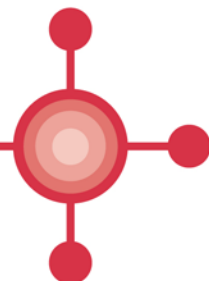


All Wales Medicines Strategy Group

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan



Polypharmacy: Guidance for Prescribing

July 2014

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CONTENTS

1.0 INTRODUCTION	2
1.1 Background	2
1.2 Medication review.....	2
2.0 GUIDANCE AIMS.....	4
Figure 1. Key Considerations for Prescribing in Frail Adults	5
Why is reviewing polypharmacy important?	5
Medicines adherence	7
Start with the basics – Can the patient manage their medicines?	8
Medication review process.....	9
High-risk medication	10
Other factors to consider when conducting a review	11
Polypharmacy in the frail elderly.....	12
Specific considerations for patients with dementia.....	13
Patients with renal dysfunction	14
Anticholinergic effects	14
Indications of shortened life expectancy.....	15
3.0 MEDICINES EFFECTIVENESS SUMMARY	16
Table 1: Medicines Effectiveness Summary	17
Abbreviation definitions.....	18
Figure 2. A Practical Guide to Stopping Medication in the Elderly	19
Antihypertensives	20
Benzodiazepines	20
Oral corticosteroids	21
Antidepressants	22
Bisphosphonates	23
Acid suppressants.....	23
Statins	23
Transdermal opioids (patches)	24
APPENDIX 1: EXAMPLE PATIENT INFORMATION LEAFLET.....	25
APPENDIX 2: TRIALS USED TO COMPLETE MEDICINES EFFECTIVENESS SUMMARY	29
APPENDIX 3: USEFUL RESOURCES	32
REFERENCES	33

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1.0 INTRODUCTION

1.1 Background

Medication is by far the most common form of medical intervention. However, up to 50% of medicines are not taken as prescribed¹. Adverse drug reactions (ADRs) account for 6.5% of hospital admissions and over 70% of ADRs are avoidable².

The proportion of patients receiving 10 or more medicines has increased from 1.9% in 1995 to 5.8% in 2010, and the average number of items per person increased by 53.8% between 2001 and 2011³.

In 2013, an audit of six GP practices in West Wales indicated that around 10% of the practice list were over the age of 74 years. Of this subgroup, it was found that between 22% and 31% were on 10 or more medicines. Similar levels were shown in Cwm Taf Health Board in 2014, when an audit of 11 GP practices showed that 6–11% of the practice population were over the age of 74 years, with an average of 22% prescribed 10 or more medicines (range 10–33%).

1.1.1 Definitions

Polypharmacy (usually considered as the use of at least four or five medicines) can be defined as ‘appropriate’ and ‘problematic’³:

- **Appropriate** – Prescribing for an individual for complex conditions or for multiple conditions in circumstances where medicines use has been optimised and where the medicines are prescribed according to best evidence.
- **Problematic** – Prescribing of multiple medications inappropriately, or where the intended benefit of the medication is not realised, e.g. treatments not evidence based, risk of harm outweighs benefits, medicines interactions present, unacceptable ‘pill burden’, difficulty achieving clinically useful medicines adherence, medicines prescribed to treat side effects of other medicines.

Patients who are considered ‘elderly’ (i.e. generally aged 65 years and over) are at highest risk of significant morbidity and mortality⁴. Frailty is well defined as a ‘reduced ability to withstand illness without loss of function’⁵. [The Gold Standards Framework \(GSF\) Prognostic Indicator Guidance](#) discusses frailty and end of life in further detail.

1.2 Medication review

Increasingly, prescribers are becoming aware of the need to review medication and consider the benefits of ‘deprescribing’. Deprescribing is not about denying effective treatment to people who will benefit, it is about ensuring people do not receive unnecessary treatment, which is unlikely to be of benefit and may cause harm⁶. This is particularly relevant where there is polypharmacy and where the patient is frail.

In line with the ethos of Prudent Health Care and [Choosing Wisely](#), this document is intended to provide guidance on how to make safe and sensible decisions on prescribing in situations where extra consideration is needed due to the complexities of both the individual’s conditions and their medication. This includes:

- when a patient is either on, or has indications to be on, multiple medications;
- when a patient is ‘frail’ in a medical sense.

There are a number of key considerations that need to be taken into account when reviewing a patient, in particular a frail adult, who is on multiple medications. These are set out in the supporting documents in [Figure 1](#). [Figure 2](#) then provides a practical guide to stopping medication in the elderly. Further supporting guidance can be found in the [Polypharmacy Supplementary Guidance on BNF Sections to Target](#).

Support tools such as NO TEARS⁷ and STOPP/START⁸ have been developed to assist prescribers and their patients in making informed and rational decisions on whether to deprescribe or not.

1.2.1 Definitions

A medication review can be defined as:

‘A structured, critical examination of a patient’s medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medication-related problems and reducing waste’⁹.

A medication review can be described in differing levels dependent on the depth of the review from Level 0 (unstructured, opportunistic) to Level 3 (full clinical face-to-face review of medicines and condition). Further information can be found at: www.npc.nhs.uk/review_medicines/intro/resources/agtmr_web1.pdf

1.2.2 Opportunities for medicines review

GP practices and community pharmacies offer opportunities for patients to discuss their medication and identify potential adverse effects and adherence concerns:

- [Medicines Use Review \(MUR\)](#) – available from community pharmacies across Wales – gives patients the opportunity to discuss their medication with a medicines expert and raise any concerns/issues around compliance and adverse effects.
- [Discharge Medication Review](#) – available from community pharmacies following a hospital admission – ensures that any changes to medication are enacted and provides patients with support and information about their medication and any changes that may have been made during their in-patient stay.
- General Practice – through the General Medical Services contract GPs are required to provide medication review for patients on an annual basis. This guidance will provide support to the discussions and possible actions following a face-to-face review. This provides an opportunity for a patient’s medication to be reviewed to ensure that it is both appropriate and continues to provide benefit to the individual.

[Appendix 1](#) provides an example patient information leaflet (PIL) on medicines review in English and Welsh.

Multidisciplinary medication review is increasingly recognised as a cornerstone of medicines management. The recent National Institute for Health and Care Excellence (NICE) guidance on ‘Managing medicines in care homes’ (where a lot of frail elderly people reside) recommends a multidisciplinary approach – involving the patient and/or their family members or carers and a local team of health and social care practitioners¹⁰.

2.0 GUIDANCE AIMS

This document aims to address some of the problems associated with the current management of polypharmacy, particularly in the frail elderly, taking into consideration that:

- Clinical guidelines usually focus on single conditions and often do not address how the risk/benefit ratio changes over time, as the patient ages.
- Healthcare professionals are frequently required to balance the recommendations of multiple guidelines in people who have numerous conditions.
- Recommendations often focus on starting treatments (particularly those used for preventing conditions that have not occurred) and are not balanced by guidance on when it might be appropriate to stop medication or reduce the dose.
- Patients may experience side effects (potentially leading to unscheduled care) from medicines providing little or no benefit, or where the risk of harm outweighs any possible benefit.
- Ongoing need for each medicine may not routinely be considered during medication reviews by both GPs and other healthcare professionals.

The guideline also aims to summarise the expected effectiveness of several of the main current medicines strategies looking at:

- What benefit do various medicines strategies hope to achieve?
- How many patients per annum need to be treated with that medicine to obtain benefit for one patient?
- Where possible, how long is it estimated that treatment was needed in therapeutic trials to show a significant difference between being on that medicine and not being on that medicine?

See [Table 1. Medicines Effectiveness Summary](#).

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 more¹¹. However, it is suggested that up to 50% of medicines are not taken as prescribed¹. Many medicines in common use can cause problems, and adverse reactions to medicines are implicated in 6.5% hospital admissions².

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 age¹². Patients are often prescribed (and may remain on) medication that causes ADRs and prescribers should consider if the harm of each medicine outweighs the benefits¹³.

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.

The NO TEARS tool⁷

Need and indication
Open questions
Tests and monitoring
Evidence and guidelines
Adverse events
Risk reduction or prevention
Simplification and switches

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.

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').

Practical tips for the management of polypharmacy³

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

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

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.

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.)

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

Medicines adherence¹⁴

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.

Please refer to the full NICE guidance <http://guidance.nice.org.uk/CG76> for further detail.

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:
 - mention a specific time (such as in the past week),
 - explain why you are asking,
 - ask about medicine-taking habits,
 - 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.

