

Polypharmacy – a dose of realism

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Declaration of interests

- I have declared that I have no interests

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Definitions: What is polypharmacy?

- “Prescription, administration, or use of more drugs than are clinically indicated”

Or

- “Taking more than three/four long-term medications”
- *Major* polypharmacy - five or more

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Definitions: What is pollypharmacy?



Case 1

Polypharmacy and diabetes

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Justifiable polypharmacy? John, age 65

- Recently found to have type-2 diabetes.
- No CV disease (yet)
- Smoker – 20/day
- BMI 34 kg/m²
- BP 156/94
- HbA1c 7.8%
- Total cholesterol 6.4 mmol/l
- OA both knees – impairs mobility

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John:
What treatment should be considered?

Write down as many options as you can think of!
(see if you can get >10)

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Q: Which of these is most important in reducing CV risk for John (after stop smoking and lifestyle change)?

- 9% 1. Reducing total cholesterol <5mmol/L (QOF)
- 67% 2. Reducing BP<140/80 (NICE target)
- 23% 3. Reducing HbA1c
- 1% 4. Antiplatelet drug

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Comparing interventions:
Collated (crudely) from Clinical Evidence

Handbook page: 137

Primary prevention of CV events or death in patients with diabetes:

	NNT (95% CI)
Tight BP control (8.4yrs)	14 (9 to 35)
Intensive BG therapy (5yrs)	46 (NS)
Intensive BG therapy, metformin (5yrs)	16 (10 to 71)
Simva statin 40mg/day (5yrs)	23 (15 to 48)
Aspirin (5yrs)	16 (12 to 47)
Ramipril (4.5yrs)	39 (21 to 716)
	22 (14 to 49)

(NB these are very rough comparisons)

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Comparing interventions:
Collated (crudely) from Clinical Evidence – including POPADAD and JPAD

Handbook page: 137

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The original “polypill” idea? The LODR
Salim Yusuf. Lancet 2002;360:2-3

Potential cumulative impact of four simple secondary-prevention treatments:

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Intervention	Relative-risk reduction	2-year event rate
No intervention	..	8%
Aspirin	25%	6%
β-blockers	25%	4.5%
Lipid lowering (by 1.5 mmol/L)	30%	3.0%
ACE inhibitors	25%	2.3%

Cumulative relative risk reduction if all four drugs are used is about 75%
But also..... smoking cessation, BP treatment, etc.....

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Let's give our diabetic patients a hand!

Don't turn the hand around

Adapted from Shaughnessy and Gleason, Lending a hand to diabetes. A pocket full of possibilities: "Just-in-Time" information at the point of care. Information Mastery Conference, Cardiff 2005.

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Case 2
Polypharmacy in older people

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Mrs Brown, aged 84

- Remarkably fit for her age. Lives on her own but fully independent. No known CV disease.
 - Takes diclofenac occasionally for OA and omeprazole for dyspepsia.
 - Takes bendroflumethiazide 2.5mg daily – she says for ankle oedema
 - Hypersensitive to aspirin
- Came for a flu jab and noted to have average BP of 164/84 (rechecked several times over a few weeks by the practice nurse)
- The nurse also checked her cholesterol – it is 7.8mmol/L

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Q: You stop her diclofenac but her BP remains high. Would you?

Increase her blood pressure treatment

72%	1. Yes
28%	2. No

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Q: You stop her diclofenac but her BP remains high. Would you?

Give her a statin

27%	1. Yes
73%	2. No

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What does NICE say about treating elderly people with raised BP?




NICE Guideline 34 2006

- Patients over 80 years of age are poorly represented in clinical trials and the effectiveness of treatment is less certain.
- However, it is reasonable to assume that older patients will receive worthwhile benefits from drug treatment, particularly in terms of reduced risk of stroke.
- Offer patients over 80 years of age the same treatment as patients over the age of 55, taking account of co-morbidity and polypharmacy.

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What does NICE say about treating isolated systolic hypertension (ISH)?



NICE Guideline 34 2006

- Patients with ISH received similar benefits from treatment to other patients with hypertension.
- Offer patients with ISH (SBP \geq 160mmHg) the same treatment as patients with both raised SBP and DBP.

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NICE CG67 Lipid Modification: What does NICE say about older people?

- People aged 75 or older should be considered at increased risk of CVD, particularly people who smoke or have raised blood pressure.
- They are likely to benefit from statin treatment.
- Assessment and treatment should be guided by the benefits and risks of treatment, informed preference and comorbidities that may make treatment inappropriate.

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"...many Western governments regard all people aged over 75 as patients"

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The Hypertension in the Very Elderly Trial (HYVET)

Beckett NS, et al. NEJM 2008;358:1887-98.

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- "There have been no conclusive results suggesting benefit in treating patients with hypertension over 80 years of age"
- "HYVET's goal was to evaluate the benefits and risks of providing medical care to very elderly individuals presenting with hypertension"
- 3,845 patients, age >80 years, systolic BP>160mmHg. 12% history of CVD, 7% DM
- Median follow up 1.8yrs
- Target BP 150/80 – indapamide +/- perindopril vs. placebo +/- placebo
- Primary Endpoint: fatal and non-fatal strokes

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HYVET Trial. Outcomes: Main Fatal and Nonfatal End Points in the Intention-to-Treat Population

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	Rate per 1000 Patient-Yr (No. of Events)		Unadjusted Hazard Ratio	p-value
	Indapamide	Placebo	(95% CI)	
	No. (%)			
PRIMARY OUTCOME Fatal/nonfatal stroke	12.4 (51)	17.7 (69)	0.70 (0.49-1.01)	0.06
Death from stroke	6.5 (27)	10.7 (42)	0.61 (0.38-0.99)	0.046
Death from any cause	47.2 (196)	59.6 (235)	0.79 (0.65-0.95)	0.02
Death from non-CV/unknown causes	23.4 (97)	28.9 (114)	0.81 (0.62-1.06)	0.12
Death from CV cause	23.9 (99)	30.7 (121)	0.77 (0.60-1.01)	0.06

BMJ Masterclasses Beckett NS, et al. NEJM 2008;358:1887-98. BMJ Learning

Is it worth treating BP in older people?

