Medication Errors: Older Patients & Their Caregivers

Denis O’Mahony,
Dept. of Medicine (Gerontology),
University College Cork &
Cork University Hospital, Ireland
Common Medication Errors in Older People

• Prescribing errors
  - Polypharmacy (caregivers sometimes complicit)
  - Potentially inappropriate medications (PIMs)
  - Potential prescribing omissions (PPOs)
  - Failure to recognise need for palliative pharmacotherapy
• Reconciliation errors
• Compliance errors
  - Packaging, presentation, formulation
  - Failure to detect cognitive problems
• Economic errors
  - Failure to prescribe generics
  - Focus of ‘new, improved’ drugs
How to counteract medication errors in older people

- Ensure correct drug indications
- Ensure no absolute drug contraindications
- Minimize adverse drug-drug, drug-disease interactions
- Minimize Potentially Inappropriate Medications (PIM’s)
- Minimize Potential Prescribing Omissions (PPO’s)
- Identify older people at high risk of and suffering the symptoms of ADR’s, ADE’s
- Identify older people who need palliative Rx
- Translate all medications to generics
- Ensure best value drug selection (BVDS)
- Maximize overall medication appropriateness
- Ensure optimal formulation, packaging, presentation
- Counsel patient and (where appropriate) caregiver
Polypharmacy is a core problem i.e. inappropriate over-prescribing in response to complex comorbidity.

Complex comorbidity → Polypharmacy → Prescribing cascades → Adverse Drug Reactions → Inappropriate medicines
Multimorbidity and Polypharmacy are *not* independent variables

Gilmartin & O’Mahony, 2012
Polypharmacy: new definition

• “The inappropriate pharmacotherapeutic response from doctors to the presence of multimorbidity, usually in an older person, that results in heightened risk of adverse drug reactions and adverse drug events. The presence of 8 or more daily medicines represents a serious risk of adverse drug-related morbidity, which should trigger corrective action.”

O’Mahony, 2012.
Adverse Drug Reaction (ADR)

• “Any noxious, unintended and undesired effect of a drug, excluding therapeutic failures, intentional or accidental poisoning, and drug abuse.”

WHO 1969

e.g. Acute haemorrhagic gastritis 48 hours after starting diclofenac 50 mg t.d.s. with no prior history of PUD and no other drug as a likely cause.

• Severe ADR →
  - Immediate discontinuation of suspect drug
  - Required resuscitative or antidote treatment
  - Caused or contributed to hospitalization
  - Caused or contributed to death
ADR Risk Factors

- Age > 65
- Female > Male
- Polypharmacy (> 6 medicines/day)
- Multimorbid illness (≥ 4 chronic diseases)
- Chronic liver disease
- Acute, chronic kidney disease (eGFR < 60 ml/min/1.73m²)
- Chronic heart failure
- Previous ADR
- Certain drugs: insulin, anticoagulants, neuroleptics, oral hypoglycaemic agents, non-steroidal anti-inflammatories
ADR epidemiology

- 6% of hospital admissions
- 4% of hospital bed-days
- Hospital stay in ADR patients 8% longer
- 0.3% of ADRs are fatal
- Mortality in ADR patients increased x 19 times
- Incidence rate increasing with global ageing
- Recent USA statistics: 5th highest cause of death
- Approx. 3% of all deaths in Sweden
- Mortality in older patients increased 7 times
- Hospital admissions for ADRs increasing
Prospective study design: July – Nov 2010
Eligibility: patients ≥ 65 years admitted via ED
Patients reviewed admission→ discharge
ADR detection: patient interview, case-note analysis, physician consultation, review of laboratory and other investigations
WHO-UMC causality criteria
Discharge letters requested on all in-patients who had an in-hospital ADR (n=135)
All 135 index hospital admissions were reviewed on the Hospital In-Patient Enquiry portal.
ADR’s in hospitalized older people

• 513 hospitalised patients; ≥ 65 years

• 135 in-hospital ADR’s identified (affecting 26% of patients)

