Prescribing in Older Adults

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Session Outline

- Describe best practice principles when prescribing in older adults
- Understand age-related changes in pharmacokinetics and pharmacodynamics
- With respect to psychiatry, recognise high risk medications that should be avoided in older adults
- Describe a psychotropic prescribing formulary for older adults, including common side-effects and interactions (drug-drug and drug-disease)

Refer to the BNF and/or Summary of Product Characteristics for detailed prescribing information, including dosage, contraindications and cautions, side-effects and drug Interactions. Some indications for use are unlicensed.

Context

- 60% of all prescriptions in England were issued to people aged 60 years and over
- 1 in 5 prescriptions to older people living in their own homes may be inappropriate
- In care homes, 91% of residents take more than 5 medicines and 65% of residents take more than 10 medicines
- Polypharmacy associated with increased hospital admissions, interactions, and adverse effects
- Ageing associated with increased burden of disease and need for evidence-based interventions
- Incremental benefit of adding additional medication to existing treatments unclear
- Older adults under-represented in trials
- Not a heterogeneous population

Clinical Pharmacology in the Elderly

Pharmacodynamics

The physiological effects of the drug

- Control over reflex actions such as BP and temperature regulation reduced
- Receptors may become more sensitive
  - Drugs affecting gut motility more likely to cause constipation e.g. anticholinergics
  - Drugs affecting BP more likely to cause falls e.g. tricyclics
- ↑incidence and severity of side-effects
- Elderly more sensitive to benzodiazepines, antipsychotics, opioids, antiparkinsonian drugs
- Therapeutic response can be delayed e.g. antidepressants → 2-3 month therapeutic trial

Clinical Pharmacology in the Elderly

Pharmacokinetics

What the body does to the drug

- Absorption
  - Slower rate of absorption, with same total amount absorbed
- Distribution
  - Older adults have proportionately more body fat, body water and less albumin
  - Increased volume of distribution, longer duration of action and increased half-life for fat soluble drugs e.g. diazepam. Plasma concentrations increased.
  - ↓amount of drug bound to albumin results in ↑ active "free drug" e.g. warfarin

Clinical Pharmacology in the Elderly

Pharmacokinetics

What the body does to the drug

- Metabolism
  - Bioavailability may be increased for drugs extensively metabolised in the liver due to loss of first pass metabolism, but not routinely problematic with normal ageing
- Excretion
  - Reduced renal clearance the most significant effect of age
  - Creatinine clearance not a good indicator of renal function → use eGFR
  - Assume all elderly have maximum 2/3rds normal renal function
  - Significant for renally excreted drugs with narrow therapeutic index e.g. lithium
  - Acute illness, pp. dehydration, may lead to rapid decline

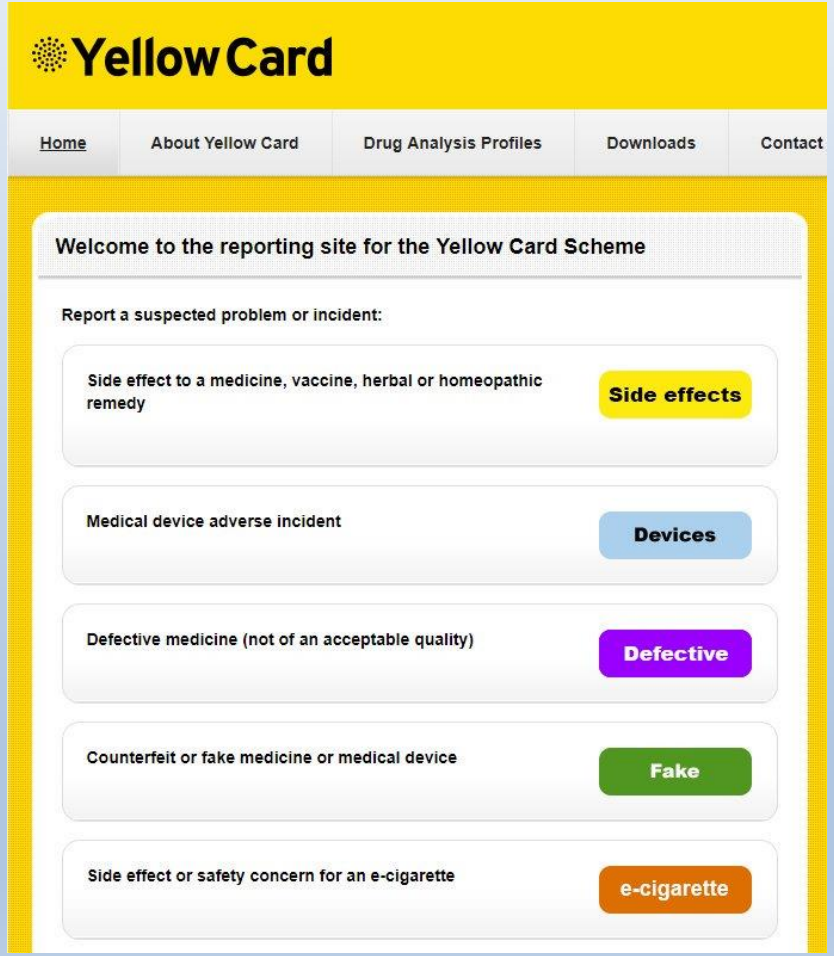
Psychotropic Drugs to avoid in Older Adults

(Reference: Beers Criteria for Potentially Inappropriate Medication Use in Older Adults)

Drug	Rationale
First-generation antihistamines e.g. chlorphenamine, promethazine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/toxicity.
Antiparkinson agents e.g. benztropine, procyclidine, trihexyphenidyl	Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease.
Alpha-adrenoceptor blockers (centrally acting) e.g. methyldopa, clonidine	High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension.

