Polypharmacy and Deprescribing for Older People

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Goals

• Learn about the impacts of polypharmacy in older people

• Understand the principles and challenges of deprescribing

• Gain skills in reviewing polypharmacy and deprescribing - David
Polypharmacy is common and increasing

Prevalence studies in older Australians since 2010
Morgan et al., MJA 2012; Hubbard et al., MJA 2015; Jokanovic et al., JAMDA 2016

Figure 4. Prevalence of polypharmacy in people aged 65 years and older in the USA, Scotland and Ireland. There has been a three- to fivefold increase in the prevalence of polypharmacy in older people over the past few decades.\textsuperscript{13,15,16}
Risks of polypharmacy in older people

• Pharmacological risks
  – ‘Inappropriate’ prescribing
  – Drug interactions
    • Drug-drug
    • Drug-disease
    • Drug-food
    • Drug-geriatric syndrome
  – Prescribing cascade

• Clinical risks
  – Adverse drug reactions
  – Geriatric syndromes
  – Hospitalisation and health care utilisation
  – Institutionalisation and death

• Patient/carer burden
  – Administration time
  – Cost

Gnjidic et al., JCE 2012
Pre-clinical Evaluation of Polypharmacy

• In observational studies, polypharmacy increases the risk of functional impairment, falls, frailty and death.
• Evaluation of the effects of polypharmacy in older adults is ethically and feasibly difficult.
Young and old male mice treated with polypharmacy (simvastatin, metoprolol, paracetamol, citalopram, omeprazole)

Locomotor activity in open field

Polypharmacy impaired physical function in old but not in young mice

Rotarod latency

Mouse clinical frailty index

Huizer-Pajkos et al., JGBS 2016
Not just number but also type and dose of medicines determines risk

A Drug Burden Index to Define the Functional Burden of Medications in Older People
Sarah N. Hilmer, MD, PhD; Donald E. Mager, PharmD, PhD; Eleanor M. Simonsick, PhD; Ying Cao, MB; Shari M. Ling, MD; E. Gwen Windham, MD; Tamara B. Harris, MD, MS; Joseph T. Hanlon, PharmD, MS; Susan M. Rubin, MPH; Ronald I. Shorr, MD, MS; Douglas C. Bauer, MD, MPH; Darrell R. Abernethy, MD, PhD

Arch Intern Med. 2007;167:781-787

\[
\frac{E}{\alpha} = \sum \frac{D}{\delta + D}.
\]

- Drug Burden Index (DBI) is a pharmacological measure of an older person’s total exposure to medicines with anticholinergic and sedative effects that impair physical and cognitive function
- Main drug classes:
  - Antipsychotics
  - Benzodiazepines and Z drugs
  - Opioids and gabapentin/pregabalin
  - Antidepressants
  - Antimuscarinics used for urgency
  - Antihistamines
Evaluation of Drug Burden Index

- DBI associated with:
  - Impaired physical function
  - Falls
  - Frailty
  - Hospitalisation and GP visits
  - Institutionalisation
  - Mortality

- Evaluated in older people from community, retirement villages, nursing homes and hospitals internationally
Drug Burden Index as a clinical risk assessment tool

- Development, validation and feasibility testing of DBI software in practice
- Trials in practice:
  - Home Medicines Reviews by pharmacists
  - Hospital inpatients
Polypharmacy and Underuse

Probably most important for IHD medications

- Polypharmacy associated with less use of medicines considered to be essential in younger adults and with increased inappropriate medications

- Tinetti *et al* BMJ 2015: cardiovascular drugs retained mortality benefit in setting of multimorbidity

- Wauters *et al* 2016 BJCP: underuse (STOPP START criteria) of aspirin (2° prevention) and ACEI (CCF) associated with increased mortality
Optimal medical therapy polypharmacy for IHD reduces mortality and institutionalisation in community dwelling older men.
Is a polypharmacy sub-group informative in clinical trials?

Polypharmacy and effects of apixaban versus warfarin in patients with atrial fibrillation: post hoc analysis of the ARISTOTLE trial

![Graph showing the relationship between polypharmacy and health outcomes](image-url)
Deprescribing is the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes.
Why do we need evidence on the effects of deprescribing?

• Risks of deprescribing
  – Adverse drug withdrawal reactions
  – Return of underlying condition or failure to prevent condition
  – Pharmacokinetic and pharmacodynamic effects on remaining medicines

• Benefits of deprescribing
  – Less adverse drug reactions
  – Less treatment burden from taking medicines: eg time, cost

• Implementation
  – Need to define and evaluate a process
Evidence on deprescribing single drug classes in older people

- **Diuretics**
  - 4 studies, 448 subjects
  - Successful 51-100% subjects (recommenced mainly if heart failure)

- **Antihypertensives**
  - 9 studies, 7188 subjects
  - 20-85% normotensive over following 6-60 mths

- **Psychotropics**
  - 15 studies, 1184 subjects
  - ↓falls ↑ cognition and/or behaviour

- **Withdrawal syndromes**
  - None reported and medicines often weaned over weeks

_Iyer et al., Drugs Aging 2008_
Deprescribing Statins in Patients with Advanced Illness

- Multicenter, parallel-group, unblinded, pragmatic clinical trial.
- Adults with an estimated life expectancy of 1 month -1 year, statin for ≥3 months, recent deterioration in function, no recent active cardiovascular disease.
- N= 381 (189 discontinued, 192 continued). Mean age 74 years, 22.0% were cognitively impaired, 49% had cancer.

