




# Medication Errors & STOPP/START criteria

Denis O'Mahony,
Dept. of Medicine (Gerontology),
University College Cork, Ireland

# What will be discussed

- Inappropriate Prescribing (IP) definition, origin
- Origin & validation of STOPP & START
- STOPP and START IP prevalence data
- IP (STOPP criteria) and Adverse Drug Events
- Use of STOPP & START to improve medication appropriateness
- IP (STOPP criteria) and resource wastage
- Role of STOPP & START in optimisation of medication in older people

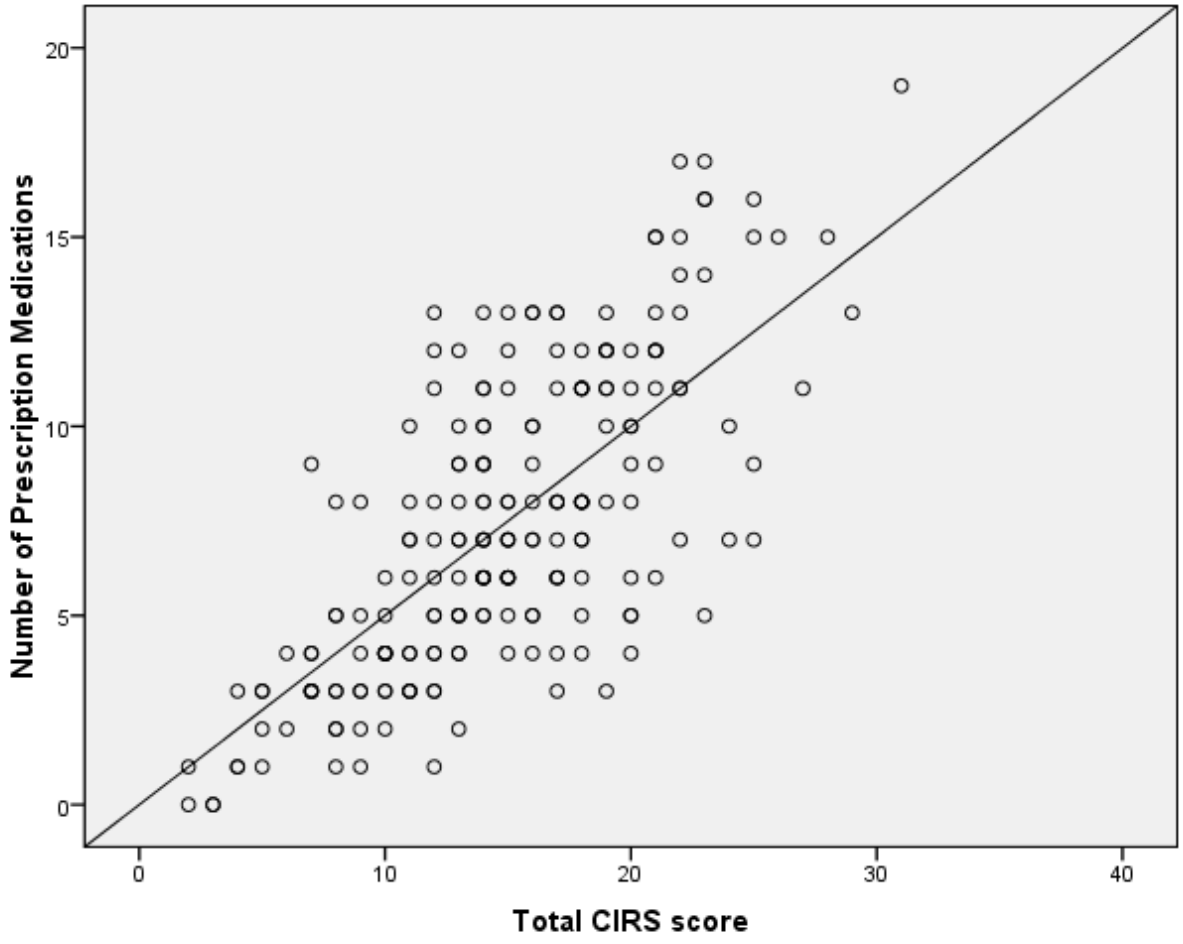
# Medications Errors

- Wrong indication
- No indication
- Treatment duration too short/too long
- Incorrect dose
- Treatment not cost-effective
- Medication not suitable for the patient's circumstances
- Drug-drug interactions not considered
- Drug-disease interactions not considered

&

- Failure to initiate appropriate, indicated pharmacotherapy (errors of omissions)

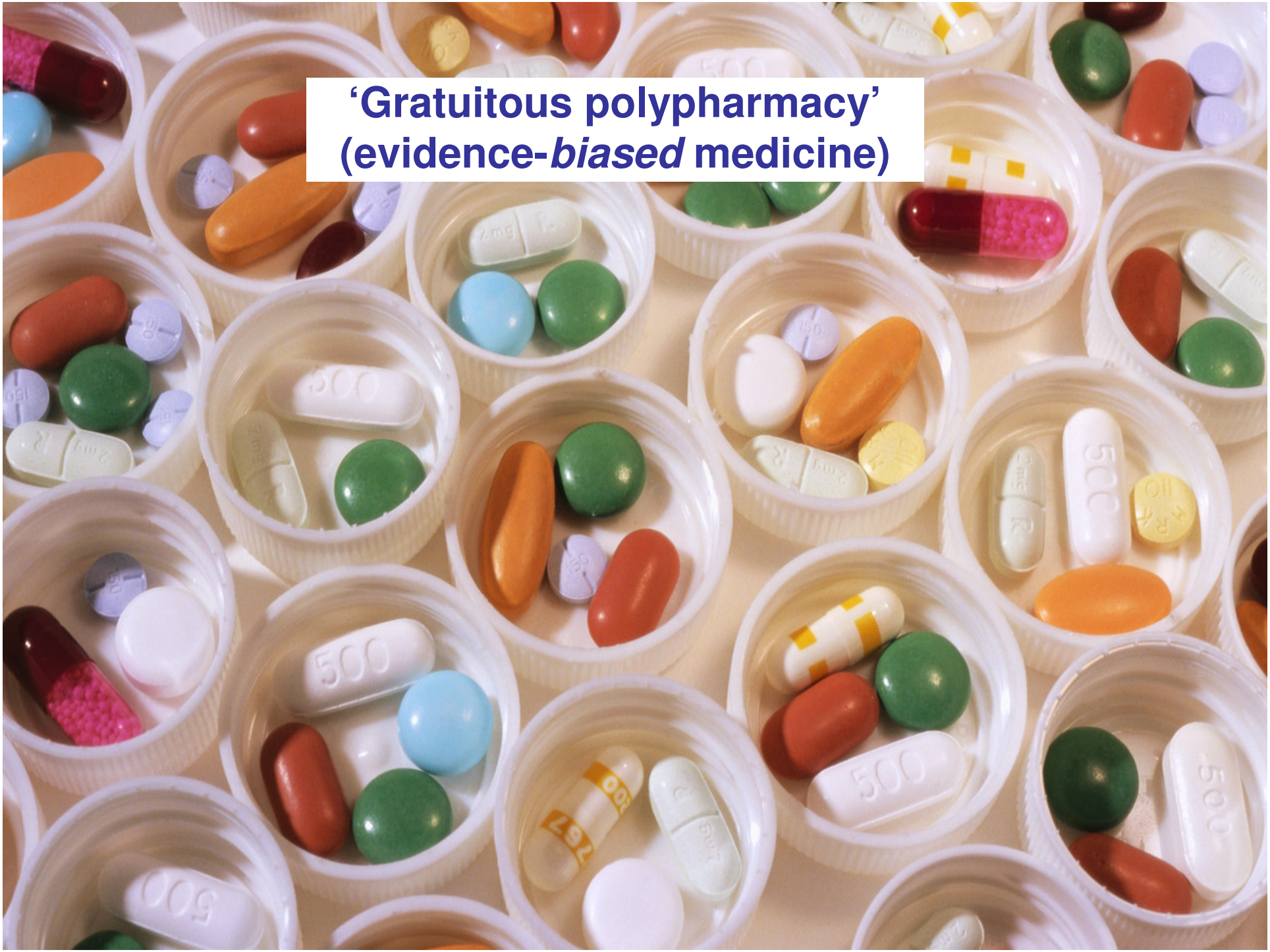
# What causes polypharmacy?




