each prescription item identify the problem it is intended to treat.

Consider introducing medicines as a trial: titrate doses and do not forget to stop if ineffective or unnecessary.

Put systems in place to ensure consistent and appropriate biochemical monitoring for high-risk medicines e.g. lithium, disease modifying anti-rheumatic drugs (DMARDs), warfarin.

Discuss complex repeat medication regimens with pharmacy colleagues for advice on safety, interactions, formulation choice and to aid with checking patient understanding.

Be aware of known pitfalls of specific medicines and recognise medicines interactions (may be ‘medicine–medicine’, ‘medicine–food’, ‘medicine–alcohol’, ‘medicine–herbal’ or ‘medicine-smoking’).

Optimise existing medicines or consider non-pharmacological alternatives where possible rather than adding additional medicines.

Ensure you are aware of medicines which may not be on the patient’s record e.g. supplied via acute specialties e.g. renal, psychiatry, memory clinic etc. Therapeutic duplication may occur when the patient has multiple prescribers.

Identify over-ordering and hoarding of medicines which can cause problems and can also indicate poor control (e.g. bronchodilators, glyceryl trinitrate sprays, opiates). Try to ensure medication quantities are synchronised to avoid potential missed doses and reduce waste.

Consider advantages and disadvantages of compliance aids for individual patients and their specific medication regimen. (N.B. Monitored dosage systems [MDS] should not be used first line as they can have disadvantages; assessment should be undertaken by the community pharmacy or dispensing doctor e.g. medicine stability and difficulty in following directions e.g. “when required” or with/after food.)
Medicines adherence

Why don’t some patients use their medicines as prescribed?
- They don’t want to – *intentional* non-adherence
- They have practical problems – *unintentional* non-adherence

What can be done about this?
- Check the patient has:
  - been given the information they need when medicines are dispensed,
  - understood the information and discussed it.
- Do not assume that PILs will meet all patients’ needs.
- Direct the patient to reliable sources of information and support after the consultation.

Increase patient involvement in decision-making
- Find out what the patient hopes the treatment will achieve.
- Listen, note any non-verbal cues and don’t make assumptions about the patient’s preference for treatment.
- Explain the medical condition clearly and help the patient to make decisions based on likely benefits and risks rather than misconception.
- Encourage and support the patient, their family and carers to keep an up-to-date list of prescription and non-prescription medicines, and allergies or adverse reactions.

Accept that the patient:
- may have different views from healthcare professionals about risks, benefits and side effects,
- has the right to decide not to take a medicine as long as they have capacity and have been given the information to make an informed decision.

If the patient decides not to take a medicine and in your view this could be harmful, record the decision and the information provided on risks and benefits.

Understand the patient’s perspective

Ask the patient what they know and believe about their medicines, including any concerns (e.g. adverse effects or dependence) and address these.
- What will happen if they don’t take the medicine
- Non-pharmacological alternatives
- Reducing or stopping long-term medicines
- Fitting medicines into their routine
- Choosing between medicines
- If the patient has specific concerns, record a summary of the discussion.

Provide clear information
- What the medicine is, how to use it and likely benefits
- Likely adverse effects and what to do if they occur
- What to do if a dose is missed
- How to obtain further supplies

Assess adherence
Whenever you prescribe, dispense or review medicines:
- Ask the patient if they have missed any doses recently:
  o mention a specific time (such as in the past week),
  o explain why you are asking,
  o ask about medicine-taking habits,
  o do not apportion blame.
- Use records of prescription re-ordering, pharmacy patient medication records and return of unused medicines to identify non-adherence and patients needing support.

Review
At agreed intervals review the patient’s knowledge, understanding and concerns about their medicines.

Please refer to the full NICE guidance [http://guidance.nice.org.uk/CG76](http://guidance.nice.org.uk/CG76) for further detail.
Potential solutions

Establish if non-adherence is because of beliefs and concerns or practical problems, and address these.
- Simplify the dosing regimen – Is there any therapeutic duplication? Are there any medicines of limited clinical value or medicines where long-term benefit is unlikely to be realised due to life expectancy?
- If side effects are a problem:
  - discuss benefits, side effects and long-term effects,
  - consider adjusting the dose, switching to another medicine, and other strategies such as changing the timing of medicines.
- Suggest the patient records their medicine-taking and monitor their condition.
- The All Wales Medicines Reminder charts can be downloaded from the following links: Medicine Reminder Chart (Standard) and Medicine Reminder Chart (Long)

Would they benefit from a compliance check from their community pharmacy? E.g. to assess options/support required e.g. MUR, compliance aids, alternative packaging etc.

