OUTLINE

IN OLDER PATIENTS

› What is deprescribing?
› What is the evidence for deprescribing?
› Opportunities and limitations of the acute setting for deprescribing
› Do we deprescribe in hospital?
› How can we optimise medicines including deprescribing in frail older inpatients
WHAT IS DEPRESCRIBING?

- Cessation/discontinuation/withdrawal of a single medication
  - Some definitions include dose reduction
  - The ‘deprescribing process’ is more than just stopping
  - The medication ‘untrial’
  - Part of the medication-use process/prescribing cycle
Patient-centred deprescribing process

**STEP 1: Comprehensive medication history**

Complete and accurate list of all medications

- prescription and OTC
- regular and PRN
- duration
- indications
- adherence
- ADRs
- patient treatment goals

**Cannot go on to STEP 2 without all of this information**
STEP 2: Identify potentially inappropriate medications

Medication appropriateness is dynamic

Decreased or no benefit
- not correct drug for disease
- tolerance to medication (e.g. benzodiazepine)
- improvement in clinical condition
- benefit for short term only (e.g. antibiotics)
- short life expectancy (e.g. statins)

Increased risk
- Patient factors:
  - increasing age (increased risk of ADRs)
  - New medical condition
- Medication factors:
  - new medications started (potential interaction, cumulative risk)

Tools:
- Beers criteria
- Improving Prescribing in the Elderly Tool (IPET)
- STOPP/START criteria
- Drug Burden Index (DBI)
- Medication Appropriateness Index (MAI)
- Good Palliative-Geriatric Practice algorithm (GP-GP)
Patient-centred deprescribing process

STEP 3: Determine if medication can be ceased and prioritisation
› Current patient condition
› Patient willingness
› Physician willingness

› Prioritise which medication to cease first, withdraw one at a time
  › clearly identify withdrawal reactions and return of symptoms
  › physician and patient priorities may differ

STEP 4: Plan and initiate withdrawal
› Tapering required
  › adverse drug withdrawal reactions
  › minimise impact of return of condition (determine lowest effective does)
  › patient comfort
› Symptom action plan
› Communication and co-ordination with the patient and carers
› Inform all health professionals involved in the patient’s care of the withdrawal plan
STEP 5: Monitoring, support and documentation

Monitor for
› withdrawal symptoms
› return of condition
   › symptoms (e.g. heartburn)
   › observations (e.g. blood pressure)
   › laboratory values (e.g. uric acid)
› beneficial effects
   › Resolution of ADRs
   › Improved cognitive/physical function, reduced falls, improved nutrition

Support
› highly valued by patients
› time spent with the health care professional
› Providing non-pharmacological therapy, eg
   › Proton pump inhibitor withdrawal – diet to reduce reflux,
   › Benzodiazepine withdrawal – sleep hygiene or psychology,
   › Antipsychotic withdrawal in BPSD – nursing strategies

› Documentation of the process and outcome
Supportive evidence for deprescribing

- Medicines are less safe in older people: good evidence of iatrogenesis
  - ‘Maleficence’

- Less evidence that medicines are efficacious or effective in older people
  - Even if trials do not exclude on chronologic age, they do so on comorbidity, comedications and/or physical and cognitive function (biologic age/frailty)
  - Uncertain ‘beneficence’
DIRECT EVIDENCE OF SAFETY AND EFFICACY OF DEPRESCRIBING

Drugs Aging 2008

Medication Withdrawal Trials in People Aged 65 Years and Older
A Systematic Review

Shoba Iyer,1 Vasi Naganathan,1 Andrew J. McLachlan1,2 and David G. Le Couteur1

- All trials 1996-2007
- Over 65 yrs, withdrawal of a single medicine
- 31 studies
- N=8972 subjects
- Variety of open label, observational, randomised, placebo controlled studies
Results - trial design

<table>
<thead>
<tr>
<th>Class</th>
<th>Randomised placebo controlled</th>
<th>Randomised no placebo</th>
<th>Prospective observational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics (n=448)</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Antihypertensive (n=7188)</td>
<td>-</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>Psychoactive (n=1184)</td>
<td>8</td>
<td>3</td>
<td>5</td>
</tr>
</tbody>
</table>

Results

› 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
Best quality evidence of safety and efficacy: withdrawal of benzodiazepines used as hypnotics and withdrawal of antipsychotics used for BPSD

- 9 trials (7 in Nursing homes) 606 subjects
- 8 of 9 no difference in success of withdrawal between groups

> 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"
Implementation/ effectiveness studies for
benzodiazepines and antipsychotics