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

Patient assessment

Who is responsible for administering medication?

E.g. self administration, family, health care support worker (HCSW), domiciliary carer etc.

Medication administered by domiciliary carers/HCSWs?

- Do administration times 'fit' the care calls?
- When required (prn) medicines?
 - State reason e.g. for pain, constipation etc.
 - Specify dose i.e. not 1 or 2

How does the patient access their community pharmacy and/or GP to arrange order or delivery of medication?

Is the patient unable to manage their medication? E.g. due to:

- Complex dosage regimen
- Over-ordering/hoarding of medication
- Forgetful/diagnosis of dementia
- Chaotic lifestyle
- Swallowing difficulties
- Poor dexterity
- Poor sight
- Unable to hear, read or understand directions
- Unable to use medication device e.g. inhalers, eye drops etc.

Is the patient intentionally poorly adherent? E.g. due to:

- Medication no longer needed (particularly prn medicines) e.g. blood glucose test strips, painkiller etc.
- Ineffective medication
- Lack of understanding of indication/importance of treatment
- Lack of immediate visible effects/benefits e.g. for hypertension
- Unpleasant side effects
- Directions unclear
- Complex administration instructions e.g. bisphosphonates, warfarin

Is the patient using any home remedies e.g. herbal products, over the counter preparations, or someone else's medication?

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?

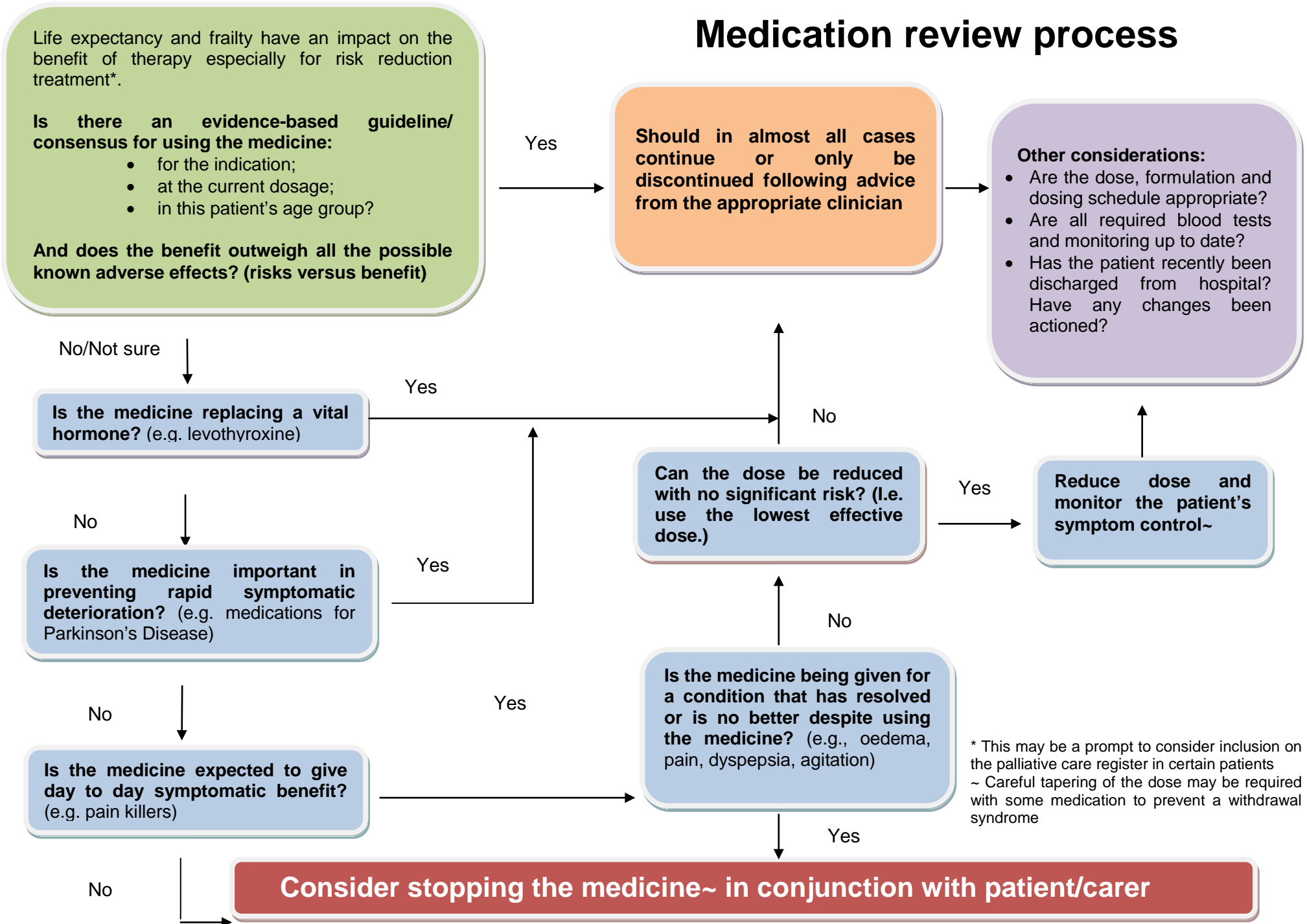
- Consider cost implications, product licence etc.
- Be aware of unlicensed specials.
- If tablets or capsules are being crushed/opened, consider impact on product licence, stability, release properties of medicine, coating etc.

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 use¹⁵ and the RPS has recommended that MDS should not automatically be the intervention of choice for all patients¹⁶. 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/ or contact local MI Centre.

Medication review process



Medication most associated with admission due to ADR

In a 2004 UK study², 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%

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.

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)

High-risk medication⁵

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

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.
- **Anti-anginal medication** – Consider reducing particularly if mobility has decreased with less need for medication.
- **Amiodarone** – Review historical use in persistent AF due to potential major toxicity.

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^{17,18}
- **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?

Other factors to consider when conducting a review^{5,19}

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.

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?

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](#).

Polypharmacy in the frail elderly

Good prescribing practice in the elderly should consider the following⁴:

- 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 appropriate³. 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 interactions²⁰.
- Physiological changes can result in changes to the body's handling of medicines; subsequently dose reductions and/or additional considerations are often required²¹.
- Polypharmacy can play an important role in prolonging a patient's life-expectancy and improving quality of life³. However, benefits should be considered alongside the increased risk and potential for reduced compliance²².

Drugs poorly tolerated in frail elderly⁵

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 falling⁵

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

Specific considerations for patients with dementia

90% of people with dementia experience behavioural and psychological symptoms, such as restlessness and shouting, at some point²³. 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 inappropriate²³.

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 medication⁵. Antipsychotics are associated with an increased risk of falls, delirium, cerebrovascular events and all-cause death.

Priority groups⁵ for reducing antipsychotic medication include:

- People in care homes (often more frail than other populations)
- People with vascular dementia (higher risk of cerebrovascular events)
- People with dementia who also have a history of cardiovascular disease, cerebrovascular disease or vascular risk factors (higher risk of cerebrovascular events)

When *not* to stop⁵ antipsychotic medication:

- Patients who have a co-morbid mental illness that is treated with antipsychotic medication, such as schizophrenia, persistent delusional disorder, psychotic depression or bipolar affective disorder should not have antipsychotic medication reduced without specialist advice.

Reduction of antipsychotics⁵:

- As with initiation of medication, reduction should be carried out slowly with monitoring of effect.
- Start with a reduction of 25% of the total daily dose.
- If the current dose is low, e.g. at the suggested starting dose (as per BNF), the medication may be stopped without tapering the dose.

Review the effect⁵ 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-instating 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.

A best practice guide for optimising treatment and care for behavioural and psychological symptoms of dementia is available from the Alzheimer's Society at:

http://alzheimers.org.uk/site/scripts/download_info.php?downloadID=609

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

Anticholinergic effects

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)²⁴. Research also suggests a link to increased mortality with the number and potency of anticholinergic agents prescribed²⁵. 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.***

1 Point	2 Points	3 Points
<ul style="list-style-type: none"> • Haloperidol • Quetiapine • Mirtazapine • Paroxetine • Trazodone • Ranitidine 	<ul style="list-style-type: none"> • Clozapine • Nortriptyline • Baclofen • Cetirizine • Loratadine • Cimetidine • Loperamide • Prochlorperazine 	<ul style="list-style-type: none"> • Chlorpromazine • Amitriptyline • Imipramine • Chlorpheniramine • Hydroxyzine • Oxybutynin

- Minimise use of anticholinergics wherever possible²⁴.
- Consider anticholinergic burden scale when prescribing anticholinergic combinations.
- Avoid prescribing anticholinergics with acetylcholinesterase inhibitors e.g. donepezil, rivastigmine (can worsen cognitive impairment)²⁴.
- Proactively monitor at regular intervals for efficacy and tolerance²⁴ 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 appropriate²⁴.
- Refer patients suffering from significant anticholinergic side effects due to psychotropic medication to an appropriate specialist²⁴.

