The epidemiology of polypharmacy

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The ageing population

ONS, 2010
The burden of multimorbidity

Barnett K, Lancet 2012
The burden of multimorbidity

Patients with these conditions...

- Cancer
  - 12
  - 4
  - 7
  - 13
  - 4
  - 5
  - 29
  - 19
  - 12

- COPD
  - 13
  - 6
  - 9
  - 24
  - 31
  - 23
  - 15

- Diabetes
  - 24
  - 11
  - 6
  - 10
  - 5
  - 28
  - 21
  - 10

- CHD
  - 23
  - 19
  - 16
  - 14
  - 10
  - 32
  - 21
  - 13

...also have these conditions

- CHD
- Diabetes
- COPD
- CHF
- Stroke
- AF
- Pain
- Depression
- Anxiety
- Dementia
<table>
<thead>
<tr>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
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</thead>
<tbody>
<tr>
<td>• Prostate cancer</td>
<td>• Medicines adherence</td>
<td>• Venous thromboembolism - reducing the risk</td>
<td>• Anxiety</td>
<td>• Epilepsy</td>
</tr>
<tr>
<td>• Osteoarthritis</td>
<td>• Antisocial personality disorder</td>
<td>• Donor breast milk banks</td>
<td>• Anaemia management in people with CKD</td>
<td>• Patient experience in adult NHS services</td>
</tr>
<tr>
<td>• Surgical management of OME</td>
<td>• Borderline personality disorder (BPD)</td>
<td>• Unstable angina and NSTEMI</td>
<td>• Alcohol dependence and harmful alcohol use</td>
<td>• Infection control</td>
</tr>
<tr>
<td>• Irritable bowel syndrome</td>
<td>• Rheumatoid arthritis</td>
<td>• Chest pain of recent onset</td>
<td>• Food allergy in children and young people</td>
<td>• Opioids in palliative care</td>
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<tr>
<td>• Antenatal care</td>
<td>• Breast cancer (early &amp; locally advanced)</td>
<td>• Neuropathic pain - pharmacological management</td>
<td>• Tuberculosis</td>
<td>• Acute upper GI bleeding</td>
</tr>
<tr>
<td>• Diabetes in pregnancy</td>
<td>• Breast cancer (advanced)</td>
<td>• Lower urinary tract symptoms</td>
<td>• Colonoscopy surveillance for prevention of colorectal cancer</td>
<td></td>
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<tr>
<td>• Prophylaxis against infective endocarditis</td>
<td>• Schizophrenia</td>
<td>• Neonatal jaundice</td>
<td>• Diabetic foot problems - inpatient management</td>
<td></td>
</tr>
<tr>
<td>• Perioperative hypothermia (inadvertent)</td>
<td>• Critical illness rehabilitation</td>
<td>• Constipation in children and young people</td>
<td>• Psychosis with coexisting substance misuse</td>
<td>• Sickle cell acute painful episode</td>
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<tr>
<td>• Type 2 diabetes</td>
<td>• Diarrhoea and vomiting in children under 5</td>
<td>• Alcohol-use disorders: physical complications</td>
<td>• Lung cancer</td>
<td>• Venous thromboembolic diseases</td>
</tr>
<tr>
<td>• Lipid modification</td>
<td>• Glaucoma</td>
<td>• Chronic obstructive pulmonary disease</td>
<td>• Ovarian cancer</td>
<td>• Spasticity in children and young people</td>
</tr>
<tr>
<td>• Stroke</td>
<td>• Coeliac disease</td>
<td>• Bacterial meningitis and meningococcal septicemia</td>
<td>• Common mental health disorders</td>
<td>• Osteoporosis fragility fracture</td>
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<td>• Respiratory tract infections</td>
<td>• Type 2 Diabetes - newer agents</td>
<td>• Delirium</td>
<td>• Hip fracture</td>
<td>• Lower limb peripheral arterial disease</td>
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<td>• Induction of labour</td>
<td>• Low back pain</td>
<td>• Metastatic malignant disease of unknown primary origin</td>
<td>• Peritoneal dialysis</td>
<td>• Urinary incontinence in neurological disease</td>
</tr>
<tr>
<td>• Familial hypercholesterolaemia</td>
<td>• When to suspect child maltreatment</td>
<td>• Motor neuron disease - non-invasive ventilation</td>
<td>• Stable angina</td>
<td>• Antibiotics for early-onset neonatal infection</td>
</tr>
<tr>
<td>• Attention deficit hyperactivity disorder (ADHD)</td>
<td>• Depression in adults</td>
<td>• Barrett's oesophagus - ablative therapy</td>
<td>• Hypertension</td>
<td>• Headaches</td>
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<tr>
<td>• Chronic kidney disease</td>
<td>• Depression with a chronic physical health problem</td>
<td>• Hypertension in pregnancy</td>
<td>• Autism in children and young people</td>
<td>• Neutropenic sepsis</td>
</tr>
<tr>
<td>• Surgical site infection</td>
<td>• Family</td>
<td>• Chronic heart failure</td>
<td>• Multiple pregnancy</td>
<td>• Crohn's disease</td>
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<tr>
<td>• Metastatic spinal cord compression</td>
<td>• To suspect child</td>
<td>• Transient loss of consciousness in adults and young people</td>
<td>• Hyperglycaemia in acute coronary syndromes</td>
<td>• Psoriasis</td>
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<tr>
<td></td>
<td></td>
<td>• Pregnancy and complex social factors</td>
<td>• Colorectal cancer</td>
<td>• Ectopic pregnancy and miscarriage</td>
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<tr>
<td></td>
<td></td>
<td>• Nocturnal enuresis - the management of bedwetting in children and young people</td>
<td>• Caesarean section</td>
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<td></td>
<td></td>
<td>• Sedation in children and young people</td>
<td>• Self-harm (longer term management)</td>
<td></td>
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<td></td>
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<td></td>
<td>• Anaphylaxis</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>• Organ donation</td>
<td></td>
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<td></td>
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<td></td>
<td>• Service user experience in adult mental health</td>
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</tbody>
</table>
Guidelines everywhere...

