Managing Polypharmacy: Thinking outside the box

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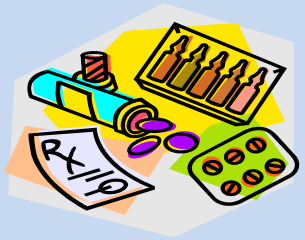
NHS Highland



Disclosure /Conflict of Interest

- No financial Interests to disclose

Questions

- Increasing age is the main driver for increasing polypharmacy in Europe
  - TRUE/ FALSE

- Adding Clopidogrel to Warfarin doubles bleeding rate
  - TRUE/FALSE

What we are going do

- Clinical Aspects of Polypharmacy Management [M Wilson]
  - Important concepts in considering polypharmacy
  - Clinical Highlights
  - Worked Example case
  - Question and answer

- Strategic Solutions and Role of the Pharmacist [C Morrison]
  - Building clinical concepts into practical management
  - The centrality of the pharmacist role in managing polypharmacy
  - Question and answer

Disclaimers

- Stopping drugs is **not** the primary goal

- Thinking openly and carefully is the goal

What is Polypharmacy

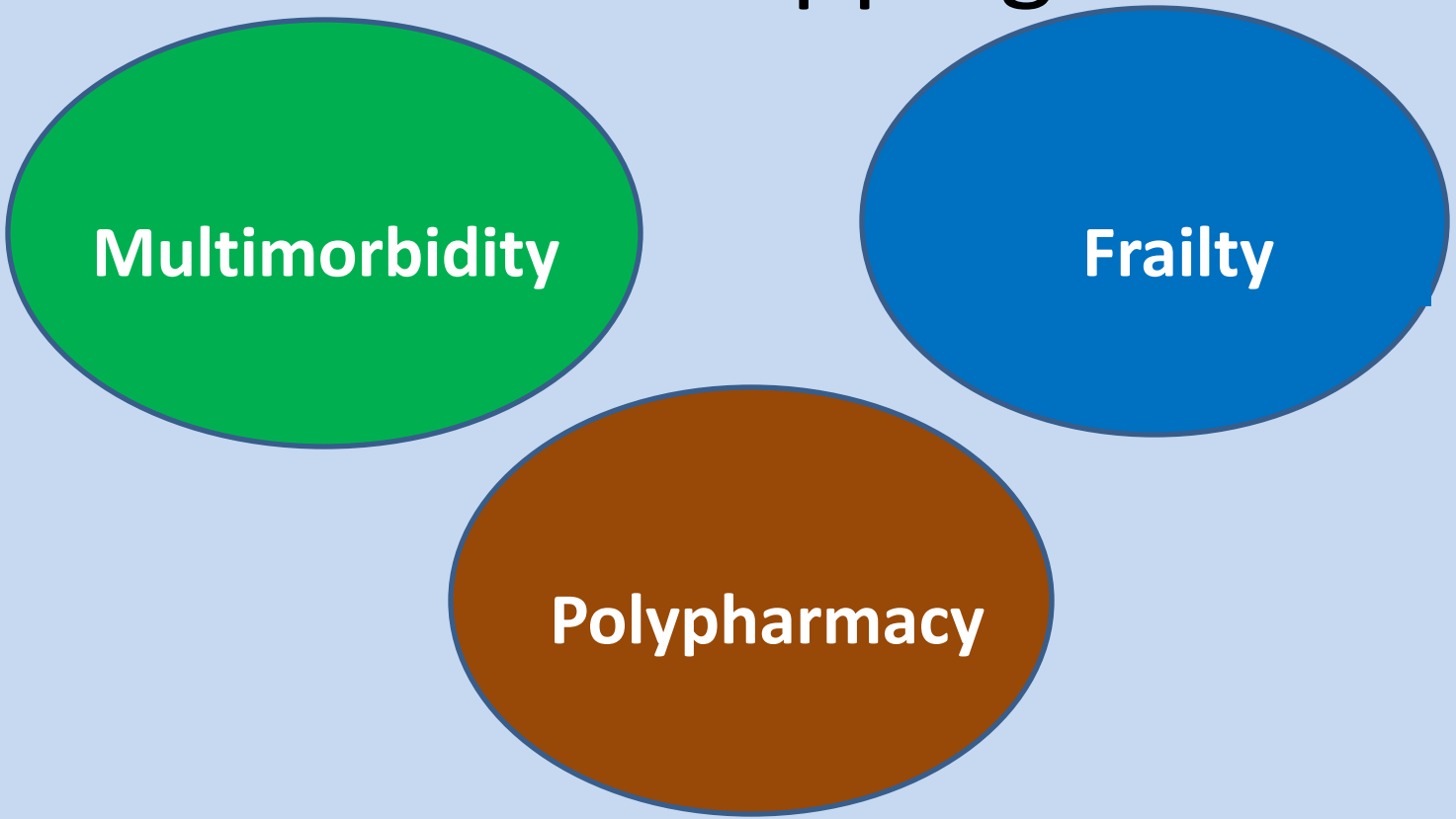
- >4
- >10
- ???
- More drugs than you need taking in to account
  - Side effects
  - Time to Benefit
  - Adherence
  - ++++++

