Rational prescribing in the older adult

Assoc Prof Craig Whitehead
Introduction

- Physiological ageing and frailty
- Medication risks in older adults
- Drug Burden
- Anticholinergic and sedative drug burden
- Cascade prescribing
- Underprescribing
- Possible solutions
Physiological ageing

Changes in the body with aging.

- **Body Fat As Proportion of Body Weight**
  - Age 20-70: ↑ 35% Increases

- **Plasma Volume**
  - Age 20-80: ↓ 8% Decreases

- **Lean Body Mass and Total Body Water**
  - Age 20-80: ↓ 17% Decreases

Elderly person

Younger person
Physiological Ageing

- Hard to define
- Rate of ageing is very different from person to person
- Gradual reduction in organ function
- Accumulate risk factors for diseases
- Diseases lead us to become disabled
Functional Implications of Organ System Aging

CARDIOVASCULAR
- VO2 max (training effects, reversibility)
- Systolic/diastolic BP (risk of cardiac/CV disease)
- Baroreceptor sensitivity (risk of orthostatic hypotension)
Functional Implications of Organ System Aging

MUSCULOSKELETAL Decreases in:
- Number of motor units/myofibrils. Muscle mass
- Muscle max power output decreases 45% from 50-80
- Muscle strength decreases 20-30% between 60 and 90 (reversible with high intensity resistance exercises)
Renal homeostenosis

Excretion

Conservation

AGE
The secret of life

- We are born
- We peak at 30 odd
- We then face a decline in ability
- We become frail and acquire diseases
- Then we become disabled
- Then we die
- Sudden death may intervene at any moment
End-of-life illness trajectories

“Polypharmacy or poly anticholinergic”
Medications the good the bad and the ugly

- Modern pharmacology has made peoples lives better
- However 10 to 18% of hospitalisations are related to a medication adverse event
- Beers criteria 20% of older adults are taking medication that are probabaly inappropriate and 3% definitely contraindicated.
- Is it too many ? wrong dose ? Or too few drugs which is the problem ?
Poly pharmacy

- Traditional teaching dictates that too many drugs are bad
- Are some drugs worse than others
- This statement has rarely been studied
- There is some limited evidence to support that too many drugs are bad for older adults
ADRs

- ADRs 2-3x higher in elderly *cf* young  
  – Cusak et al, 1997

- Reportedly 5th leading cause of death in US  
  – Lazarou et al, JAMA 1998

- Contributes to 10% of geriatric admissions  
  – Williamson and Chopin, 1980
## ADRs

<table>
<thead>
<tr>
<th>No. of drugs</th>
<th>Risk of ADR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>5%</td>
</tr>
<tr>
<td>6-10</td>
<td>10%</td>
</tr>
<tr>
<td>11-15</td>
<td>30%</td>
</tr>
<tr>
<td>16-20</td>
<td>55%</td>
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</table>

– May et al, Clin Pharmacol Ther 1977
Falls
Drugs as a risk factor for falls

- A large body of literature of observational studies/case control
- Few RCTs in older adults measure falls as an adverse event (esp. psychotropic trials)
- A good metaanalysis was published in 1999
Total number of drugs

- Fairly consistent finding that more than 4 drugs increases risk (OR 2.07-2.91)
- Part of one successful multi-component intervention was to reduce drugs to <4
- Not clear if this definition is only prescription drugs or includes over the counter
- Current evidence base for common conditions start at 4 drug regimes
Psychotropic drugs

- Neuroleptics OR 1.99
- Anti depressants OR 1.62
- Sedative/Hypnotics OR 1.25
- Benzodiazepines OR 1.4
- TCAs OR of 1.4
- ie Small but significant
Psychotopic drugs

- Risk probably independent of cofounders
- Risk maybe biased by indication
- Risk goes up probably with
  - More than one
  - Higher dose
  - ? On initiation rather than chronic use
Psychotropic Drugs

- Short acting BZDs are as risky as Long acting
- New antidepressants may not be safer
- The only study suggested SSRIs may be worse than TCAs but ? patient selection
Other drugs

- Analgesics inc NSAIDs and Opiates don’t increase risk
- Digoxin OR 1.59 and Diuretics OR 1.09 may increase falls
- Other antihypertensives don’t increase risk
- Postural hypotension as a rule doesn’t increase falls risk (but maybe important for an individual)
Drugs and nutritional status

- Loss of weight typically involves loss of muscle mass
- Muscular weakness has been shown to be a risk factor for falls
- Weight loss is a big risk factor for disability
Drugs and Nutritional status

- Anorexient: Digoxin, SSRIs, perhexiline, Amiodarone other cardiovascular drugs, metformin
- Metabolically active: Thyroxine, Insulin, Cortico steroids
- Cognitive Impairment/ sedative: antipsychotics, benzodiazepines
- Swallowing/mastication anticholinergic drugs, EPSE from antipsychotics
Drugs and Delirium

- Psychoactive drugs
  - Withdrawal/Discontinuation syndromes
  - Toxicity (serotonin syndrome)

- Non-psychoactive drugs
  - H2 blockers, steroids, cardiac drugs, NSAIDs, antibiotics, opioids

- Drugs with anticholinergic effects
Anticholinergic drugs and delirium

- Moderate to high anticholinergic activity
  - atropine, benzhexol, hyoscine, oxybutinin, propantheline, tricyclic antidepressants, some antipsychotics

