Polypharmacy and Deprescribing

Dr Matthew Thomas - Portfolio GP, Swindon TPD

6th April 2022

Who am I?

- Portfolio GP - mixture of salaried, locum and urgent care roles
- I also work for the BSW Training Hub and have recently been appointed as a training programme director for GP trainees in Swindon
- My main clinical job is as a salaried GP at Elm Hayes in Paulton
- I have an interest in clinical pharmacology and polypharmacy

Why am I here?

- I frequently see the iatrogenic harms we inadvertently create through our prescribing
- In primary care we're responsible for the vast bulk of prescribing
- I want to improve how we prescribe - means better compliance, fewer side effects and better health

How do we do this?

- First and foremost through better prescribing of *new* medications - on this front we're making huge progress (eg opioids, benzodiazepines, antibiotics)
- Room for improvement in deprescribing unnecessary or harmful medications
- As pharmacists you're the vanguard of this - as doctors we're often reactively changing medications when harm has already occurred - you have the opportunity to proactively prevent harm in the first place

SMRs

- A great opportunity to reduced iatrogenic harm from inappropriate medications
- Potentially unrealistic ambitions for how many of these can be done leading to huge time pressures on what is a complicated bit of work
- Often very successful and ensuring correct dosing and avoiding interactions
- Aren’t always successful in stopping inappropriate medications

Aims for today

- I want to hear from you! Do you feel supported when doing SMRs? What common challenges do your face? How can things be improved?
- I'll talk a bit about common issues I see and how I approach them
- Time at the end for questions and feedback - this is a learning opportunity for me and I would really value your input

Outline

1. Introduce our ‘soon to be published’ deprescribing guidelines
2. How I approach deprescribing discussions
3. Hypertension in the elderly
4. Benzodiazapines/Z-drugs
5. Anticholinergics
6. Discussion

Deprescribing Guidelines

Deprescribing Guidelines

- Developed jointly with Gayle Wynn and Robin Fackrell
- Aims to be a ‘quick reference’ guide to deprescribing medications in patients living with moderate and severe frailty
- Currently out for feedback pending formal approval by the CCG

CLINICAL FRAILTY SCALE

1 **VERY FIT**

People who are robust, active, energetic and motivated. They tend to exercise regularly and are among the fittest for their age.

2 **FIT**

People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g., seasonally.

3 **MANAGING WELL**

People whose **medical problems are well controlled**, even if occasionally symptomatic, but often are **not regularly active** beyond routine walking.

4 **LIVING WITH VERY MILD FRAILTY**

Previously "vulnerable," this category marks early transition from complete independence. While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up" and/or being tired during the day.

5 **LIVING WITH MILD FRAILTY**

People who often have **more evident slowing**, and need help with **high order instrumental activities of daily living** (finances, transportation, heavy housework). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, medications and begins to restrict light housework.

6 **LIVING WITH MODERATE FRAILTY**

People who need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **LIVING WITH SEVERE FRAILTY**

Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).

8 **LIVING WITH VERY SEVERE FRAILTY**

Completely dependent for personal care and approaching end of life. Typically, they could not recover even from a minor illness.

9 **TERMINALLY ILL**

Approaching the end of life. This category applies to people with a **life expectancy <6 months**, who are **not otherwise living with severe frailty.** (Many terminally ill people can still exercise until very close to death.)

SCORING FRAILTY IN PEOPLE WITH DEMENTIA

The degree of frailty generally corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

In **very severe dementia** they are often bedfast. Many are virtually mute.

DALHOUSIE UNIVERSITY

Rockwood K et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–495.