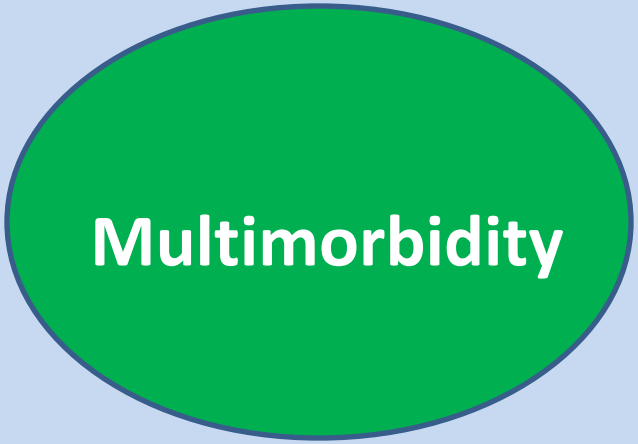
Key Concepts

- Frailty
  - a decreased ability to withstand illness without loss of function

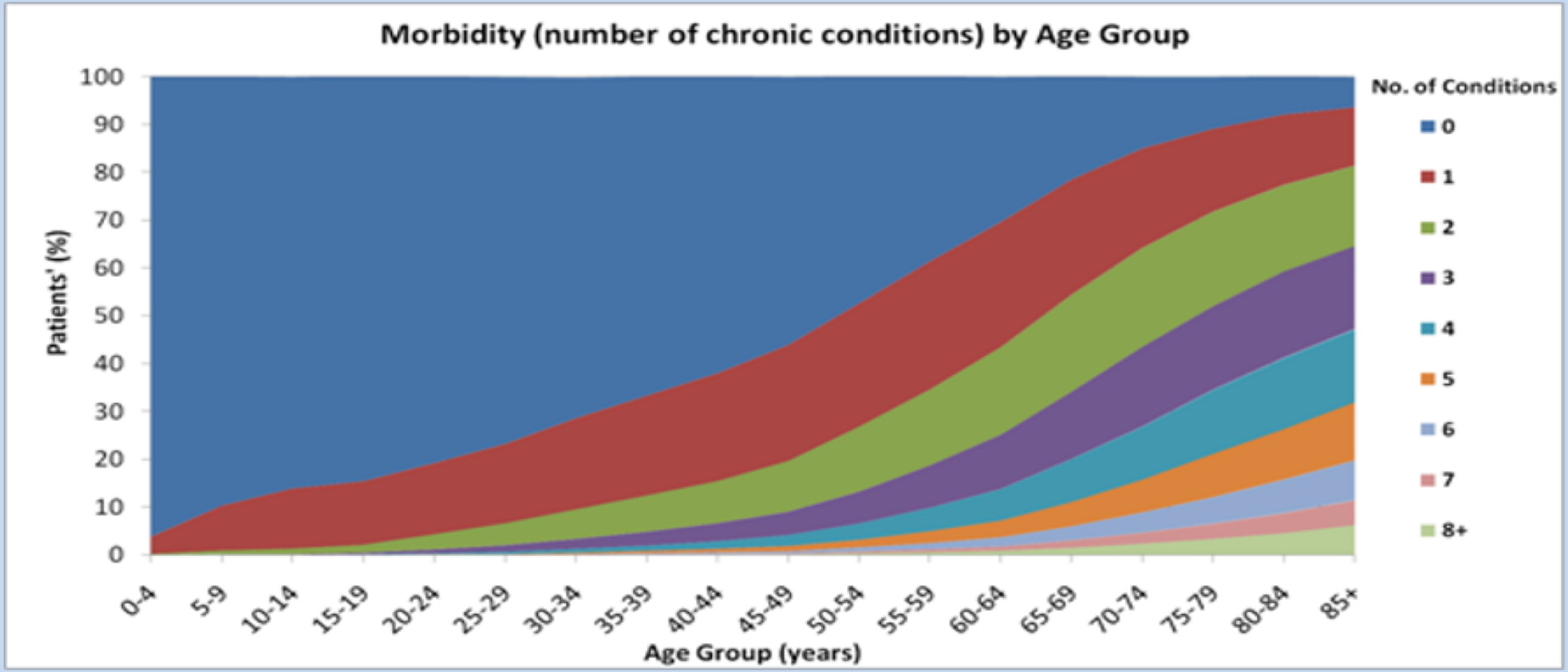
- Age is next to useless

Three overlapping areas

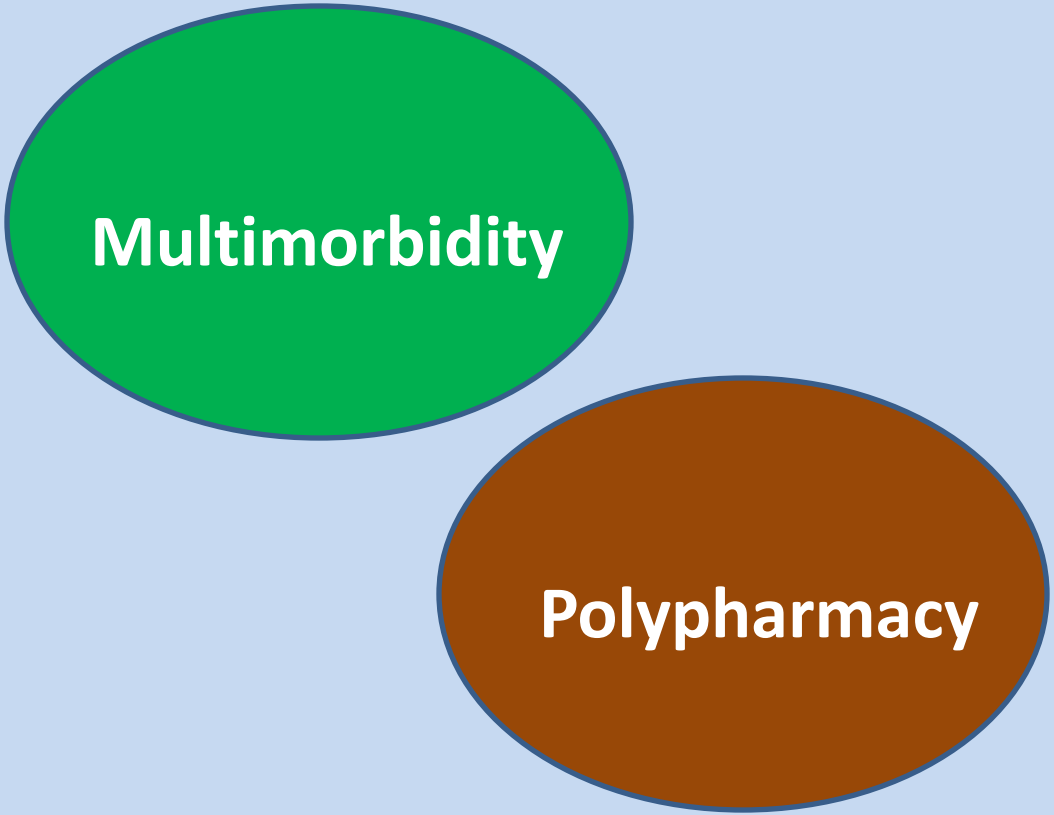


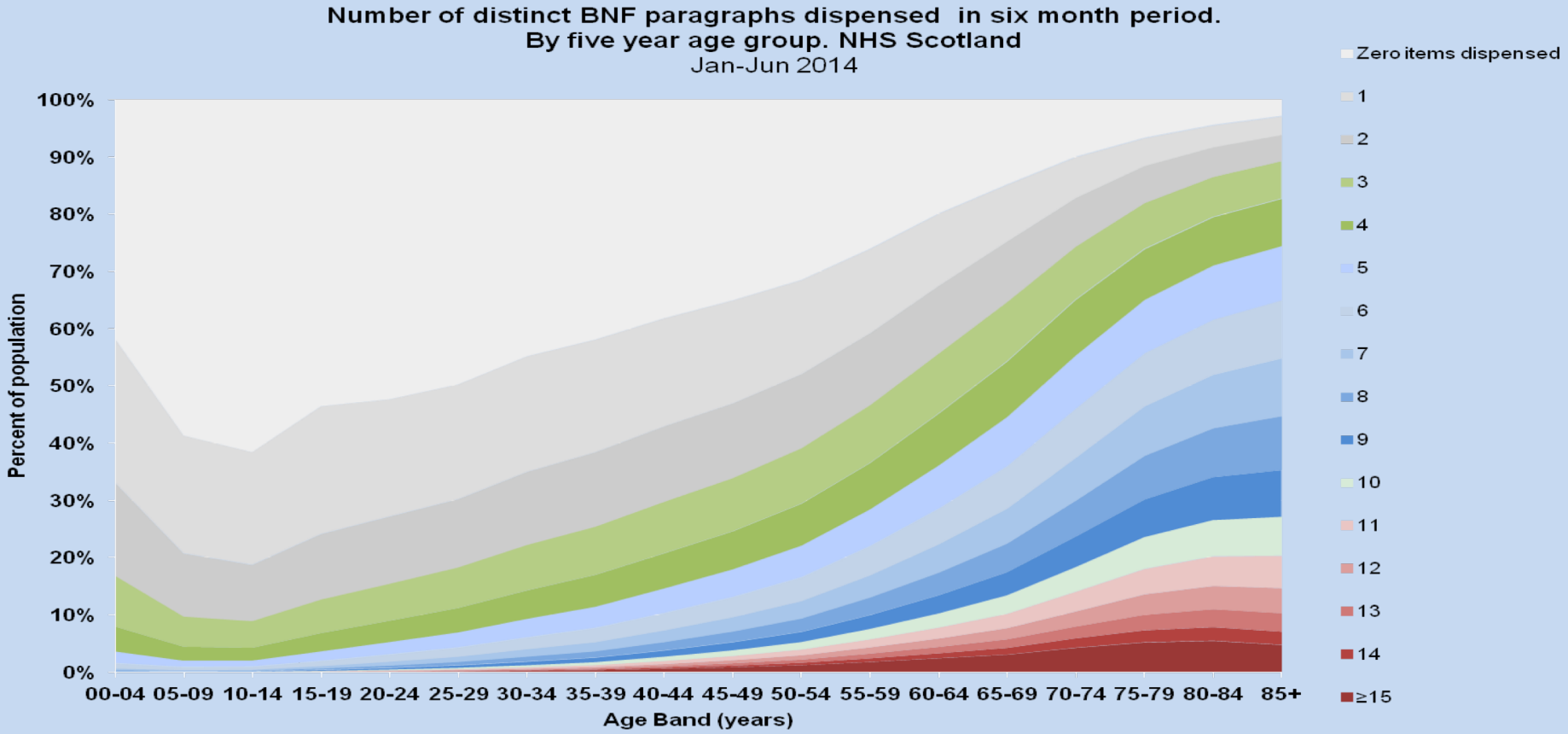

Multimorbidity

Multimorbidity is common



Barnett K, Mercer SW, Norbury M et al. Epidemiology of multi-morbidity and implications for healthcare, research, and medical education: a cross sectional study. The Lancet 2012:380:37-43