Patients with renal dysfunction

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 creatinine¹⁷. It is wise to assume at least mild impairment of renal function when prescribing in the elderly¹⁷.

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 clearance¹⁷.

However, there are two exceptions¹⁷, 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 lithium¹⁷.
- **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 dosages¹⁷.

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:

- 1) <http://archinte.jamanetwork.com/article.aspx?articleid=414049>
- 2) <http://onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.2011.03491.x/pdf>
- 3) <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 include²⁶:

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.
2. Choice/need – Where a patient with advanced disease is making a choice for comfort care rather than 'curative' treatment.
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/ 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.
- <http://book.pallcare.info/> Palliative Care Adult Network Guidance – **Symptom control**.
- 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.
- www.diabetes.org.uk/upload/Position%20statements/End-of-life-care_strategy_Doc111113.pdf A key document for supporting palliative and end of life care for people with diabetes.

3.0 MEDICINES EFFECTIVENESS SUMMARY

Table 1 below summarises the expected effect of various commonly prescribed medicine strategies represented in terms of numbers needed to treat (NNT) per annum to achieve a desired effect. The medicines included were chosen due to the following criteria:

- Is a medicine commonly associated with admission due to ADR, or;
- Is a medicine commonly prescribed in patients with multiple co-morbidities?

Details of the trials used to compile this table are given in [Appendix 2](#).

Where possible, emphasis has been given to trials that include older age groups, and where possible, meta-analysis and reviews of multiple trials from reputable sources (e.g. Cochrane Library) have been used to try and obtain the best estimates of overall effect.

In most cases the analysis demonstrates that these strategies can be very effective if given to enough people for a long enough period of time.

Limitations

It is recognised that no data in any trial or meta-analysis will ever give an exact figure for an individual patient and this table is not intended to be an accurate indicator of outcomes. It is reasonable to assume, however, that the figures give a reasonable estimate of the magnitude of effect.

It is noted that patients in medicines trials will tend on average to be younger, fitter and have less co-morbidity than those not in trials.

This is not an exhaustive list of medicines that fit the above criteria.

Table 1: Medicines Effectiveness Summary

Please note: This table is not intended to be an accurate indicator of outcome, but rather a reasonable estimate of the magnitude of effect. An update of the data is expected by autumn 2014 and this table will be revised accordingly.

Indication/medication	NNT per annum	To do what	Notes
ACE INHIBITORS			
Elevated vascular risk (normal LV function)	280	Prevent one death (all causes)	Trial ran for 5 years
Impaired LV function – mild/moderate	30	Prevent one death (all causes)	Likely symptomatic benefit
Chronic kidney disease (CKD)	See Notes	Increase time to dialysis, reduce cardiovascular risk	ACE inhibitors unlikely to show benefit greater than other antihypertensives unless protein: creatinine ratio (PCR) > 100; in frail adults unlikely unless severe proteinuria PCR > 500 mg/mmol due to time to show effect.
Combination therapy including ACE			
ACE + indapamide	55	Prevent one stroke	Trial ran for 5 years
Secondary prevention post myocardial infarction (MI) > 80 yrs	33	Prevent one death	
ACE + beta-blocker for impaired LV	14	Prevent one death	Likely symptomatic benefit
Impaired LV mild/moderate ACE + beta-blocker	15	Prevent one death	Likely symptomatic benefit
Impaired LV severe ACE + beta-blocker + spironolactone	7	Prevent one death	Likely symptomatic benefit
ASPIRIN primary prevention			
ASPIRIN post stroke/transient ischaemic attack (TIA)	Enormous	No longer recommended	
ASPIRIN post stroke/transient ischaemic attack (TIA)	100	Prevent one stroke or MI or vascular death	
DIPYRIDAMOLE in addition to ASPIRIN post stroke/TIA	100	Prevent one vascular event	BNF caution in cardiac disease
CLOPIDOGREL post stroke or TIA	Dipyridamole + aspirin	Prevent one vascular event	
WARFARIN			
Atrial fibrillation (AF) + another risk factor v ASPIRIN	40	Prevent one stroke – no difference in mortality	
HYPERTENSION			
BP > 140/190 trial predominantly systolic hypertension			
Cardiovascular morbidity and mortality > 80 yrs			
Low risk	80	Avoid one cardiovascular event	2 years for effect
High risk (diabetes, vascular disease)	32	Avoid one cardiovascular event	2 years for effect
Cerebrovascular morbidity and mortality > 80 yrs			
Low risk	122	Avoid one cerebrovascular event	2 years for effect
Cardiovascular morbidity and mortality > 60 yrs			
Low risk	107	Avoid one cardiovascular event	4.5 years for effect
High risk (diabetes, vascular disease)	40	Avoid one cardiovascular event	4.5 years for effect
Cerebrovascular morbidity and mortality > 60 yrs			
Low risk	225	Avoid one cerebrovascular event	4.5 years for effect

Medicines Effectiveness Summary (continued)

STATINS	NNT per annum	To do what	Notes
MI or angina	80–170	Prevent one major coronary event	No difference in mortality to 5 years
Post stroke (atorvastatin 80 v placebo)	165	Prevent one cardiovascular event	No difference in mortality to 5 years
Tight HbA1c control strategies			
<i>Microvascular risk</i>			
ADVANCE (HbA1c 7.3% v 6.5%)	333	Prevent one microvascular event (predominantly retinal)	Trial ran for 5 years
UKPDS (HbA1c 7.9% v 7%)	200	Prevent one microvascular event (predominantly retinal)	Trial ran for 10 years
<i>Macrovascular risk</i>	No difference at 10 years		
Metformin			
Overweight/obese diabetic	50	Prevent one MI or diabetes event or death	10 year follow up
Standard < 140BP in control in diabetes			
Any means	57	Prevent one stroke or major diabetes event or death	8 year follow up
Tight BP control in diabetes			
BP 120 v BP 134	500	Prevent one stroke	4 years minimum for effect
<i>Number needed to harm for this strategy</i>	50		
Osteoporosis (alendronate + calcium/VitD)	Secondary prevention vertebral fractures*	Secondary prevention hip fractures*	Notes for osteoporosis
70–74 years	65	430	NNT per annum to prevent further fractures
75–79 years	45	180	Potential symptomatic benefit re vertebral fractures
80–84 years	60	105	Normally 2 years needed to see effect
85–89 years	55	45	
90+ years	40	40	
NNTs are a guide – they do not give exact figures for individual patients. *NNT for fractures calculated for annual NNT from 5 year NNTs			

Abbreviation definitions

Number needed to treat (NNT)