- **Mild frailty** (Rockwood 3-4): Needing help with ‘high order instrumental activities of daily living’ - finances, shopping, etc
- **Moderate frailty** (Rockwood 5-6): Needing help with personal care
- **Severe frailty** (Rockwood 7-9): Dependent for personal care

Prescribing Guidance for Moderately to Severely Frail Patients

Severe frailty (Rockwood score 7-9): dependent for personal care. **Moderate** frailty (Rockwood score 5-6): need help with personal care.
If only **mild** frailty (Rockwood score 3-4) continue usual prescribing

Deprescribing algorithms for specific drugs and further information in PrescQIPP IMPACT tool, available here: https://prescribing.bswccg.nhs.uk/?wpdmdl=873

DIABETES Code as moderate or severe frailty for QOF		
Moderate Frailty	Aims	Control of symptoms. Avoid HbA1c <60. QOF HbA1c target: <75
	Actions	Maximum two agents unless for symptom control. Do not restrict diet if low weight or losing weight.
Severe Frailty	Aims	Only aim to prevent symptoms of hyper or hypoglycaemia.
	Actions	Avoid sulphonlyurea (gliclazide) or insulin (in type 2 DM). Watch for falling weight. Review after move to care home: potential increased medication compliance & change in diet

HYPERTENSION Always measure lying and standing in >75yrs. Review after a fall.		
Moderate Frailty	Aims	BP <160/100 **and** no postural drop
	Actions	Avoid alpha blockers and thiazides
Severe Frailty	Aims	No BP target
	Actions	Stop anti-hypertensives

CHOLESTEROL REDUCTION		
Moderate Frailty	Aims	Primary prevention reduces CV risk if <75 yrs (no risk factors) or if <85 yrs with risk factors (particularly diabetes).
	Actions	If for primary prevention and not diabetic then stop Rx. If for secondary prevention (CV/stroke/PVD) or diabetic - continue.
Severe Frailty	Aims	No added value in the severely frail.
	Actions	Stop cholesterol drugs regardless of indication.

ANGINA Refer/discuss if uncontrolled on 2 agents or first line treatments not tolerated		
Moderate Frailty	Aims	Usually fewer symptoms as mobility decreases.
	Actions	If asymptomatic or falling/hypotensive stop one drug at a time. Usually ISMN or calcium channel blocker first to stop. Usually continue aspirin and statin.
Severe Frailty	Aims	Reduce & stop angina drugs; symptoms less likely if inactive/immobile.
	Actions	Stop aspirin and statin (NNT to prevent ischaemic event 250/yr, and no sig reduction in mortality). Stop angina drugs if asymptomatic.

DEMENTIA Consider referral to RICE/Old age psychiatry		
Moderate Frailty	Aims	Relieve symptoms, slow progression. Advanced care plans agreed & documented.
	Actions	Continue dementia drugs if benefit - only taper/stop if no benefit. Taper & stop antipsychotics after 12 weeks if only for dementia and symptoms now settled. Minimise anticholinergic burden (ACB) e.g. antimuscarinics, antihistamine, tricyclics.
Severe Frailty	Aims	Minimise medication burden.
	Actions	Continue dementia drugs if benefit to behavioural symptoms. Stop if unable to take e.g. unreliable swallow. Minimise other drugs to reduce risk of delirium.

HEART FAILURE If normal NTpro-BNP consider other causes of symptoms		
Moderate Frailty	Aims	Symptom control & avoidance of hospital admission. Optimise Rx with loop diuretic (bumetanide has lowest ACB score) + ACEi/ARB + β blocker. NNT 15 to prevent one death/year.
	Actions	In confirmed HF, continue treatment as advised by specialist. Involve Community HF service. If not confirmed HF, consider titrating down diuretics & consider alternative causes of oedema eg dependency, Ca channel blocker.
Severe Frailty	Aims	Continue Rx to reduce risk of terminal CCF.
	Actions	Manage symptoms, less concern regarding renal function. Continue ACE & diuretic even where BP is low, as long as not dizzy or syncope. Furosemide in syringe driver is an option at end of life.

ANALGESIA Usually not to exceed: Morphine 60mg bd; Fentanyl 25 mcg patch		
Moderate Frailty	Aims	Use lowest effective dose of analgesia - significant risk of side effects e.g. gabapentinoids & falls. Stop if cause of pain resolved e.g. post joint replacement in OA.
	Actions	Avoid amitriptyline as highly anticholinergic. Co-prescribe laxatives with opiates: stimulant + softener. Taper opioids when stopping e.g. 10% every 1-2 weeks. Avoid NSAID if possible, if no other option & eGFR >30: 2 weeks max, plus gastroprotection.
Severe Frailty	Aims	Titrate down analgesia to lowest effective dose and stop if able.
	Actions	Titrate down doses with weight loss. Titrate all drugs down if delirium. Consider pain or constipation as a cause of delirium.