Drug	Rationale
Tricyclic antidepressants e.g. amitriptyline, clomipramine, dosulepin, imipramine, trimipramine	Highly anticholinergic, sedating, and cause orthostatic hypotension
Antipsychotics, first- (conventional) and second- (atypical) generation	Increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia. Avoid use for behavioural problems of dementia unless non-pharmacologic options have failed and patient is threat to self or others.
Benzodiazepines	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults.
“Z” drugs e.g. zopiclone,	As per benzodiazepines

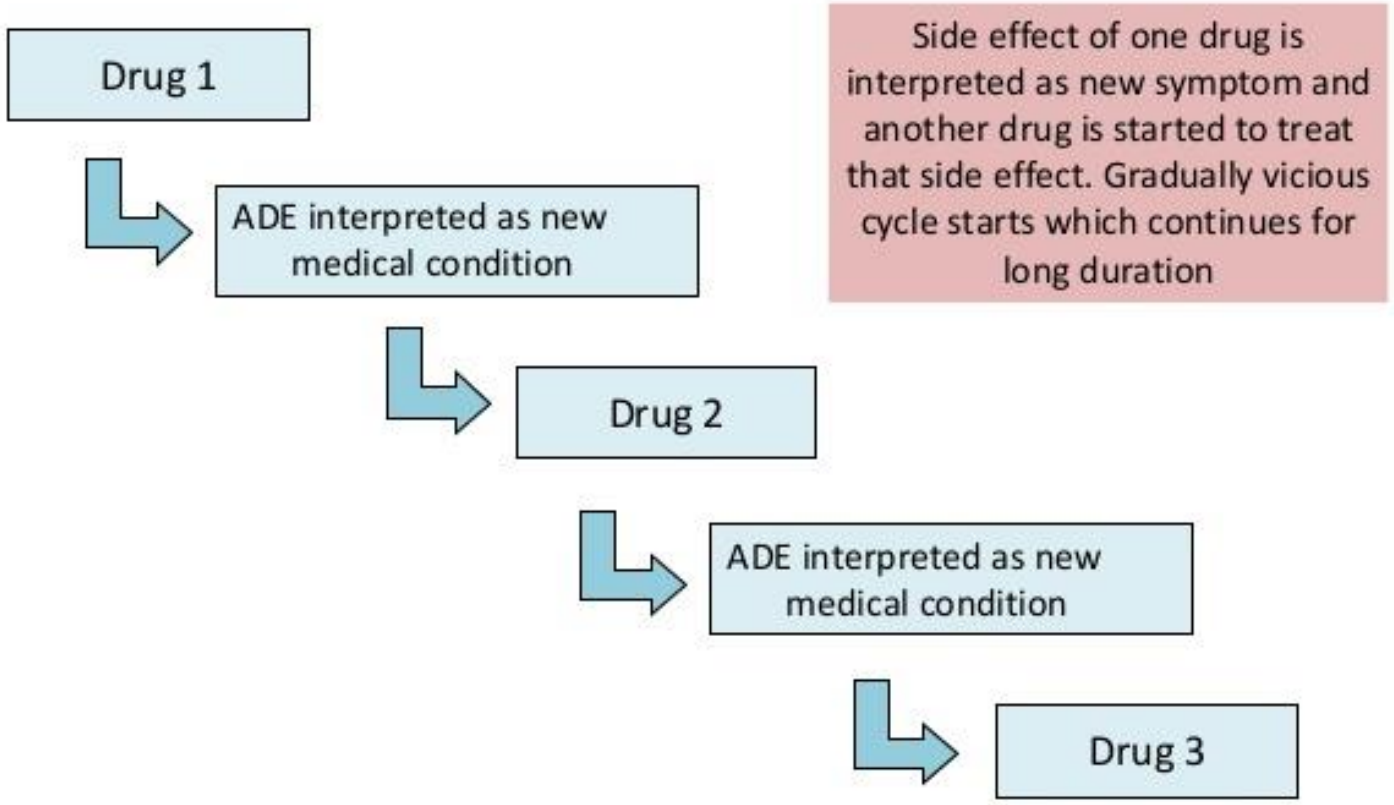
Adverse Drug Reactions



- ADRs in older adults often vague and non-specific
- Confusion may be caused by most drugs
- Constipation, dizziness, dry mouth, blurred vision are common
- Postural hypotension and falls risk with psychotropics and anti-hypertensives
- Consider iatrogenic disease

→ REVIEW OF MEDICATION

Prescribing Cascade



Depression → Tricyclic AD → Constipation → Laxative
Agitation → Antipsychotic → EPSE → Parkinson's medication
Dementia → Cholinesterase inhibitor → Incontinence → anticholinergic
Arthritis → NSAID → ↑BP → Antihypertensive