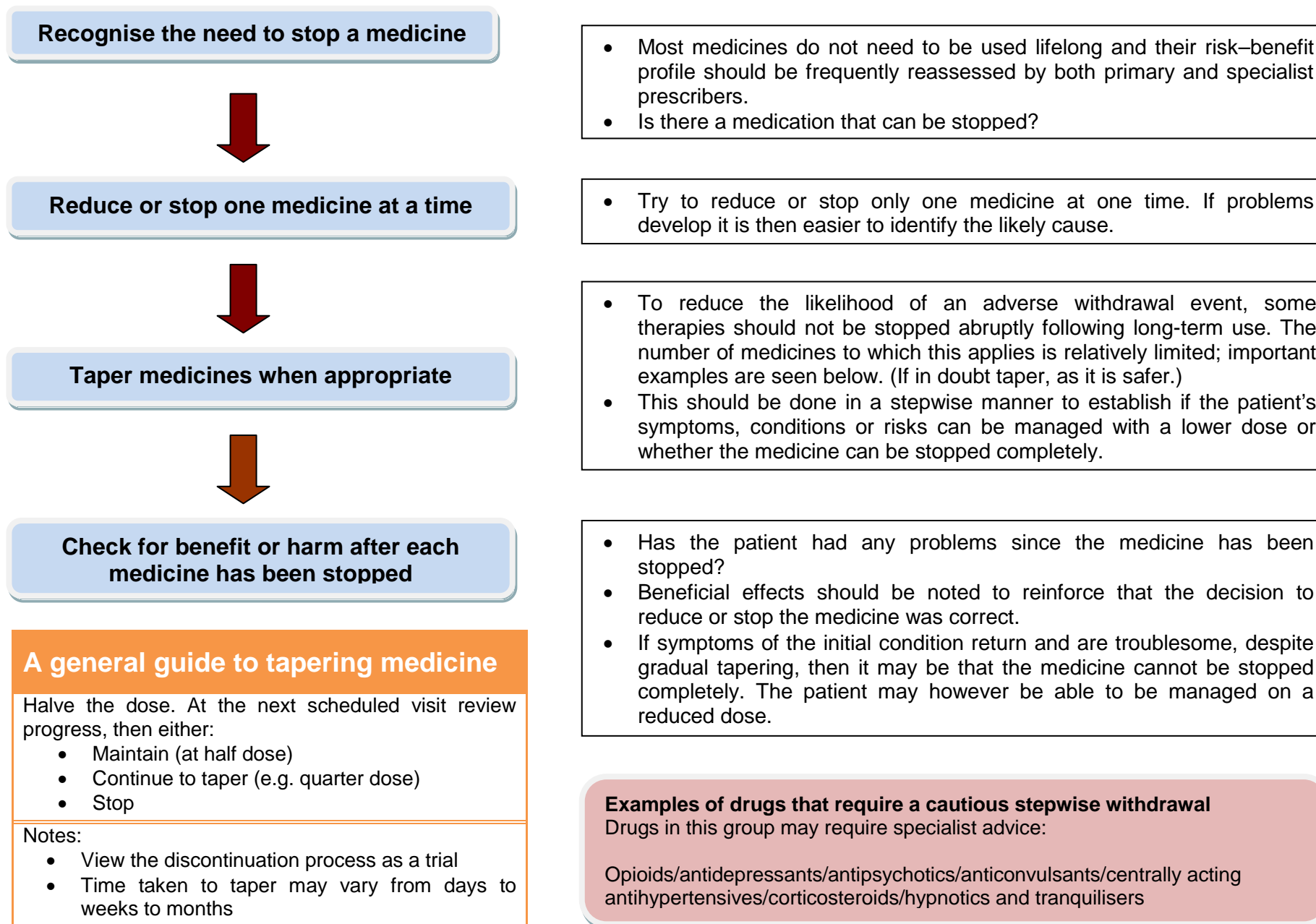
- Number of patients needed to treat to avoid a single additional adverse outcome.
- Needs to refer both to what adverse outcome is avoided and over what timescale (calculated as 1/ARR).

Absolute risk reduction (ARR)

- The absolute difference in adverse outcomes between groups.

Relative risk reduction (RRR)

- The relative difference in outcomes between groups.

Figure 2. A Practical Guide to Stopping Medication in the Elderly²⁷

Antihypertensives¹⁹

Why consider stopping?

- Check if there is a valid indication for prescribing – is the blood pressure (BP) at a normal level or too low?
- Do the known possible ADRs outweigh the possible benefits? E.g. risk of falls; loop diuretic for ankle oedema – following an appropriate assessment, would compression hosiery be more appropriate?

General tapering guide

- If > one antihypertensive is used, stop one at a time, maintaining the dose of the others without change. Restart antihypertensives if BP increases above 90 mm Hg diastolic and/or 150 mm Hg systolic (160 mm Hg if no organ damage).

Withdrawal effect:

- Wide range depending on the specific medicine and the condition being treated.
- Beta-blockers are often associated with adverse withdrawal events. Abrupt withdrawal may cause rebound hypertension, tachycardia, arrhythmia or angina. Gradual dose reduction is required

Benzodiazepines¹⁷

Why consider stopping?

Regular and prolonged use should be avoided because of the risk of tolerance to effects, dependence and an increased risk of adverse effects.

General tapering guide

Withdrawal should be gradual in steps of about one-eighth (range one-tenth to one-quarter) of the daily dose every fortnight.

1. Transfer patient to equivalent daily dose of diazepam, preferably at night.
2. Reduce diazepam dose every 2–3 weeks; if withdrawal symptoms occur, maintain this dose until symptoms improve.
3. Reduce dose further, if necessary in smaller steps; it is better to reduce too slowly rather than too quickly.
4. Stop completely; period needed for withdrawal can vary from about four weeks to a year or more.

Approximate equivalent doses, **diazepam 5 mg**

- | | |
|----------------------------|-------------------|
| • Chlordiazepoxide 15 mg | • Nitrazepam 5 mg |
| • Loprazolam 0.5 mg–1 mg | • Oxazepam 15 mg |
| • Lorazepam 0.5 mg–1 mg | • Temazepam 10 mg |
| • Lormetazepam 0.5 mg–1 mg | |

Withdrawal effects

- These may develop at any time up to three weeks after stopping a long-acting benzodiazepine, but may occur within a day in the case of a short-acting one.
- Characterised by insomnia, anxiety, loss of appetite and of body-weight, tremor, perspiration, tinnitus, and perceptual disturbances. Some symptoms may be similar to the original complaint and encourage further prescribing; some symptoms may continue for weeks or months after stopping benzodiazepines.
- Seek advice from benzodiazepine withdrawal service if one in your area.

Useful link:

www.wemerec.org/Documents/enotes/WithdrawingBenzodiazepine2009.pdf

Oral corticosteroids¹⁷

Why consider stopping?

- The consequences of the common adverse effects (such as osteoporosis, diabetes, glaucoma and GI toxicity) may be more serious in elderly people, especially for those receiving long-term treatment.

General tapering guide

The magnitude and speed of dose reduction should be determined on a case-by-case basis, taking into consideration the underlying condition that is being treated, the likelihood of relapse and the duration of corticosteroid treatment.

Gradual withdrawal should be considered in those whose disease is unlikely to relapse and have:

- received more than 40 mg prednisolone (or equivalent) daily for more than one week;
- been given repeat doses in the evening or received more than three weeks' treatment;
- recently received repeated courses (particularly if taken for longer than three weeks)/taken a short course within one year of stopping long-term therapy;
- other possible causes of adrenal suppression.

The dose may be reduced rapidly down to physiological doses (equivalent to prednisolone 7.5 mg daily) e.g. 2.5–5 mg every 1–3 days.

Reduce more slowly initially if it is likely that the disease will relapse e.g. 2.5–5 mg every 1–3 weeks.

Once the dose has reached 5–10 mg daily, reduce the dose more slowly, e.g. by 1 mg each week.

Patients on longer term treatment may require withdrawal at a more gradual rate over many months (such as a reduction of 1 mg every 1–4 weeks).

Withdrawal effects

Include:

Anorexia, hypotension, nausea, weakness, fever, myalgia, arthralgia, weight loss

Antidepressants^{17,19}

Why consider stopping?

- Check if there is a valid indication for prescribing. For a single episode of depression treat for 6–9 months; for multiple episodes, treat for at least two years, no upper duration of treatment has been identified.
- Dosulepin should not be routinely initiated as treatment for depression.
- Do the known possible ADRs outweigh the possible benefits? E.g. TCAs can worsen dementia, glaucoma, constipation, urinary retention; SSRIs may induce clinically significant hyponatraemia.
- Are TCAs being taken with other medicines that have anticholinergic activity and can increase risk of cognitive impairment e.g. chlorpromazine, oxybutynin, chlorphenamine?

General tapering guide

Dose should preferably be reduced gradually over about four weeks, or longer if withdrawal symptoms emerge

For people with severe adverse reactions to treatment (e.g. cardiac arrhythmia with a TCA) – a more abrupt discontinuation may be necessary.

For people on shorter half-life medication such as paroxetine or venlafaxine a longer period is needed.

For people who have been receiving longer term maintenance treatment – may need to be tapered for much longer e.g. over six months.

Fluoxetine has a long half life and active metabolites, therefore can be stopped abruptly. Patients taking higher doses (40–60 mg) may require a more gradual withdrawal.

Withdrawal effects

- Discontinuation symptoms include dizziness, nausea, paraesthesiae, anxiety, diarrhoea, flu-like symptoms, and headache. They may occur when stopping or reducing the dose of any antidepressant.
- Onset is usually around five days of stopping therapy. Occasionally, symptoms occur during tapering or after missed doses.
- These symptoms are usually mild and self-limiting, rarely lasting for more than 1–2 weeks. However, occasionally they can be severe, particularly if the drug is stopped abruptly.
- Discontinuation symptoms are more likely with antidepressants with a short half-life, in people who developed anxiety symptoms at the start of treatment, and in people taking other centrally acting drugs.