**R = 0.726**

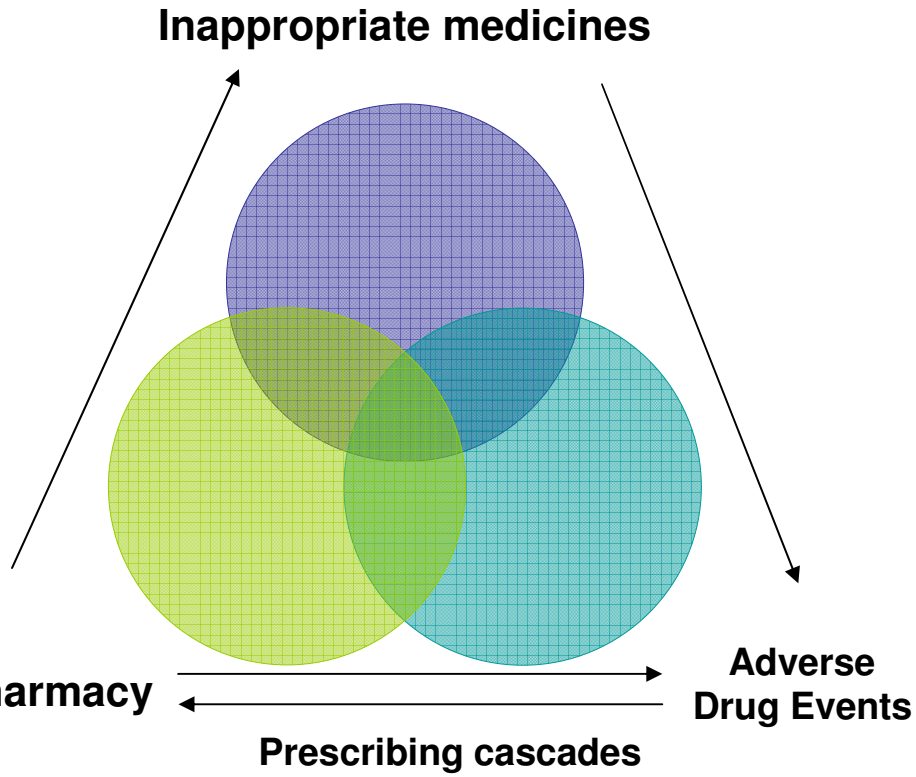
**Gilmartin & O'Mahony, 2012**

**CIRS = Cumulative Illness Rating Scale (Geriatric)**


‘Gratuitous polypharmacy’
(evidence-*biased* medicine)

# Unifying Theory/Concept

***Polypharmacy*** **is a core problem i.e. inappropriate over-prescribing in response to complex comorbidity**



# Official ADR data – Ireland 2010

- 3202 adverse drug reaction (ADR) reports received by Irish Medicines Board (779 ADR reports relating to H1N1 vaccines)

versus

- 329 adverse drug *events* (ADEs) in 3 months in *one hospital* in patients ≥ 65 yrs)

# Inappropriate Prescribing: Definition

The use of a drug

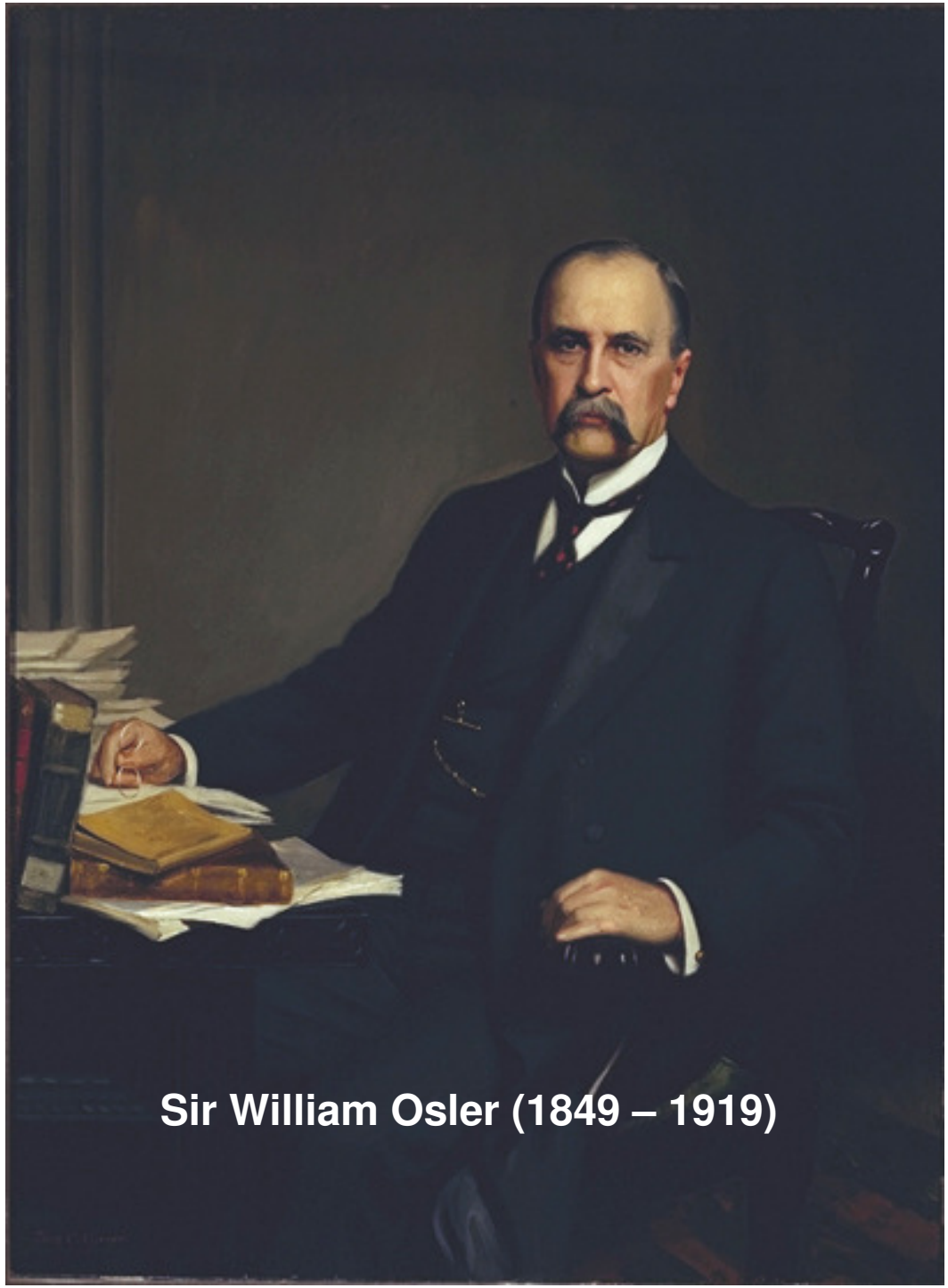
- that has the wrong indication
- that has no indication
- that has a high risk of Adverse Drug Reaction (ADR) i.e. adverse drug-drug or drug-disease interactions or Adverse Drug Event (ADE)
- that is unnecessarily expensive
- for too short or too long a time period

or

The failure to prescribe appropriate drug therapy for irrational or ageist reasons

**“One of the first duties of the physician is to educate the masses *not* to take (inappropriate) medicine.”**

**“Imperative drugging – the ordering of medicine in any and every malady (i.e. polypharmacy) - is no longer regarded as the chief function of the doctor.”**



**Sir William Osler (1849 – 1919)**

# Beers Criteria for Inappropriate Prescribing in Older People: 1991, 1997, 2003

**(A) Independent of Diagnosis**

**(B) Considering Diagnosis**

**Designed for use in any clinical setting**
**"Should be routine"**
**"Should improve outcomes"**

# Beers Criteria: 2012

- For publication May 2012 (JAGS)
- AGS-endorsed
- Interdisciplinary panel of 11 experts
- 53 medications/drug classes
- 3 groups:

(i) potentially inappropriate in all older people

(ii) potentially inappropriate in older people with certain diseases

(iii) drugs to be used with caution in older people

- 'Efficacy' of new Beers Criteria uncertain.

# Problems with Beers Criteria - 1

| | | |
|---|---|---|
| **Trimethobenzamide** | **Methocarbamol** | **Carisoprolol** |
| **Metaxalone** | **Cyclobenzaprine** | **Meprobamate** |
| **Halazepam** | **Reserpine** | **Chlorpropamide** |
| **Hydroxyzine** | **Hyoscyamine** | **Clidinium** |
| **Cyclandelate** | **Cyproheptadine** | **Tripelenamine** |
| **Guanedrel** | **Oxaprozin** | **Guanethidine** |
| **Mesoridazine** | **Isoxsurpine** | **Thiordiazine** |
| **Amphetamines** | **Clonidine** | **Ethacrynic acid** |
| **Dicyclomine** | **Phenylpropanolamine** | **Dessicated thyroid** |

**>50% drugs NOT AVAILABLE IN EUROPE**

- Are amitriptyline, amiodarone, nitrofurantoin, doxazosin and propranolol inappropriate?
- No drug-drug interactions
- No therapeutic duplication
- No under-prescribing
- Few prospective studies done using all criteria
- No RCTs using criteria as an intervention

?