OVER ACTIVE BLADDER		
Moderate Frailty	Aims	Avoid anticholinergic OAB drugs - all have ACB score = 3. 2 year mortality 20% with total ACB score ≥4 vs 7% with ACB score 0.
	Actions	If drug treatment needed use mirabegron. Refer for continence support. Stop anticholinergics.
Severe Frailty	Aims	Review need for any OAB drug.
	Actions	Avoid/stop drug treatment if significant functional or cognitive impairment; incontinent; catheterised; immobile.

OSTEOPOROSIS		
Moderate Frailty	Aims	Prevent fracture: bisphosphonate NNT 40-90 to prevent one fracture over 1-3 years.
	Actions	Continue bisphosphonate if on oral steroids. Review at 5yrs, consider extending to 10yrs if >75yrs or previous NOF/vertebral #.
Severe Frailty	Aims	No benefit if life expectancy <1yr or immobile.
	Actions	Stop bisphosphonates.

Deprescribing Discussions

Deprescribing in SMRs

- Understandably difficult to stop medication started by another doctor - GPs often worry about this too
- We worry more about causing harm through action than through inaction
- Patients may be resistant to pharmacists changing their medications - often poor understanding of your expertise
- Can be intimidating when there is a long list of medications

My approach

- First scan through the medications - do they look appropriate? *Appropriate* polypharmacy isn't necessarily harmful
- General statement to start - 'you seem to be taking a lot of tablets - how are you getting on with them?'
- If you think a medicine should be stopped explain why - ultimately it's the patient's choice (unless clear risk of harm that would necessitate immediate cessation)
- Likewise identify medications that they patient should definitely continue - eg aspirin/statin/ACE-I/beta blocker following MI
- Offer a trial and follow up after a few weeks to review
- If on high doses (eg amitriptyline or gabapentinoids) wean and review

Hypertension in the Elderly

Evidence based guidelines for prescribing in the moderately/severely frail

That list in full!

- Bisphosphonates: NICE CKS for Multimorbidity
- Er…
- That's it

The NEW ENGLAND JOURNAL of MEDICINE

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Treatment of Hypertension in Patients 80 Years of Age or Older

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ABSTRACT

of whom 84.5% were receiving antihypertensive medication, reported a shorter survival for those with systolic blood pressure levels below 140 mm Hg, even after adjustment for known predictors of death.[10] Randomized controlled trials involving older adults either have excluded those 80 years of age or older[11,12] or have recruited too few to show an advantage of treatment.[13-16] A meta-analysis of results regarding the treatment of hypertension specifically in this age group suggested that the benefit — a 36% reduction in the risk of stroke — might be offset by possible adverse effects, given a nearly significant increase, by 14%, in the risk of death from any cause (P=0.05).[17] These positive results were not robust, since addition of data from just one hypothetical, properly designed trial that showed no treatment effect would render the results not significant.

The results of the pilot study for the Hypertension in the Very Elderly Trial (HYVET)[18] were consistent with those from the meta-analysis. Both results suggest that treatment for hypertension was associated with a reduction in stroke but also a possible increase in death from any cause, such that for each stroke prevented, there was one

who were at Imperial College London. The interim analyses were performed by, and the final analysis verified by, an academic author, independently of Imperial College London. All the authors contributed to the writing of the manuscript and the lead authors vouch for the completeness and accuracy of the results.