Anticholinergic Burden

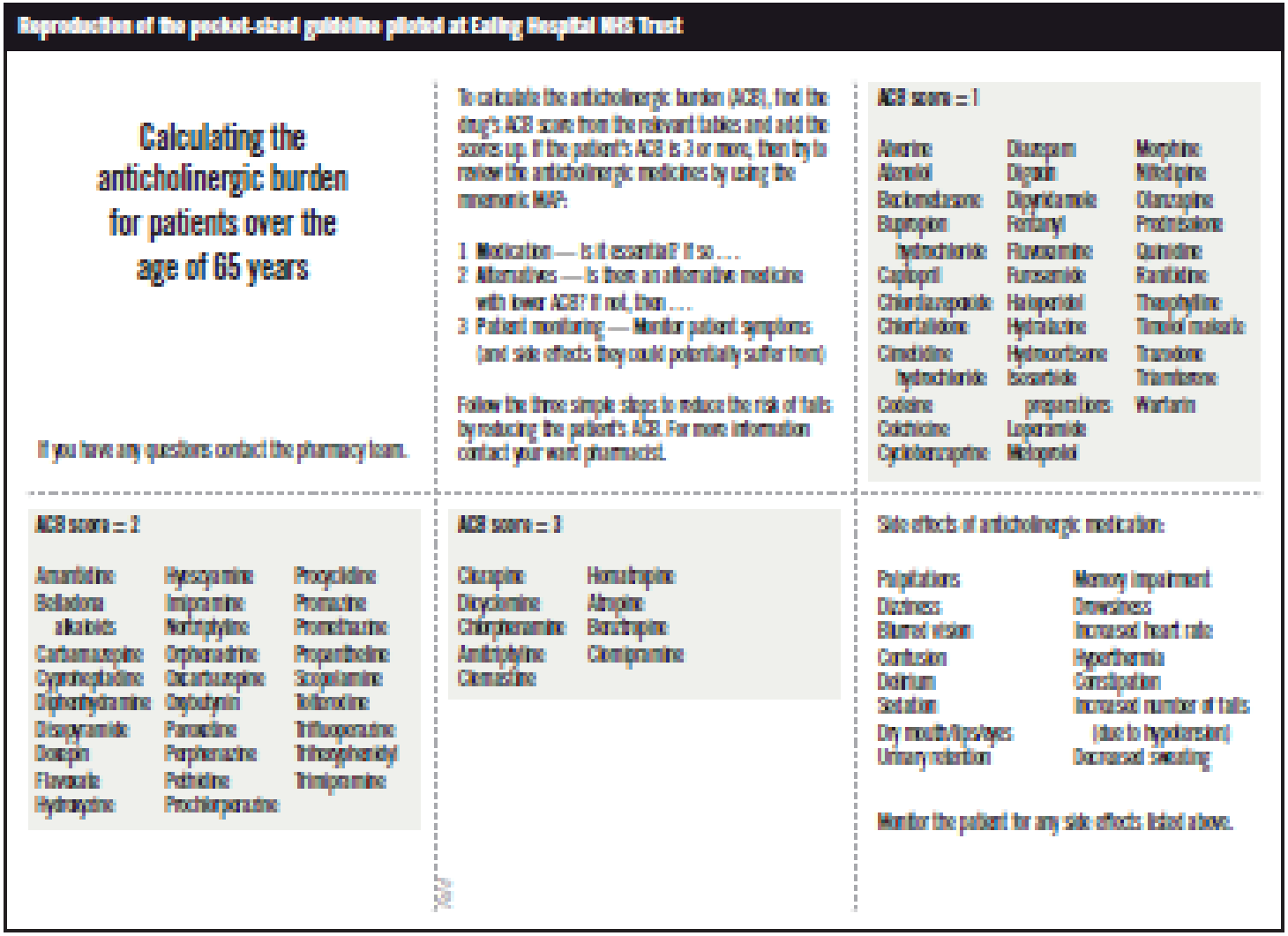
- Anticholinergic drugs (ACD) block muscarinic receptors
  - Causes central adverse effects such as confusion, disorientation, memory impairment, hallucinations and delirium.
- Use of ACD in the elderly is associated with increased risk of cognitive decline, dementia, and early death.

Case control study found association between anticholinergic use and risk of community acquired pneumonia

Further Background Information

- Anticholinergic drugs DIRECTLY OPPOSE the action of acetylcholinesterase inhibitors
  - Concurrent use will reduce the clinical efficacy of the Acetylcholinesterase inhibitors
- For the ACD to cause cognitive impairment it must also be able to penetrate the blood-brain barrier
  - Various risk scales have been developed to evaluate potency. Receptor specificity and subtypes or ability to enter the brain have not always been considered.

Ealing Hospital NHS Trust Anticholinergic Burden pocket guide



Reproduction of the pocket-sized guideline piloted at Ealing Hospital NHS Trust

Calculating the anticholinergic burden for patients over the age of 65 years

If you have any questions contact the pharmacy team.

To calculate the anticholinergic burden (ACB), find the drug's ACB score from the relevant tables and add the scores up. If the patient's ACB is 3 or more, then try to review the anticholinergic medicines by using the mnemonic MAP:

1 Medication — Is it essential? If so ....
2 Alternatives — Is there an alternative medicine with lower ACB? If not, then ....
3 Patient monitoring — Monitor patient symptoms (and side effects they could potentially suffer from)

Follow the three simple steps to reduce the risk of falls by reducing the patient's ACB. For more information contact your ward pharmacist.