Multimorbidity
Polypharmacy


Number of distinct BNF paragraphs dispensed in six month period.
By five year age group. NHS Scotland
Jan-Jun 2014
Percent of population
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
00-04 05-09 10-14 15-19 20-24 25-29 30-34 35-39 40-44 45-49 50-54 55-59 60-64 65-69 70-74 75-79 80-84 85+
Age Band (years)
Zero items dispensed
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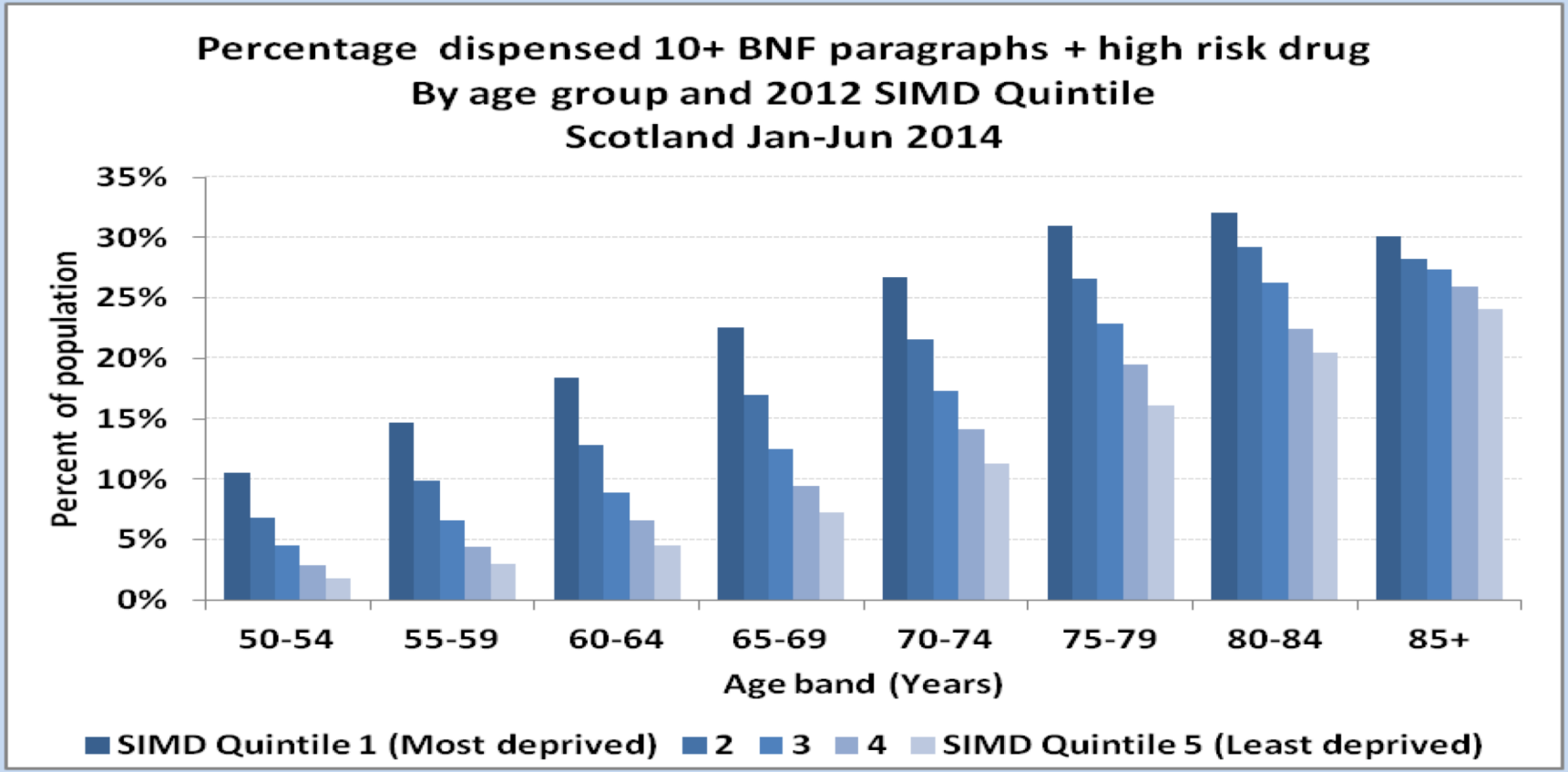
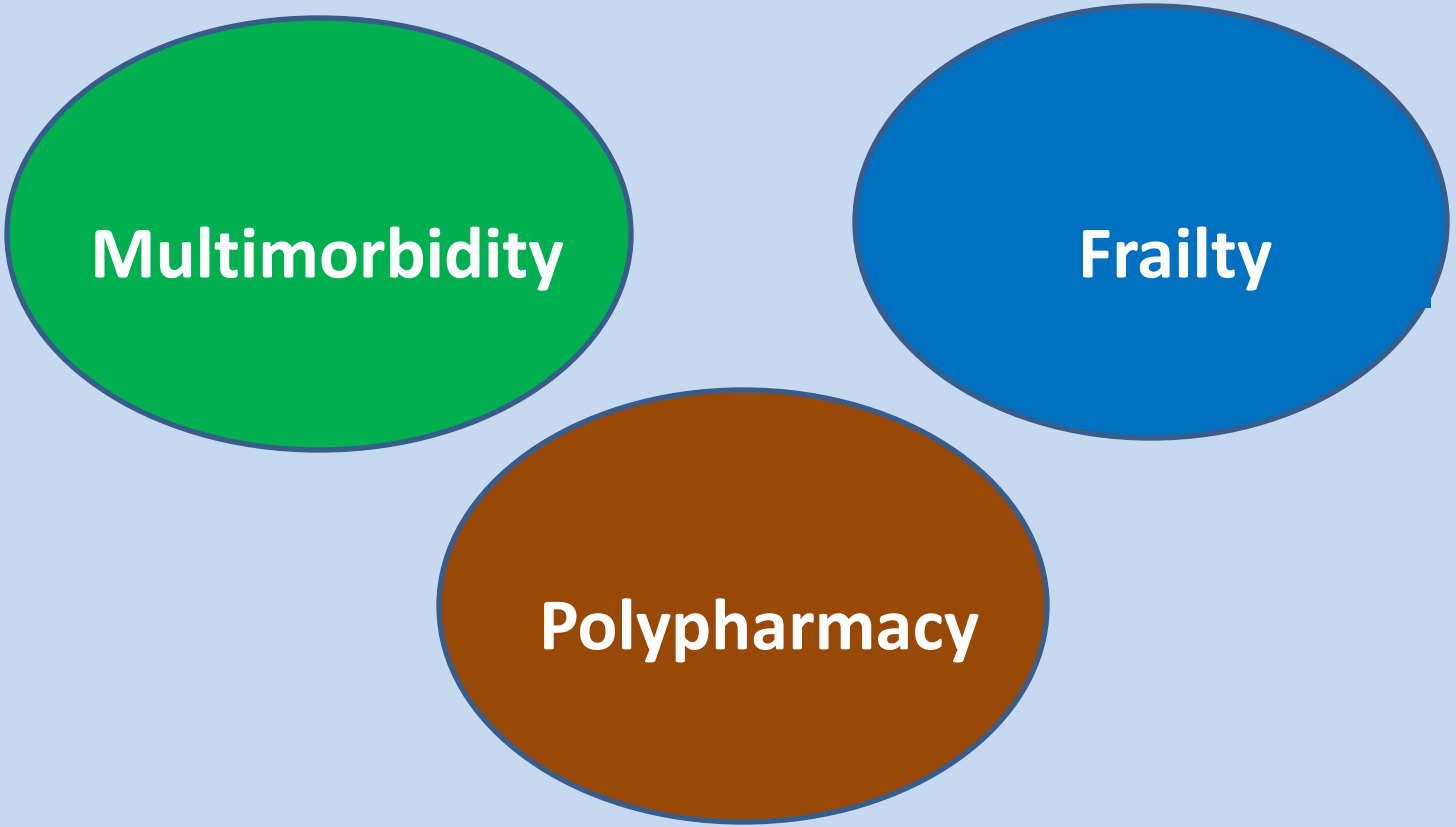
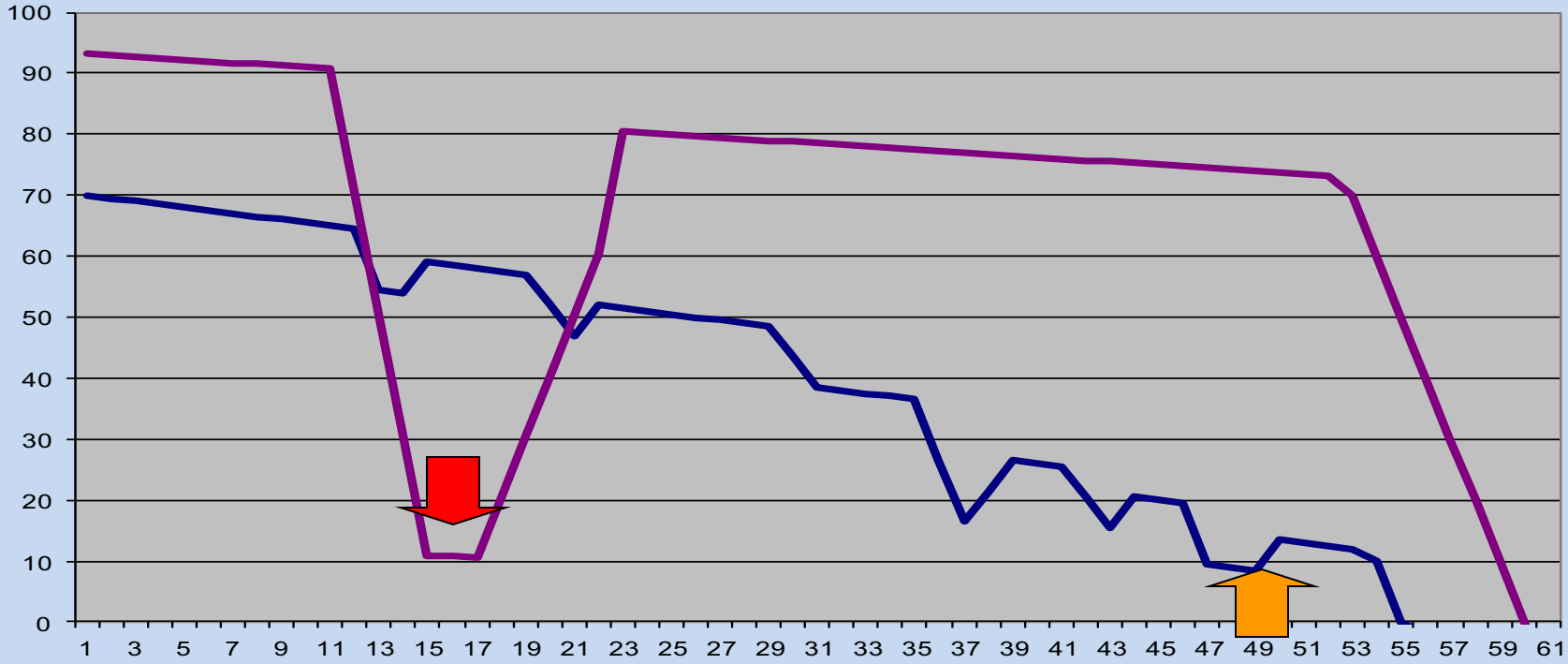
ISD