# Problems with Beers Criteria - 2

- Focused on US prescriber
- Unstructured
- Not used in routine clinical practice
- Lack of efficacy data in relation to:

  (i) ADE prevention

  (ii) Cost reduction
- Lack of significant association between Beers IP drugs and risk of ADE's
- Do not include several important instances of IP

# No mention in Beers Criteria of…

**(i) Loop diuretic for dependent ankle oedema only, i.e. no clinical signs of heart failure (no evidence of efficacy, compression hosiery usually more appropriate).**
**(ii) Thiazide diuretic with a history of gout (may exacerbate gout).**
**(iii) Aspirin to treat dizziness not clearly attributable to cerebrovascular disease (not indicated).**
**(iv) Tricyclic anti-depressants with glaucoma (likely to exacerbate glaucoma).**
**(v) Long-term (i.e. >1 month) neuroleptics as long-term hypnotics (risk of confusion, hypotension, extra-pyramidal side-effects, falls).**
**(vi) Anti-cholinergics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anti-cholinergic toxicity).**
**(vii) Prochlorperazine (Stemetil) with Parkinsonism (risk of exacerbating Parkinsonism).**
**(viii) Proton pump inhibitor for peptic ulcer disease at full therapeutic dosage for >8 weeks (dose reduction or earlier discontinuation indicated).**
**(ix) Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).**
**(x) Non-steroidal anti-inflammatory drugs (NSAIDs) with moderate to severe hypertension (risk of exacerbation of hypertension).**
**(xi) NSAID with heart failure (risk of exacerbation of heart failure).**
**(xii) NSAID with chronic renal failure (risk of deterioration in renal function).**
**(xiii) Alpha-blockers in males with frequent urinary incontinence, i.e. one or more episodes of incontinence daily (risk of urinary frequency and worsening of incontinence).**
**(xiv) Beta-blockers in those with diabetes mellitus and frequent hypoglycaemic episodes, i.e. ≥1 episode per month (risk of masking hypoglycaemic symptoms).**
**(xv) Oestrogens with a history of venous thromboembolism (increased risk of recurrence).**
**(xvi) Neuroleptics and recurrent falls (may cause gait dyspraxia and Parkinsonism, leading to further falls).**
**(xvii) Vasodilator drugs with persistent postural hypotension, i.e. recurrent >20 mmHg drop in systolic blood pressure (risk of syncope, falls).**
**(xviii) Long-term opiates, i.e. >3 months in those with chronic constipation without concurrent use of laxatives (risk of severe constipation).**
**(xix) Any duplicate drug class prescription, e.g. two concurrent opiates, NSAIDs, loop diuretics, ACE inhibitors (optimisation of monotherapy within a single drug class should be observed prior to considering a new agent).**

**O'Mahony & Gallagher, *Age & Ageing*, 2008**

# New IP Criteria?

- Errors of prescribing commission
- Errors of prescribing omission
- Structured according to physiological systems (alá drug formularies)
- Recognize specific high risk groups particularly fallers, patients with dementia
- Reflect current prescribing practice
- Designed for application in all clinical settings

# New Draft IP Criteria

- (A) **S**creening **T**ool of **O**lder **P**ersons' potentially inappropriate **P**rescriptions (acronym, **STOPP**): 68 draft criteria

- (B) **S**creening **T**ool to **A**lert doctors to **R**ight (i.e. indicated, appropriate) **T**reatment (acronym, **START**): 22 draft criteria

# Validation of STOPP & START

- Consensus panel of 18 experts in Geriatric Pharmacotherapy in Ireland & UK
- Geriatric Medicine, Clinical Pharmacology, Old Age Psychiatry, Clinical Pharmacy, Primary Care Medicine
- Delphi process (2 rounds)
- Final agreed list of STOPP criteria (n=65), START criteria (n=22)
- Good inter-rater reliability (STOPP k = 0.75; START k = 0.68)

**Gallagher P et al., *Int J Clin Pharmacol Ther* 2008; 46: 72-83**

# STOPP: Screening Tool of Older People's potentially inappropriate Prescriptions

**The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age.**

## Cardiovascular System

1. **Digoxin at a long-term dose > 125μg/day with impaired renal function***
2. **Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure**
3. **Loop diuretic as first-line monotherapy for hypertension**
4. **Thiazide diuretic with a history of gout.**
5. **Non-cardioselective beta-blocker with Chronic Obstructive Pulmonary Disease (COPD).**
6. **Beta-blocker in combination with verapamil**
7. **Use of diltiazem or verapamil with NYHA Class III or IV heart failure**
8. **Calcium channel blockers with chronic constipation**
9. **Use of aspirin and warfarin in combination without histamine H2 receptor antagonist (except cimetidine because of interaction with warfarin) or PPI**
10. **Dipyridamole as monotherapy for cardiovascular secondary prevention**
11. **Aspirin with a past history of peptic ulcer disease without histamine H2 receptor antagonist or proton pump inhibitor**
12. **Aspirin at dose > 150mg day**
13. **Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event**
14. **Aspirin to treat dizziness not clearly attributable to cerebrovascular disease**
15. **Warfarin for first, uncomplicated deep venous thrombosis for > 6 months**
16. **Warfarin for first uncomplicated pulmonary embolus for > 12 months**
17. **Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder**

**** eGFR <50ml/min.***

## Central Nervous System and Psychotropic Drugs

1. **Tricyclic antidepressants (TCA's) with dementia**
2. **TCA's with glaucoma**
3. **TCA's with cardiac conductive abnormalities**
4. **TCA's with constipation**
5. **TCA's with an opiate or calcium channel blocker**
6. **TCA's with prostatism or prior history of urinary retention**
7. **Long-term (i.e. > 1 month), long-acting benzodiazepines e.g. chlordiazepoxide, fluazepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites e.g. diazepam**
8. **Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics**
9. **Long-term neuroleptics in those with parkinsonism**
10. **Phenothiazines in patients with epilepsy**
11. **Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications**
12. **Selective serotonin re-uptake inhibitors (SSRI's) with a history of clinically significant hyponatraemia**
13. **Prolonged use (> 1 week) of first generation antihistamines i.e. diphenydramine, cyclizine, chlorpheniramine, promethazine**

## Gastrointestinal System

1. Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause
2. Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis i.e. bloody diarrhoea, high fever or severe systemic toxicity
3. Prochlorperazine (Stemetil) or metoclopramide with Parkinsonism
4. PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks
5. Anticholinergic antispasmodic drugs with chronic constipation

## Respiratory System

1. Theophylline as monotherapy for COPD
2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD
3. Nebulised ipratropium with glaucoma

## Musculoskeletal System

1. Non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or GI bleeding, unless with concurrent H2 receptor antagonist, PPI or misoprostol
2. NSAID with moderate-severe hypertension
3. NSAID with heart failure
4. Long-term use of NSAID (>3 months) for symptom relief of mild osteoarthtitis
5. Warfarin and NSAID together
6. NSAID with chronic renal failure*
7. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis or osterarthritis.
8. Long-term NSAID or colchicine for chronic treatment of gout where no contraindication to allopurinol

## Urogenital System

1. Bladder antimuscarinic drugs with dementia
2. Antimuscarinic drugs with chronic glaucoma
3. Antimuscarinic drugs with chronic constipation
4. Antimuscarinic drugs with chronic prostatism
5. Alpha-blockers in males with frequent incontinence
6. Alpha-blockers with long-term urinary catheter

## Endocrine System

1. Glibenclamide or chlorpropamide with type 2 DM
2. Beta-blockers in those with DM and frequent hypoglycaemic episodes
3. Oestrogens with a history of breast cancer or venous thromboembolism
4. Oestrogens without progestogen in patients with intact uterus

**Drugs that adversely affect those prone to falls**

1. **Benzodiazepines**
2. **Neuroleptic drugs**
3. **First generation antihistamines**
4. **Vasodilator drugs with persistent postural hypotension**
5. **Long-term opiates**

**Analgesic Drugs**

1. **Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain**
2. **Regular opiates for >2 weeks in those with chronic constipation without concurrent laxative**
3. **Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome**

**Duplicate Drug Classes**

1. **Any duplicate drug class prescription e.g. concurrent opiates, NSAID's, SSRI's, loop diuretics, ACE inhibitors**

**i.e. 65 rules relating to the most common and the most potentially dangerous instances of inappropriate prescribing in older people.**

# START: Screening Tool to Alert doctors to Right i.e. appropriate, indicated Treatment.

**These medications should be considered for people ≥ 65 years of age with the following conditions, where no contraindication to prescription exists.**

**Cardiovascular System**

1. Warfarin in the presence of chronic atrial fibrillation
2. Aspirin in the presence of chronic atrial fibrillation, where warfarin is contraindicated, but not aspirin
3. Aspirin or clopidogrel with a history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm
4. Antihypertensive therapy where systolic BP consistently >160 mmHg
5. Statin therapy with a history of coronary, cerebral or peripheral vascular disease, where functional status remains independent for activities of daily living and life expectancy is > 5 years
6. Angiotensin Converting Enzyme (ACE) inhibitor with chronic heart failure
7. ACE inhibitor following acute myocardial infarction
8. Beta-blocker with chronic stable angina

