Polypharmacy is not always hazardous
Retrospective cohort analysis using linked electronic health records from primary and secondary care

RA Payne, GA Abel, AJ Avery, SW Mercer, M Roland
The ageing, multimorbid population

Barnett K, Lancet 2012
ONS, 2010
<table>
<thead>
<tr>
<th>2008</th>
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<tbody>
<tr>
<td>Prostate cancer</td>
<td>Medicines adherence</td>
<td>Venous thromboembolism - reducing the risk</td>
<td>Anxiety</td>
<td>Epilepsy</td>
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<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>
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<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>
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<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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<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>
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<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>Autism in adults</td>
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<td>Prophylaxis against infective endocarditis</td>
<td>Schizophrenia</td>
<td>Neonatal jaundice</td>
<td>Diabetic foot problems - inpatient management</td>
<td>Sickle cell acute painful episode</td>
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<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>Venous thromboembolic diseases</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>Spasticity in children and young people</td>
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<tr>
<td>Lipid modification</td>
<td>Glaucma</td>
<td>Chronic obstructive pulmonary disease</td>
<td>Ovarian cancer</td>
<td>Osteoporosis fragility fracture</td>
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<td>Stroke</td>
<td>Coeliac disease</td>
<td>Bacterial meningitis and meningococcal septicaemia</td>
<td>Common mental health disorders</td>
<td>Lower limb peripheral arterial disease</td>
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<tr>
<td>Respiratory tract infections</td>
<td>Type 2 Diabetes - newer agents</td>
<td>Delirium</td>
<td>Hip fracture</td>
<td>Urinary incontinence in neurological 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>Antibiotics for early-onset neonatal infection</td>
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<td>Familial hypercholesterolaemia</td>
<td>When to suspect child maltreatment</td>
<td>Motor neurone disease - non-invasive ventilation</td>
<td>Stable angina</td>
<td>Headaches</td>
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<td>Attention deficit hyperactivity disorder (ADHD)</td>
<td>Depression in adults</td>
<td>Barrett's oesophagus - ablative therapy</td>
<td>Hypertension</td>
<td>Neutropenic sepsis</td>
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<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>Crohn's disease</td>
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<td>Surgical site infection</td>
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<td>Chronic heart failure</td>
<td>Multiple pregnancy</td>
<td>Psoriasis</td>
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<td>Metastatic spinal cord compression</td>
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<td>Transient loss of consciousness in adults and young people</td>
<td>Hyperglycaemia in acute coronary syndromes</td>
<td>Ectopic pregnancy and miscarriage</td>
</tr>
</tbody>
</table>
Guidelines everywhere...

Multiple medicines are often advocated, but it may be unclear when or how to stop them.

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

\(A + C + D + \text{consider further diuretic}^{10,21}\)

\text{or alpha-blocker or beta-blocker}^{22}

Consider seeking expert advice
Prescribing is increasing

![Graph showing increasing number of prescribed items (millions) from 1994 to 2010.](image)

![Bar chart showing percentage of patients receiving multiple medicines in 1995 and 2010.](image)

Guthrie B, SAPC 2012
Prescribing Cost Analysis, England
Adverse consequences of polypharmacy

Guthrie B, BMJ 2011
Aim

• To examine the association between number of prescribed medicines and unplanned hospital admission.
Methods

- Analysis of adult patients (age >20 years) from 40 representative GP surgeries across Scotland
- Primary care data (demographics, prescribing, 40 long-term diagnoses*)
- Linked secondary care admission data

* Barnett K, Lancet 2012
Methods

• Mixed-effects binary logistic regression model

• Outcome
  • 1-year follow-up for unplanned (emergency) hospital admission

• Predictor variables
  • Age, gender, deprivation, repeat medication count, co-morbidity count
  • Interaction term: medication count \times co-morbidity count
  • Random effect for GP surgery
Results
Study population

- 180,815 adult patients
- 49.3% male
- Median age 49 years (IQR 36 to 63)

- Number of recorded clinical conditions:
Prevalence of use of multiple medicines
Prevalence of use of multiple medicines
Prevalence of use of multiple medicines

Number of medicines:
- None
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10 or more

Percentage of all adults:
- 0%
- 5%
- 10%
- 15%
- 20%
- 25%
- 30%
- 35%
- 40%

Number of clinical conditions:
- None
- 1
- 2
- 3
- 4 or 5
- 6+
Unadjusted numbers of patients admitted

<table>
<thead>
<tr>
<th>Number of medicines</th>
<th>Patients admitted</th>
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<tbody>
<tr>
<td>None</td>
<td>2736</td>
</tr>
<tr>
<td>1 to 3</td>
<td>2356</td>
</tr>
<tr>
<td>4 to 6</td>
<td>2043</td>
</tr>
<tr>
<td>7 to 9</td>
<td>1647</td>
</tr>
<tr>
<td>10+</td>
<td>2046</td>
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</table>
Association between admission and polypharmacy

<table>
<thead>
<tr>
<th>Number of medications</th>
<th>None</th>
<th>1 to 3 (reference)</th>
<th>4 to 6</th>
<th>7 to 9</th>
<th>10 or more</th>
</tr>
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<tr>
<td>None</td>
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</tbody>
</table>

Number of clinical conditions

None 1 2 3 4 or 5 6 or more
Summary of results

- Rates of unplanned hospital admission are strongly associated with number of regular medicines.
- The effect is much reduced in patients with multiple conditions, with only the most extreme levels of polypharmacy being associated with an increase in unplanned hospitalisation.
What this adds to previous work

• First large study to examine in detail the association between number of medicines and hospital admission
  • Not limited to older patients
  • Avoids treating polypharmacy as dichotomous variable
  • Accounts for interplay between polypharmacy and multimorbidity
• Highlights importance of avoiding under-prescribing
Why?

- Increased medicines increased the risk of drug interactions, prescribing errors, poorer adherence, etc.
- May reflect generally poorer quality of care (e.g. lack of continuity of care, suboptimal medication review)

…but…

- Increased morbidity requires more (appropriate) treatment with medication
Conclusion

• Number of medications is associated with hospitalisation

• The effect is greatly reduced in multimorbid patients

• Numbers of medicines should be
  • interpreted as a continuum
  • considered in the context of co-morbidity

• Polypharmacy should not be misinterpreted as a characteristic of care inevitably leading to adverse outcomes