Reduction of Inappropriate Benzodiazepine Prescriptions
Among Older Adults Through Direct Patient Education
The EMPOWER Cluster Randomized Trial

Cara Tannenbaum, MD, MSc; Philippe Martin, BSc; Robyn Tamblyn, PhD;
Andrea Benedetti, PhD; Sara Ahmed, PhD

Table 2. Prevalence, Risk Difference, and Odds Ratios for Discontinuation and Discontinuation Plus Benzodiazepine Dose Reduction
at the 6-Month Follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Participants, No.</th>
<th>Outcome, No. (%)</th>
<th>Risk Difference (95% CI)</th>
<th>No. Needed to Treat</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation of benzodiazepine use</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Intention to treat analysis</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>148</td>
<td>40 (27.0)</td>
<td>0.23 (0.14-0.32)</td>
<td>4.35</td>
<td>8.05 (5.81-18.47)</td>
<td>8.33 (3.32-20.93)</td>
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<tr>
<td>Usual care</td>
<td>155</td>
<td>7 (4.5)</td>
<td></td>
<td>4.03</td>
<td>7.33 (2.16-24.68)</td>
<td>7.73 (2.05-29.82)</td>
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<tr>
<td>Intracohort correlation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.008</td>
<td>0.008</td>
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<tr>
<td>Per protocol analysis</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>123</td>
<td>38 (30.9)</td>
<td>0.26 (0.16-0.36)</td>
<td>3.85</td>
<td>8.53 (3.69-19.76)</td>
<td>8.10 (3.34-19.66)</td>
</tr>
<tr>
<td>Usual care</td>
<td>138</td>
<td>7 (5.1)</td>
<td></td>
<td>3.90</td>
<td>7.00 (1.86-27.42)</td>
<td>7.00 (1.86-27.42)</td>
</tr>
<tr>
<td>Intracohort correlation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.007</td>
<td>0.007</td>
</tr>
<tr>
<td>Discontinuation plus benzodiazepine dose reduction</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Intention to treat analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>148</td>
<td>56 (37.8)</td>
<td>0.27 (0.18-0.37)</td>
<td>3.70</td>
<td>5.05 (2.66-9.59)</td>
<td>5.49 (2.78-10.84)</td>
</tr>
<tr>
<td>Usual care</td>
<td>155</td>
<td>17 (11.0)</td>
<td></td>
<td>3.90</td>
<td>7.00 (1.86-27.42)</td>
<td>7.00 (1.86-27.42)</td>
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<tr>
<td>Intracohort correlation</td>
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<td></td>
<td></td>
<td></td>
<td>0.006</td>
<td>0.006</td>
</tr>
<tr>
<td>Per protocol analysis</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>123</td>
<td>54 (43.9)</td>
<td>0.34 (0.22-0.46)</td>
<td>2.94</td>
<td>6.33 (3.10-12.92)</td>
<td>6.73 (3.12-14.55)</td>
</tr>
<tr>
<td>Usual care</td>
<td>138</td>
<td>16 (11.0)</td>
<td></td>
<td>3.90</td>
<td>7.00 (1.86-27.42)</td>
<td>7.00 (1.86-27.42)</td>
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<tr>
<td>Intracohort correlation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.030</td>
<td>0.030</td>
</tr>
</tbody>
</table>

*95% Confidence intervals were calculated using robust standard errors.

**Adjusted for age, sex, education, health status, indication of benzodiazepine use for insomnia, anxiety disorder, benzodiazepine dose, previous attempt at tapering, duration of benzodiazepine use, and number of medications.
Deprescribing antipsychotics for behavioural and psychological symptoms of dementia

HALT

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, medicare local 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.
Deprescribing psychotropics in long term care

RedUSe: Reducing Use of Sedatives and Aged Care Facilities

› Involves RACFs and their staff, GPs, the supply community pharmacy, as well as the pharmacist providing the QUM services for the RACF.
› Multi-strategic, includes:
  - audits of sedative use
  - educational sessions for nursing staff
  - ‘good practice’ guidelines
  - academic detailing for GPs attending the RACF
  - information provided to relatives and residents
  - involvement of NPS MedicineWise and the PSA

› CI: Juanita Westbury, University of Tasmania
› Funded by Australian Government Department of Social Services under the Aged Care Service Improvement and Healthy Ageing Grant Fund.
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
- Examples: nitrates stopped if not chest pain for 3 months, H2 blockers stopped if no bleeding or symptoms for 12 months, K and Fe supplements, antihypertensives
- Failure of withdrawal defined
- Not randomised