What support is available?
Child resistant/wing topped bottles, devices to aid popping tablets from blisters, devices to aid administration of eye drops/inhalers, large print labels/PILs, reminder charts, text alerts

Would a liquid or soluble preparation be more appropriate?
- Consider cost implications, product licence etc.
- Be aware of unlicensed specials.
- If tablets or capsules are being crushed/opened, consider impact on product licence, stability, release properties of medicine, coating etc.

MDS, e.g. Nomad trays, Dossette, are an option but should not be used first line
- A Cochrane Review exploring the effectiveness of the use of MDS demonstrated that the evidence was weak in support of their widespread use\(^9\) and the RPS has recommended that MDS should not automatically be the intervention of choice for all patients.\(^10\) AWMSG has published further guidance on the use of Monitored Dosage Systems.
- UK Medicines Information (UKMi) has a database for stability of drugs when used in an MDS: [www.ukmi.nhs.uk/applications/mca/](http://www.ukmi.nhs.uk/applications/mca/) or contact local MI Centre.
Life expectancy and frailty have an impact on the benefit of therapy especially for risk reduction treatment*.

Is there an evidence-based guideline/consensus for using the medicine:
- for the indication;
- at the current dosage;
- in this patient’s age group?

And does the benefit outweigh all the possible known adverse effects? (risks versus benefit)

Is the medicine replacing a vital hormone? (e.g. levothyroxine)

Is the medicine important in preventing rapid symptomatic deterioration? (e.g. medications for Parkinson’s Disease)

Is the medicine expected to give day to day symptomatic benefit? (e.g. pain killers)

Should in almost all cases continue or only be discontinued following advice from the appropriate clinician

Can the dose be reduced with no significant risk? (i.e. use the lowest effective dose.)

Is the medicine being given for a condition that has resolved or is no better despite using the medicine? (e.g., oedema, pain, dyspepsia, agitation)

Other considerations:
- Are the dose, formulation and dosing schedule appropriate?
- Are all required blood tests and monitoring up to date?
- Has the patient recently been discharged from hospital? Have any changes been actioned?

* This may be a prompt to consider inclusion on the palliative care register in certain patients
~ Careful tapering of the dose may be required with some medication to prevent a withdrawal syndrome

Reduce dose and monitor the patient’s symptom control~

Consider stopping the medicine~ in conjunction with patient/carer
Polypharmacy – Figure 1. Key Considerations for Prescribing in Frail Adults

Medicines and dehydration
It may be indicated to WITHHOLD the following in patients diagnosed with severe dehydration (e.g. those suffering from vomiting/diarrhoea):
- ACE inhibitors/angiotensin 2 receptor blockers (ARBs)
- NSAIDs
- Diuretics
- Metformin

These can then be restarted when the patient has improved (e.g. after 24 to 48 hours of eating and drinking normally).

Adults with advanced heart failure can decompensate rapidly off medication and will need specialist advice.

Medicines most associated with admission due to ADR
In a 2004 UK study, the most common medicine groups associated with admission due to ADRs were:

1. Non-steroidal anti-inflammatory drugs (NSAIDs) 29.6%
2. Diuretics 27.3%
3. Warfarin 10.5%
4. Angiotensin-converting enzyme (ACE) inhibitors 7.7%
5. Antidepressants 7.1%
6. Beta-blockers 6.8%
7. Opiates 6.0%
8. Digoxin 2.9%
9. Prednisolone 2.5%
10. Clopidogrel 2.4%

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Medicines that can be associated with rapid symptomatic decline if stopped, or require cautious stepwise withdrawal
Medicines in this group may require specialist advice.
- ACE inhibitors in heart failure (left ventricular (LV) impairment).
- Diuretics in heart failure.
- Medicines for heart rate or rhythm control (beta-blockers; digoxin).
- Opioids/antidepressants/antipsychotics/ anti-epileptics/medication for Parkinson’s disease/clonidine/baclofen/steroids/corticosteroids/benzodiazepines.

Medicines for which specialist advice is strongly advised before altering include:
- Anticonvulsants for epilepsy.
- Antidepressants initiated in secondary care.
- Antipsychotic and mood stabilising medicines (e.g. lithium).
- Medicines for the management of Parkinson’s Disease.
- Amiodarone.
- DMARDs.
- Medicines prescribed by specialist teams e.g. renal unit.