Kutner et al., JAMA Internal Medicine, 2015

Figure 2. Product-Limit Survival Estimates

Figure 3. Summary of Patient-Reported Outcomes
• 9 trials (7 in Nursing homes) 606 subjects
• 8 of 9 no difference in success of withdrawal between groups
• No difference in psychiatric symptoms except subsets with severe symptoms or psychosis/agitation and have responded
• “We recommend that programmes that aim to withdraw older nursing home residents from long-term antipsychotics should be incorporated into routine clinical practice, especially if the NPS are not severe”

Figure 3. Forest plot of comparison: 1 Discontinuation versus continuation of antipsychotic medication: continuous data, analysis method mean difference, outcome: 1.1. Behavioural assessment by using Neuropsychiatric Inventory (NPI) measuring neuropsychiatric symptoms (NPS) at 3 months (Ballard 2004 and Ballard DART-AD) (forest plot 1).
Implementation of deprescribing antipsychotics for BPSD

Longitudinal study design

**Primary objective:** Reduce use of antipsychotic medication in aged care residents, without increase in substitute psychotropic drugs

**Intervention:** involves study pharmacist, patient’s GP, PHN GP, nursing home champion, nursing training

CI: Prof Henry Brodaty, UNSW

Funding: Australian Government Department of Social Services under the Aged Care Service Improvement and Healthy Ageing Grant Fund.
META-ANALYSIS

Impact of strategies to reduce polypharmacy on clinically relevant endpoints: a systematic review and meta-analysis

25 studies n=10980, 21 RCTs and 4 non-RCTs, 7.4 meds reduced by 0.2 meds per person
No effect on mortality

Johansson et al BJCP 2016
132 papers
- 34,143 participants aged 73.8 ± 5.4 years
- Effect of deprescribing polypharmacy on mortality:
  - Non-randomized studies:
    - significant decrease in mortality (OR 0.32, 95% CI: 0.17–0.60)
  - Randomized studies:
    - no significant change in mortality (OR 0.82, 95% CI 0.61–1.11)
The war against Polypharmacy: A New Cost-Effective Geriatric-Palliative Approach for Improving Drug Therapy in Disabled Elderly People

Doron Garfinkel MD¹, Sarah Zur-Gil MA² and Joshua Ben-Israel MD³

¹Department of Evaluation & Rehabilitation, ²Pharmacy, and ³Directorate, Shoham Geriatric Medical Center, Pardes Hana, Israel

- 6 nursing departments
- Stop or reduce as many drugs as possible using an algorithm
- Restart if necessary using algorithm
Success rate after one year follow-up according to types of drugs discontinued

<table>
<thead>
<tr>
<th>Drug Group</th>
<th>No of pts drug stopped</th>
<th>Failures (signs/symptoms)</th>
<th>Success Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrates</td>
<td>22</td>
<td>0</td>
<td>100</td>
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<tr>
<td>H2 Blockers</td>
<td>35</td>
<td>2</td>
<td>91</td>
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<td>Antihypertensives</td>
<td>51</td>
<td>9</td>
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<td>Diuretics</td>
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<td>Pentoxifylline</td>
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<td>100</td>
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<td>Potassium Supps</td>
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<tr>
<td>Iron Supps</td>
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<tr>
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<td>Antidepressants</td>
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<td>5</td>
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</tr>
<tr>
<td>Antipsychotics</td>
<td>13</td>
<td>4</td>
<td>69</td>
</tr>
</tbody>
</table>

**BETTER CLINICAL OUTCOMES IN STUDY (DEPREScribing) GROUP**

- One year mortality rate: 45% control group vs 21% study group (p < 0.001)
- Annual referral rate to acute care facilities: 30% control group vs 11.8% study group (p < 0.002)
OPTIMED Trial

• A randomized controlled trial of deprescribing to optimize medical therapy for frail older people: The Opti-med Study
• NHMRC Project $1,444,996 over 5 years
• CIs: Beer, Potter, Hilmer, Naganathan, McLachlan, Commans
• Primary aim to determine whether deprescribing is safe among older people living in residential aged care facilities (RACF)
• Secondary outcomes: functional, QOL, prescribing
From why to how...

• Polypharmacy is common in older people with multimorbidity and is associated with significant risks of adverse outcomes

• Need to take opportunities to review medicines during admission, on transfer to RACF, and when patient’s condition or goals of care change

• Deprescribing is one of many outcomes of a medication review

• There is emerging evidence on the outcomes and implementation of deprescribing to inform our practice