Aged under 55 years

Aged over 55 years or black person of African or Caribbean family origin of any age

A

A + C

A + C + D

Resistant hypertension
A + C + D + consider further diuretic\textsuperscript{10,21} or alpha-blocker or beta-blocker\textsuperscript{22}
Consider seeking expert advice

No of antihypertensive drugs:
- ≥3
- 2
- 1
- 0

Tight control of blood pressure

Patients receiving antihypertensive treatment (%)

Years since randomisation

NICE, CG127, Hypertension
UKPDS38, BMJ 1998
Guidelines everywhere…

Blood-glucose-lowering therapy

Consider sulfonylurea⁴ here if:
- not overweight (tailor the assessment of body-weight-associated risk according to ethnic group⁶), or
- metformin is not tolerated or is contraindicated, or
- a rapid therapeutic response is required because of hyperglycaemic symptoms.

Consider a rapid-acting insulin secretagogue for people with erratic lifestyles.

Consider substituting a DPP-4 inhibitor⁹ or a thiazolidinedione¹⁰ for the sulfonylurea if there is a significant risk of hypoglycaemia (or its consequences) or a sulfonylurea is contraindicated or not tolerated.

Consider adding a DPP-4 inhibitor⁹ or a thiazolidinedione¹⁰ instead of insulin if insulin is unacceptable (because of employment, social, recreational or other personal issues, or obesity).

Consider adding exenatide⁶ to metformin and a sulfonylurea if:
- BMI ≥ 35 kg/m² in people of European descent⁷ and there are problems associated with high weight, or
- BMI < 35 kg/m² and insulin is unacceptable because of occupational implications or weight loss would benefit other comorbidities.

Add insulin²–⁹ (see page 11); particularly if the person is markedly hyperglycaemic

Insulin + metformin + sulfonylurea⁴

Metformin² (see page 10)

Nephropathy

Dyslipidaemia

Antithrombotic

Neuropathic pain

Gastroparesis

Erectile dysfunction

Exenatide

Glitazones

Glipins

Sulphonylurea

Metformin

Insulin

HbA₁c ≥ 6.5%¹ after trial of lifestyle interventions

HbA₁c ≥ 6.5%¹

HbA₁c ≥ 7.5%¹

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Add insulin²–⁹ (see page 11), particularly if the person is markedly hyperglycaemic

Insulin + metformin + sulfonylurea⁴

HbA₁c ≥ 7.5%¹

HbA₁c < 7.5%¹

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Guidelines everywhere…

Guidelines generally fail to make it clear when or how to stop drugs
Guidelines everywhere…
age + multimorbidity + guidelines = lots of medicines
Prevalence of use of multiple medicines

- Analysis of 180,815 adult patient (age >20 years)
- 40 representative GP surgeries across Scotland
- Primary care data (demographics, prescribing, 40 long-term diagnoses)
- Linked secondary care admission data
Prevalence of use of multiple medicines

Prevalence of polypharmacy in a Scottish primary care population

Percentage of population

Number of regular medicines

Payne RA, unpublished data
Prescribing is increasing
Prescribing is increasing
Prescribing is increasing

![Bar chart showing the percentage of patients receiving multiple medicines in 1995 and 2010. The chart compares the percentage of patients with different numbers of medications: None, 1 to 4, 5 to 9, 10 or more.](image-url)
Factors associated with polypharmacy

Prevalence of polypharmacy in a Scottish primary care population

Payne RA, unpublished data
Factors associated with polypharmacy

Prevalence of polypharmacy in a Scottish primary care population

Payne RA, unpublished data
Factors associated with polypharmacy

Payne RA, unpublished data
Factors associated with polypharmacy

- Heart failure
- IHD
- Diabetes
- Dementia
- Epilepsy
- Chronic pain
- COPD
- Skin condition
- Inflamm. bowel
- Cancer
- Depression

Payne RA, unpublished data
Factors associated with polypharmacy

Unadjusted gender differences in prescribing rates

Percentage of population receiving given number of medicines

Number of medicines

Payne RA, unpublished data
Factors associated with polypharmacy

Percentage of patients on given number of medicines with mental health condition

Payne RA, unpublished data
Factors associated with polypharmacy

Payne RA, unpublished data
Factors associated with polypharmacy

Effect of acute hospitalisation on medication count

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Before admission</th>
<th>After admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>65–75</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>76–85</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>&gt;85</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