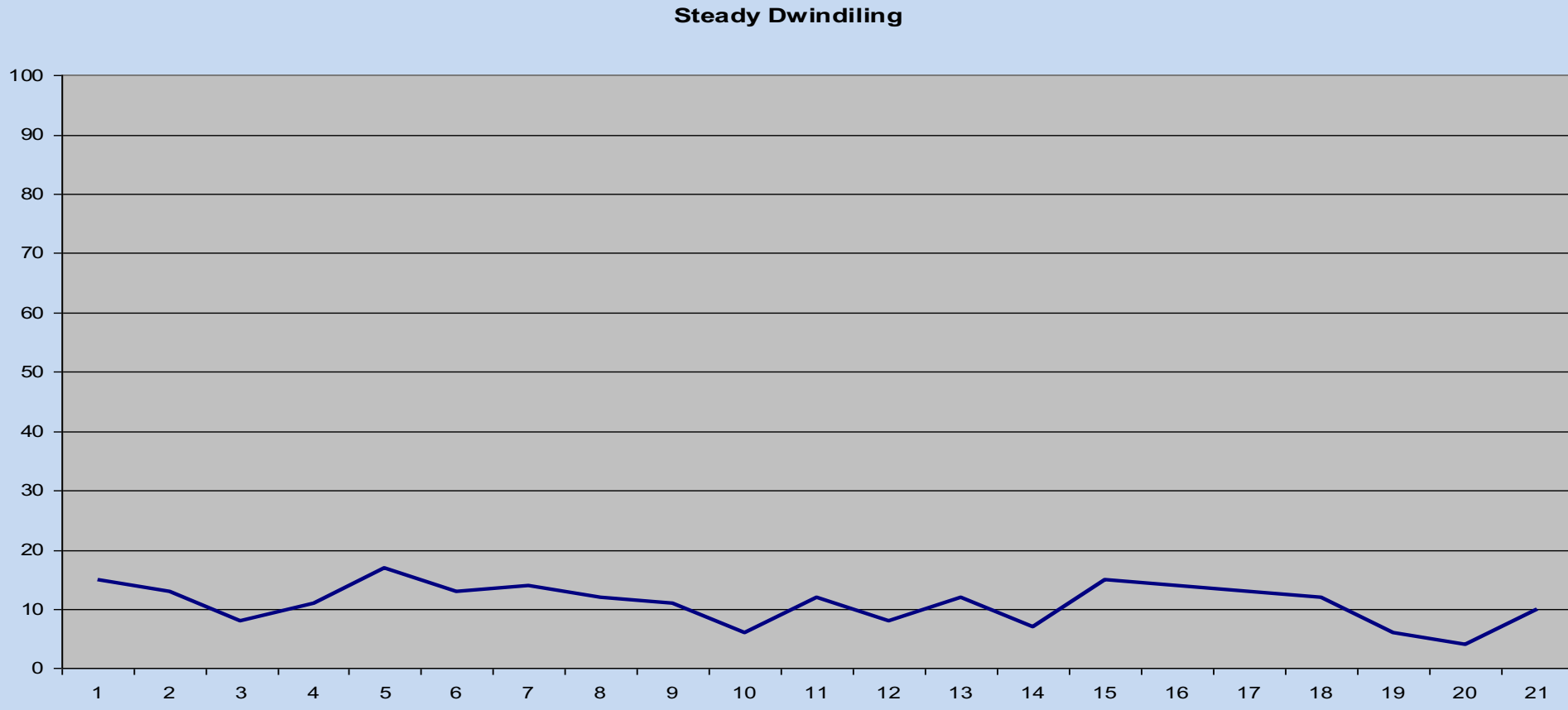

Percentage dispensed 10+ BNF paragraphs + high risk drug
By age group and 2012 SIMD Quintile
Scotland Jan-Jun 2014
Percent of population
35%
30%
25%
20%
15%
10%
5%
0%
50-54
55-59
60-64
65-69
70-74
75-79
80-84
85+
Age band (Years)
SIMD Quintile 1 (Most deprived)
2
3
4
SIMD Quintile 5 (Least deprived)

Source ISD


Multimorbidity
Frailty
Polypharmacy

Functional history as important as Past Medical History




Steady Dwindiling
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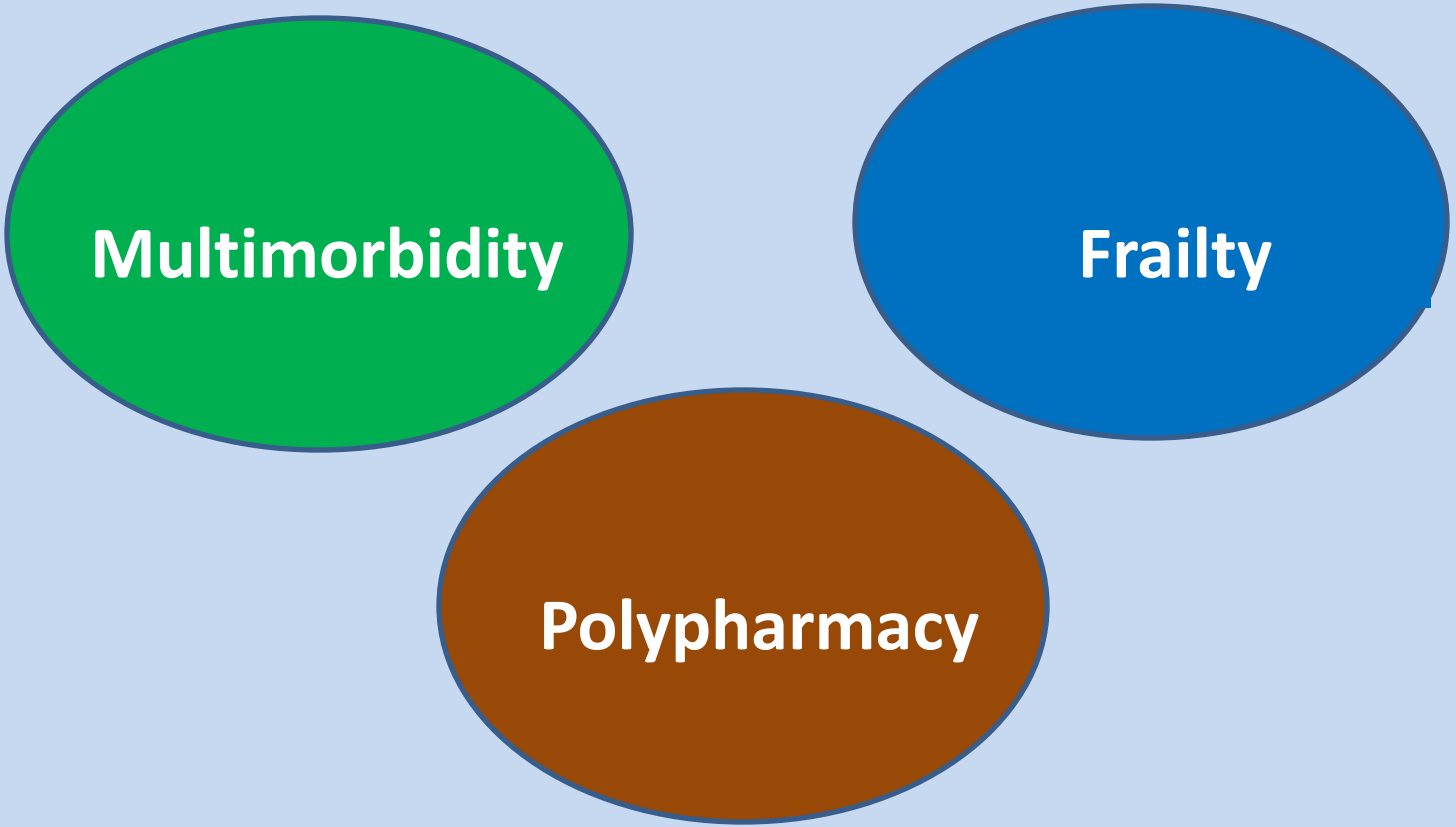
Where does chronological age fit in?



Where does chronological age fit in?

- Usually does not help much UNLESS Super old

- So if 90+ and **not** frail
  - Normally minimal or no co-morbidity
    - Or would have died sooner
  - Tiny sets of case notes
  - Tend to be independent
    - Loss of function often herald of very rapid decline.
  - ‘Learned immortality’ an issue

- 90+ and frail

So how old is your patient?

- Lots of old folk who are physiologically younger than years
  - Most of whom will be rich

- Lots of younger folk who are physiologically older than years
  - Many of whom be deprived

How do guidelines help us manage these groups?

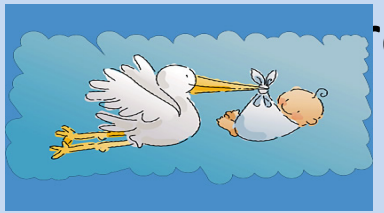
Honesty about Guidelines

- Done with a SINGLE disease in mind
- Based on studies in non- frail
- Are not made with the frail or multimorbid in mind

- They are GUIDElines but
  - Can feel VERY hard to ‘defy’ them

- Almost no trial evidence in frail adults
  - Different pharmacology
  - Huge comorbidity

- Use the best we have ie younger adults
  - Different Absolute Risk



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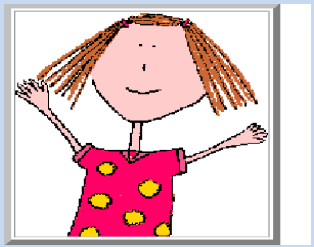
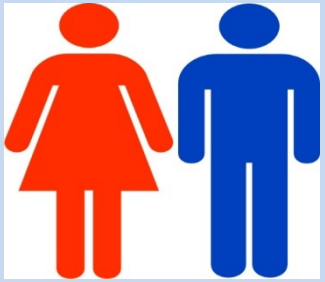


- Almost no trial evidence in frail adults
  - Different pharmacology
  - Huge comorbidity

- Use the best we have ie younger adults
  - Different Absolute Risk
  - rent Harm [illegible].

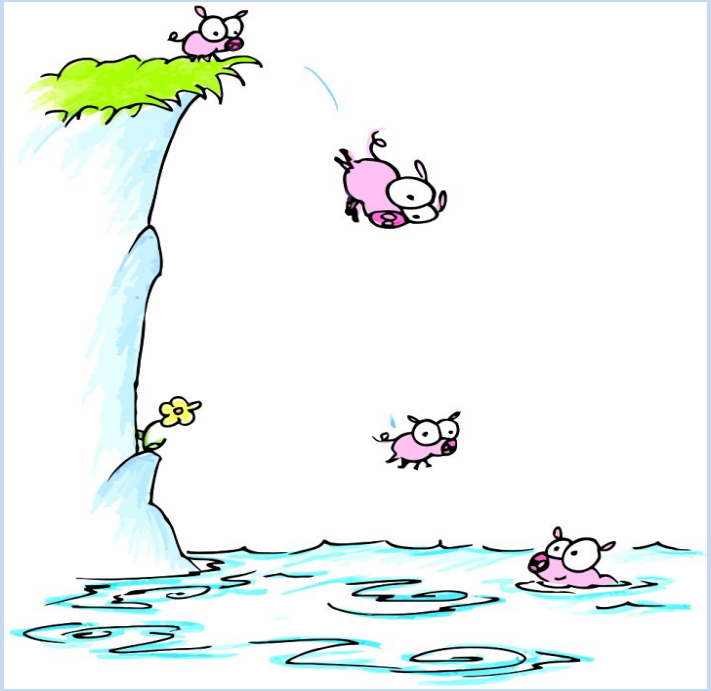



Game changing concepts

If guideline says Prescribe X drug it is GUIDANCE not INSTRUCTION and not prescribing may well be acceptable (and often desirable) in a range of situations

One size does not fit all.....