ACB score = 1

Alverine
Alimidol
Baclofen/diazepam
Bupropion hydrochloride
Captopril
Chlordiazepoxide
Chlortalidone
Cimetidine hydrochloride
Codeine
Colchicine
Cyproheptadine
Diazepam
Digoxin
Disopyramide
Fentanyl
Fluvoxamine
Furosemide
Haloperidol
Hydralazine
Hydrocortisone
Losartan/sartan preparations
Loperamide
Metoprolol
Morphine
Nifedipine
Olanzapine
Prednisolone
Quinidine
Ranitidine
Theophylline
Timolol maleate/ophthalmic
Tramadol
Triamterene
Warfarin

ACB score = 2

Amantadine
Belladonna alkaloids
Carbamazepine
Cyproheptadine
Diphenhydramine
Disopyramide
Doxepin
Flavoxate
Hydroxyzine
Hyoscyamine
Imipramine
Nortriptyline
Orphenadrine
Oxcarbazepine
Oxybutynin
Paroxetine
Perphenazine
Pethidine
Prochlorperazine
Procyclidine
Promazine
Promethazine
Propantheline
Scopolamine
Tolterodine
Trifluoperazine
Trihexyphenidyl
Trimipramine

ACB score = 3

Clozapine
Dicyclomine
Chlorpheniramine
Amitriptyline
Clomazine
Homatropine
Atropine
Benztropine
Clomipramine

Side effects of anticholinergic medication:

Palpitations
Dizziness
Blurred vision
Confusion
Delirium
Sedation
Dry mouth/lips/eyes
Urinary retention
Memory impairment
Drowsiness
Increased heart rate
Hyperthermia
Constipation
Increased number of falls (due to hypotension)
Decreased sweating

Monitor the patient for any side effects listed above.

Appropriate Prescribing Tools

Screening Tool of Older People's Prescriptions
and
Screening Tool to Alert to Right Treatment

The NO TEARS tool

Need and indication

Open questions

Tests and monitoring

Evidence and guidelines

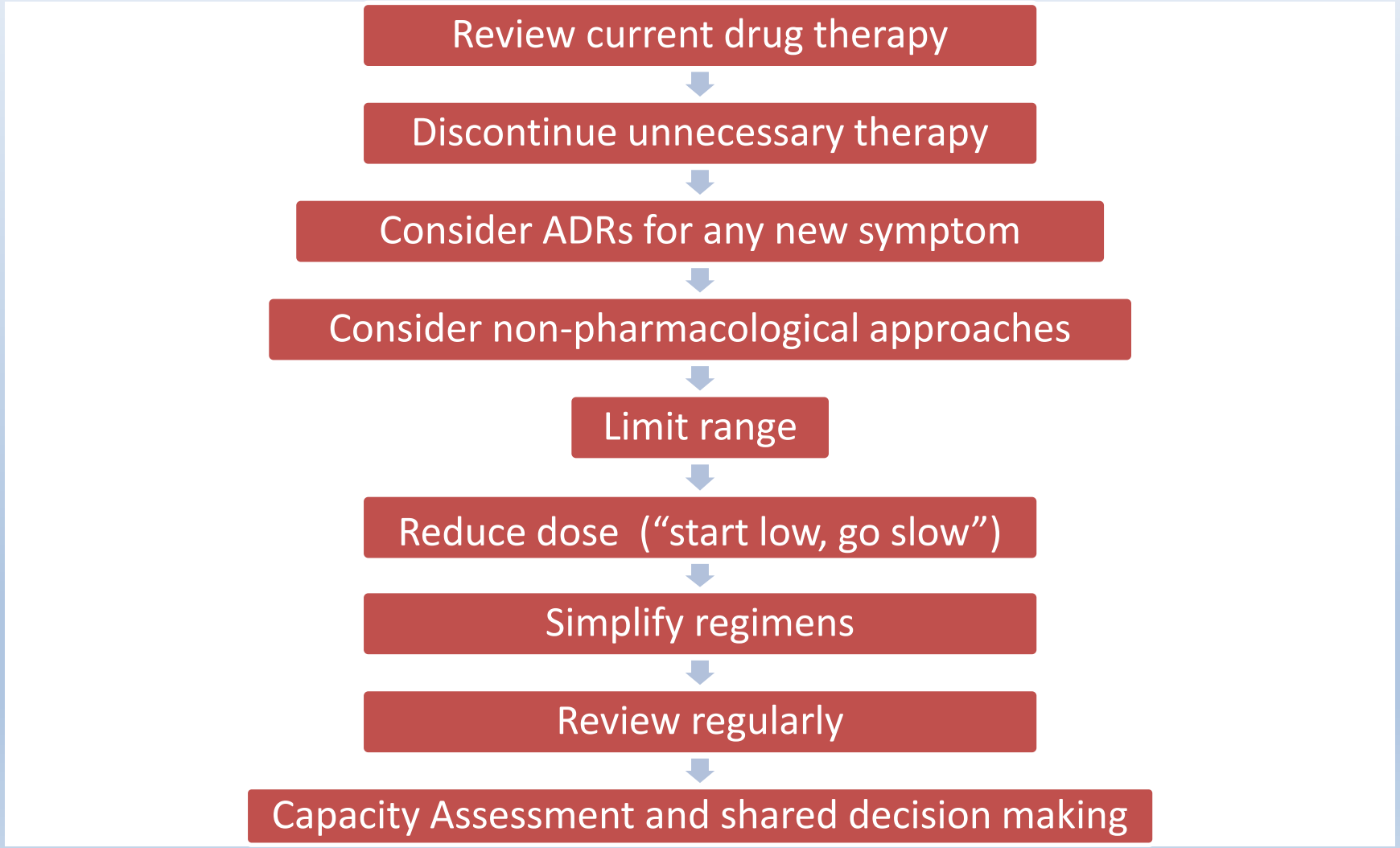
Adverse events

Risk reduction or prevention

Simplification and switches

Lewis T. Using the NO TEARS tool for medication review. 2004. 329:434

Stepwise Approach to Prescribing



Case Study

Sarah is a 77 year old care home resident with a history of Alzheimer's dementia.