**Respiratory System**

1. Regular inhaled beta 2 agonist or anticholinergic for mild to moderate asthma or COPD
2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where predicted FEV1 <50%
3. Home continuous oxygen with documented chronic type 1 respiratory failure or type 2 respiratory failure

**Central Nervous System**

1. L-DOPA in idiopathic Parkinson's disease with functional impairment and disability
2. Antidepressant with moderate-severe depressive symptoms

**Gastrointestinal System**

1. Proton Pump Inhibitor with severe GORD or peptic stricture requiring dilatation
2. Fibre supplement for chronic, symptomatic diverticular disease with constipation

**Musculoskeletal System**

1. Disease-modifying anti-rheumatic drug (DMARD) with active rheumatoid disease lasting > 12 weeks
2. Bisphosphonates in patients taking maintenance corticosteroid therapy
3. Calcium/Vitamin D supplement in patients with osteoporosis (fragility fracture, dorsal kyphosis)

**Endocrine System**

1. Metformin with type 2 diabetes +/- metabolic syndrome (in the absence of renal impairment*)
2. ACE inhibitor or ARB in diabetes with nephropathy i.e. proteinuria or micoralbuminuria +/- renal impairment*
3. Antiplatelet therapy in diabetes mellitus with co-existing cardiovascular risk factors
4. Statin therapy in diabetes mellitus if co-existing major cardiovascular risk factors present

** eGFR <50ml/min.*

**i.e. 22 rules relating to common instances of prescribing omission**

# 6 European Centres:

- **Ireland (Cork)**
  - D O'Mahony
  - P Gallagher
- **Switzerland (Geneva)**
  - JP Michel
  - PO Lang
- **Belgium (Ostende)**
  - JP Baeyens
  - H Baeyens
- **Spain (Madrid)**
  - A Cruz-Jentoft
  - B Montero
- **Czech Rep (Prague)**
  - E Topinkova
  - P Madlova
- **Italy (Perugia)**
  - A Cherubini
  - B Gasperini

**Inter-rater reliability of STOPP and START criteria between 9 hospital physicians on 20 datasets with 181 medications in 6 different European countries.**

| Rater combination | A | B | C | D | Ppos | Pneg | Kappa (95% CI) |
|---|---|---|---|---|---|---|---|
| **STOPP criteria** | | | | | | | |
| Rater 1 ∗ rater 2 | 1,255 | 4 | 0 | 41 | 0.99 | 0.95 | 0.95 (0.91–0.99) |
| Rater 1 ∗ rater 3 | 1,254 | 5 | 3 | 38 | 0.99 | 0.90 | 0.90 (0.83–0.97) |
| Rater 1 ∗ rater 4 | 1,254 | 5 | 3 | 38 | 0.99 | 0.90 | 0.90 (0.83–0.99) |
| Rater 1 ∗ rater 5 | 1,255 | 4 | 0 | 41 | 0.99 | 0.95 | 0.95 (0.91–0.99) |
| Rater 1 ∗ rater 6 | 1,258 | 1 | 2 | 39 | 0.99 | 0.96 | 0.96 (0.92–1) |
| Rater 1 ∗ rater 7 | 1,257 | 2 | 1 | 40 | 0.99 | 0.96 | 0.96 (0.92–1) |
| Rater 1 ∗ rater 8 | 1,253 | 6 | 3 | 38 | 0.99 | 0.89 | 0.89 (0.82–0.96) |
| Rater 1 ∗ rater 9 | 1,250 | 9 | 0 | 41 | 0.99 | 0.90 | 0.90 (0.83–0.96) |
| Median (IQR) | | | | | 0.99 | 0.93 | 0.93 (0.90–0.96) |
| **START criteria** | | | | | | | |
| Rater 1 ∗ rater 2 | 417 | 3 | 2 | 18 | 0.99 | 0.88 | 0.87 (0.76–0.98) |
| Rater 1 ∗ rater 3 | 417 | 3 | 3 | 17 | 0.99 | 0.85 | 0.84 (0.72–0.97) |
| Rater 1 ∗ rater 4 | 418 | 2 | 1 | 19 | 0.99 | 0.92 | 0.92 (0.84–1) |
| Rater 1 ∗ rater 5 | 417 | 3 | 0 | 20 | 0.99 | 0.93 | 0.93 (0.84–1) |
| Rater 1 ∗ rater 6 | 416 | 4 | 3 | 17 | 0.99 | 0.83 | 0.82 (0.69–0.95) |
| Rater 1 ∗ rater 7 | 415 | 5 | 5 | 15 | 0.98 | 0.75 | 0.74 (0.58–0.89) |
| Rater 1 ∗ rater 8 | 413 | 7 | 1 | 19 | 0.99 | 0.83 | 0.82 (0.69–0.94) |
| Rater 1 ∗ rater 9 | 414 | 6 | 0 | 20 | 0.99 | 0.87 | 0.86 (0.75–0.97) |
| Median (IQR) | | | | | 0.99 | 0.86 | 0.85 (0.82–0.91) |

A, both raters agreed criterion not fulfilled; B, rater 1 scored criterion not fulfilled and rater 2 scored criterion as being fulfilled; C, rater 1 scored criterion as fulfilled and rater 2 scored criterion as not fulfilled; D, both raters scored criterion as being fulfilled; ppos, proportion of positive agreement; pneg, proportion of negative agreement; CI, confidence interval; IQR, interquartile range.

**Gallagher et al., *Age Ageing* 2009**

# Application of STOPP, START

- Define prevalence rates of IP in different clinical settings:
  - Primary Care (general practice)
  - Secondary Care (hospital)
  - Nursing Home/Continuing Care
- Compare IP rates in different countries
- Can STOPP predict ADE's?
- Can STOPP & START be used clinically to:
  (i) improve medication appropriateness?
  (ii) reduce ADE incidence?
  (iii) reduce cost of pharmacotherapy?

# Prevalence rates of IP in Ireland (STOPP criteria & Beers criteria)

- **Primary Care:**
  - STOPP: 21.4%
  - Beers: 18.3%

**Ryan C et al., *Br J Clin Pharmacol* 2009**

- **Secondary Care:**
  - STOPP: 34.5%
  - Beers: 25%

**Gallagher P & O'Mahony D, *Age Ageing* 2008**

- **Nursing Home Care**
  - STOPP: 60% - 70%

**O'Sullivan D et al., *Eur Ger Med* 2010**
**Ryan C et al., *Age Ageing* 2012 (in press)**

# Prevalence Rates of PPO's in Ireland (START criteria)

- Primary Care: 22.7%

**Ryan C et al., *Br J Clin Pharmacol* 2009**

- Secondary Care: 57.9%

**Barry P et al., *Age Ageing* 2007**

- Nursing Homes: 42%

**Ryan C et al., *Age Ageing* 2012 (in press)**

# Risk Factors for Prescribing Omission

- Age > 85 years (odds ratio 2.08; p< 0.01)
- Female gender (odds ratio 2.29; p< 0.01)
- Greater Charlson Index (comorbidity) scores (CI score > 2: odds ratio 3.25; p<0.001)
- > 10 daily drugs (odds ratio 7.22; p< 0.001)