**IMAJ 2007;9:430–434**

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**DEFINED INTERVENTION**

- Discuss the following with the patient/guardian

**DEFINED INTERVENTION FAILURE**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Symptom or Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frusemide</td>
<td>Symptoms of CCF</td>
</tr>
<tr>
<td>H2 Blocker</td>
<td>Dyspepsia</td>
</tr>
<tr>
<td>L-DOPA</td>
<td>Parkinsonism</td>
</tr>
<tr>
<td>Antihyperten</td>
<td>BP &gt; 160/90 or 150/90 if target organ damage</td>
</tr>
<tr>
<td>Iron Supps</td>
<td>Anaemia</td>
</tr>
<tr>
<td>Potassium supps</td>
<td>Hypokalaemia</td>
</tr>
</tbody>
</table>
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>
</tr>
<tr>
<td>H2 Blockers</td>
<td>35</td>
<td>2</td>
<td>91</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td>51</td>
<td>9</td>
<td>82</td>
</tr>
<tr>
<td>Diuretics</td>
<td>27</td>
<td>4</td>
<td>85</td>
</tr>
<tr>
<td>Pentoxifylline</td>
<td>15</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Potassium Supps</td>
<td>20</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Iron Supps</td>
<td>19</td>
<td>1</td>
<td>95</td>
</tr>
<tr>
<td>Sedatives</td>
<td>16</td>
<td>2</td>
<td>88</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>19</td>
<td>5</td>
<td>74</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>13</td>
<td>4</td>
<td>69</td>
</tr>
</tbody>
</table>

**BETTER CLINICAL OUTCOMES**

- 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)

Need higher quality evidence of safety and efficacy of deprescribing in the setting of multimorbidity and polypharmacy
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

- Quality of life
- Anticholinergic and sedative drug exposure (DBI)
- Number of potentially inappropriate medicines
- Number of regular and PRN prescription medicines
- Hospital admissions
- Independence in activities of daily living
- Cognitive function
- Falls
- Fractures
OPTIMED Design

- Double blind RCT with open intervention arm
- Uses encapsulation to hide medication
- Protocol driven medication reduction based on Garfinkel derived by trial pharmacists
- Up to 1,000 participants
- Randomised to:
  - blinded control group
  - blinded intervention group
  - open intervention group
- Most outcomes measured at 3, 6, 9 and 12 months
- ADWE monitored 1 week after any possible change in medication

Target high risk medications with less obvious functional effects: DBI as a trigger to deprescribe

Drug Burden Index: cumulative exposure to anticholinergic and sedative medicines associated with functional impairment

- Development of Drug Burden Index calculator
- Feasibility study with Home Medicines Review
- Primary Aim: Reduce DBI
- Secondary Aim: Improve function

<table>
<thead>
<tr>
<th></th>
<th>DBI decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>6/19 (32%)</td>
</tr>
<tr>
<td>Control</td>
<td>6/31 (19%)</td>
</tr>
</tbody>
</table>

https://www.drugburdenindex.com

Gnjidic et al., Annals of Pharmacotherapy, 2010

Lisa Kouladjian, PhD student
What’s the evidence for deprescribing in older people?

› Limited for both safety and efficacy for most deprescribing interventions (level III or IV)
› Strongest for antipsychotics in BPSD (level I)
› Evidence being generated currently for safety, efficacy and implementation of deprescribing interventions

<table>
<thead>
<tr>
<th>Level</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>A systematic review of level II studies</td>
</tr>
<tr>
<td>II</td>
<td>A randomised controlled trial</td>
</tr>
<tr>
<td>III-1</td>
<td>A pseudorandomised controlled trial (i.e. alternate allocation or some other method)</td>
</tr>
</tbody>
</table>
| III-2 | A comparative study with concurrent controls:  
- Non-randomised, experimental trial  
- Cohort study  
- Case-control study  
- Interrupted time series with a control group |
| III-3 | A comparative study without concurrent controls:  
- Historical control study  
- Two or more single arm studies  
- Interrupted time series without a parallel control group |
| IV    | Case series with either post-test or pre-test/post-test outcomes |

NHMRC Evidence Hierarchy

Opportunities and limitations of the acute setting for deprescribing
Patient-centred deprescribing process in the acute setting

Step 1: Comprehensive medication history
- Available through medication reconciliation
- May be difficult to obtain, e.g., indications for medicines

Step 2: Identify potentially inappropriate medications
- Multidisciplinary review of care goals: may change
- New diagnosis, new medicines
- Specialist and pharmacist review
- Management of acute illness may take priority
- Tools not used in clinical practice

Step 3: Determine if the medication can be ceased and prioritisation
- Discussions with patient/carer, admitting team, pharmacist, GP, other health practitioners involved
- Patient may be delirious/anxious/distracted
- Management of acute illness may take priority