• 95% were defined as certain/probable (WHO-UMC criteria)
<table>
<thead>
<tr>
<th>Drug/Drug Class</th>
<th>Adverse Drug Reaction</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>Acute kidney injury/electrolyte disturbance</td>
<td>45 (25%)</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Fall(s)</td>
<td>32 (18%)</td>
</tr>
<tr>
<td>Opiates</td>
<td>Acute confusion/ falls/sedation/constipation</td>
<td>32 (18%)</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Symptomatic bradycardia/Orthostatic hypotension</td>
<td>16 (9%)</td>
</tr>
<tr>
<td>Anti-hypertensive’s (excluding diuretics + beta blockers)</td>
<td>Orthostatic hypotension/Acute Kidney Injury/Hyperkalemia</td>
<td>14 (7.8%)</td>
</tr>
<tr>
<td>NSAID’s (excluding Aspirin)</td>
<td>Gastritis/peptic ulceration/acute kidney injury</td>
<td>10 (5.6%)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Haemorrhage</td>
<td>8 (4.5%)</td>
</tr>
<tr>
<td>Anti-platelets</td>
<td>Haemorrhage/gastritis</td>
<td>6 (3.3%)</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Falls/parkinsonism</td>
<td>3 (1.6%)</td>
</tr>
<tr>
<td>Selective Serotonin Reuptake Inhibitors</td>
<td>Hyponatraemia</td>
<td>3 (1.6%)</td>
</tr>
<tr>
<td>Antibiotics (Cephalosporins)</td>
<td>Clostridium difficile colitis</td>
<td>3 (1.6%)</td>
</tr>
</tbody>
</table>
## Recording of ADR’s in hospital

### HIPE coded data
- 135 records analysed (100%)
- 27/135 (20%) detailed the medication and associated ADR

### Hospital Discharge summary
- 124/135 (92%) discharge letters analysed
- 24/124 (19%) reported that patient had an ADR in hospital
  - 8/24 :detailed description of the ADR
  - 16/24: detailed the drug only but not the ADR

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Insufficient recording of ADR’s by hospitals → Grossly under-reported rate of ADR’s by Irish Medicines Board.
### Can ADR risk be predicted?

<table>
<thead>
<tr>
<th>Multi-Variate Analysis Variable</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p -value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>2.12</td>
<td>1.22</td>
<td>3.69</td>
</tr>
<tr>
<td>75-84</td>
<td>2.22</td>
<td>1.68</td>
<td>4.23</td>
</tr>
<tr>
<td>≥ 85</td>
<td>2.22</td>
<td>1.68</td>
<td>4.23</td>
</tr>
<tr>
<td>Renal Failure (eGFR &lt; 60)</td>
<td>1.81</td>
<td>1.12</td>
<td>2.92</td>
</tr>
<tr>
<td>Liver Disease</td>
<td>1.86</td>
<td>0.90</td>
<td>3.84</td>
</tr>
<tr>
<td>Number of STOPP medications</td>
<td>2.40</td>
<td>1.26</td>
<td>4.59</td>
</tr>
<tr>
<td>Number of Medications</td>
<td>1.09</td>
<td>1.02</td>
<td>1.17</td>
</tr>
<tr>
<td>Assistance ≥ 1 activity of daily living</td>
<td>0.75</td>
<td>0.45</td>
<td>1.26</td>
</tr>
</tbody>
</table>

O’Connor MN et al., 2012
Evidence-based ADR prevention

• Pharmacist-led medication review (17 studies):
  odds ratio 0.64 (95% CI: 0.43 – 0.96) prevents ADR-related admissions
  
  Royal S et al., Qual Saf Health Care 2005
  (Systematic review and meta-analysis)

• Outpatient geriatric clinic care using Comprehensive Geriatric Assessment (one RCT):
  odds ratio 0.65 (95% CI: 0.45 – 0.93) prevents serious ADRs (outside hospital)
  
  Schmader KE et al., Am J Med 2004
  (Randomized controlled trial)

• In-patient structured education programme on ADR recognition, prevention (one RCT in the rehabilitation setting):
  odds ratio: 0.61 (95% CI not cited) prevents ADRs (in hospital)
  