Barry et al., *Age Ageing*, 2007

Gallagher et al., *Eur J Clin Pharmacol*, 2011

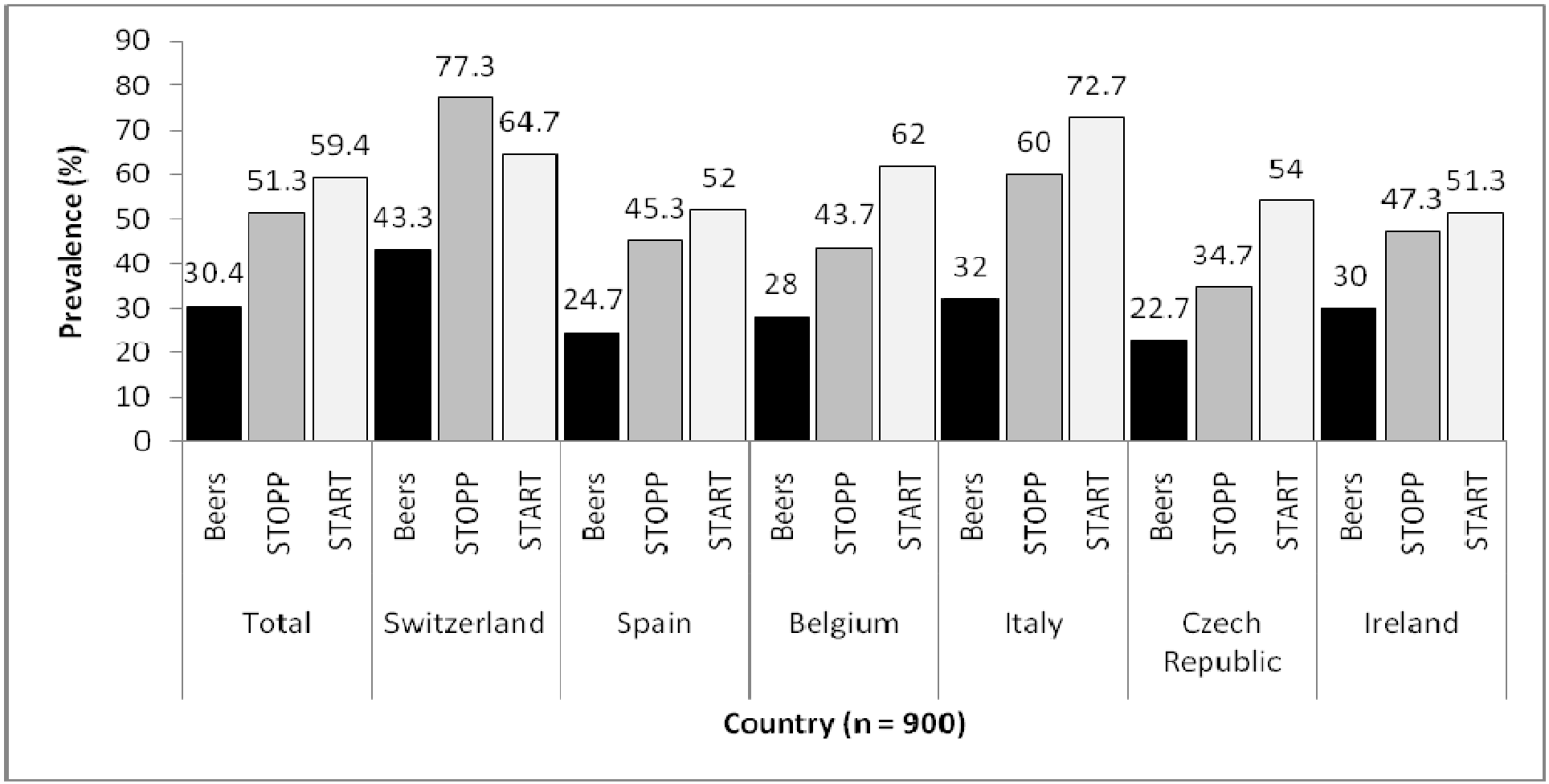
# IP rates in different countries

- 6 European centres:

  Cork Madrid Geneva Ostende

  Prague Perugia
- 150 consecutive cases in each centre
- STOPP, Beers' Criteria → PIM's
- START → PPO's
- Criteria applied by trained geriatricians

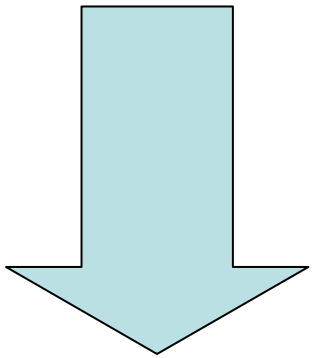
# Rates of PIM's & PPO's in 6 European Centres




Gallagher et al., *Eur J Clin Pharmacol*, 2011

# Inappropriate Prescribing & Adverse Drug Events (ADEs)

- Laroche et al. (2007): 2018 pts
- Onder et al. (2005): 5152 pts



PIMs *not* significantly associated with ADEs in older hospitalised pts, *using Beers' Criteria*

Laroche *et al*., *Br J Clin Pharmacol* 2007
Onder *et al*., *Eur J Clin Pharmacol* 2005

# ADEs in older people on admission to hospital

- Cork University Hospital data 2006-7
- 715 consecutive patients with acute illness in one 3 month period
- Age ≥ 65 years
- Retrospective assessment of ADE occurrence
- STOPP criteria PIMs causal/contributory to acute admission in **11.5%**
- Beers' criteria PIMs causal/contributory to acute admission in **6%**

Gallagher & O'Mahony, *Age Ageing*, 2008

ORIGINAL INVESTIGATION

LESS IS MORE

# Potentially Inappropriate Medications Defined by STOPP Criteria and the Risk of Adverse Drug Events in Older Hospitalized Patients

*Hilary Hamilton, MB, MRCPI; Paul Gallagher, PhD, MRCPI; Cristin Ryan, PhD, MPSI; Stephen Byrne, PhD, MPSI; Denis O'Mahony, MD, FRCPI*

Archives of Internal Medicine,
June, 2011

# Definition of an Adverse Drug Event (ADE)

- "Harm caused by the use of a drug"

  Nebeker et al., *Ann Intern Med*, 2004

- Severe ADE →
  - Immediate discontinuation of suspect drug
  - Required resuscitative or antidote treatment
  - Caused or contributed to hospitalization
  - Caused or contributed to death

# ADE Causality: WHO-UMC criteria

| Categories | Time sequence | Other drugs and diseases excluded | Dechallenge | Rechallenge |
|---|---|---|---|---|
| Certain | Yes | Yes | Yes | Yes |
| Probable | Yes | Yes | Yes | No |
| Possible | Yes | No | No | No |
| Unlikely | No | No | No | No |

**www.who-umc.org**

# ADEs on arrival to hospital

- 600 consecutive pts aged ≥ 65 → CUH
- Acute unselected illness, requiring admission
- 40% male; median age 77
- 34% taking ≤ 5 meds;
- 46% taking 6-10 meds;
- 20% taking > 10 meds
- 329 ADEs identified in 158 pts (26.3%)


Gold standard ADE definition: expert consensus panel

# ADEs & Acute Hospital Admission

- 36/329 ADEs (10.9%) the ***prime cause of hospital admission*** in ADE-affected patients
  i.e. ***6% of total*** cohort of 600 patients

- 183/329 ADEs (55.6%) ***significantly contributed to hospital admission*** in ADE-affected patients
  i.e. ***14.7% of total*** cohort of 600 patients