Useful link: www.wemerec.org/Documents/enotes/Stoppingantidepressantse-notes.pdf

Acid suppressants

Why consider stopping?

- PPIs have been implicated with an increased risk of infection including pneumonia and *C. difficile*.
- More recently reports have also highlighted potential increases in bone fracture rates, hyponatraemia and hypomagnesaemia seen in patients taking long-term PPIs.

General tapering guide

- Tapering the dose of an acid suppressant (both PPIs and H₂RAs) is recommended because of the risk of rebound hypersecretion of gastric acid.
- A step down approach can be employed for certain patients, alongside recommendations for appropriate trials of antacids or alginates and lifestyle changes.
- Halve the dose for 4–8 weeks then stop (or step down to a less potent agent).

Withdrawal effects

- Rebound hypersecretion (which may last up to 6–8 weeks)
- If rebound hyperacidity is mistaken for a return of the underlying condition then acid suppressants may be restarted unnecessarily

Useful link: www.wemerec.org/Documents/enotes/StoppingPPIsenotes.pdf

Bisphosphonates¹⁹

Why consider stopping?

- Check if there is a valid indication for prescribing.
- Has treatment been taken for five years or more?
- Do the known possible ADRs outweigh the possible benefits?
- If the patient is at low risk of falls, are these still needed?
- Prolonged immobility is a risk factor for low bone mineral density.
- Compliance is often poor.
- Alendronate can be stopped abruptly without the need for tapering.

Useful link:

www.wemerec.org/Documents/enotes/Stoppingbisphosphonatese-notes.pdf

Statins

Why consider stopping?

The decision to stop a statin is based on an assessment of individual benefits and risks.

- Stopping may be justified in a person at relatively low risk of a cardiovascular event, who is also poorly compliant or experiencing troublesome adverse effects.
- Statins should be stopped in palliative patients.

Transdermal opioids (patches)

Why consider stopping?

- Modified release morphine is the recommended first choice strong opioid.
- There is increasing prescribing of opioid transdermal preparations, which has both safety and cost implications. (Perhaps it's because patches seem simple that we get complacent about the potential risks.) www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON087796

Is a transdermal patch appropriate? Can the patient be switched to oral medication?

- Patches are only for patients with **stable** pain AND significant side effects to morphine or when the oral route is unacceptable e.g. dysphagia.
- They are NOT suitable for patients with unstable pain.

What are the problems associated with transdermal patches?

- Analgesic patches are all similar in their indications but vary greatly in their potency. Fever or external heat, e.g. a hot bath or sauna, may increase absorption and hence increase risk of adverse effects.
- Transdermal adhesion problems – patches do not always stay tightly bound to the skin's surface e.g. during excessive sweating.

When is a transdermal patch appropriate?

- Stable analgesia requirements where dexterity/confusion are issues for taking oral medication.
- Chronic nausea/vomiting, or malabsorption/bowel obstruction.
- Transdermal patches may be particularly suitable for frail elderly people requiring steady drug levels or where daily administration is difficult.

Buprenorphine patches are *approximately* equivalent to the following 24-hour doses of oral morphine¹⁷

morphine salt 12 mg daily	≡	BuTrans® '5' patch	7-day patches
morphine salt 24 mg daily	≡	BuTrans® '10' patch	7-day patches
morphine salt 48 mg daily	≡	BuTrans® '20' patch	7-day patches
morphine salt 84 mg daily	≡	Transtec® '35' patch	4-day patches
morphine salt 126 mg daily	≡	Transtec® '52.5' patch	4-day patches
morphine salt 168 mg daily	≡	Transtec® '70' patch	4-day patches

72-hour fentanyl patches are *approximately* equivalent to the following 24-hour doses of oral morphine¹⁷

morphine salt 30 mg daily	≡	fentanyl '12' patch
morphine salt 60 mg daily	≡	fentanyl '25' patch
morphine salt 120 mg daily	≡	fentanyl '50' patch
morphine salt 180 mg daily	≡	fentanyl '75' patch
morphine salt 240 mg daily	≡	fentanyl '100' patch

Reference: BNF April 2014. Conversion ratios vary and these figures are a guide only. There are numerous available opioid dose conversion charts and tools show considerable variation. The important thing is to **remember that all these conversions are approximations only**. See <http://book.pallcare.info/index.php> for more detail.

APPENDIX 1: EXAMPLE PATIENT
INFORMATION LEAFLET

What questions will I be asked at my medicines review?

At the medicines review, you will be asked about how you are getting on with your medicines. Some of the questions you might be asked at your medicines review include:

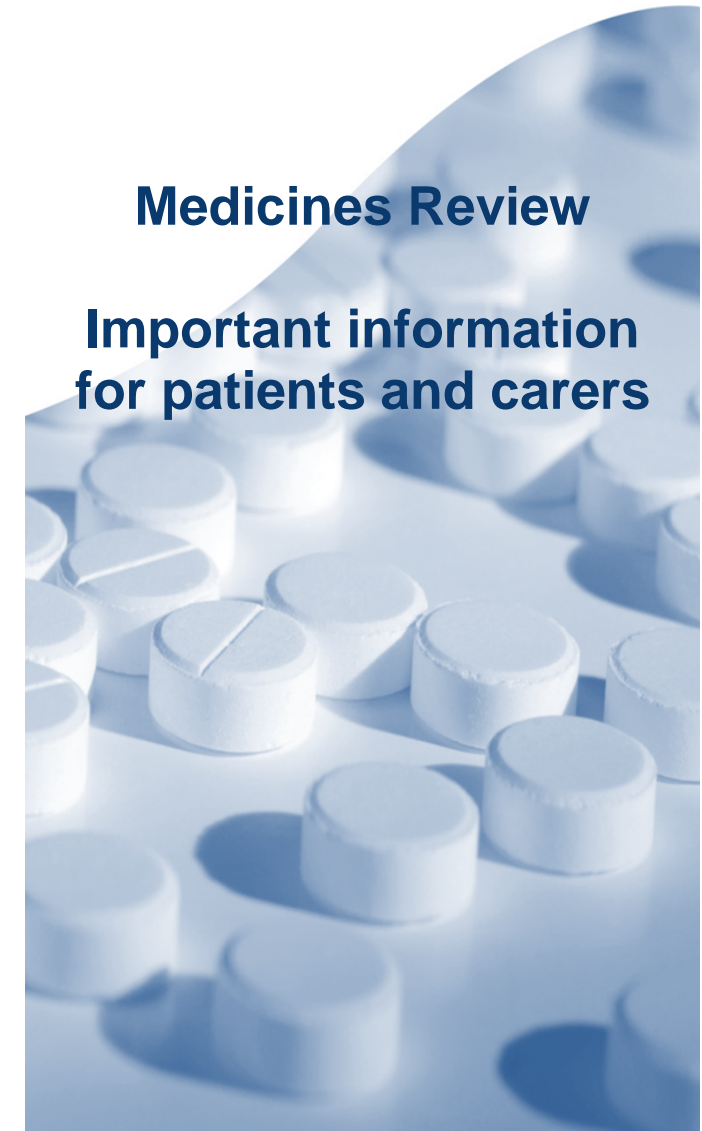
- Are you taking all of your medicines?
- Are there any you miss out or forget to take?
- Can you take/use the medicine properly?
- Do you feel you are having any side effects from your medicines?
- Do you have any concerns about your medicines?
- Do you take any other medicines, such as those bought in a pharmacy or supermarket?

Where can I get more information?

For further information about your medicines, please contact:

- Your GP Surgery.
- Your community pharmacy (chemist).

NHS Direct Wales (web:
www.nhsdirect.wales.nhs.uk/ or telephone:
0845 46 47)



Introduction

A medicines review is a meeting with your doctor, pharmacist or nurse to talk about your medicines. Your medicines should be reviewed regularly (usually once a year) to check that they are right for you.

Why are medicines reviews needed?

When you are first prescribed a medicine, your doctor, pharmacist and/or nurse checks that it is the best medicine for you. However, things can change, for example:

- You might have developed a side effect from the medicine.
- Your health might have changed, such as developing a long-term condition.
- You might have started taking other additional medicines.
- The guidelines for treating your condition might have changed.
- You may be taking a large number of medicines (known as “polypharmacy”).
- A medicine you are on may be no longer essential for your health day to day.