High-risk medicine combinations to avoid
The following are highlighted as being particularly high-risk combinations and should be avoided where possible and clearly justified when considered necessary. This list is NOT exhaustive, and the safety of other medicines has to be considered depending on individual circumstances.

NSAID
- ACE inhibitor or ARB + diuretic (‘triple whammy’ combo)
- eGFR less than 60 ml/min
- Diagnosis heart failure
- Warfarin or new oral anticoagulants (NOACs) e.g. dabigatran, apixaban, rivaroxaban
- Age > 75 without PPI

Warfarin
- Another antiplatelet. Although specific indications for this exist, in a frail group of patients the risk is high and combination should be challenged – it is important to check who initiated the combination
- NSAID
- Macrolide and quinolone antibiotics, metronidazole (If concomitant use is essential ensure increased international normalised ratio [INR] monitoring)
- Azole antifungal including miconazole oral gel (If essential ensure increased INR monitoring)
- NOAC

Heart failure diagnosis
- Glitazone
- NSAID
- Tricyclic antidepressant (TCA)
Cardiovascular system in general

- **Warfarin** – Do patients have an active indication for anticoagulant therapy? Is monitoring robust? Is the INR within the recommended therapeutic range? Are there frequent falls (> one per week)?
- **Antiplatelets** – Does the patient have a history of coronary, cerebral or peripheral symptoms/events? If not – consider stopping. Ensure aspirin/ clopidogrel combination reviewed as per cardiology advice. Reduce aspirin to evidence-based doses.
- **Statins** – Re-evaluate risk profile for primary/secondary prevention.
- **Diuretics** – For dependent ankle oedema – consider alternative ways of managing oedema; consider medication causes e.g. calcium channel blocker.
- **Digoxin** in the presence of chronic kidney disease – consider reducing the dose, or stopping.
- **Peripheral vasodilators e.g. cilostazol, pentoxifylline** – clinical effectiveness not often established.
- **Quinine** – Review long-term use – see Medicines and Healthcare Products Regulatory Agency (MHRA) advice.

Central nervous system and psychotropic medication

- **Hypnotics and anxiolytics** – Discuss reducing long-term therapy with the aim of stopping.
- **Antidepressants** – Review combinations e.g. TCAs for analgesia used in combination with other antidepressants for depression.
- **Selective serotonin reuptake inhibitors (SSRIs)** – Are in general better tolerated in people with dementia who also have depression.
- **Metoclopramide** – Review long-term use
- **Vertigo** – Review long-term use of medicines such as prochlorperazine and cinnarizine.
- Consider cumulative gastro-intestinal (GI) effects when co-prescribing SSRIs + NSAIDs/aspirin.

Endocrine system

- **Metformin** – use with caution in renal impairment due to risk of lactic acidosis.
- **Oral corticosteroids** for long-term use – maintenance dose should be kept as low as possible with withdrawal considered where feasible. When possible, local treatments e.g. inhalations, creams etc should be used in preference.
- **Bisphosphonates** – Has treatment been taken for > five years?

Gastrointestinal system

- **Proton pump inhibitors (PPIs) and H2 receptor antagonists (H2RAs)** – Consider reducing the dose or stopping, especially if antibiotics are required (remember increase in risk of *Clostridium difficile* – stop if confirmed).
- **Laxatives** – Reduce overuse if possible. Rationalise those with the same mode of action. Opioids stopped?

Analgesic medication

- **Strong opioids** – Long-term use for mild/moderate pain – review diagnosis (is pain neuropathic or otherwise not responsive to opiates) and effectiveness – discuss stepping down therapy
- Consider non-pharmacological treatment such as gentle exercise, relaxation or TENS
- Check compliance with long-term analgesia
- Check effectiveness – step up or step down analgesia using the World Health Organisation (WHO) analgesic ladder available
- Check safety – reduce use of NSAIDs and opioids and amitriptyline if possible. Prescribe laxatives with opioids.

Other factors to consider when conducting a review

- **Urogenital system**
  - **α-blockers/5α reductase inhibitors** for benign prostatic hyperplasia in men with long-term urinary catheters – consider stopping. Patients with catheters may inadvertently be on long-term antibiotics, yet the biofilm formed on the inside of the catheters may render them ineffective
  - **Antimuscarinics e.g. solifenacin**. Is there still a valid indication?