Patients had to be 80 years of age or older (confirmed by national documentation) with persistent hypertension (defined as a sustained systolic blood pressure of 160 mm Hg). Exclusion criteria included a contraindication to use of the trial medications, accelerated hypertension, secondary hypertension, hemorrhagic stroke in the previous 6 months, heart failure requiring treatment with antihypertensive medication, a serum creatinine level greater than 150 μmol per liter (1.7 mg per deciliter), a serum potassium level of less than 3.5 mmol per liter or more than 5.5 mmol per liter, gout, a diagnosis of clinical dementia, and a requirement of nursing care.

Patients were instructed to stop all antihypertensive treatment and to take a single placebo tablet daily for at least 2 months and to undergo two blood-pressure measurements during each of

Reviewing antihypertensives

- First priority is to avoid postural drop - over 80 years old need a lying and standing BP
- Likewise if you have a home BP diary don't just look at the average - consider how low the BP is dropping
- Far more harm to be caused from a fall - but consider the patient's degree of frailty
- First priority is stop alpha blockers (doxazosin), thiazides (bendroflumethiazide/indapamide)
- Atenolol is mildly anticholinergic and may be a good target for cessation
- Watch out for CCB induced oedema - may be able to switch amlodipine to lercanidipine

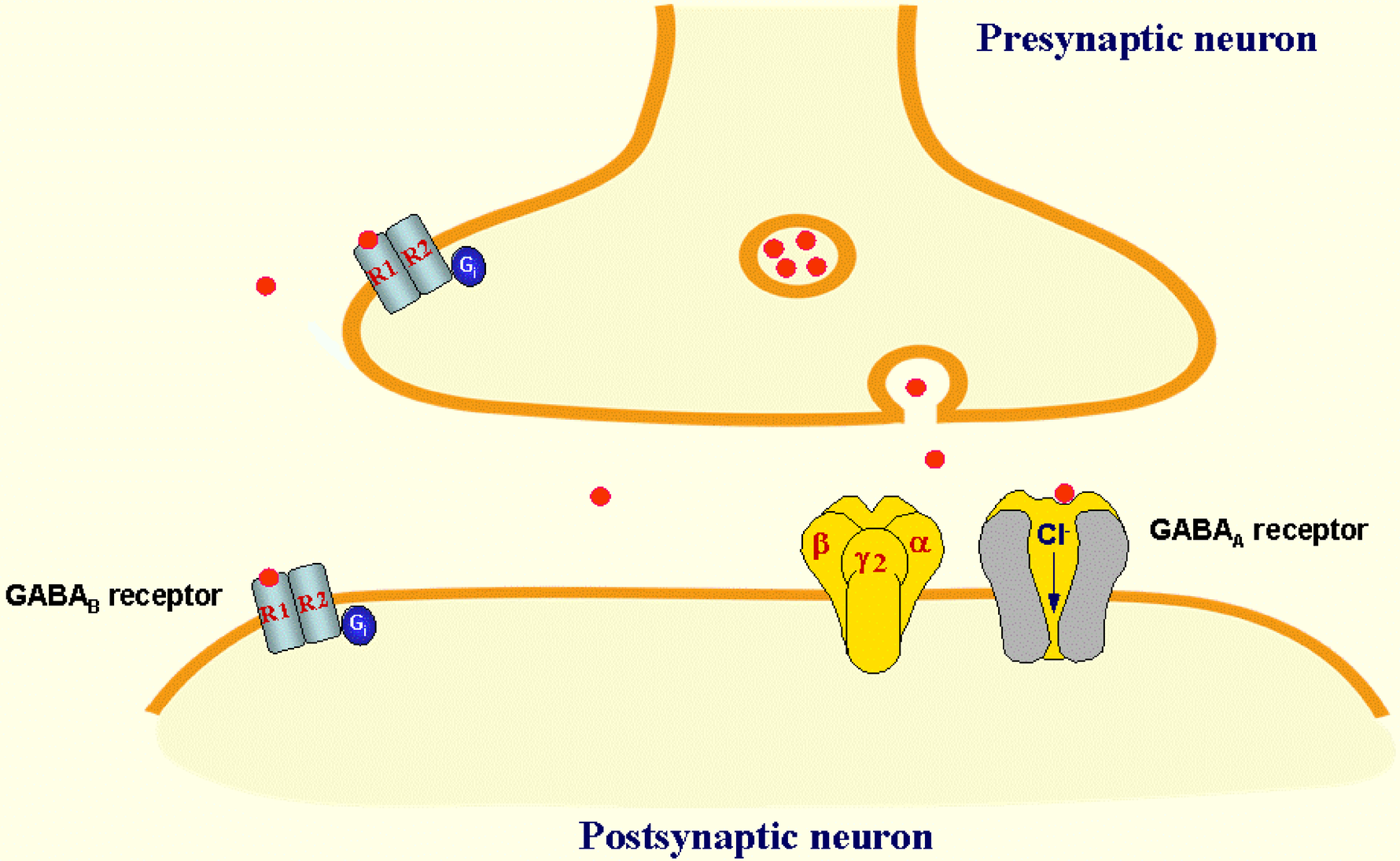
Reviewing antihypertensives

- If changing medications always offer a review
- May need an honest risk/benefit discussion with the patient
- Some elderly patients have incredibly resistant hypertension - most likely due to poor vessel compliance

Benzodiazepines/Z-drugs

Benzodiazepine/Z-drug Pharmacology

- Different drugs but act in a similar manner
- Work to potentiate the action of GABA - an inhibitory neurotransmitter
- Act upon different subunits of the GABA receptor - z-drugs acting particularly on those neurones involved in wakefulness
- Barbituates (no longer used) have a similar effect - they act upon the same receptor to prolong the duration of it's opening - however this can easily lead to overwhelming CNS and respiratory depression