All of these factors can affect whether a medicine remains the best choice for you.

What is “polypharmacy”?

You might have heard your doctor, pharmacist or nurse talk about “polypharmacy”. Polypharmacy just means “lots of pharmacy” or, in other words, taking a large number of medicines.

Medicines reviews are particularly useful for people who take lots of medicines so they are sometimes called “polypharmacy reviews”.

What happens at a medicines review?

You will be asked to make an appointment with your doctor, pharmacist or nurse for a medicines review. The review will take between 10 and 30 minutes.

The review will involve the doctor/pharmacist/nurse gathering information from you and from your medical record. This information will be used to check that you are taking the most appropriate medicines.

It might be necessary for the doctor/pharmacist/nurse to recommend some changes to your medicines. The reasons for these changes will be explained to you and you will be asked for your agreement before any changes are made.

What changes to my medicines might be recommended?

Some common changes your doctor/pharmacist/nurse might recommend to your medicines are:

- A medicine may be changed to a form that is easier to take (e.g., once a day rather than three times a day).
- A medicine may be started or changed to a newer version.
- A medicine may be stopped.

Do I need to take anything to my medicines review?

It would be very useful if you could bring all of your medicines with you, including any you have bought in a pharmacy or shop. If you buy vitamins or herbal or homoeopathic remedies, please bring them too.

Medicines often have two names (a generic name and a brand name) so having the medicines with you will prevent any confusion if the doctor/pharmacist/nurse calls the medicine by a different name to the name you normally use.

Pa gwestiynau gaiff eu gofyn yn fy adolygiad meddyginiaethau?

Yn eich adolygiad meddyginiaethau gofynnir i chi sut ydych yn ymdopi â'ch meddyginiaethau. Gall rhai o'r cwestiynau a ofynnir i chi gynnwys:

- A ydych yn cymryd eich holl feddyginiaethau?
- A oes rhai yr ydych yn anghofio eu cymryd?
- A allwch gymryd/ddefnyddio y feddyginiaeth yn gywir?
- A ydych yn teimlo eich bod yn dioddef unrhyw sgîl-ffeithiau oherwydd eich meddyginiaethau?
- A oes gennych unrhyw bryderon ynglŷn â'ch meddyginiaethau?
- A ydych yn cymryd unrhyw feddyginiaethau eraill, megis y rheini a brynir mewn fferyllfa neu archfarchnad?

Lle gallaf gael rhagor o wybodaeth?

Am ragor o wybodaeth am eich meddyginiaethau, cysylltwch â'ch:

- Meddygfa meddyg teulu.
- Fferyllfa gymunedol (fferyllydd).

Galw Iechyd Cymru (gwefan:

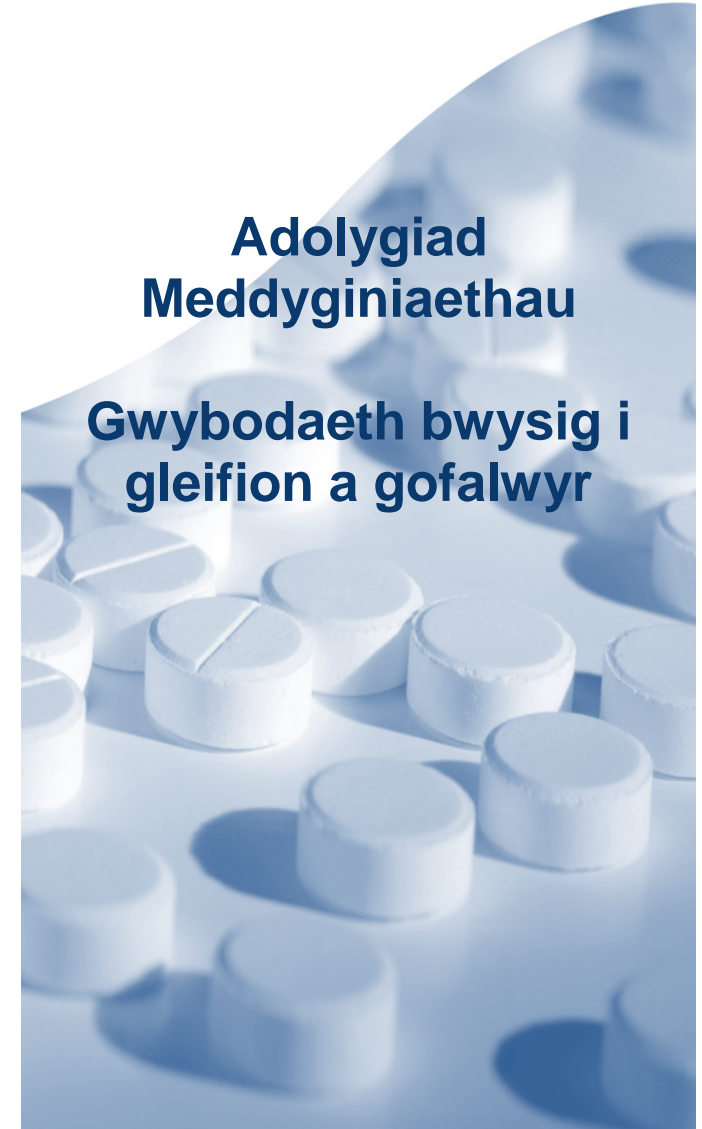
www.nhsdirect.wales.nhs.uk/ neu ffoniwch:

0845 46 47)

ATODIAD 1: ENGHRAIFFT O DAFLEN GWYBODAETH I GLEIFION

Adolygiad Meddyginiaethau

Gwybodaeth bwysig i gleifion a gofalwyr



Rhagymadrodd

Cyfarfod i siarad am eich meddyginiaethau gyda'ch meddyg, fferyllydd neu nyrs yw adolygiad meddyginiaethau. Dylid adolygu eich meddyginiaethau yn rheolaidd (fel arfer unwaith y flwyddyn) i wirio eu bod yn iawn ar eich cyfer.

Pam mae angen adolygiadau meddyginiaethau?

Pan ragnodir meddyginiaeth i chi am y tro cyntaf mae eich meddyg, fferyllydd a/neu eich nyrs yn gwirio mai hon yw'r feddyginiaeth orau ar eich cyfer. Fodd bynnag, gall pethau newid, er enghraifft:

- Efallai eich bod wedi datblygu sgîl effaith oherwydd y feddyginiaeth.
- Efallai bod eich iechyd wedi newid, megis datblygu cyflwr hir dymor.
- Efallai eich bod wedi dechrau cymryd meddyginiaethau ychwanegol eraill.
- Gallai'r canllawiau ar gyfer trin eich cyflwr fod wedi newid.
- Efallai eich bod yn cymryd nifer fawr o feddyginiaethau (a adwaenir fel "polyfferylliaeth").
- Efallai nad yw'r feddyginiaeth yr ydych yn ei chymryd yn hanfodol mwyach ar gyfer eich iechyd bob dydd.

Gall yr holl ffactorau hyn gynorthwyo i benderfynu a yw meddyginiaeth yn parhau i fod yn ddewis gorau ar eich cyfer.

Beth yw "polyfferylliaeth"?

Efallai eich bod wedi clywed eich meddyg, fferyllydd neu nyrs yn sôn am "polyfferylliaeth". Ystyr hyn yw cymryd nifer fawr o feddyginiaethau.

Mae adolygiadau meddyginiaethau yn arbennig o ddefnyddiol ar gyfer pobl sy'n cymryd llawer o feddyginiaethau felly fe'u gelwir weithiau yn "adolygiadau polyfferylliaeth".

Beth sy'n digwydd mewn adolygiad meddyginiaethau?

Gofynnir i chi wneud apwyntiad gyda'ch meddyg, fferyllydd neu nyrs ar gyfer adolygiad meddyginiaethau. Bydd yr adolygiad yn para rhwng 10 a 30 munud.

Yn yr adolygiad bydd y meddyg/fferyllydd/nyrs yn casglu gwybodaeth gennych chi ac o'ch cofnodion meddygol. Defnyddir y wybodaeth hon i wirio eich bod yn cymryd y meddyginiaethau mwyaf priodol.

Efallai y bydd angen i'r meddyg/fferyllydd/nyrs argymhell rhai newidiadau yn eich meddyginiaethau. Caiff y rhesymau am y newidiadau hyn eu hegluro i chi a gofynnir am eich cydsyniad cyn y caiff unrhyw newidiadau eu gwneud.