Two months ago the GP commenced risperidone 500 micrograms BD for agitation and nocturnal wandering. Two days ago she was seen in A&E following a fall where she sustained a left Colles' fracture. She was treated conservatively and was discharged from the department with tramadol 50mg QDS prn. No underlying cardiac or neurological event was identified as the cause of the fall. Sarah's other medical problems are depression, hypertension, and insomnia.

Her current medications are: amlodipine 5mg OM, zopiclone 7.5mg ON, donepezil 5mg ON, risperidone 500mcg BD, paroxetine 20mg OM, and tramadol 50mg QDS prn

1. List three potential causes for Sarah's fall (exc cardiac or cerebrovascular event)
2. Identify at least two possible drug interactions and potential effects
3. List any changes your would consider making to Sarah's medication regimen (in order of priority)
4. List up to three reasons why the elderly are more prone to ADRs and drug interactions

Psychotropic Prescribing Formulary - Depression

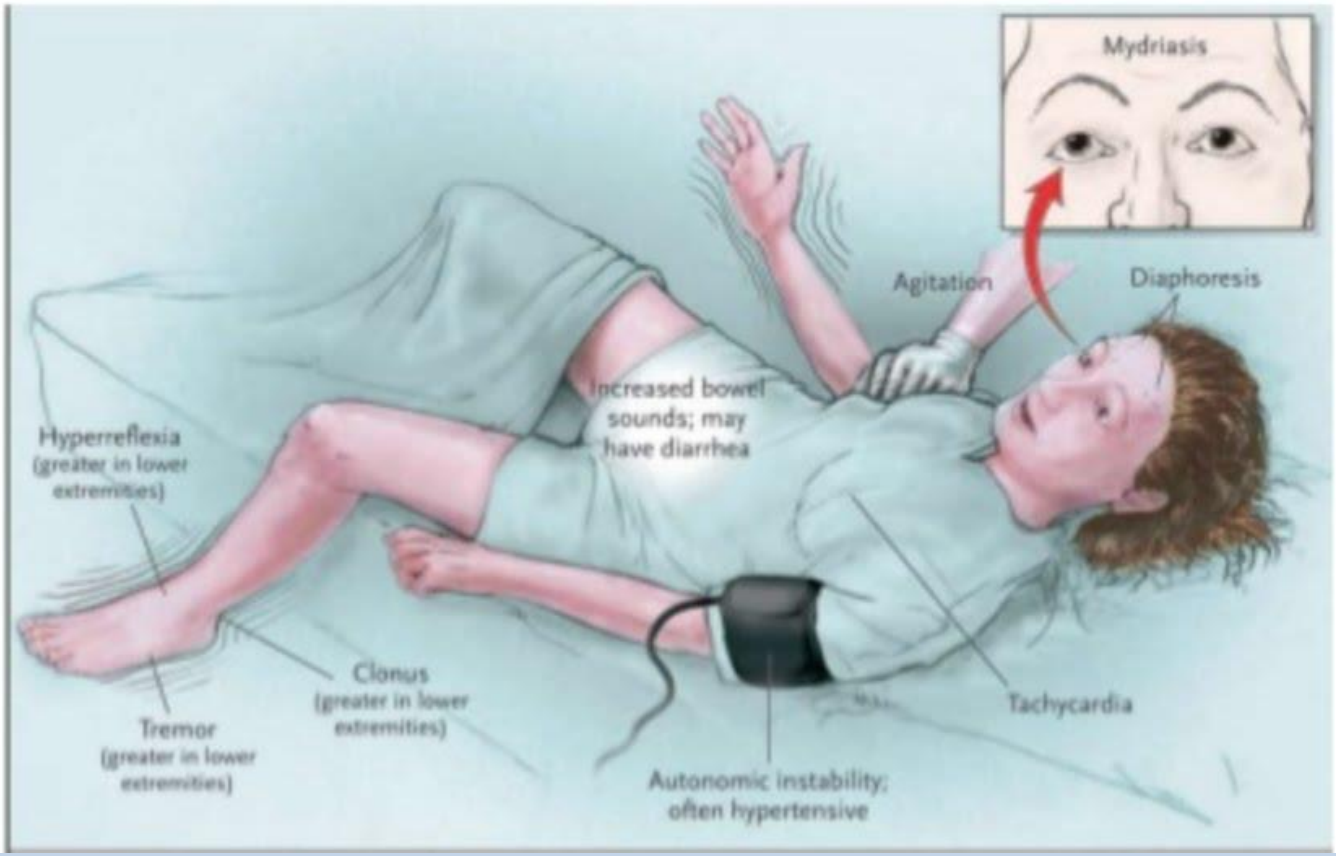
Drug	Drug Class	Starting Dose	Side Effects	Drug Interactions
Citalopram	Selective serotonin re-uptake inhibitor (SSRI)	**Starting** 10mg OM **Maintenance** 10-20mg OM **Maximum** 20mg OM	GI side-effects Headaches Increased risk GI bleed QTc prolongation (citalopram) Contra-indicated: epilepsy	NSAIDs → GI bleed (co-prescribe PPI) Anticoagulants (↑ risk GI bleed) Serotonin syndrome Other drugs that prolong QTc (citalopram)
Sertraline		**Starting** 25-50mg OM **Maintenance** 50-100mg OM **Maximum** 100mg OM (Occasionally 150mg OM)		
Mirtazapine	Noradrenergic and specific serotonergic antidepressant)NaSSA)	**Starting** (7.5mg) 15mg ON **Maintenance** 15-30mg ON **Maximum** 45mg ON	Sedation (histamine inhibition) Weight gain Neutropenia	Serotonin syndrome Warfarin (monitor INR)
Trazodone	Serotonin antagonist and reuptake inhibitor	**Starting** 50mg BD **Maintenance** 100mg OD – 100mg BD **Maximum** 300mg daily	Contra-indicated: arrhythmias and post-MI	
Venlafaxine	Serotonin norepinephrine reuptake inhibitor (SNRI)	**Starting** 37.5mg OM **Maintenance** 37.5mg BD – 75mg BD **Maximum** 112.5mg BD	GI side-effects Hypertension (monitor BP) QTc prolongation Contra-indicated: arrhythmias, uncontrolled hypertension	Serotonin syndrome Drugs that prolong QTc Anticoagulants (↑ risk GI bleed) NSAIDs (↑ risk GI bleed)