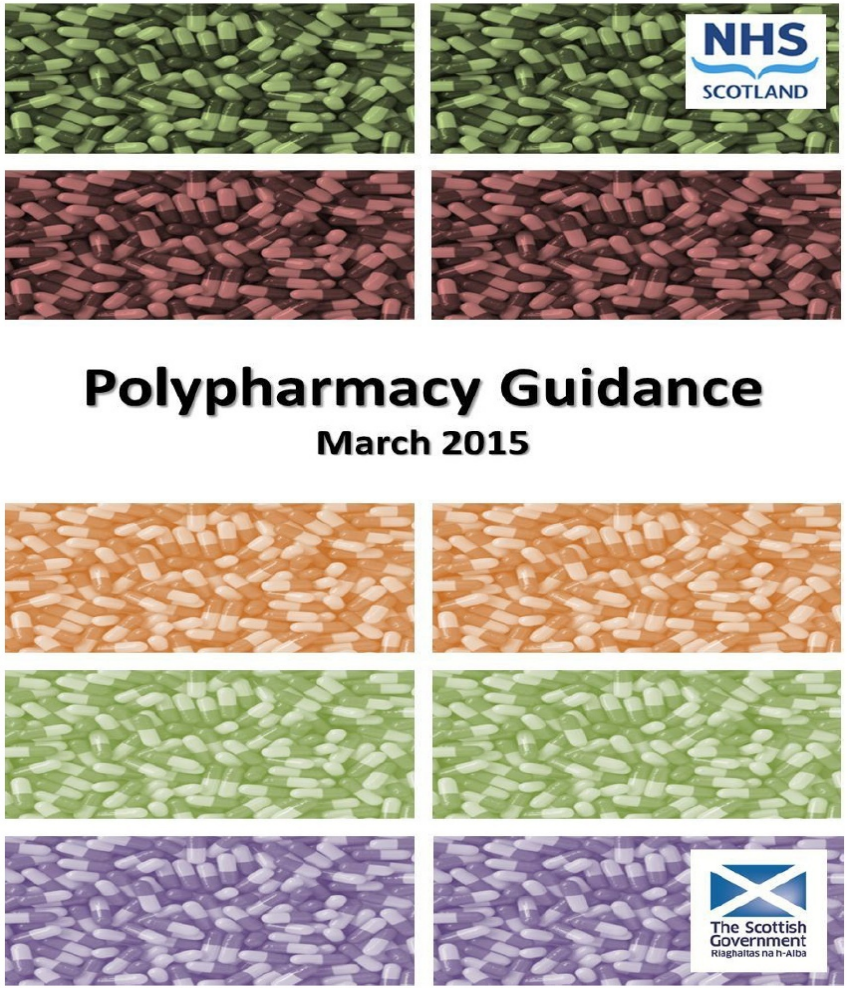
Why did you jump off a cliff?



Because the Guideline told me to.

Game changing concepts

A lot of commonly prescribed medication is not as effective in a patient specific basis than the drive to get the drugs prescribed would imply.



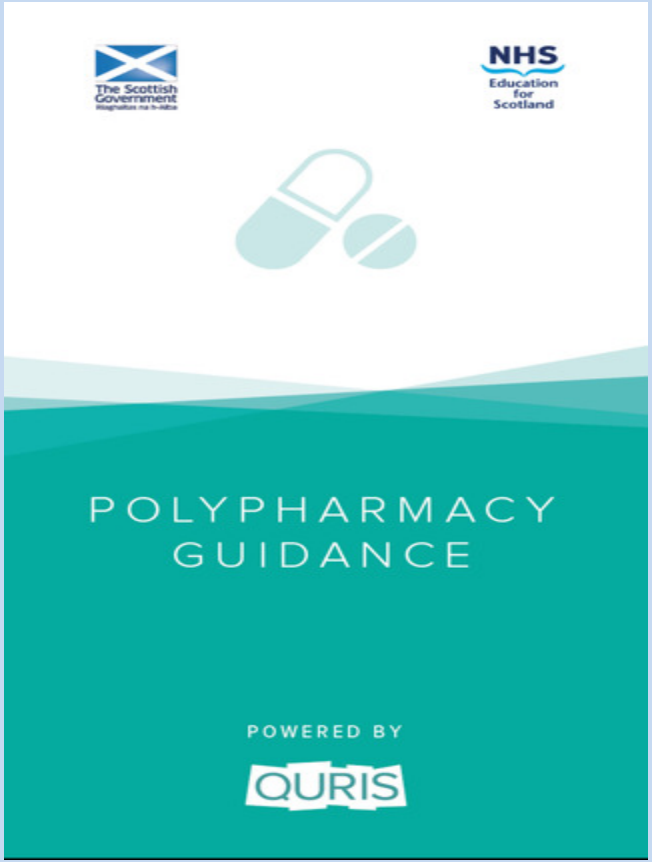
NICE National Institute for Health and Care Excellence

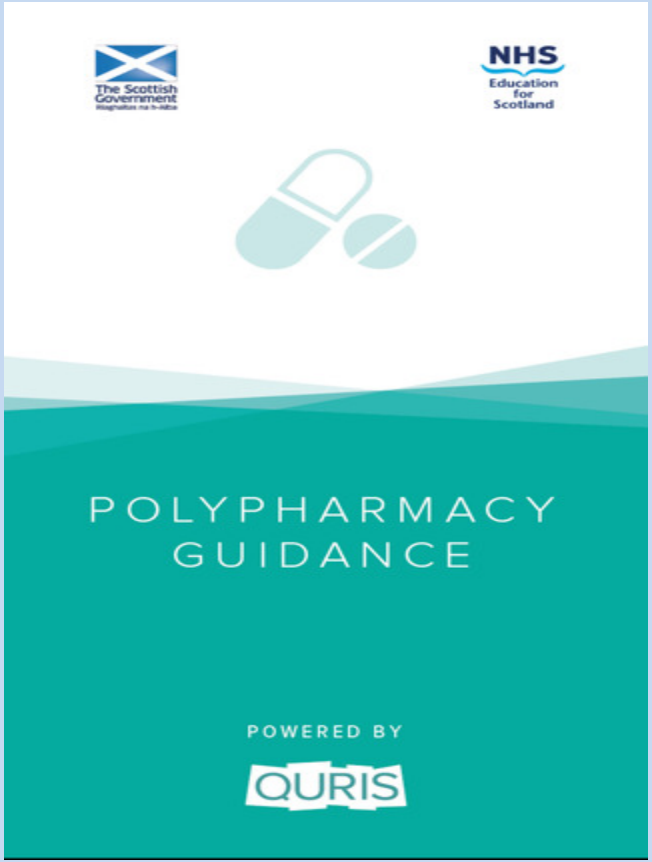
NICE guideline

Multimorbidity: clinical assessment and management

NICE guideline
Published: 21 September 2016
nice.org.uk/guidance/ng56

NHS Scotland Poly APP !!




The Scottish Government
NHS Education for Scotland
POLYPHARMACY GUIDANCE
POWERED BY
QURIS


Carrier
1:46 PM
Polypharmacy
7 Steps
Medicines
NNT
ADR
General principles
Hot topics

INTENSIVE SULPHONYLUREA WITH INSULIN TO ACHIEVE FASTING PLASMA GLUCOSE LESS THAN 6.0MMOL/ VS CONVENTIONAL TREATMENT WITH DIET TO AIM FOR FASTING BLOOD GLUCOSE LESS THAN 15MMOL/L

Study population:

Newly diagnosed type 2 diabetes patients - between 25-65 years.

Comments:

Mean age of patients was 54 years [23]
Any diabetes-related endpoint was defined as sudden death, death from hyperglycaemia or hypoglycaemia, fatal or non-fatal myocardial infarction, angina, heart failure, stroke, renal failure, digital amputation, vitreous haemorrhage, retinopathy requiring photocoagulation, blindness in one eye, or cataract extraction
Diabetes-related death was death due to myocardial infarction, stroke, peripheral vascular disease, renal disease, hyperglycaemia or hypoglycaemia, and sudden death
Median HbA1c over 10 years 7.0% in intensive group versus 7.9% in conventional group
Intensive group had more hypo-glycaemic episodes per year and higher weight gain than conventional group
Reduction in micro-vascular events were mostly retina

Outcome	Duration	NNT	Annualised NNT
Any diabetes end point	10 years (median duration of followup)	20	200
Diabetes related death	10 years (median duration of followup)	91	910
Micro-vascular complications	10 years (median duration of followup)	36	360

References:

²³UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998; 352: 837-53

Aiming blood sugar < 6 v < 15 [*achieved 7% v 8 %]*

Outcome	Duration	NNT	Annualised NNT
Any Diabetes related end point	10 years	20	200
Diabetes related death	10 years	91	910
Microvascular complication	10 years	36	360