Pa newidiadau all gael eu hargymell i fy meddyginiaethau?

Rhai newidiadau cyffredin y gall eich meddyg/fferyllydd/nyrs eu cynnig ar gyfer eich meddyginiaethau yw:

- Meddyginiaeth yn cael ei newid i ffurf sy'n haws ei chymryd (e.e. unwaith y dydd yn hytrach na theirgwaith y dydd)
- Meddyginiaeth yn cael ei dechrau neu ei newid i fersiwn mwy newydd.
- Meddyginiaeth yn cael ei hatal.

A oes angen i mi ddod â rhywbeth gyda mi i'r adolygiad meddyginiaethau?

Byddai'n ddefnyddiol iawn pe byddech yn dod a'ch holl feddyginiaethau gyda chi, yn cynnwys unrhyw rai a brynwyd gennych mewn fferyllfa neu siop. Os ydych yn prynu fitaminau neu feddyginiaethau llysieuol neu homeopathig, dewch â hwy gyda chi hefyd.

Yn aml bydd gan feddyginiaethau ddau enw (enw generig ac enw brand), felly bydd bod a'ch meddyginiaethau gyda chi yn atal unrhyw ddryswch os bydd y meddyg/fferyllydd/nyrs yn defnyddio enw gwahanol i'r enw fyddwch chi'n ei ddefnyddio fel arfer.

APPENDIX 2: TRIALS USED TO COMPLETE MEDICINES EFFECTIVENESS SUMMARY

Cardiac Trials

The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991; 325(5):293-302

The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000; 342(3):145–153

The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. *Lancet* 1999; 353(9146):9-13

The Randomized Aldactone Evaluation Study [RALES] Investigators. The Effect of Spironolactone on Morbidity and Mortality in Patients with Severe Heart Failure. (Pitt B; Zannad F; Remme WJ; Cody R; Castaigne A; Perez A; Palensky J; Wittes J) *N Engl J Med* 1999; 341(10):709-717

Setoguchi S; Glynn RJ; Avorn J; Mittleman MA; Levin R; Winkelmayr WC. Improvements in long-term mortality after myocardial infarction and increased use of cardiovascular drugs after discharge: a 10-year trend analysis. *J Am Coll Cardiol* 2008; 51(13):1247-1254

Stroke Secondary Prevention

Anti-thrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002; 324(7329):71-86

PROGRESS Collaborative Group. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet* 2001; 358(9287):1033-1041

Holman RR; Paul SK; Bethel MA; Matthews DR; Neil HAW. 10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes. *N Engl J Med* 2008; 359(15):1577-1589

Halkes PH; Gray LJ; Bath PM; Diener HC; Guiraud-Chaumeil B; Yatsu FM; Algra A. Dipyridamole plus aspirin versus aspirin alone in secondary prevention after TIA or stroke: a meta-analysis by risk. *J Neurol Neurosurg Psychiatry* 2008; 79(11):1218-1223

Rashid P; Leonardi-Bee J; Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. *Stroke* 2003; 34(11):2741-2748.

The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators. High-Dose Atorvastatin after Stroke or Transient Ischemic Attack. *N Engl J Med* 2006; 355(6):549-559

NICE. Technology Appraisal 210: Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (review of technology appraisal guidance 90). 2010

Warfarin

Mant J; Hobbs FD; Fletcher K; Roalfe A; Fitzmaurice D; Lip GY; Murray E; BAFTA investigators; Midland Research Practices Network (MidReC). Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): a randomised controlled trial. *Lancet* 2007; 370(9586):493-503

Hypertension

Musini VM; Tejani AM; Bassett K; Wright JM. Pharmacotherapy for hypertension in the elderly. *Cochrane Database of Syst Rev* 2009; Issue 4. Art. No.: CD000028. DOI: 10.1002/14651858.CD000028.pub2.

Statins

Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994; 344(8934):1383-1389

LaRosa JC; He J; Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. *JAMA* 1999; 282(24):2340-2346

Goldberg RB; Mellies MJ; Sacks FM; Moye LA; Howard BV; Howard WJ; Davis BR; Cole TG; Pfeffer MA; Braunwald E. Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the Cholesterol and Recurrent Events (CARE) trial. *Circulation* 1998; 98(23):2513-2519

West of Scotland Coronary Prevention Group. West of Scotland Coronary Prevention Study: identification of high-risk groups and comparison with other cardiovascular intervention trials. *Lancet* 1996; 348(9038):1339-1342

Colhoun HM; Betteridge DJ; Durrington PN; Hitman GA; Neil HA; Livingstone SJ; Thomason MJ; Mackness MI; Charlton-Menys V; Fuller JH; CARDS investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo controlled trial. *Lancet* 2004; 364(9435):685-696

Action to Control Cardiovascular Risk in Diabetes Study Group; Gerstein HC; Miller ME; Byington RP; Goff DC Jr; Bigger JT; Buse JB; Cushman WC; Genuth S; Ismail-Beigi F; Grimm RH Jr; Probstfield JL; Simons-Morton DG; Friedewald WT. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 2008; 358(24):2545-2559

Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo controlled trial. *Lancet* 2002; 360(9326):7-22

Diabetes

Currie CJ; Peters JR; Tynan A; Evans M; Heine RJ; Bracco OL; Zagar T; Poole CD. Survival as a function of HbA1c in people with type 2 diabetes: a retrospective cohort study. *Lancet* 2010; 375 (9713): 481-489

Ray KK; Seshasai SRK; Wijesuriya S; Sivakumaran R; Nethercott S; Preiss D; Erqou S; Sattar N. Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials. *Lancet* 2009; 373(9677):1765-1772

The ADVANCE Collaborative Group. Intensive Blood Glucose Control and Vascular Outcomes in Patient with Type 2 Diabetes. *N Engl J Med* 2008; 358:2560-2572

The ACCORD Study Group. Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus. 2010. *N Engl J Med* 2010; 362:1575-1585

Osteoporosis

Wells GA; Cranney A; Peterson J; Boucher M; Shea B; Robinson V; Coyle D; Tugwell P. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database Syst Rev* 2008; Issue 1. Art. No.: CD001155. DOI: 10.1002/14651858.CD001155.pub2.

Renal

The Gisen Group. Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy [REIN study]. *Lancet* 1997; 349(9069):1857-1863

The Gisen Group. Renal function and requirement for dialysis in chronic nephropathy patients on long-term ramipril: REIN follow-up trial. *Lancet* 1998; 352(9136):1252-1256

Casas JP; Chua W; Loukogeorgakis S; Vallance P; Smeeth L; Hingorani AD; MacAllister RJ. Effect of inhibitors of the renin-angiotensin system and other antihypertensive drugs on renal outcomes: systematic reviews and meta-analysis. *Lancet* 2005; 366(9502):2026-2033

Bleeding Risk and Antiplatelet Strategies

Hansen ML; Sorensen R; Clausen MT; Fog-Petersen ML; Raunsø J; Gadsbøll N; Gislason GH; Folke F; Andersen SS; Schramm TK; Abildstrøm SZ; Poulsen HE; Køber L; Torp-Pedersen C. Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation. *Arch Intern Med* 2010; 170(16):1433-1441

Aspirin in Secondary Prevention

Rodriguez LAG; Cea-Soriano L; Martin-Merino E; Johansson S. Discontinuation of low dose aspirin and risk of myocardial infarction: case-control study in UK primary care. *BMJ* 2011; 343:d4094

Other

Boyd CM; Darer J; Boult C; Fried LP; Boult L; Wu AW. Clinical Practice Guidelines and Quality of Care for Older Patients with Multiple Comorbid Diseases: implications for pay for performance. *JAMA* 2005; 294(6):716-724

Guthrie B; McCowan C; Davey P; Simpson CR; Dreischulte T; Barnett K. High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice. *BMJ* 2011; 342:d3514 Source of high risk drug group information.

APPENDIX 3: USEFUL RESOURCES

The following sources provide additional information to support effective medication reviews; many of these have been used to compile this document.