Please note that this list is not exhaustive and further detail can be found in Polypharmacy Supplementary Guidance – BNF Sections to Target.
Good prescribing practice in the elderly should consider the following:\(^7\):

- Use medicines that are familiar
- Use the lowest effective dose
- Anticipate medicines interactions
- Be alert to ADRs
- Monitor therapy
- Avoid the prescribing cascade (when ADRs are treated with new medication)
- Promote concordance in collaboration with the patient
- Involve carers where reasonable

Although polypharmacy is not exclusively an issue that affects older people, it is particularly important that medication reviews are undertaken regularly for this age group to support scaling back or indeed increasing treatment where appropriate.\(^2\) Particular problems in elderly patients include:

- Elderly patients appear to be particularly at risk of ADRs and are often prescribed multiple medicines, further increasing their risk of ADRs and medicines interactions.\(^6\)
- Physiological changes can result in changes to the body’s handling of medicines; subsequently dose reductions and/or additional considerations are often required.\(^7\)
- Polypharmacy can play an important role in prolonging a patient’s life-expectancy and improving quality of life.\(^7\) However, benefits should be considered alongside the increased risk and potential for reduced compliance.\(^8\)

**Drugs poorly tolerated in frail elderly**\(^11\)

Although sometimes necessary, the following groups of drugs are noted to be poorly tolerated and associated with adverse events (especially falls). It is particularly important to clarify if patients on the following have a valid and current indication and if treatment is still felt to be effective.

Attention is still needed when considering stopping some of these drugs.

- Digoxin in doses of 187.5 mcg or greater
- Benzodiazepines and ‘Z’ drugs particularly for long-term use
- Phenothiazines (e.g. prochlorperazine)
- Antipsychotics
- TCAs
- Anticholinergics
- Combination analgesics (e.g. co-codamol)

**Patients at risk of falling**\(^11\)

Medication review should be considered as part of a multifactorial assessment in patients at risk of falling. See NICE Clinical Guideline 161 on falls for further details.

The medicines listed below are associated with an increased risk of falls; therefore clinicians should review the need for the following:

- Any long-acting or long-term hypnotic or anxiolytic
- Antihypertensives, beta-blockers
- Diuretics
- Antidepressants, antipsychotics, anti-epileptic medication (especially if used for pain)
- First generation (sedating) antihistamines
- Medicines used for Parkinson’s Disease (review in conjunction with specialist)
- Anti-cholinergic medication used for bladder spasm or other medicines with anti-cholinergic side effects e.g. TCAs
90% of people with dementia experience behavioural and psychological symptoms, such as restlessness and shouting, at some point. These distressing symptoms can often be prevented or managed without medication. However, antipsychotic medications are frequently prescribed as a first resort. It has been estimated that around two thirds of these prescriptions are inappropriate.

Some longer-term clinical trials appear to show that the benefits of antipsychotic medications are limited over longer periods. Patients who have dementia and who have been on antipsychotics for more than three months and have stable symptoms should be reviewed with a view to reducing/stopping antipsychotic medication.

Antipsychotics are associated with an increased risk of falls, delirium, cerebrovascular events and all-cause death. Review the effect after one week to assess for:

- The re-emergence of the initial 'target' symptoms.
- Discontinuation symptoms such as nausea, vomiting, anorexia, diarrhoea, rhinorrhoea, sweating, myalgia, paraesthesia, insomnia, restlessness, anxiety and agitation. These symptoms are more common with abrupt withdrawal of antipsychotic medication and generally begin within 1–4 days of withdrawal and abate within 7–14 days.
- If either of the above occurs the clinicians should make an assessment of the risk and benefits of re-instituting the previous dose of antipsychotic. Further attempts to reduce the antipsychotic should be made one month later with smaller decrements for example 10% of the total daily dose.
- If there are no particular problems after one week then the dose should remain the same with further review after week 4 (for risperidone and haloperidol) or fortnightly (for quetiapine).
- If the reduction has been tolerated without any discontinuation symptoms then reduce by a further 25% and repeat the process.
- Availability of smaller doses may be a problem so discuss with a pharmacist.
- Once the total daily dose is reduced to the recommended starting dose for the individual antipsychotic, it may be stopped.