Be Aware Long Term Strategies

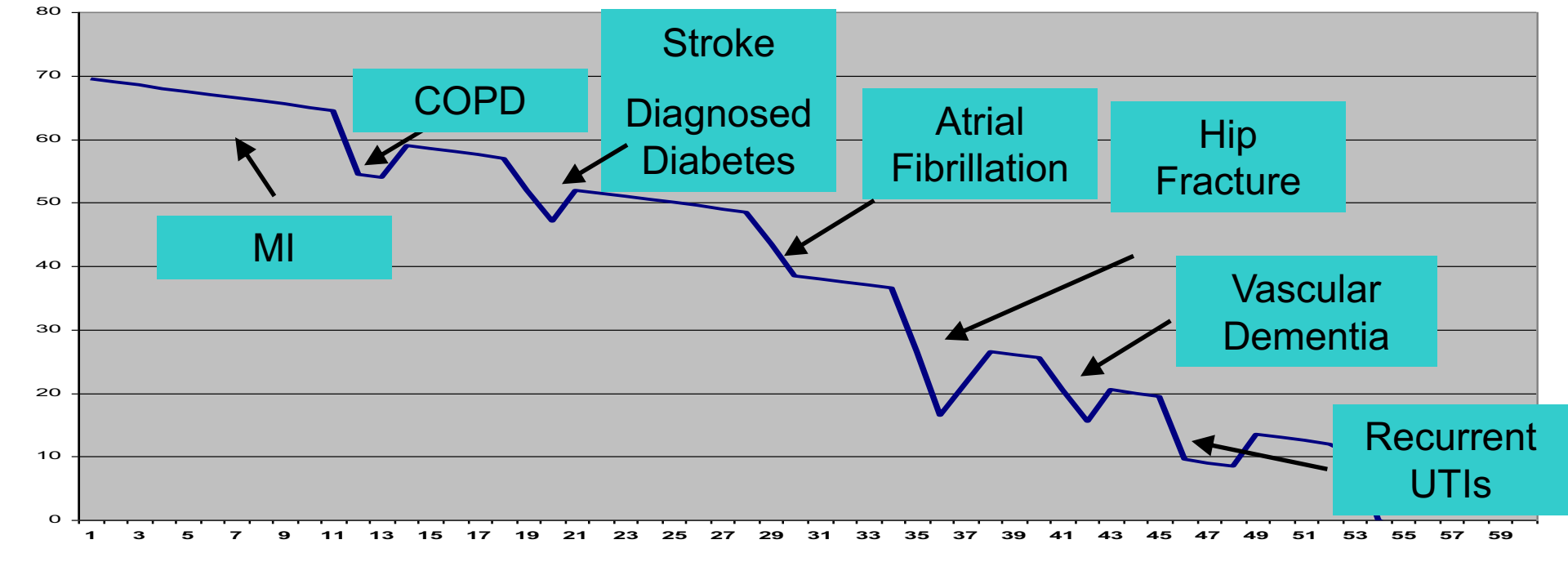
Need a long time

Domain	Steps		Process
Aims	1.	What matters to the patient	**Review diagnoses and identify therapeutic objectives with respect to:** • What matter to me (the patient)? • Understanding of objectives of drug therapy • Management of existing health problems • Prevention of future health problems
Need	2.	Identify essential drug therapy	**Identify essential drugs (not to be stopped without specialist advice)** • Drugs that have essential replacement functions (e.g. thyroxine) • Drugs to prevent rapid symptomatic decline (e.g. drugs for Parkinson's disease, heart failure)
	3.	Does the patient take unnecessary drug therapy?	**Identify and review the (continued) need for drugs:** • With temporary indications • With higher than usual maintenance doses • With limited benefit in general for the indication they are used for • With limited benefit in the patient under review (see Drug efficacy & applicability (NNT) table)
Effectiveness	4.	Are therapeutic objectives being achieved?	**Identify the need for adding/intensifying drug therapy in order to achieve therapeutic objectives:** • To achieve symptom control • To achieve biochemical/clinical targets • To prevent disease progression/exacerbation
Safety	5.	Does the patient have ADR/Side Effects or is at risk of ADRs/Side Effects? Does the patient know what to do if they're ill?	**Identify patient safety risks by checking for** • Drug-disease interactions • Drug-drug interactions (see ADR table) • Robustness of monitoring mechanisms for high-risk drugs • Drug-drug and drug-disease interactions • Risk of accidental overdosing (see Yellow Card Scheme) **Identify adverse drug effects by checking for** • Specific symptoms/laboratory markers (e.g. hypokalaemia) • Cumulative adverse drug effects (see ADR table) • Drugs that may be used to treat ADRs caused by other drugs **Sick Day rule cards**
Cost-effectiveness	6.	Is drug therapy cost-effective?	**Identify unnecessarily costly drug therapy by:** • Consider more cost-effective alternatives (but balance against effectiveness, safety, convenience)
Patient centeredness	7.	Is the patient willing and able to take drug therapy as intended?	**Does the patient understand the outcomes of the review?** • Does the patient understand why they need to take their medication? • Consider Teach back **Ensure drug therapy changes are tailored to patient preferences by** • Is the medication in a form the patient can take? • Is the dosing schedule convenient? • Consider what assistance the patient might have and when this is available • Is the patient able to take medicines as intended? **Agree and Communicate Plan** • Discuss with the patient/carer/welfare proxy therapeutic objectives and treatment priorities • Decide with the patient/carer/welfare proxies what medicines have an effect of sufficient magnitude to consider continuation or discontinuation • Inform relevant healthcare and social care carers change in treatments across the care interfaces

1. Identify Objectives
2. Identify Essentials
3. Identify unneccesary meds
4. Identify Undertreatment
5. Safety Check
6. Can they take it ? /Can we afford it ?
7. Do they know what they are taking and why and agree ?

Now on to the scenario

Lets meet Mrs Jones..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MI
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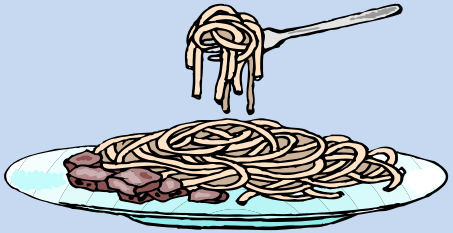
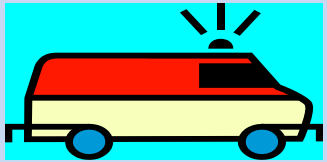
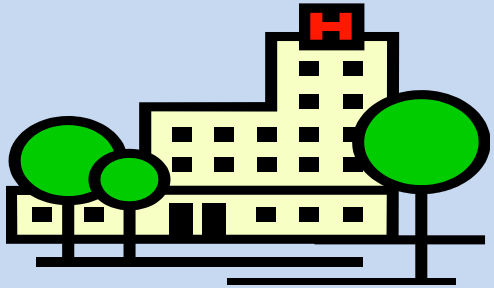
Hip
Fracture
Vascular
Dementia
Recurrent
UTIs

Current Function



Now lets admit her to hospital and see what happens...





Admitted to Hospital

- Fall
- Assessed in Accident and emergency.
- No fracture but unable to mobilise
- Admitted for pain control and rehab
- Pharmacist asked to review medication

Medication

- Metformin 1 g TDS
- Gliclazide 160mg bd
- Calcichew D3 forte 1 tab twice a day
- Alendronate 70mg once a week
- Perindopril 4mg once a day
- Indapamide 2.5mg once a day
- Warfarin as per INR
- Seretide 250 1 puff twice a day
- Salbutamol as required
- Ipratropium Inhaler 4 times a day
- Clopidogrel 75mg once a day
- Atorvastatin 80mg once a day
- Mirtazapine 30mg nocte
- Zopicolone 7.5 mg at night
- Oxybutinin 5mg bd
- Thyroxine 150mcg once a day
- Ipratropium inhaler 4 times a day.
- Paracetamol 1g QDS
- Omeprazole 20mg once a day
- Trimethoprim 200mg once a day prophylaxis

Medication

- DIABETES
  - Metformin 1 g TDS
  - Gliclazide 160mg bd
- OSTEOPOROSIS
  - Calcichew D3 forte 1 tab twice a day
  - Alendronate 70mg once a week
- POST CVA
  - Perindopril 4mg once a day
  - Indapamide 2.5mg once a day
  - Warfarin as per INR
- COPD
  - Seretide 250 1 puff twice a day
  - Salbutamol as required
  - Atrovent inhaler 4 times a day
- POST MI
  - Clopidogrel 75mg once a day
  - Atorvastatin 80mg once a day
- MOOD /BEHAVIOUR
  - Mirtazapine 30mg nocte
  - Zopicolone 7.5 mg at night
- BLADDER
  - Oxybutinin 5mg bd
- ENDOCRINE
  - Thyroxine 150mcg once a day
- OTHER
  - Paracetamol 1g QDS
  - Omeprazole 20mg once a day
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Facts and figures

- BP 106/56
- HbA1c 40 mmmol/mol 6.6%
- Urine Albumin/Creat ratio
  - trace microalbuminuria
- Creatinine 124 eGFR 45
- Weight 43kg

Identify Objectives

Synchronising understanding

- Identify Essentials
- Identify unnecessary medication
- Identify under treatment
- Safety check

Which would you say was the most effective medication she was on ?

- Atorvastatin
- Warfarin
- Perindopril
- Thyroxine
- Alendronate /Calcichew D3 Forte
- Gliclazide

Medication

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- OTHER
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Which of her medications does her husband think helps the most ?

- Atorvastatin
- Warfarin
- Perindopril
- Thyroxine
- Alendronate /Calcichew D3 Forte
- Gliclazide

Medication

- DIABETES
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Which of her medications does her husband think helps the most ?

- Oxybutinin
- Zopicolone
- Mirtazapine
- Paracetamol
- Omeprazole
- None

Medication

- DIABETES
  - Metformin 1 g TDS
  - Gliclazide 160mg bd
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- OTHER
  - Paracetamol 1g QDS
  - Omeprazole 20mg once a day
  - Trimethoprim 200mg once a day prophylaxis

Which of her medications do you think is potentially the most harmful ?

- Warfarin / Clopidogrel
- Oxybutinin
- Zopicolone
- Perindopril
- Alendronate
- Atorvastatin
- One of the others.

When thinking about this lady what proportion of her medication did you assume her husband gets into her?

- 100%
- 90%
- 70%
- 50%
- <40%
- Did not consider that…

So where would you start ?

- Metformin 1 g TDS
- Gliclazide 160mg bd
- Calcichew D3 forte 1 tab twice a day
- Alendronate 70mg once a week
- Perindopril 4mg once a day
- Indapamide 2.5mg once a day
- Warfarin as per INR
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- Omeprazole 20mg once a day
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Example Run through

Reality will always be a bit (a lot) less clear cut.