- **AWMSG.** Advises health boards on the use of medicines within NHS Wales and responsible for the development of prescribing resources. Available at: www.awmsg.org/
- **Electronic Medicines Compendium (eMC).** Searches the latest approved prescribing information (e.g. SPCs) and patient information leaflets for licensed medicines. Available at: www.medicines.org.uk/emc/
- **MHRA.** Drug Safety Updates and Yellow Card Reporting. Available at: www.mhra.gov.uk/index.htm
- **NICE.** Guidelines and pathways available at: www.nice.org.uk/
- **NICE Clinical Knowledge Summaries.** Provides primary care practitioners with summaries of current evidence base and practical guidance. Available at: <http://cks.nice.org.uk/>
- **NICE Evidence Search.** Search engine available at: www.evidence.nhs.uk/
- **NICE Clinical Guideline 76. Medicines adherence: involving patients in decisions about prescribed medicines and supporting adherence.** Available at: www.nice.org.uk/CG76
- **Optimising treatment and care for people with behavioural and psychological symptoms of dementia: A best practice guide for health and social care professionals.** (Alzheimer's Society) 2011. Available at: http://alzheimers.org.uk/site/scripts/download_info.php?downloadID=609
- **Prescribing for Older People.** Bulletin produced by WeMeReC. Available at: www.wemerec.org/Documents/Bulletins/Prescribing4OlderBulletin-online.pdf
- **Stopping Medicines.** Bulletin produced by WeMeReC. Available at: www.wemerec.org/Documents/Bulletins/StoppingMedicinesBulletinOnline.pdf
- **STOPP and START criteria: A new approach to detecting potentially inappropriate prescribing in old age.** The STOPP START criteria form a medication review tool designed to identify medication where the risks outweigh the benefits in elderly patients (aged > 65 years) and vice versa (*access requires OpenAthens login or subscription to journal*). Available at: www.sciencedirect.com/science/article/pii/S1878764910000112
- **The King's Fund: Polypharmacy and medicines optimisation.** Contains useful case studies and practical advice. Available at: www.kingsfund.org.uk/publications/polypharmacy-and-medicines-optimisation
- **The Medication Appropriateness Index.** Designed to assist clinicians and pharmacists in assessing the appropriateness of a medication given to a patient and consists of 10 explicit criteria. See page 18 of The King's Fund Polypharmacy and medicines optimisation document. Available at: www.kingsfund.org.uk/publications/polypharmacy-and-medicines-optimisation
- **The NO TEARS tool.** A useful prompt to aid efficient medication review and maximise the potential of the 10-minute consultation. The one-page BMJ article is available at: www.bmj.com/highwire/filestream/382551/field_highwire_article_pdf/0/434
- **Facilitating Avoidance of Medication-Related Admissions.** Material produced by Betsi Cadwaladr University Health Board. Available at: <http://yhiec.org.uk/wp-content/uploads/2012/05/PSC2011-Facilitating-Avoidance-of-medication-related-admissions-pdf.pdf>
- **Responding to Suspected Avoidable Antimicrobial-related Admissions.** Material produced by Betsi Cadwaladr University Health Board. Available at: www.ukcpa.net/wp-content/uploads/2014/01/Example-poster-Janet-Thomas-BCUHB-Autumn-Symp-2013-poster-winner.pdf

REFERENCES

- 1 World Health Organisation. Failure to take prescribed medicine for chronic diseases is a massive, world-wide problem. 2003. Available at: <http://www.who.int/mediacentre/news/releases/2003/pr54/en/>. Accessed May 2014.
- 2 Pirmohamed M, James S, Meakin S et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *British Medical Journal* 2004; 329 (7456): 15-9.
- 3 Duerden M, Avery T, Payne R. Polypharmacy and medicines optimisation. Making it safe and sound. The King's Fund; Nov 2013. Available at: http://www.kingsfund.org.uk/sites/files/kf/field/field_publication_file/polypharmacy-and-medicines-optimisation-kingsfund-nov13.pdf. Accessed Mar 2014.
- 4 Welsh Medicines Resource Centre. Prescribing for older people. Jun 2011. Available at: <http://www.wemerec.org/Documents/Bulletins/Prescribing4OlderBulletin-online.pdf>. Accessed Apr 2014.
- 5 NHS Scotland. Polypharmacy guidance. Oct 2012. Available at: <http://www.central.knowledge.scot.nhs.uk/upload/Polypharmacy%20full%20guidance%20v2.pdf>. Accessed Apr 2014.
- 6 Allred D. Deprescribing: a brave new world? *International Journal of Pharmacy Practice* 2014; 22: 2-3.
- 7 Lewis T. Using the NO TEARS tool for medication review. 2004. 329:434. Available at: <http://www.bmj.com/content/329/7463/434>. Accessed Mar 2014.
- 8 Gallagher P, Ryan C, Byrne S et al. STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. *International Journal of Clinical Pharmacology and Therapeutics* 2008; 46: 72-83.
- 9 Task Force on Medicines Partnership and The National Collaborative Medicines Management Services Programme. Room for review. A guide to medication review: the agenda for patients, practitioners and managers. 2002. Available at: http://www.npc.nhs.uk/review_medicines/intro/resources/room_for_review.pdf. Accessed Apr 2014.
- 10 National Institute for Health and Care Excellence. Managing medicines in care homes. 2014. Available at: <http://www.nice.org.uk/guidance/sc/SC1.jsp>. Accessed May 2014.
- 11 NHS Employers. Quality and Outcomes Framework for 2012/13. Apr 2012. Available at: http://www.nhsemployers.org/Aboutus/Publications/Documents/QOF_2012-13.pdf. Accessed Feb 2014.
- 12 Zhang M, Holman CD, Price SD et al. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. *British Medical Journal* 2009; 338 (a2752).
- 13 Guthrie B, McCowan C, Davey P et al. High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice. *British Medical Journal* 2011; 342 (d3514).
- 14 East Lancashire Health Economy Medicines Management Board. NICE Bites. Mar 2009. Report No.: 3. Available at: <http://www.elmmb.nhs.uk/newsletters-minutes/nice-bites/?assetdetesctl486923=32536&p=3>. Accessed Apr 2014.
- 15 Mahtani KR, Heneghan CJ, Glasziou PP et al. Reminder packaging for improving adherence to self-administered long-term medications (Review). *Cochrane Database of Systematic Reviews* 2011; (9). Available at: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005025.pub3/pdf>.
- 16 Royal Pharmaceutical Society. Improving patient outcomes. The better use of multi-compartment compliance aids. 2013. Available at:

- <http://www.rpharms.com/support-pdfs/rps-mca-july-2013.pdf>. Accessed Nov 2014.
- 17 British Medical Association, Royal Pharmaceutical Society of Great Britain. British National Formulary. Apr 2014. Available at: <http://www.bnf.org/bnf/index.htm>. Accessed Apr 2014.
 - 18 Drug and Therapeutics Bulletin. Metformin OK in CKD? 2014. Available at: http://dtb.bmj.com/content/52/4/37.extract?utm_medium=email&utm_campaign=14238&utm_content=Metformin%20OK%20in%20CKD%3F&utm_term=&utm_source=Aestra_BMJ%20Evidence%20Centre. Accessed May 2014.
 - 19 NHS Midlands and East. PrescQIPP - optimising safe and appropriate medicines use. 2014.
 - 20 Routledge PA, O'Mahony MS, Woodhouse KW. Adverse drug reactions in elderly patients. *British Journal of Clinical Pharmacology* 2003; 57 (2): 121-6.
 - 21 Walker R, Whittlesea C. *Clinical pharmacy and therapeutics*. 5th ed. Churchill Livingstone; 2011.
 - 22 Sergi G, De Rui M, Sarti S et al. Polypharmacy in the elderly: can comprehensive geriatric assessment reduce inappropriate medications use? *Drugs and Aging* 2011; 28 (7): 509-18.
 - 23 Alzheimer's Society. Antipsychotic drugs. Apr 2013. Available at: http://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=548. Accessed Apr 2014.
 - 24 Coastal West Sussex Clinical Commissioning Group. Medicines optimisation prescribing guidance: key therapeutic areas. 2013. Available at: <http://www.coastalwestsussexccg.nhs.uk/home>.
 - 25 Fox C, Richardson K, Maidment ID et al. Anticholinergic medication use and cognitive impairment in the older population. *Journal of the American Geriatrics Society* 2011; 59 (8): 1477-83.
 - 26 The Gold Standards Framework Centre in End of Life Care CIC. Prognostic indicator guidance (PIG) 4th edition. Oct 2011. Available at: <http://www.goldstandardsframework.org.uk/cd-content/uploads/files/General%20Files/Prognostic%20Indicator%20Guidance%20October%202011.pdf>. Accessed Apr 2014.
 - 27 Best Practice Journal. A practical guide to stopping medicines in older people. *Best Practice Journal* 2010; (27).