Presynaptic neuron
R1
R2
G_i
$GABA_B$ receptor
R1
R2
G_i
β
γ2
α
Cl^-
$GABA_A$ receptor
Postsynaptic neuron

Z-Drugs and Insomnia

- Increase in total sleep time vs placebo = 25mins
- Time to get to sleep reduced by 10mins
- Mean number of awakenings reduced by 0.63/night

Benzodiazepines/Z-Drugs - Problems

- Long term use leads to reduction in efficacy and negative-feedback induced decline in GABA production - resulting in tolerance and dose escalation
- Simultaneously long lasting enhanced GABA action results in reduced production of excitatory neurotransmitters
- No causative link established between use and dementia but there is a strong association between the two (increased odds of 49-78%)
- Significant increase in falls risk (35-60% during even short term use)
- Also cause anterograde amnesia, disinhibition and delirium, much more so in the elderly

Patient Choice

- One study (Int J Geriatr Psychiatry 1992; 7:89–93) showed that tapering of benzodiazepines in non-demented elderly patients living in residential care did improve memory BUT the patients strongly preferred to continue the medication for its sedative effect despite this
- If someone doesn't want to stop they probably won't
- Some practices have been very proactive about this - mandating patients wean off benzodiazepines
- Different approaches are needed for the young/elderly
- Don't forget to ask about illicit medication use (one patient was taking 150mg (!) zopiclone a night)

Anticholinergics

Anticholinergic Burden(ACB)

Significant increase in:

- Dementia
- Death
- Falls (all types)
- Postural hypotension
- Dry mouth
- Hallucinations/Delirium
- Worsened glaucoma
- Constipation
- Urinary retention

JAMA Internal Medicine | Original Investigation

Anticholinergic Drug Exposure and the Risk of Dementia
A Nested Case-Control Study

Carol A. C. Coupland, PhD; Trevor Hill, MSc; Tom Dening, MD; Richard Morriss, MD;
Michael Moore, MSc; Julia Hippisley-Cox, MD

3 month exposure to anticholinergic medications
increases risk of dementia by 46%

Anticholinergic drugs and risk of dementia: Time for action?