Drugs for Depression - Hyponatraemia

- Hyponatraemia is common. Risk factors include: >80 years, female, previous Hx, reduced renal function, low body weight
- Monitor for clinical signs (confusion, nausea, cramps, muscle weakness, oedema, seizures)
- U&Es at baseline, after 2/52, after 4/52 then 3-monthly
- Mirtazapine may be a suitable option in those with a history of hyponatraemia

Serotonin Syndrome

- Cluster of autonomic, motor & mental status changes resulting from excess 5-HT (5-HT_{2A})



<u>Agents</u>
MAO-Is
TCA
SSRIs
opiate analgesics
cough medicines (OTC)
antibiotics
triptans
anti-nausea
herbal products
abused drugs

Refractory Depression

- Augmentation with lithium (aim for serum lithium 0.5 mmol/l)
- Combination antidepressant: e.g. mirtazapine and venlafaxine. (Care →risk of serotonin syndrome)
- Augmentation with antipsychotic (aripiprazole, olanzapine, quetiapine, risperidone)

Side Effects of Lithium and Signs of Toxicity

Side Effects

- Fine Tremor
- Gastrointestinal disturbances
- Polyuria, polydypsia
- Weight gain & oedema
- Hair loss, Acne, Psoriasis
- Hypothyroidism, hyperparathyroidism
- Hyperglycaemia,
- Hypocalcaemia,
- Hypomagnesaemia
- Metallic taste

Toxicity – potentially fatal

- Lithium level > 1.5 mmol/L
- Blurred vision
- Increased gastrointestinal disturbances (anorexia, vomiting, diarrhoea)
- Muscle weakness
- Drowsiness / sluggishness
- Slurred speech
- CNS disturbances (drowsiness, lethargy, ataxia, coarse tremor, impaired co-ordination, dysarthia – unclear pronunciation)
- Risk ↑ with dehydration

Narrow therapeutic index. Aim for 0.5 mmol/L (0.4 – 0.6 mmol/L) in elderly
Levels should be done 12 hours post dose
Prescribing by Brand

Lithium Monitoring

Baseline monitoring

Electrolytes including blood urea, serum creatinine and calcium, T3, T4 and TSH

Full blood count (FBC)