Betteridge TM, Int Med J 2011
So what?
Drug interactions

• Pharmacodynamic
  • Common effects
  • Common receptors
  • Indirect effects

• Pharmacokinetic
  • Absorption
    (chelation, gut motility, gastric pH)
  • Distribution
    (plasma protein binding competition)
  • Metabolism
    (cytochrome P450 induction/inhibition)
  • Excretion
    (renal, bile)
Adverse drug reactions

- Hospitalisation for ADRs in UK
  - 6.5% of admissions
  - Mean stay 8 days
  - £466 million
  - Most are avoidable

Calderón-Larrañaga A, BJGP 2012
## Medication errors

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>0.66</td>
<td>0.48-0.92</td>
</tr>
<tr>
<td><strong>Number of drugs</strong></td>
<td>1.16</td>
<td>1.12-1.19</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 14</td>
<td>1.87</td>
<td>1.19-2.94</td>
</tr>
<tr>
<td>15 to 64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 to 74</td>
<td>1.68</td>
<td>1.04-2.73</td>
</tr>
<tr>
<td>75+</td>
<td>1.95</td>
<td>1.19-3.19</td>
</tr>
<tr>
<td>Practice</td>
<td></td>
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</tr>
<tr>
<td>Dispensing</td>
<td>0.70</td>
<td>0.26-1.88</td>
</tr>
<tr>
<td>Non-training</td>
<td>1.39</td>
<td>0.97-2.01</td>
</tr>
<tr>
<td>Rural (cf. urban)</td>
<td>1.06</td>
<td>0.43-2.58</td>
</tr>
<tr>
<td>List size</td>
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<tr>
<td>&lt;5000</td>
<td>0.88</td>
<td>0.58-1.33</td>
</tr>
<tr>
<td>5000-10000</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>&gt;10000</td>
<td>0.56</td>
<td>0.31-0.99</td>
</tr>
</tbody>
</table>

### Medication errors in UK primary care
- 1 in 8 patients
- 1 in 20 prescription items
- Most mild-moderate severity

### Type of prescribing error

<table>
<thead>
<tr>
<th>Type of prescribing error</th>
<th>% of all errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete information</td>
<td>30</td>
</tr>
<tr>
<td>Dose/strength</td>
<td>17.8</td>
</tr>
<tr>
<td>Timing</td>
<td>10.5</td>
</tr>
<tr>
<td>Frequency</td>
<td>8.1</td>
</tr>
<tr>
<td>Omission of concomitant Rx</td>
<td>7.7</td>
</tr>
<tr>
<td>Other</td>
<td>25.9</td>
</tr>
</tbody>
</table>

Avery AJ, The PRACtICe Study, 2012
High-risk prescribing

Adjusted odds ratio (95% CI) for high-risk prescribing

Number of repeat prescriptions

Guthrie B, BMJ 2011
Medication adherence

Polypharmacy and adherence

Gazmararian 2006
(>3 drugs)

Chapman 2008
(>5 drugs)

Stoehr 2008
(>4 drugs)

Turner 2009
(>3 drugs)

Odds ratio for medication adherence

Gellad WF, Am J Geriatr Pharmacother 2011
The elderly

• Altered pharmacokinetics
  • Altered absorption
  • Changes in fat distribution
  • Impaired renal function
  • Impaired liver function

• Altered sensitivity to adverse reactions
  • Impaired gait/balance
  • Cognitive impairment
Polypharmacy is sometimes bad
Polypharmacy is sometimes not bad

Payne RA, unpublished data
Polypharmacy is sometimes not bad

Odds ratio (95% CI) for non-CV admission

<table>
<thead>
<tr>
<th>Number of cardiovascular medicines</th>
<th>None</th>
<th>1-2</th>
<th>3-4</th>
<th>5-6</th>
<th>7+</th>
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<tbody>
<tr>
<td>Ref</td>
<td>1</td>
<td></td>
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</tr>
</tbody>
</table>

Emergency admission

- p<0.001

Potentially preventable emergency admission

- p=0.79

Appleton S, unpublished data
Revisiting the definition of polypharmacy

• Consider polypharmacy as a continuum
• Consider polypharmacy in context

• Appropriate polypharmacy
  • Prescribing for an individual for multiple/complex conditions in circumstances where medicines use can be optimised and the medicines are prescribed according to best evidence. The intent should be maintaining quality of life or improving longevity, whilst minimising harm

• Problematic polypharmacy
  • Prescribing of multiple medications inappropriately, or where the intended benefit of the medication is not realised
Summary

• Our population is ageing and multimorbidity is the norm, and polypharmacy is increasingly common

• Polypharmacy is driven by various patient factors, as well as evidence-based clinical guidance

• Polypharmacy is associated with various adverse outcomes, such as prescribing errors, ADRs and non-adherence

• Polypharmacy can be both appropriate and problematic, and this should be considered when defining it