- 110/329 (33.5%) ADEs ***not causal or contributory to admission***

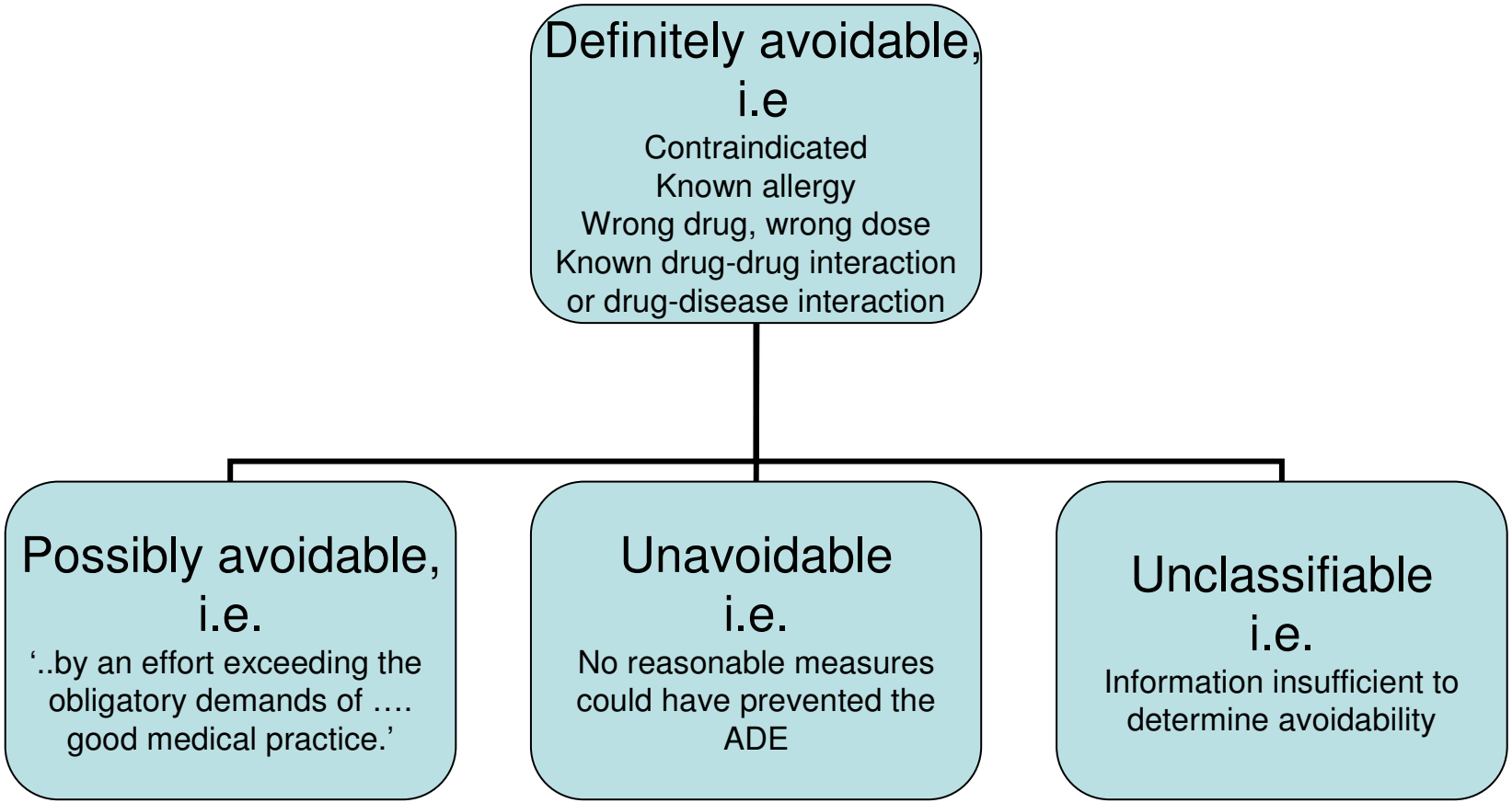
# ADE+ versus ADE- patients

**Table 1. Baseline Characteristics of Patients With and Without ADEs on Admission to Hospital**

| Variable | No. (%) | | Test Statistic For Difference Between Groups | *P* Value |
|---|---|---|---|---|
| | Patients With At Least 1 ADE | Patients With No ADE | | |
| Age, y | | | | |
| Median (IQR) | 79 (73-84) | 77 (72-83) | Mann-Whitney=31545.00 | .07 |
| 65-74 | 48 (30.4) | 159 (36) | | |
| 75-84 | 77 (48.7) | 195 (44.1) | $\chi^2_2$=1.658 | .44 |
| ≥85 | 33 (20.9) | 88 (19.9) | | |
| Sex | | | $\chi^2_1$=4.698 | .03 |
| Female | 106 (67.1) | 253 (57.2) | | |
| Male | 52 (32.9) | 189 (42.8) | | |
| Place of residence | | | $\chi^2_2$=21.680 | <.001 |
| Home | 125 (79.1) | 408 (92.3) | | |
| Nursing home | 25 (15.8) | 29 (6.6) | | |
| Sheltered accommodation | 8 (5.1) | 5 (1.1) | | |
| Functional level | | | $\chi^2$=19.677 | <.001 |
| Independent in ADLs | 86 (54.4) | 325 (73.5) | | |
| Needs help with ≥1 ADL | 72 (45.6) | 117 (26.5) | | |
| Falls | | | $\chi^2_1$=22.560 | <.001 |
| ≥1 fall in 3 mo before admission | 125 (79.1) | 256 (57.9) | | |
| No fall in 3 mo before admission | 33 (20.9) | 186 (42.1) | | |
| Hospitalization | | | $\chi^2_3$=6.104 | .64 |
| ≥1 in previous year | 71 (44.9) | 186 (42.1) | | |
| None in previous year | 87 (55.1) | 256 (57.9) | | |

Abbreviation: ADEs, adverse drug events; ADL, activity of daily living; IQR, interquartile range.

# ADR/ADE avoidability criteria




*Hallas J et al., *J Intern Med* 1990

# Avoidable ADEs that caused or contributed to hospitalisation

- 36 ADEs *caused* admission; 19 ADEs *definitely* avoidable; 7 ADRs *possibly* avoidable
- 183 ADEs *contributed* to admission; 88 ADEs *definitely* avoidable; 36 ADEs *possibly* avoidable
- i.e. **107/219 ADEs causal/contributory to admission *definitely* avoidable (i.e. 49% of ADEs)**
- i.e. **43/219 ADEs causal/contributory to admission *possibly* avoidable (i.e. 20% of ADEs)**

# STOPP vs. Beers: *avoidable* ADEs that cause or contribute to hospitalization

**Table 4. Comparison of STOPP Criteria and Beers Criteria in Terms of Total ADEs Identified and Total ADEs Deemed Avoidable (Hallas Criteria)[a]**

| | STOPP Criteria | Beers Criteria |
|---|---|---|
| No. of ADEs of the 329 ADEs identified by expert consensus panel and simultaneously listed in PIM criteria | 170[b] | 67 |
| No. of consensus panel–identified ADEs deemed avoidable or potentially avoidable (n=235) and simultaneously identified by PIM criteria | 159[b] | 67 |
| No. of consensus panel–identified ADEs deemed causal or contributory to index hospital admission and simultaneously avoidable or potentially avoidable (n=151) identified by PIM criteria | 94[b] | 34 |

Abbreviations: ADEs, adverse drug events; PIM, potentially inappropriate medicine; STOPP, Screening Tool of Older Persons' potentially inappropriate Prescriptions.

[a]The expert panel identified 329 ADEs in 158 of the 600 patients (26.3%), independent of STOPP criteria and Beers criteria. Of the 329 ADEs, 235 were judged to be avoidable or potentially avoidable.

[b]Significant difference ($\chi^2$ test, $P<.001$).

Hamilton et al., *Arch Intern Med* June, 2011

# STOPP vs Beers: Summary

After adjusting for age, sex, comorbidity, dementia, baseline ADLs, number of medications……

- Clinically significant ADEs were listed in STOPP **2.54 times** more often than in Beers criteria
- Risk of a severe, avoidable ADE ***is*** increased significantly with STOPP medications (**OR=1.85**, 95% CI 1.51-2.26, p<0.001)
- Risk of a severe, avoidable ADE ***is not*** increased significantly with Beers medications (OR=1.28, 95% CI 0.94-1.72,p=0.11)

# Common *avoidable* ADEs that caused or contributed to hospital admission

| Adverse Drug Event | n | STOPP PIMs | Beers PIMs |
|---|---|---|---|
| Injurious falls and benzodiazepines | 24 | 24 | 22 |
| Metabolic / electrolyte disturbance and diuretics | 15 | 1 | 0 |
| Injurious falls and opiates | 11 | 11 | 1 |
| Symptomatic orthostatic hypotension and ACEIs or ARBs | 8 | 7 | 0 |
| Injurious falls and sedative hypnotics | 7 | 0 | 0 |
| Acute kidney injury and diuretics/nephrotoxic drugs | 7 | 4 | 0 |
| Major constipation and opiates | 7 | 6 | 0 |
| Gastritis / Peptic Ulcer Disease and NSAIDs | 7 | 6 | 1 |
| Injurious falls and antipsychotics | 5 | 5 | 0 |
| Symptomatic orthostatic hypotension and diuretics | 4 | 4 | 0 |
| Symptomatic orthostatic hypotension and alpha blockers | 4 | 4 | 1 |
| Symptomatic bradycardia and beta blockers | 4 | 0 | 0 |
| Symptomatic orthostatic hypotension and beta blockers | 3 | 3 | 0 |
| ADEs (of total 159) | 106 | 75 | 25 |

PIMs = Potentially Inappropriate Medicines

# Can STOPP & START criteria help to optimise prescribing in older people?

- Improve medication appropriateness?
- Reduce incidence of ADEs?
- Reduce drug costs?

# Prevention of Potentially Inappropriate Prescribing for Elderly Patients: A Randomized Controlled Trial Using STOPP/START Criteria

PF Gallagher[1], MN O'Connor[1] and D O'Mahony[1,2]