Brian Bell[1] | **Anthony Avery**[1] | **Delia Bishara**[2] | **Carol Coupland**[1] | **Darren Ashcroft**[3] | **Martin Orrell**[4]

Pharmacol Res Perspect. 2021;9:e00793.
https://doi.org/10.1002/prp2.793

utynin satisfies the Bradford Hill criteria to be considered *causative* of Alzheimer's dementia - should we

the principle of fully informed consent - would you consent to a treatment that could potentially *cause* A

https://pubmed.ncbi.nlm.nih.gov/34087056/

ACB Score

- Freely available calculator at acbcalc.com
- Drugs are given a score of 1-3 depending on severity of their effect
- Score is cumulative - the more anticholinergic drugs the greater the impact
- One study in patients >65yrs found over a two year period 20% mortality in patients with an ACB score of 4 compared to 7% in patients with a score of 0[4]

Drugs with an ACB score of 3

Nortriptyline	Chlorpromazine	**Oxybutynin**	**Paroxetine**
Cyclizine	**Tolterodine**	Olanzapine	Dosulepin
Clozapine	**Solifenacin**	Imipramine	**Chlorphenamine (Piriton)**
Trospium	Hyoscine Hydrobromide	Hydroxyzine	
Amitriptyline	Promethazine	Clomipramine	

Drugs with an ACB score of 2

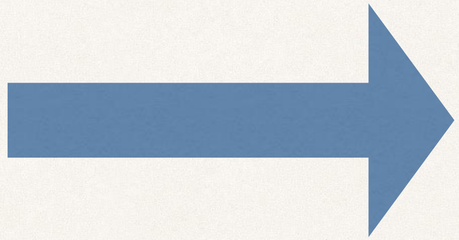
Loratadine	**Loperamide**	Carbamazapine
Sertraline	Cimetidine	Baclofen
Procholorperazine	**Cetirizine**	

Drugs with an ACB score of 1

Diazepam	Levodopa (Sinemet)	Fentanyl	**Furosemide**
Fluoxetine	**Mirtazapine**	Colchicine	**Codeine**
Citalopram	Metoclopramide	Alprazolam	Captopril
Tramadol	**Co-codamol**	**Atenolol**	**Warfarin**
Quetiapine	**Digoxin**	**Venlafaxine**	**Ranitidine**
Prednisolone	**Nifedipine**	Morphine	Mertoprolol
ISMN/ISDN	Hydrocortisone	Haloperidol	Trazodone

Reducing ACB Risk - Antihistamines

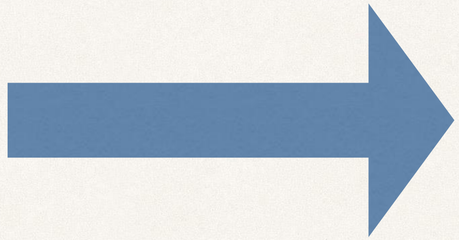
From:
Cetirizine (2)
Lortadine (2)
Piriton (3)



To:
Fexofenadine (0)

Reducing ACB Risk - H2 Antagonists

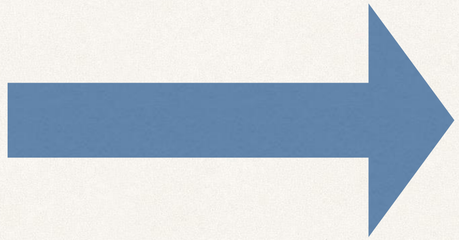
From:
Cimetidine (2)
Ranitidine (1)



To:
PPIs (0)
?famotidine (no data)

Reducing ACB Risk - Diuretics

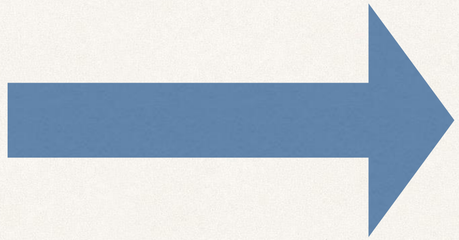
From:
Furosemide (1)



To:
Bumetanide (0)

Reducing ACB Risk - Overactive Bladder

From:
Solifenacin (3)
Oxybutynin (3)
Trospium (3)
Tolterodine (3)



To:
Mirabegron (0)

Any questions?

I want to hear from you!

- What would be most useful for you?
- Would a ‘liaison GP’ be helpful?
- What challenges have you faced?
- If you want to get in touch:

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