ECG

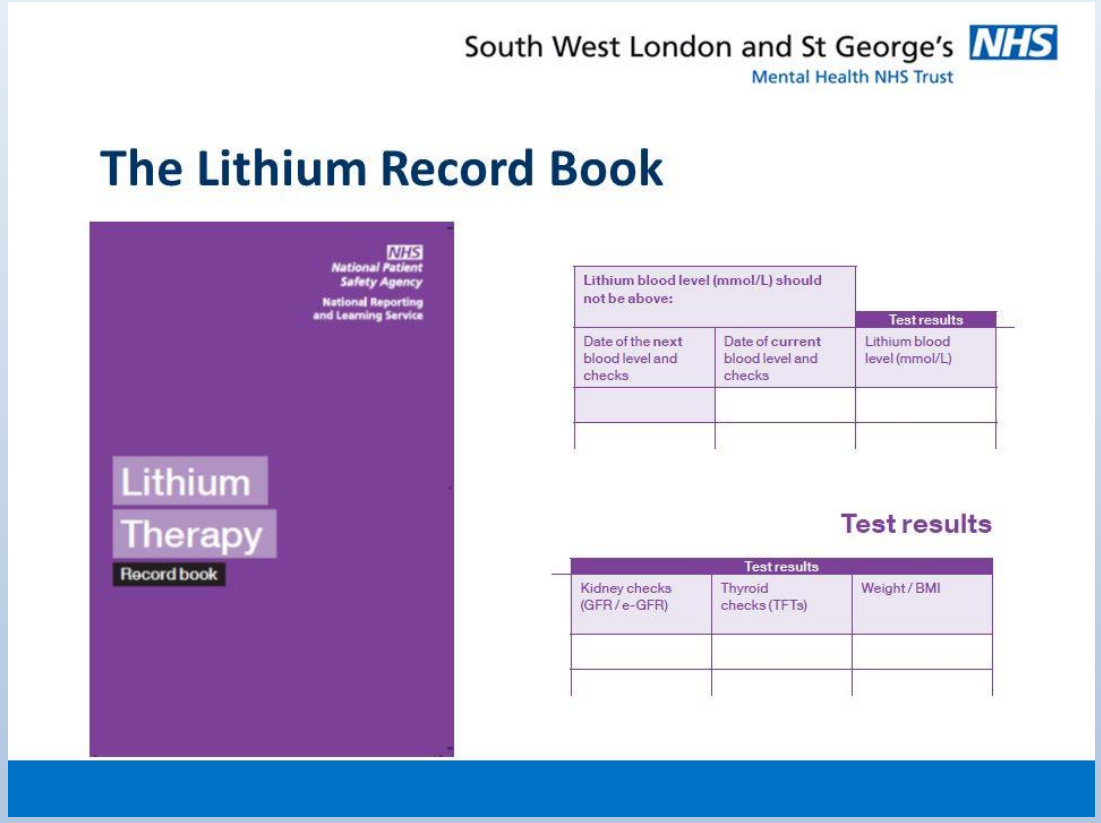
Routine monitoring

Serum lithium (0.4 –0.6mmol/l in elderly) every 3 – 6 months.

Serum creatinine, T3, T4 and TSH,FBC and electrolytes, including calcium;

watch for toxicity signs

warn patients about changes in diet or dehydration.



Lithium – common drug interactions

- **Analgesics:** Excretion of Lithium is reduced by **NSAIDS** e.g. Ibuprofen, Diclofenac, Indomethacin
- **ACE inhibitors** by reducing glomerular perfusion pressure increases re absorption of lithium and hence, toxicity.
- **Diuretics** – Thiazides > loop diuretics. Increased toxicity with medications that cause sodium depletion.
- Neurotoxic effect with carbamazepine, diltiazem
- **Anti Psychotics**: Neurotoxic and increased risk of extra pyramidal side effects but can be used with caution
- **Antidepressants:** increase lithium toxicity with SSRIs, Venlafaxine, and Tricyclics.
- **Antacids:** excretion of lithium is increased by sodium bicarbonate
- Drugs that ↑ **serotonin**, → serotonin syndrome e.g. tramadol, SSRIs, SNRIs, triptans
- Drugs that **prolong the QT interval** e.g. quetiapine, tamoxifen, clarithromycin

Psychotropic Prescribing Formulary - Psychosis

- Antipsychotic common side-effects: postural hypotension, falls, anticholinergic effects and EPSEs
- Review response to treatment and dose regularly. Consider dose reduction by up to 25% every 4 weeks
- Monitoring at baseline, at 3 months, and then annually:
  - BP, pulse, weight, waist circumference
  - Fasting glucose (or HbA1c), U&Es (inc. eGFR), FBC, LFTs, lipids, prolactin
  - ECG (where indicated in SPC, in-patient, or cardiovascular risk)
  - Side-effects and emergence of movement disorders
  - Assessment of nutritional status, diet and level of physical activity.
- Avoid antipsychotics in people with dementia (↑ risk CVA and mortality)

Psychotropic Prescribing Formulary - Psychosis

Drug	Dose
Amisulpride	**Starting** 25-50mg daily **Maintenance** 50-100mg daily **Maximum** 200mg daily (caution > 100mg daily)
Aripiprazole	**Starting** 5mg OM (takes 2 weeks to reach therapeutic blood levels) **Maintenance** 5-15mg OM **Maximum** 20mg OM
Risperidone	**Starting** 500 micrograms once a day **Maintenance** 1mg daily **Maximum** 2mg daily

Clozapine

- Lower doses due to age-related differences in metabolism
- Older adults more at risk of neutropenia
- Slower titration and lower maintenance doses
- Sedation may be profound
- Postural hypotension dose related
- Urinary retention and other anticholinergic side effects

Psychotropic Prescribing Formulary - Dementia

Alzheimer's Disease

- Acetylcholinesterase (AChE)inhibitors (donepezil, galantamine and rivastigmine) licensed for **mild to moderate dementia** in Alzheimer's disease
- Memantine an antagonist at N-methyl-D-aspartate (NMDA) glutamate receptors. Option for **moderate** Alzheimer's Disease when AChE inhibitors not an option, or in **severe** Alzheimer's
- **Combination** AChE inhibitor and memantine to be considered / offered for those with moderate and severe AD

Non-Alzheimer's dementia

- Consult NICE guidance for details of treatment recommendations for non-Alzheimer's dementia

Behavioural and Psychological Symptoms of Dementia (BPSD)