First get rid of the obvious poisons

Medication

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  - Gliclazide 160mg bd
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  - Alendronate 70mg once a week
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  - Oxybutinin 5mg bd
- ENDOCRINE
  - Thyroxine 150mcg once a day
- OTHER
  - Paracetamol 1g QDS
  - Omeprazole 20mg once a day
  - Trimethoprim 200mg once a day prophylaxis

Risk of bleeding with combination antiplatelet / anticoagulation

- Taking **warfarin** as baseline [ie 1] risk of bleeding at one is as follows
- Aspirin 0.93 [0.88 - 0.98]
- Clopidogrel 1.06 [0.87 - 1.29]
- Aspirin + Clopidogrel 1.66 [1.34 -2.04]
- Warfarin + Aspirin 1.83 [1.72-1.96]
- Warfarin + Clopidogrel 3.08 [2.32 - 3.91]
  13.9% bleed risk /patient year
- Warfarin + Aspirin + Clopidogrel *15.7% bleed risk /patient year* 3.7 [2.89 - 4.76]

Hansen ML, Sorensen R, Clausen MT, et al. **Risk of bleeding with single, dual, or triple therapy with warfarin, aspirin, and clopidogrel in patients with atrial fibrillation.** Arch Intern Med. 2010 Sep 13;170 (16):1433-41.

Medication

- DIABETES
  - Metformin 1 g TDS
  - Gliclazide 160mg bd
- OSTEOPOROSIS
  - Calcichew D3 forte 1 tab twice a day
  - Alendronate 70mg once a week
- POST CVA
  - Perindopril 4mg once a day
  - Indapamide 2.5mg once a day
  - Warfarin as per INR
- COPD
  - Seretide 250 1 puff twice a day
  - Salbutamol as required
- POST MI
  - Atorvastatin 80mg once a day
- MOOD /BEHAVIOUR
  - Mirtazapine 30mg nocte
  - Zopicolone 7.5 mg at night
- BLADDER
  - Oxybutinin 5mg bd
- ENDOCRINE
  - Thyroxine 150mcg once a day
- OTHER
  - Paracetamol 1g QDS
  - Omeprazole 20mg once a day

Medicine Sick Day Rules

When you are unwell with any of the following:

- Vomiting or diarrhoea (unless only minor)
- Fevers, sweats and shaking

Then STOP taking the medicines listed overleaf

Restart when you are well (after 24-48 hours of eating and drinking normally)

If you are in any doubt, contact your pharmacist, GP or nurse

Medicines to stop on sick days

ACE inhibitors: medicine names ending in "pril"
eg, lisinopril, perindopril, ramipril

ARBs: medicine names ending in "sartan"
eg, losartan, candesartan, valsartan

NSAIDs: anti-inflammatory pain killers
eg, ibuprofen, diclofenac, naproxen

Diuretics: sometimes called "water pills"
eg, furosemide, spironolactone, indapamide, bendroflumethiazide

Metformin: a medicine for diabetes

Produced April 2013. Authorised by: NHS Highland SPSP Primary Care working group

BP reduction in the very frail

- PARTAGE trial
  - **increase** in mortality over 2 years in nursing home residents (mean age 87.6 years) when blood pressure ran < 130 on 2 or more blood pressure agents.
    - Number needed to harm 10 patients treated for one extra death over 2 years.
    - [Mortality over two years 30% v 20% so this is perhaps a fairly fit Care home group.].
  - There is also emerging concern about low diastolic blood pressures in older adults.

Treatment with Multiple Blood Pressure Medications, Achieved Blood Pressure and Mortality in Older Nursing Home Residents The PARTAGE Study. Benetos Et Al *Jama Intern Med* 2015;175(6) 989 -995

Medication

- DIABETES
  - Metformin 1 g TDS
  - Gliclazide 160mg bd
- OSTEOPOROSIS
  - Calcichew D3 forte 1 tab twice a day
  - Alendronate 70mg once a week
- POST CVA
  - Warfarin as per INR
- COPD
  - Seretide 250 1 puff twice a day
  - Salbutamol as required
  - Atrovent inhaler 4 times a day
- POST MI
  - Atorvastatin 80mg once a day
- MOOD /BEHAVIOUR
  - Mirtazapine 30mg nocte
  - Zopicolone 7.5 mg at night
- BLADDER
  - Oxybutinin 5mg bd
- ENDOCRINE
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- OTHER
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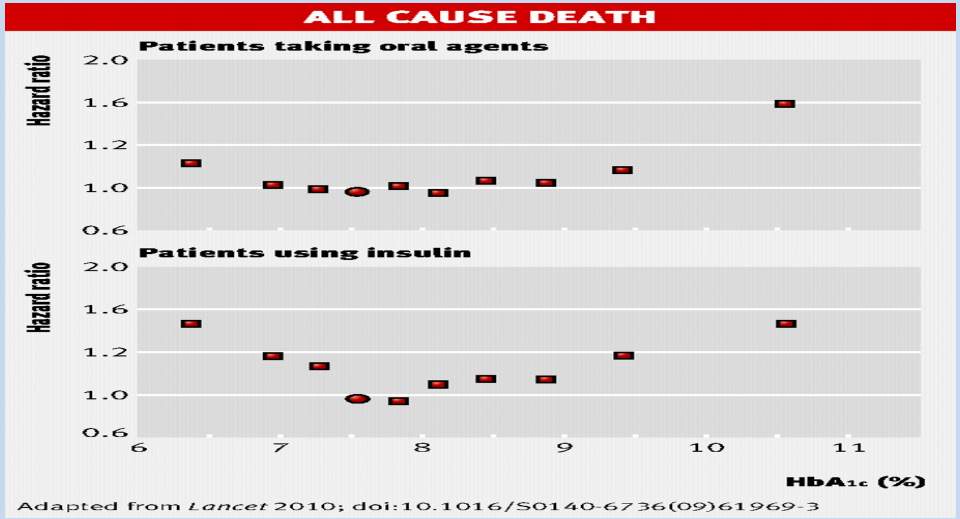
  - Omeprazole 20mg once a day

Diabetic drugs

- Hb AIC 5.8% - dangerous



- Reduce diabetic meds ++
  1. Pioglitazone
  2. Gliclazide

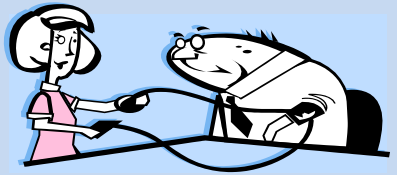
In short.....

- Beware
  - Systolic BP <130
  - Diastolic < 70
  - Pulse < 60
  - Hba1c < 60

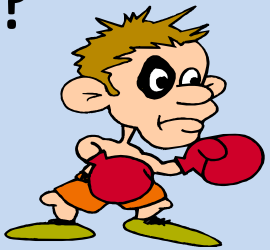
    - Unless super strong indication

Key risk/ benefit Questions

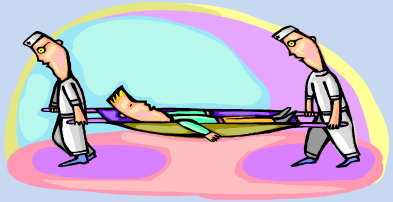
- [Postural] Blood Pressure too low ?



- Blood Sugar [Hba1c] too low?



- Blood too thin [ed]?



- Kidneys too vulnerable?

Medication

- DIABETES
- OSTEOPOROSIS
  - Calcichew D3 forte 1 tab twice a day
  - Alendronate 70mg once a week
- POST CVA
  - Warfarin as per INR
- COPD
  - Seretide 250 1 puff twice a day
  - Salbutamol as required
  - Atrovent inhaler 4 times a day
- POST MI
  - Atorvastatin 80mg once a day
- MOOD /BEHAVIOUR
  - Mirtazapine 30mg nocte
  - Zopicolone 7.5 mg at night
- BLADDER
  - Oxybutinin 5mg bd
- ENDOCRINE
  - Thyroxine 150mcg once a day
- OTHER
  - Paracetamol 1g QDS
  - Omeprazole 20mg once a day
  - Trimethoprim 200mg once a day prophylaxis

Medication

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  - Trimethoprim 200mg once a day prophylaxis

Drugs husband may think helps the most

- Oxybutinin
- Zopicolone
- Mirtazapine

Drugs that every frail adults guideline will suggest you stop

- Oxybutinin
- Zopicolone
- Mirtazapine

Anticholinergic Risk Scale

1 Point	2 Points	3 points
Haloperidol Quetiapine Mirtazapine Paroxetine Trazadone Ranitidine	Clozapine Nortryptyline Baclofen Cetirizine Loratadine Cimetidine Loperamide Prochlorperazine **Tolteridone**	Chlorpromazine Amitrytyline Imipramine Chlorpheniramine **Hydroxyzine** Oxybutinin

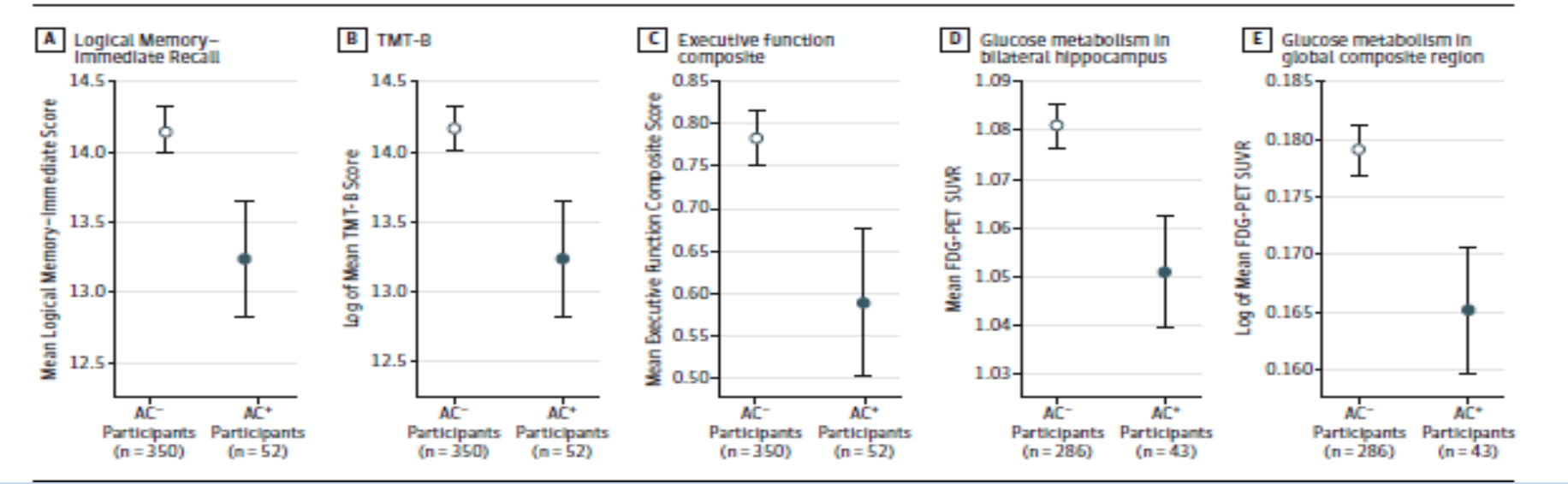
The Anticholinergic Risk Scale and Anticholinergic Adverse Effects in Older Persons. Rudolph JI et al *Arch Intern Med. 2008;168(5):508-513*

Anticholinergics and accelerated decline?