Step 4: Plan and initiate withdrawal
- Can plan
- Difficult to initiate withdrawal of some medicines in hospital or with acute illness
- Management of acute illness may take priority

Step 5: Monitoring, support and documentation
- Needs follow up and support beyond acute setting: communication with and agreement of GP essential
- Documentation in detail on discharge summary

Do we deprescribe in hospital?
We do deprescribe but we prescribe too

Sydney teaching hospital, 329 aged care or rehabilitation patients (Best et al., IMJ 2013)

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>Discharge</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of medicines</td>
<td>7.61 (7.19–8.03)</td>
<td>7.83 (7.43–8.23)</td>
<td>0.22 (−0.07–0.51)</td>
<td>0.1</td>
</tr>
<tr>
<td>DBI</td>
<td>0.41 (0.34–0.47)</td>
<td>0.36 (0.30–0.41)</td>
<td>−0.05 (−0.012–−0.095)</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Psychotropics decreased
Opioids increased

DBI from admission to discharge

Decrease
No Change
Increase

Prescribing for Frail and Robust Inpatients Admitted after a fall

Sydney Teaching Hospital, n=204

<table>
<thead>
<tr>
<th>Medication exposure</th>
<th>Total (n = 204)</th>
<th>Robust (n = 101)</th>
<th>Frail (n = 103)</th>
<th>P value (frail vs. robust)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRID count admission</td>
<td>2.5 ± 2.1</td>
<td>1.6 ± 1.5</td>
<td>3.4 ± 2.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FRID count discharge</td>
<td>2.5 ± 1.9</td>
<td>1.7 ± 1.3</td>
<td>3.3 ± 2.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FRID change: discharge admission</td>
<td>0 ± 2.8</td>
<td>0.1 ± 2.0</td>
<td>−0.1 ± 3.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medication count admission</td>
<td>7.1 ± 4.7</td>
<td>4.4 ± 5.3</td>
<td>9.8 ± 4.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medication count discharge</td>
<td>7.7 ± 4.6</td>
<td>4.9 ± 3.3</td>
<td>10.3 ± 4.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medication change: discharge admission</td>
<td>0.6 ± 6.5*</td>
<td>0.2 ± 4.6*</td>
<td>0.5 ± 6.0*</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DBI admission</td>
<td>40 (20)</td>
<td>5 (5)</td>
<td>35 (35)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DBI discharge</td>
<td>40 (20)</td>
<td>10 (10)</td>
<td>30 (30)</td>
<td>0.001</td>
</tr>
<tr>
<td>DBI change: discharge admission</td>
<td>0 (0)</td>
<td>5 (5)</td>
<td>−5 (−5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Complementary medicines count</td>
<td>1.1 ± 1.2</td>
<td>0.7 ± 1.2</td>
<td>1.5 ± 1.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Chi-squared analysis, McNemar’s test for proportions and Mann Whitney U test as appropriate. Significance determined as P < 0.05. Data presented as mean ± SD or number (percentage of robust/frail population).

DBIs: drug interactions. FRIDs: fall-risk-increasing drugs.

* Represents significant changes in medication exposure from admission to discharge.

Number of medications on discharge was significantly associated with recurrent hospitalisation, falls, and functional decline in the total population.

Number of Falls Risk Increasing Drugs (FRIDs) was significantly associated with recurrent falls, institutionalisation, and functional decline in the total population after 2 months.
- Threshold for recurrent falls: 1.5 FRIDs frail, 2.5 FRIDs robust
How can we optimise medicines including deprescribing in frail older inpatients

Specific considerations for frail (cf robust) older people

› Pharmacokinetics
  - Sarcopaenic obesity impacts on loading dose
  - Reductions in hepatic and renal clearance impact on maintenance dose

› Pharmacodynamics
  - Reduced physiological reserve
  - Inflammatory state, pro-coagulant (?)

› Higher risk of interactions:
  - Higher prevalence of polypharmacy: pharmacokinetic and pharmacodynamic drug-drug interactions
  - Higher prevalence of comorbidity: Drug-disease interactions (therapeutic competition)

› Less clinical trial evidence of efficacy

› Therapeutic aims often towards optimising function

› Medicines may increase risk of frailty
Patient-centred deprescribing and prescribing process for frail older inpatients

Step 1: Comprehensive medication history

Step 2: Identify potentially inappropriate and potentially appropriate medications and doses

Step 3: Determine if the medication can be ceased or started and prioritisation

Step 4: Plan and initiate withdrawal or initiation or dose change

Step 5: Monitoring, support and documentation