  Trivalle C et al., J Nutr Aging Health 2010
  (Randomized controlled trial)
Prevention of Potentially Inappropriate Prescribing for Elderly Patients: A Randomized Controlled Trial Using STOPP/START Criteria

PF Gallagher¹, MN O’Connor¹ and D O’Mahony¹,²


Effect of STOPP on Medication Appropriateness

Effect of START on Omission of Appropriate Medications

**Post-randomization follow-up**  
*** P<0.001
STOPP/START RCT
Primary outcome:
ADR incidence in acutely ill older patients

Patients admitted between May 2011 and May 2012. Assessed for eligibility (n=1042)

Excluded (n= 310)
- Expected length of stay ≤ 48 hours (n=110)
- Not meeting inclusion criteria (n=174)
- Declined to participate (n=20)
- Terminal Illness (=6)

Randomly assigned (n=732)

Control (n=372)
Normal pharmaceutical care

Follow-up:
Patient, nursing staff & physician interview
ADR detection, causality & preventability

In-hospital death (n=9)
Discharged (n= 363)

Intervention (n=360)
STOPP/START criteria

Application of STOPP/START criteria at 48-72 hours post-admission

Follow-up:
Patient, nursing staff & physician interview
ADR detection, causality & preventability

In-hospital death (n= 11)
Discharged (n= 349)

NIH trial number: NCT01467050
### ADR’s caused by medications listed in STOPP/START criteria

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>Number (%) of patients with at least one instance of IP according to STOPP/START criteria at randomization</th>
<th>Number (%) of ADR’s attributable to medications listed in STOPP/START criteria</th>
<th>Number (%) of ADR’s not attributable to medications listed in STOPP/START criteria</th>
<th>Total number of ADR’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>158 (42.5%)</td>
<td>51 (57%)</td>
<td>38 (43%)</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td>(n = 372)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>176 (48.9%)</td>
<td>15 (33%)</td>
<td>30 (66%)</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>(n = 360)</td>
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</tbody>
</table>

i.e. ADR rate in Intervention Group = 23.9% vs. ADR rate in control Group = 12.5%

**Absolute Risk Reduction = 11.4%; NNT = 9**

Adjusting for number of drugs, PIMs, renal failure, liver disease, heart failure, age, dementia and falls...........

**ADR risk Odds Ratio = 0.43 (CI: 0.28 - 0.67)**
Prescribing Optimization: Starting with a ‘blank canvas’

Drug indications

Drug-drug interaction

Drug-disease interaction

Medications reconciliation

Potential inappropriateness

Potential prescribing omissions

ADR/ADE risk factors

Indications for palliative drug therapy

Generic drug list

Cheapest brands

Assessment of overall medication appropriateness
Age, sex, weight, height

Known diagnoses & severity

Drugs & doses

Drug formulations

Laboratory data:
- biochemistry incl. eGFR
- haematology
- ECG rhythm, ischaemia

Scales: AMTS, Barthel, MNA-sf, CIRS-geriatric

Geriatric syndromes
Present or not?

SHiM screening

Full medication reconciliation

British National Formulary:
Indications, contraindications,
First Data Bank: drug-drug,
drug-disease interactions

ADR risk scale

STOPP criteria

START criteria

1-year mortality risk >50%
→ palliative therapy

Generic medication list

Least expensive brand list

Medication Appropriateness Index
KEEP IT SIMPLE!
THERE IS MORE TO LIFE THAN TAKING TABLETS.

DON’T ADD TO CAREGIVER BURDEN BY COMPLEX DRUG REGIMENS
Summary

• Prevention of ADR’s is vital, most ADR’s are predictable.
• Avoidance of medication errors/medication optimization in multimorbid older people is often complex and challenging ......i.e. there are no simple solutions.
• Polypharmacy, Inappropriate Prescribing, ADR’s not economically sustainable.
• Evidence-based interventions exist.
• Systematic scrutiny of medication essential.
• Co-ordinated, integrated efforts of prescribers and pharmacists is essential for medication optimization.
• EU-wide investment in R&D of effective and efficient pharmacotherapy optimization software systems is needed.
Insanity:
Doing the same thing over and over again and expecting different results.

Albert Einstein