- Long term follow up of cognitive normal adults
  - Cognitive testing
  - Imaging
- Looking for clues re development dementia
- Looking at those on Anticholingergics v none

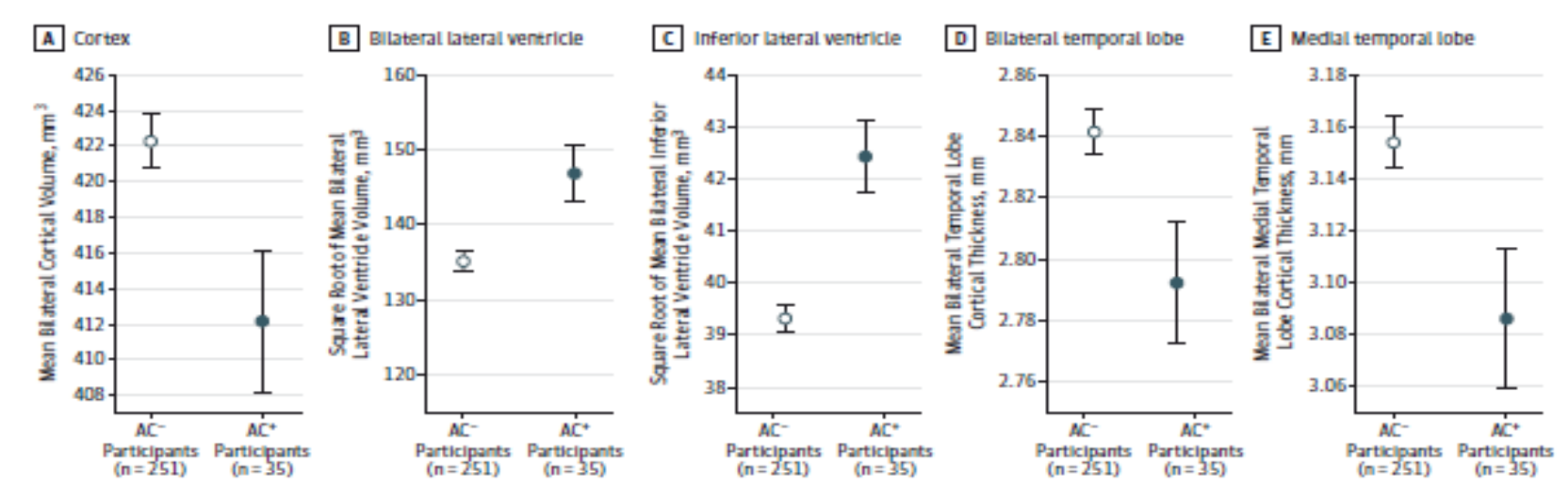
Association Between Anticholinergic Medication Use and Cognition, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults Risacher et al, JAMA Neurol. 2016;73(6):721-732

Accelerate Cognitive loss??



Association Between Anticholinergic Medication Use and Cognition, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults Risacher et al, JAMA Neurol. 2016;73(6):721-732

Accelerate Brain Atrophy??



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Anticholinergics and accelerated decline?

- Will be a while before definitive
  - Confoundings abound

- But
  - Adults are often brighter off anticholinergics
  - Cognition a high stakes risk

So this is interesting..

- Go slow
- A lot of time the problems are equally bad on and off the meds
- Try the confidence building medication stops first.
- Be willing to give up

Medication

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  - Warfarin as per INR
- COPD
  - Seretide 250 1 puff twice a day
  - Salbutamol as required
  - Atrovent inhaler 4 times a day
- POST MI
  - Atorvastatin 80mg once a day
- MOOD /BEHAVIOUR
  - Mirtazapine 30mg nocte
  - Zopicolone 7.5 mg at night
- BLADDER
  - Oxybutinin 5mg bd
- ENDOCRINE
  - Thyroxine 150mcg once a day
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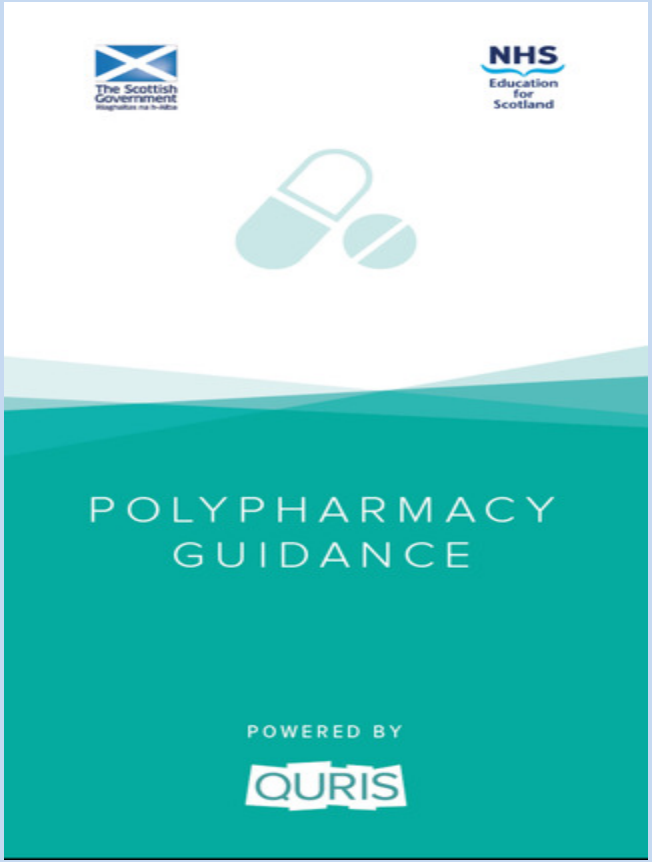
Drugs that are not actively harming but ? efficacy

Questions to ponder

- Is this a population treatment or an individual treatment ?
- Does this individual look anything like the trial population?
- Do they have long enough to benefit?


The Scottish Government
NHS Education for Scotland
POLYPHARMACY GUIDANCE
POWERED BY
QURIS


Carrier
1:46 PM
Polypharmacy
7 Steps
Medicines
NNT
ADR
General principles
Hot topics

Medication

- DIABETES
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  - Gliclazide 160mg bd
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  - Perindopril 4mg once a day
  - Indapamide 2.5mg once a day
  - Warfarin as per INR
- COPD
  - Seretide 250 1 puff twice a day
  - Salbutamol as required
  - Atrovent inhaler 4 times a day
- POST MI
  - Clopidogrel 75mg once a day
  - Atorvastatin 80mg once a day
- MOOD /BEHAVIOUR
  - Mirtazapine 30mg nocte
  - Zopicolone 7.5 mg at night
- BLADDER
  - Oxybutinin 5mg bd
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  - Thyroxine 150mcg once a day
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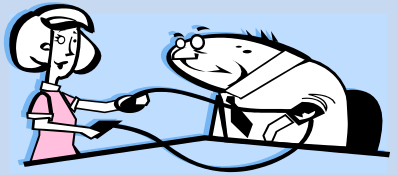
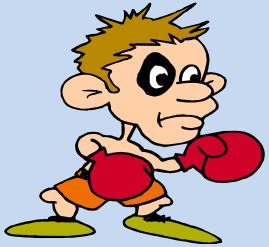
- BLADDER
- ENDOCRINE
  - Thyroxine 150mcg once a day
- OTHER
  - Paracetamol 1g QDS

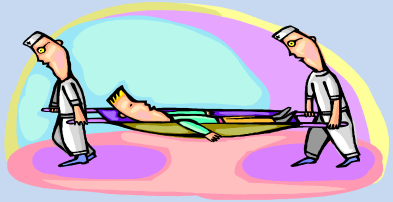
Summary of that

- Idealistic drug review
  - Rarely manage that radical a change
- But it does lead to benefit.
  - Focus on Food
  - Carer Stress
  - Iatrogenic harm reduced
  - Big picture story telling

- [Postural] Blood Pressure too low ?
- Blood Sugar too low?
- Blood too thin [ed]?
- Kidneys too vulnerable?
- Any Messy drugs ?







Hard Heads and Soft Hearts

- Hard Heads
  - Study learn and know what we can re medication efficacy
  - Be willing and active in challenging prescribing
  - Be confident enough to be seen as leaders in how to prescribe

- Soft Hearts
  - Adult focussed goals
  - Teach train and develop others
  - Always ensure focus goes on the patient not the pills

What happens next ?

Questions

- Increasing age is the main driver for increasing polypharmacy in Europe
  - FALSE Deprivation and presence of mental health condition weight more strongly
- Adding Clopidogrel to Warfarin doubles bleeding rate
  - FALSE Rate is nearer treble