Meta-analysis of blood pressure trials for isolated systolic hypertension
Staessan JA et al. Lancet 2000;355:865-872. Handbook page: 136

	Number of patients to treat for 5 years to prevent one event. Reduction in systolic blood pressure approximately 10mmHg.	
	Fatal or non-fatal CV event	95% Confidence Interval
All Patients	26	25-27
Male	18	17-19
Female	38	36-40
Age 60-69	39	36-41
Age >70	19	18-20
No previous CV event	37	35-39
Previous CV event	16	15-17

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Is it worth treating CV risk in older people?

Usually more so.
Where risk is greatest, so is benefit.
The biggest problem may be under-treatment:

- Diabetes
- Hypertension
- Heart failure
- Established CHD
- Depression

It's also worth lifestyle advice.....

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'The elderly' : Prescribing in those over 65
Derived from: Dept. of Health, 2001. Medicines and older people: Implementing medicines-related aspects of the NSF for older people.

- 18% of the population and rising
- Receive **45% of all prescription items**
- 78% of all items are on repeat scripts
- 60% of those over 65 are on regular medications, 80% of those over 75
- 5-17% of admissions for elderly patients relate to **adverse drug reactions**
- Of those over 75, 36% take 4 or more drugs (= **polypharmacy**)
- 50% don't take "as expected" (= **waste?**)
- Nursing home use is considerable

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Case 3
Polypharmacy and ADRs

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Annette is 60. She had breast cancer diagnosed several years ago and takes tamoxifen.

She has been troubled with thoracic spine pain, right hypochondrial pain and is known to have metastatic disease. She recently had a fit – thought to be due to brain metastases. She comes to see you in surgery.

- She has been pain free for several months taking **naproxen** and **paracetamol** but the pain is now bad
- She has a burning discomfort in her right arm and it feels numb
- She is also taking **tramadol**
- She is depressed and takes **fluoxetine**
- She has developed congestive heart failure and is on **furosemide** and **lisinopril**, she remains SOB
- *She has dyspepsia, as well*

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List potential medication problems in this case

[If you identify less than 4, you're not really trying!]

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Interactions/ADRs: Did you identify the following?

- SSRI and tramadol? – seizure threshold
- SSRI and tramadol – 5-HT syndrome
- SSRI and NSAID? – bleeding
- NSAID and ACEI? – nephrotoxicity
- Furosemide and NSAID? – fluid retention, counteraction

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Q: You urgently arrange assessment by the palliative care team. In the meantime what is the **priority medication intervention?**

32%	1. Stop NSAID
39%	2. Start morphine
7%	3. Stop fluoxetine
10%	4. Start proton pump inhibitor
12%	5. Start gabapentin

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Back-of-the-envelope calculation for NSAID ADRs
 Bandler 2000; Number 79: 6-8.

Event due to NSAID	Estimated Number of Cases per year per PCT
Acute renal failure	10
Upper GI bleed	18
Congestive heart failure	22

Information based on an average PCT of 100,000 patients where 3,800 over '65s take NSAIDs

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Drug Safety Update Volume 2, Issue 7 February 2009 from MHRA and CHM

- ..some increase in thrombotic cardiovascular risk may apply to all NSAIDs users, irrespective of their baseline risk, and not only to chronic users.
- The absolute increase in risk for 'healthy' users is very low. Current advice remains that patients should use the lowest effective dose and the shortest duration of treatment necessary to control symptoms.
- Overall evidence continues to indicate that naproxen is associated with a lower thrombotic risk than coxibs.
- For ibuprofen, no significant increase in risk has been identified for doses of up to 1200 mg daily

<http://www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/CON038625>

The real world

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Prescribing, diabetes and the real world

- A 64-year-old lady comes to the annual diabetes review clinic
- She is blind in her left eye
- Her HbA1c is 8.6%
- BP is 177/73 mmHg
- Serum cholesterol is 7.3 mmol/L

What medication should she be on?

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According to the medical notes she is on the following treatment:

- Aspirin 150mg daily
- Gliclazide 160mg twice daily
- Metformin 850mg three times daily
- Ramipril 5mg daily
- Simvastatin 80mg daily
- Diclofenac 75mg SR twice daily
- Co-proxamol 2 prn
- Clobazam 10mg three times daily

How come she is so poorly controlled?

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Because she does this! She insisted that she took 7 tablets from the bottle daily



BMJ Masterclasses Pills in the bottle as produced by the patient BMJ Learning

But which ones? The answer to polypharmacy – pick'n mix!



Figure 1b. The combination of tablets

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SUMMARY:

Good prescribing practice and polypharmacy

Handbook page: 134

- Polypharmacy should never be thoughtless.
- Within reason, establish the diagnosis rather than treat symptoms.
- Promote patient and carer understanding of prescribed drugs. Establish concordance.
- Try to substitute rather than add to medication regimes.
- Think of introduced drugs as a trial: Do not forget to stop treatment that is unnecessary or ineffective.
- Combination products may seem like a good idea but can add to the complexity with little room for titration of individual constituents.
- Anticipate interactions and be alert to side-effects.
- **Remember** to harness the 4 Ps: prompts, plans, partners, pharmacists

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