- Medications not usually associated with anticholinergic activity
Drug burden

![Bar chart showing drug burden by condition.}

- Addiction: $366 billion
- Alzheimer's Disease: $148 billion
- Obesity: $123 billion
- Chronic Pain: $95 billion
- Depressive Disorders: $83 billion
- Attention Disorders: $77 billion
- Sleep Disorders: $75 billion
- Stroke: $57 billion
- Vision: $52 billion
- Hearing Loss: $50 billion
- Anxiety: $47 billion
- Schizophrenia: $33 billion
- Epilepsy: $16 billion
- Parkinson's Disease: $10 billion
- Multiple Sclerosis: $9 billion
Drug Burden Index

\[ DB = \sum \frac{D_{AC}}{\delta_{AC} + D_{AC}} + \sum \frac{D_{S}}{\delta_{S} + D_{S}} \]

- **DB**: Drug Burden
- **AC**: Medications with anticholinergic properties
- **S**: Medications with sedative properties
- **D**: Daily dose
- **\(\delta\)**: Minimum recommended daily dose approved by US Food and Drug Administration; estimate of DR\(_{50}\)
Correlate Drug Burden Index with Function in the Health, Aging and Body Composition (Health ABC) Study Participants

Population

Random sample of 3075 Medicare recipients
Pittsburgh, Pennsylvania and Memphis, Tennessee
70-79 years, high functioning, community dwelling

Medication Inventory

“Brown Bag”
All medications actually taken in past 2 weeks

Objective Functional Measures
Longitudinal Association Between Drug Burden and Function in Health ABC Study Participants

Association of

– Drug Burden Index at each time point
– Cumulative drug burden exposure

with function over 5 years
# Health ABC Study Participants with Longitudinal Functional Measures

<table>
<thead>
<tr>
<th>Baseline (Year 1) Characteristics</th>
<th>Included</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>2172</td>
<td>903 (501 dead)</td>
</tr>
<tr>
<td>Age*</td>
<td>73 ± 3</td>
<td>74 ± 3</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>Race (% black)*</td>
<td>37</td>
<td>53</td>
</tr>
<tr>
<td>Drug burden Index over zero (%)</td>
<td>34</td>
<td>37</td>
</tr>
<tr>
<td>Mean number of physical comorbidities*</td>
<td>1.9 ± 1.3</td>
<td>2.3 ± 1.4</td>
</tr>
<tr>
<td>% with significant depression, anxiety or cognitive impairment*</td>
<td>25</td>
<td>29</td>
</tr>
</tbody>
</table>

* p<0.01 for difference between included and excluded participants
Covariates

- Socio-demographics
- Cumulative physical comorbidities
- Cumulative significant depression, anxiety or cognitive impairment
- Significant sleep disturbance
- Body Mass Index (BMI)
Objective Functional Outcomes

- **Short Physical Performance Battery (SPPB)**
  - Observed measures for:
    - Gait speed on 4 or 6 m walk
    - Chair stands
    - Standing balance

- **Gait Speed on 4 or 6 m walk**
  - Component of SPPB

- **Grip Strength**
  - Isometric dynamometer
  - Loss of grip strength:
    - strong predictor of disability and mortality in older people
    - associated with frailty
Association between Drug Burden Index and 4 m or 6 m Walk Speed at Year 6

Subjects with four or six meter gait speed at year 6 (n=2192)

<table>
<thead>
<tr>
<th>Drug burden</th>
<th>Year 1</th>
<th>Year 3</th>
<th>Year 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1457</td>
<td>1619</td>
<td>1566</td>
</tr>
<tr>
<td>0-1</td>
<td>624</td>
<td>516</td>
<td>556</td>
</tr>
<tr>
<td>≥ 1</td>
<td>111</td>
<td>57</td>
<td>70</td>
</tr>
</tbody>
</table>

Drug burden exposure at each timepoint
Association between Drug Burden Index and Grip Strength at Year 6

Subjects with grip strength at year 6 (n=2099)

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<th>Year 3</th>
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<tr>
<td>0</td>
<td>1397</td>
<td>1550</td>
<td>1506</td>
</tr>
<tr>
<td>0-1</td>
<td>600</td>
<td>495</td>
<td>530</td>
</tr>
<tr>
<td>≥ 1</td>
<td>102</td>
<td>54</td>
<td>63</td>
</tr>
</tbody>
</table>
Higher Baseline Drug Burden Index Associated with Lower Function Year 6

- Multivariate regression analysis
- One unit increase in drug burden in year 1 would predict at year 6 an independent decrease in:
  - SPPB of 0.32 (p < 0.005)
  - Gait speed of 0.05 (p < 0.0005)
  - Grip strength of 0.62 (p=0.05)

- Degree of change
  - > that of 2 additional physical or mental comorbidities for each outcome
Substance abuse in older adults

- Poorly studied
- In my experience benzodiazepine abuse and alcohol abuse are common problems
- Dementia can predispose to alcohol abuse in particular
  - They forget that they have been drinking
Substance abuse in older adults

- The issues of psychological and physical dependency plague prescribing.
- Common in therapeutic doses of benzodiazepines.
- Also common with drugs like Protn Pump Inhibitors and Diuretics for example.
Conclusions

- The therapeutic risks of prescribing in late life centres on nutrition, falls and cognition
- Worse in misuse
- Alcohol is the worse drug
- The issues of psychological and physical dependency are common in older adults