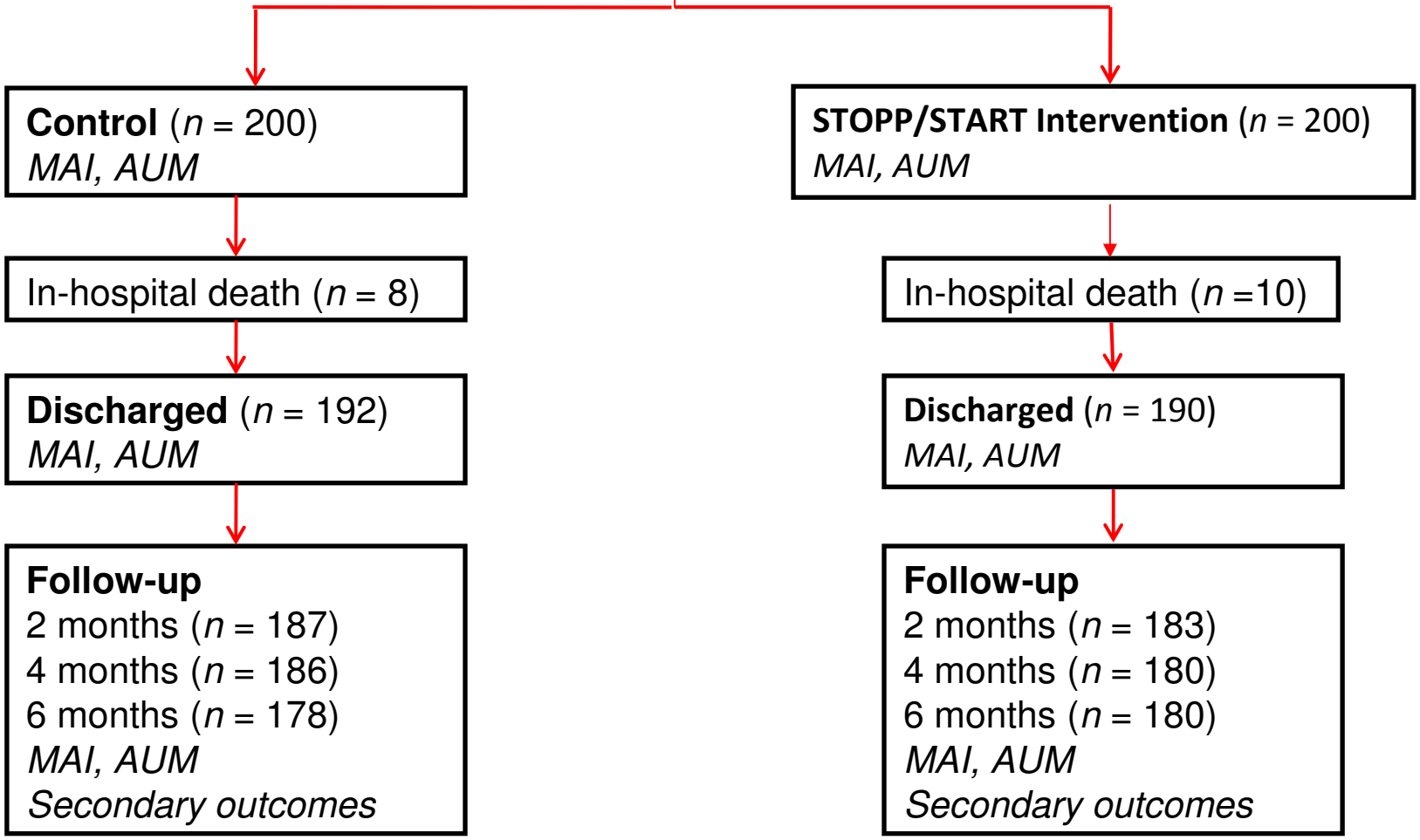
Clinical Pharmacology & Therapeutics (Nature) 2011; 41(6): 841-54.

# Single-centre RCT: Does application of STOPP & START rules improve medication appropriateness?

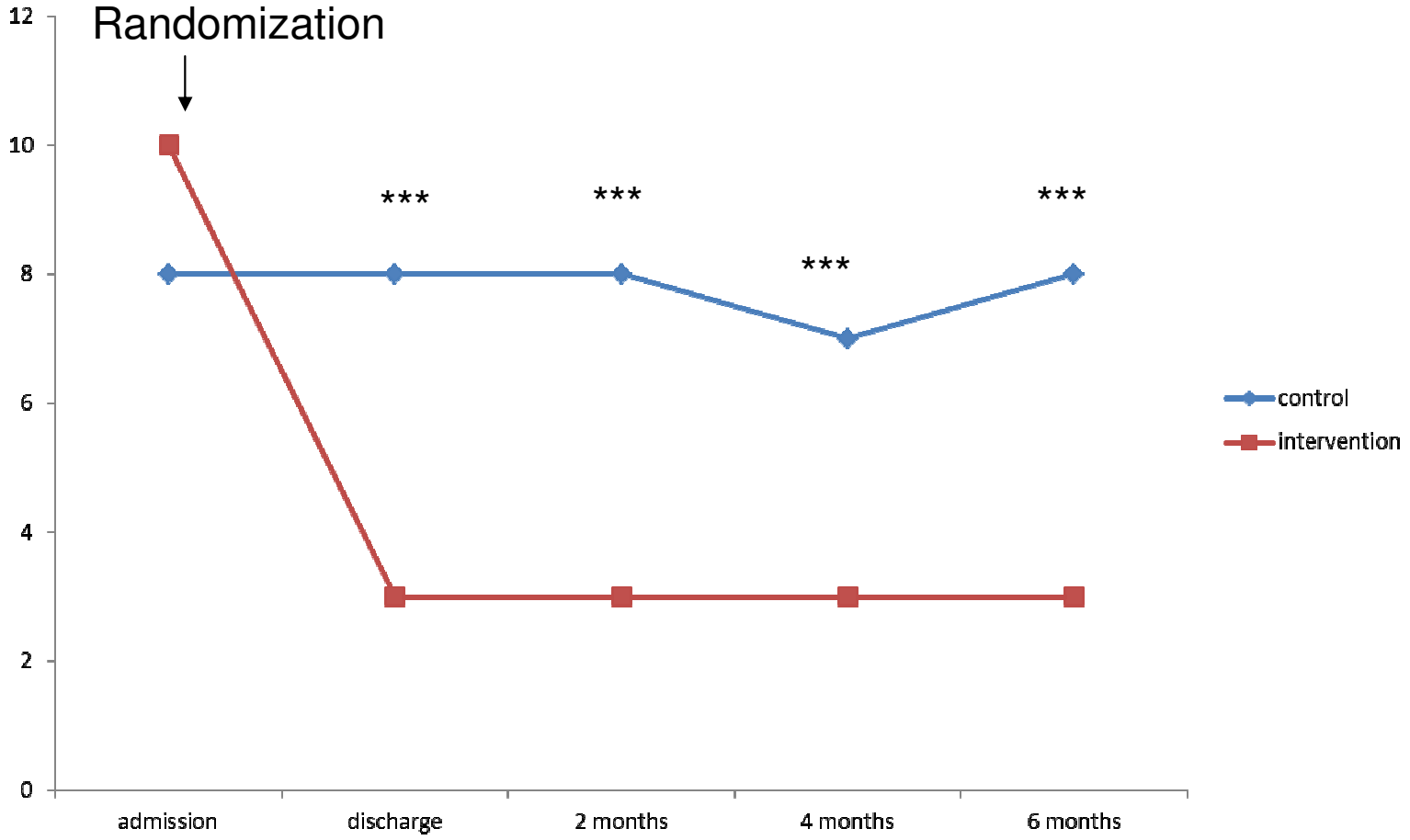
**MAI: Medication Appropriateness Index**
**AUM: Assessment of Underutlization of Medication**

Patients admitted Dec 2007 – Nov 2008
Randomly assigned (*n* = 400)