Consider clinical or environmental causes

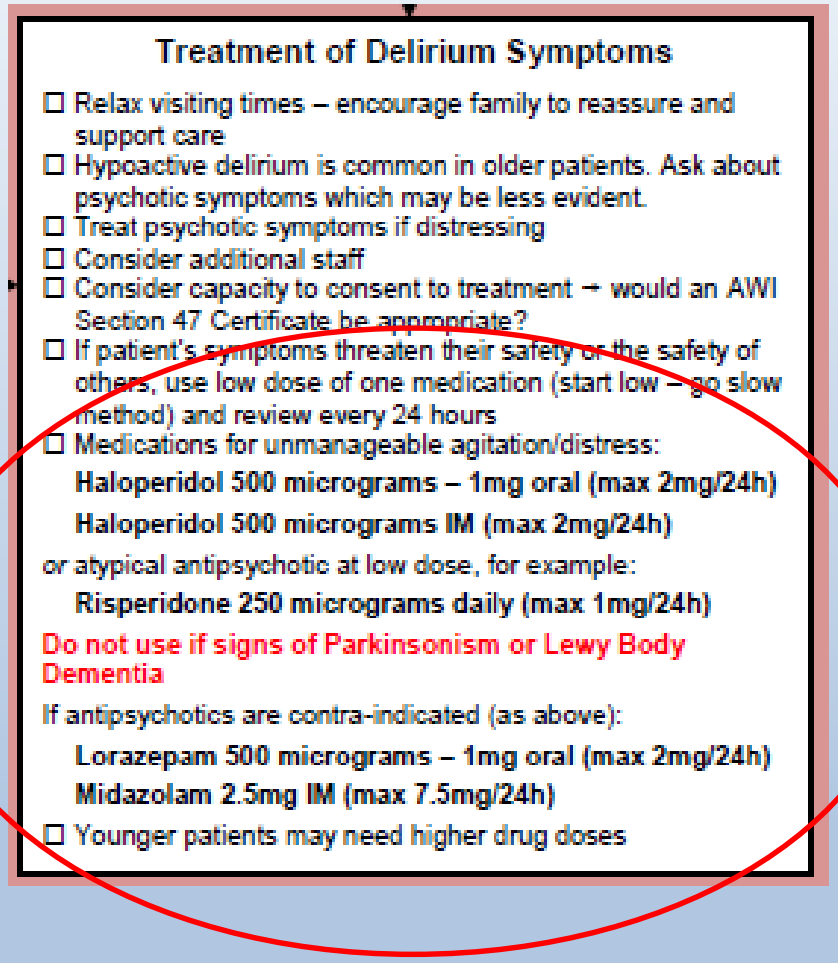
- Check for
  - pain (trial with paracetamol)
  - delirium
  - inappropriate care
- Offer psychosocial and environmental interventions

Offer antipsychotics only if

- individual at risk of harming themselves or others or
- experiencing agitation, hallucinations or delusions that are causing them severe distress.
- (Extreme caution dementia with Lewy bodies or Parkinson's disease dementia)
- Assess ongoing benefit and discontinue if ineffective
- Best evidence for risperidone (licensed for short-term use)

Delirium

- Treat underlying cause, inc possible ADR to medication (*opioids, benzodiazepines, and anticholinergics)*



Treatment of Delirium Symptoms

- ☐ Relax visiting times – encourage family to reassure and support care
- ☐ Hypoactive delirium is common in older patients. Ask about psychotic symptoms which may be less evident.
- ☐ Treat psychotic symptoms if distressing
- ☐ Consider additional staff
- ☐ Consider capacity to consent to treatment → would an AWI Section 47 Certificate be appropriate?
- ☐ If patient's symptoms threaten their safety or the safety of others, use low dose of one medication (start low – go slow method) and review every 24 hours
- ☐ Medications for unmanageable agitation/distress:

Haloperidol 500 micrograms – 1mg oral (max 2mg/24h)

Haloperidol 500 micrograms IM (max 2mg/24h)

or atypical antipsychotic at low dose, for example:

Risperidone 250 micrograms daily (max 1mg/24h)

Do not use if signs of Parkinsonism or Lewy Body Dementia

If antipsychotics are contra-indicated (as above):

Lorazepam 500 micrograms – 1mg oral (max 2mg/24h)

Midazolam 2.5mg IM (max 7.5mg/24h)

- ☐ Younger patients may need higher drug doses

Scottish Delirium Association.
Delirium Management Comprehensive Pathway v2

Psychotropic Use in Old Age Summary (Bazire 2016)

	Lower Risk	Moderate Risk	Higher Risk
Antipsychotics	Lurasidone Risperidone	Amisulpride Aripiprazole Olanzapine Paliperidone Quetiapine Thioxanthenes	Clozapine Haloperidol Phenothiazines Pimozide
Antidepressants	Agomelatine Duloxetine Lofepramine Mirtazapine Moclobemide SSRIs Venlafaxine	MAOIs Mianserin Nortriptyline Reboxetine Trazodone Vortioxetine	Tricyclics (most)
Anxiolytics and hypnotics	Lorazepam Melatonin Oxazepam Zaleplon, Zopiclone	Benzodiazepines (short acting) Temazepam Zolpidem	Benzodiazepines (long acting)
Mood and bipolar		Carbamazepine Lamotrigine Lithium, Olanzapine Quetiapine, Valproate	

Covert Administration

Suggested reading

- Best practice guidance in covert administration of medication

- What legal and pharmaceutical issues should be considered when administering medicines covertly?

Further Reading

- General
  - Maudsley Prescribing Guidelines (current edition) Use of Psychotropic Drugs in the Elderly
  - Bazire Psychotropic Drug Directory (current edition) Drug Use in Old Age
  - NHS England (2017) Mental Health in Older People A Practice Primer
  - NICE (2015) Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes
  - All Wales Medicines Strategy Group (2014) Polypharmacy: Guidance for Prescribing in Frail Adults
  - NHS Cumbria and NECS (2016) Stopp Start Toolkit Supporting Medication Review v2
  - UpToDate (2018) Drug prescribing for older adults

- Affective disorders
  - NICE (2016) Depression in adults: recognition and management [CG90]
  - NICE (2009) Depression in adults with a chronic physical health problem: recognition and management [CG91]
  - NICE (2014) Bipolar disorder: assessment and management [CG185]
- Schizophrenia
  - NICE (2014) Psychosis and schizophrenia in adults: prevention and management [CG 178]
- Dementia
  - NICE (2018) Dementia: assessment, management and support for people living with dementia and their carers [NG97]