1000 Lives Plus is working with NHS organisations across Wales to reduced inappropriate use of anti-psychotic medications in patient with dementia: www.1000livesplus.wales.nhs.uk/antipsychotics-column
Anticholinergics should be prescribed with caution as elderly patients are more likely to experience adverse effects such as constipation, urinary retention, dry mouth/eyes, sedation, confusion, delirium, photophobia, falls and reduced cognition (may lead to wrong diagnosis of dementia)\(^\text{20}\). Research also suggests a link to increased mortality with the number and potency of anticholinergic agents prescribed\(^\text{21}\). The **Anticholinergic Risk Scale** is useful to raise awareness of anticholinergic effects of different medicines. A number of studies have been published which aim to assign drugs with one, two or three points; **the higher the number, the stronger the anticholinergic effect**.*

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<td>• Quetiapine</td>
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- Minimise use of anticholinergics wherever possible\(^\text{20}\).
- Consider anticholinergic burden scale when prescribing anticholinergic combinations.
- Avoid prescribing anticholinergics with acetylcholinesterase inhibitors e.g. donepezil, rivastigmine (can worsen cognitive impairment)\(^\text{20}\).
- Proactively monitor at regular intervals for efficacy and tolerance\(^\text{20}\) e.g. annually (or 6 monthly in patients over 75 years) once clinically stable.
- If suspicion of anticholinergic induced impaired cognition, carry out a mini mental state examination (or equivalent) and consider switching or stopping if confirmed and clinically appropriate\(^\text{20}\).
- Refer patients suffering from significant anticholinergic side effects due to psychotropic medication to an appropriate specialist\(^\text{20}\).

Renal function declines with age; many elderly patients have renal impairment but because of reduced muscle mass, this may not be indicated by a raised serum creatinine\(^\text{12}\). It is wise to assume at least mild impairment of renal function when prescribing in the elderly\(^\text{12}\).

For most medicines and for most patients (over 18 years) of average build and height estimated glomerular filtration rate (eGFR) can be used to determine dosage adjustments in place of creatinine clearance\(^\text{12}\).

However, there are two exceptions\(^\text{12}\), both of which may be particularly relevant in the elderly population:

- **Toxic drugs** – for potentially toxic drugs with a small safety margin, creatinine clearance should be used to adjust dosages in addition to plasma-drug concentration and clinical response; for example digoxin and lithium\(^\text{12}\).
- **Patients at extremes of weight** – In patients at both extremes of weight (BMI < 18 or > 30) the absolute GFR or creatinine clearance should be used to adjust drug dosages\(^\text{12}\).

Commonly prescribed medicines which often require dose adjustment in renal impairment include some anti-epileptics, antibiotics and opioid analgesics. See **BNF/SPC** for full details.

*Further details of these studies can be found at:
3) [http://www.uea.ac.uk/mac/comm/media/press/2011/June/Anticholinergics+study+drug+list](http://www.uea.ac.uk/mac/comm/media/press/2011/June/Anticholinergics+study+drug+list)
Indications of shortened life expectancy

It is important to re-evaluate the role of medicines once a patient has entered the terminal phases of an illness, as there should be a shift in treatment goals. Stopping medication will reduce the medicine load and potential adverse effects, while shifting the therapeutic focus to end-of-life issues that are important to the patient.

Triggers that suggest that patients are nearing the end of life include:

1. When the answer to the question: ‘Would you be surprised if this person were to die in the next 6–12 months?’ is No.


3. Specific clinical indicators related to certain conditions – often associated with patients requiring help with multiple activities of daily living either at home or in a care home due to:
   - Advanced organ failure
   - Cancer
   - Multiple co-morbidity giving significant impairment in day to day function
   - Advanced dementia

For more information: www.goldstandardsframework.org.uk

Prescribing in palliative care

It is important to consider the risk/benefit of the medication being prescribed, particularly with change in prognosis/patient goals, with the aim of improving the patient’s quality of life. Many preventive therapies such as medicines used to treat hypertension, osteoporosis and hyperlipidaemia take many months and even years before their benefit is established. They have limited value in patients with a short life expectancy.

Useful links

- [www.wales.pallcare.info/](http://www.wales.pallcare.info/) Palliative Care website for Wales. Provides information on:
  - Advance Care Planning – follow link wIPADS for information about Advance Care Planning (ACP), including identifying appropriate patients for ACP, communication skills, best-interests decisions, Advance Decisions to Refuse Treatment (ADRT) and guidance about resuscitation decisions. Follow the link 'Anticipatory Prescribing' for information about the Just in Case box and prescribing for palliative patients.
- [www.goldstandardsframework.org.uk](http://www.goldstandardsframework.org.uk) It is recommended that the guidance contained in the prognostic indicators guidance in the GSF is followed to identify patients nearing the end of life.
REFERENCES