**Patient population aged > 65, admitted with acute illness under care of non-geriatric physicians**



# Effect of STOPP on Medication Appropriateness

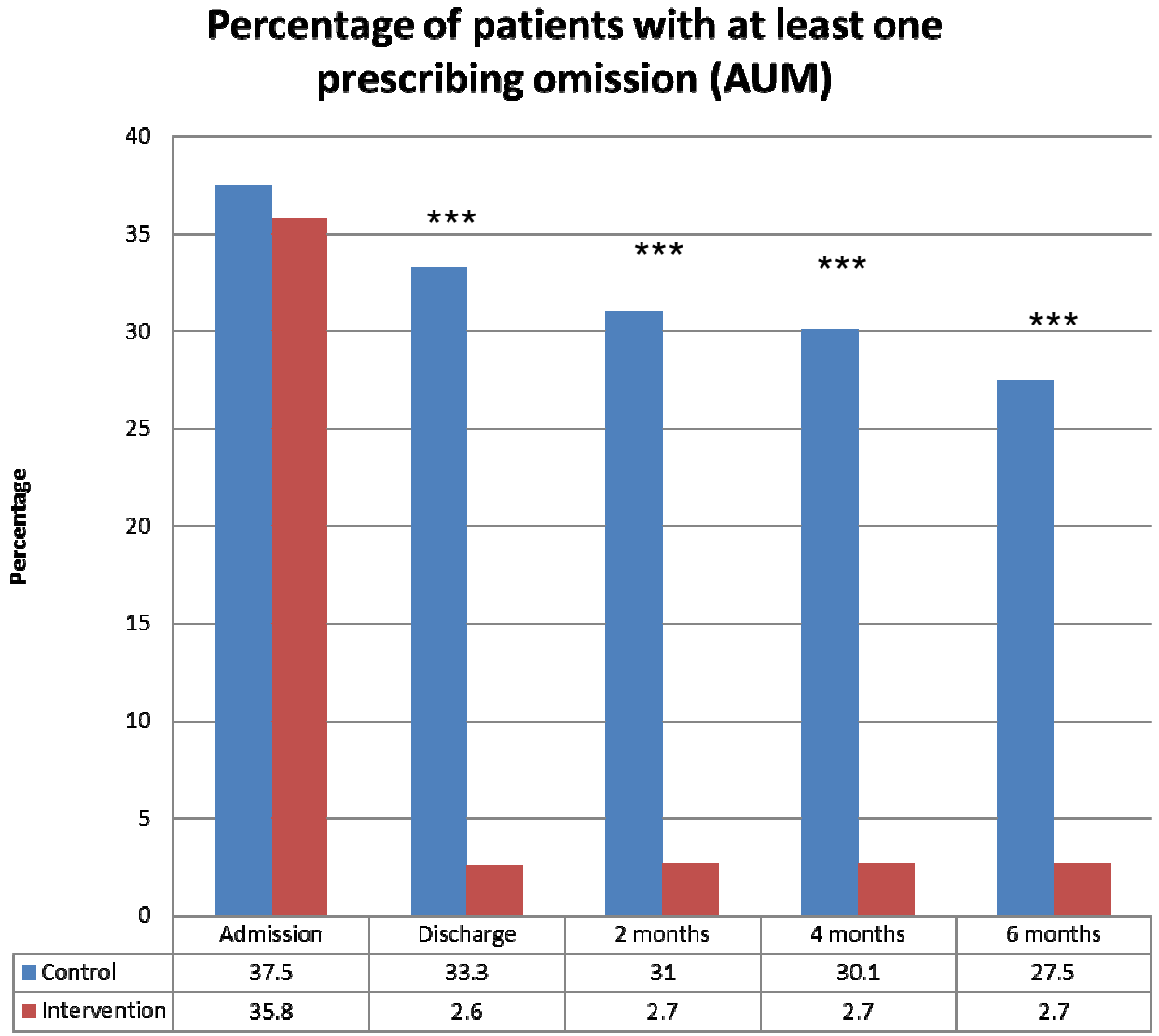



MAI score

Post-randomization follow-up

*** P<0.001

# Effect of START on Omission of Appropriate Medications




| | Admission | Discharge | 2 months | 4 months | 6 months |
|---|---|---|---|---|---|
| Control | 37.5 | 33.3 | 31 | 30.1 | 27.5 |
| Intervention | 35.8 | 2.6 | 2.7 | 2.7 | 2.7 |

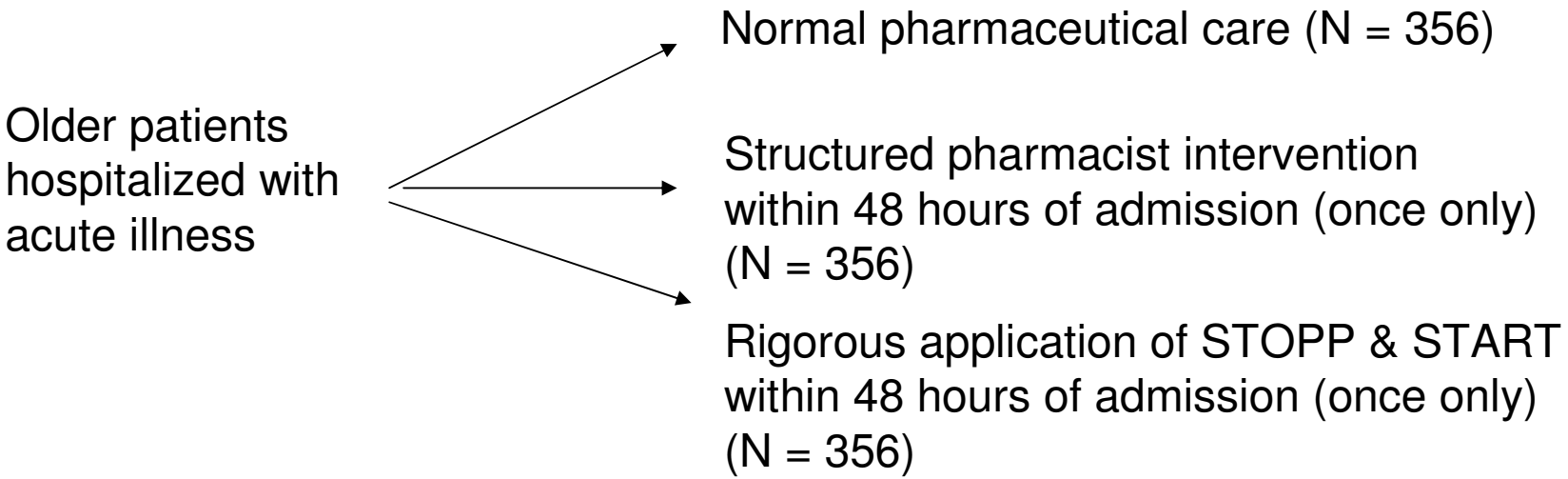
*** P< 0.001

# STOPP PIM's: Implications for drug budget in older people

- 338801 persons aged ≥ 70 years in Ireland during 2007
- Primary Care Reimbursement database (uses ATC drug classification)
- 30 out of 65 STOPP criteria → PIM prevalence rate of 36%
- Main PIM's were:
  - PPI's at full dose > 8 weeks
  - NSAID's for > 3/12
  - Long half-life BZD's > 4/12
  - Duplicate drug classes
- Polypharmacy was the main risk factor for PIM's
- Expenditure on STOPP PIM's = €45.6 Million = 9% of total spent on drugs for persons aged ≥ 70 years in Ireland during 2007)

Cahir C et al., *Br J Clin Pharmacol* 2010

# New Randomized Controlled Trial: May 2011 – May 2012




1º outcomes:
- ADE incidence at Day 3-5, at discharge, 3 months post-discharge
- Medication appropriateness (MAI score)

2º outcomes:
- Drug costs
- Composite healthcare costs
- Mortality

Trial number: NCT01467050

# ADE's defined by 'trigger events'

| |
|---|
| **1. New-onset falls/new-onset movement disorder** |
| **2. Acute kidney injury** i.e estimated GFR reduction by ≥ 50% or a twofold increase in serum creatinine concentration or a drop in urine output to ≤0.5mls/kg/hr for at least 12 hrs<br>or **Major serum electrolyte derangement** i.e. Sodium < 130 mmol/l or >150 mmol/l; Potassium < 3.0 mmol/l or > 5.6 mmol/l |
| **3. New-onset orthostatic hypotension (symptomatic or not)**<br>≥20mmHg drop in Systolic BP or ≥10mmHg Diastolic BP from supine to erect posture. |
| **4. Bradycardia** i.e heart rate ≤ 40 /min or heart rate ≤ 60/min with symptoms of lightheadedness, dizziness, fatigue, dyspnoea. |
| **5. New-onset major constipation** i.e. no bowel movement for > 72 hrs or requiring new prescription of regular laxatives |
| **6. Acute bleeding** i.e causing a drop in Haemoglobin concentration of > 1g/dl or cessation of antiplatelet or anticoagulant therapy or requiring transfusion or prescription of an antidote (e.g. Vitamin K, Prothrombin complex concentrate) |
| **7. Acute dyspepsia** i.e. epigastric pain or fullness, needing new prescription of antacid or proton pump inhibitor. |
| **8. Acute diarrhoea** i.e. ≥3 loose stool in 24 hrs or documented Bristol Stool Chart score ≥ 6 |
| **9. Acute cognitive deterioration** i.e reduction in Abbreviated Mental Test Score (AMTS) of ≥ 2 points compared to the AMTS score on admission. |
| **10. Other clear-cut, well-recognised, incontrovertible common ADRs** (e.g. proven digoxin toxicity, symptomatic hypoglycaemia with insulin) |

# RCT Data so far (March 2012)

- 61 serious ADEs in 303 control patients (20.1%)
- 34 serious ADEs in 316 intervention patients (10.7%)
- Absolute risk reduction: 9.4%
- NNT = 11 to prevent one serious ADE

# Watch this space……

- STOPP/START version 2: 2012
  - STOPP v.2 (draft): 96 criteria
  (v.1 has 65 criteria)
  - START v.2 (draft): 38 criteria
  (v.1 has 22 criteria)
  - For full Delphi validation in 2012
  - 26 European experts in Geriatric Pharmacology
- Commercialized STOPP/START software

# Summary

- STOPP & START are new, validated, reliable systems-based criteria for potentially inappropriate prescribing
- High prevalence of PIMs and PPOs in acutely ill older people in European hospitals according to new criteria
- STOPP drugs significantly predict ADEs (in contrast to Beers' criteria drugs)
- Rigorous application of STOPP & START improves medication appropriateness & (probably) prevents ADEs

# STOPP/START in perspective

- STOPP/START criteria are designed to highlight inappropriate prescriptions and prevent ADEs
- STOPP/START criteria are *not* the complete answer to preventing medication errors….but they help
- The future: versatile software engines designed to optimize pharmacotherapy at the point of initiation and at routine medication review

# The future is electronic!

Stephen Byrne, PhD

Paul Gallagher, PhD

Pat Barry, MD

Cristin Ryan, PhD

David O'Sullivan, MPharm

Hilary Hamilton, MRCPI

Marie O'Connor, MRCPI