Beers and Beyond: a 2016 update on Potentially Inappropriate Medications

Marilyn N. Bulloch PharmD, BCPS
mjn0004@auburn.edu

Objectives

• Review medication use in older adults
• Understand the impact of age-related physiologic changes on medication use in the older adult
• Recognize risk factors for adverse drug events in geriatric patients
• Explain potentially inappropriate medication use
• Compare and contrast updated and new instruments available to evaluate for potentially inappropriate medications and/or underprescribing in older adults

Older Adults and Medication Use

• Geriatric Population
  • Current ~ 13%
  • 2030 ~ 20%
  • 2050 ~23%
  • 2100 ~33%
• Average number of medications – 5
  • Including over-the-counter: average 6 medications
  • Age > 85 years: average 7 medications
  • 48% of LTC patients use ≥ 9 medications
Question 1
Which age-related pharmacokinetic parameter change may result in the need to adjust the dosing regimen of medications?
A. Absorption
B. Distribution
C. Metabolism
D. Excretion
E. All of the above

Age Related Physiologic Changes
- PO - Delayed
- Inhaled - Decreased
- SQ/IM - Decreased predictability
- Eye - Increased
doubling time (lipophilic drugs)

Liver - Decreased size & blood flow
CYP enzymes - Decreased activity
Phase II – No change
GFR - Decreased

Hydrophilic - Decreased
Lipophilic - Increased
Protein binding - Decreased
Risk Factors for Adverse Drug Events

**Medications**
- Antiepileptics
- Diuretics
- Anticoagulants
- NSAIDs
- NSAID + anticoagulant
- Insulin
- Oral antidiabetics
- Digoxin
- Tricyclic antidepressants
- Anticholinergics
- Benzodiazepines
- Opioids
- Corticosteroids

**Others**
- Missing information
- Patient understanding
- Previous ADE
- Difficult to handle medication
- Impaired manual skills
- Language barriers
- Hepatic impairment
- Self-medication

Inappropriate Medication Use
- Overprescribing – clinically not indicated
- Underprescribing – omission of therapy for a given indication
- Mis-prescribing – incorrect prescription of an indicated medication
  - Drug choice – better alternatives
  - Dose – too low, too high, adjusted for patient characteristics
  - Duration – too long, too short
  - Duplication
  - Interactions – drug-drug, drug-disease, drug-nutrient

Potentially Inappropriate Medication (PIM) Use
- Prevalence – 20-79%
- 6% of all geriatric hospitalizations could be avoided if no PIMs were prescribed
- Up to 50% of adverse drug events (ADE) and ADE-related hospitalizations could be avoided by avoiding PIMs
Who are PIM Users?

- Endres et al.
  - 67% female
  - Mean age 73 years
  - Average 16.4 ICD-10 code diagnoses
  - 8.4% require long-term care
  - Average 4.8 medications
    - Average 2.06 potentially inappropriate medications per quarter
    - 32% take ≥ 6 medications

Endres et al. PLOS One. 2016. DOI:10.1371/journal.pone.0146811

Tools to Evaluate PIM Use

- Over 46 published tools
  - 20 (43%) relate to previously published tools.
    - 18 use Beers Criteria for their basis
    - 28 use explicit criteria
    - 36 are directly targeted for geriatrics
- Inappropriate use focus
  - Overprescribing – 14
  - Underprescribing – 6
  - Non-adherence – 8
  - Cost - 5

Limitations of Explicit Criteria

• Limited evidence-based medicine—weaker evidence grading
• Cannot account for all subpopulations and special considerations
• Potential for missed studies during literature search
• Does not address all aspects of prescribing
• Does not evaluate the patient’s full regimen
• Potential for false-positives—inflexible without individual consideration


American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel

• For use in all ambulatory, acute, and institutionalized settings for patients ≥ 65 years
  • Exception: Hospice and Palliative Care
• Intentions
  • Improve medication selection
  • Educate clinicians and patients
  • Reduce adverse drug events
  • Evaluate quality of care, cost, and patterns in older adults
• Goal
  • To improve the care of older adults by reducing their exposure to potentially inappropriate medications


• What the criteria are NOT intended for:
  • Punitive application
  • Be applied as a quality measure when subgroups of individuals who should be exempt from a criteria cannot be easily identified through structured and readily accessible electronic health data.

• 13 member interdisciplinary panel
  • Ex-officio members – Centers for Medicare and Medicaid Services, National Committee for Quality Assurance, Pharmacy Quality Alliance

• Literature Search
  • August 1, 2011 to July 1, 2014
  • Drugs, classes, and conditions in 2012 version used as initial search terms
  • Generally focused on adverse drug events and adverse drug reactions
  • 20,748 initial citations → 1,188 unduplicated citations ultimately selected for full panel review + additional searches until December 15, 2014


• Tables
  • Medications to avoid for many/most older adults
  • Medications to avoid in older adults with specific diseases/syndromes
  • Medications to be used with caution in older adults
  • Potentially clinically important drug-drug interactions ***NEW***
    • Excludes antimicrobials
  • Medications to avoid/adjust dose in older adults based on kidney function ***NEW***
    • Excludes antimicrobials

• Medications to avoid for many/most older adults
  • Organized by organ system → therapeutic category → medication

• Rationale
  • Concerns with use – i.e. adverse effects
  • Some address efficacy – or alternative's relative efficacy
  • Some address role in therapy – i.e. avoid in treatment for certain conditions

• Recommendation
  • Majority – avoid without discussion
  • Many have caveats to clarify more specifically when the use of the medication becomes potentially inappropriate.

• Quality of evidence
• Strength of recommendations
Medications to avoid for many/most older adults – Removals

- Avoid nitrofurantoin in CrCl < 60 mL/min
- Still recommends to avoid long-term use of nitrofurantoin - irreversible pulmonary fibrosis, liver toxicity, peripheral neuropathy
- Antiarrhythmics (Classes 1a, 1c, III) as 1st line therapy for atrial fibrillation
  - Amiodarone - still considered a PIM except in heart failure or substantial left ventricular hypertrophy
  - Dronedarone – avoid in permanent atrial fibrillation or with severe or recently decompensated heart failure
  - Disopyramide (Class 1a) – highly anticholinergic
  - Digoxin – not 1st line therapy or doses > 0.125 mcg
- Trimethobenzamide
  - No longer available – mesoridazine, chloral hydrate

Medications to avoid in older adults with specific diseases/syndromes

- 12 conditions
  - Heart failure, syncope, seizures/epilepsy, delirium, dementia/cognitive impairment, history of falls/fractures, insomnia, Parkinson disease, history of gastric/duodenal ulcers, CKD (Stage ≥ 4), urinary incontinence (women), BPH
- Changes
  - Dementia/cognitive impairment – added Nonbenzodiazepine hypnotics
  - History of falls/fractures – added opioids
  - Exception – pain management for recent fractures or joint replacement
  - Delirium – added antipsychotics (as 1st line treatment)
  - Exception – alternatives are not possible AND patient is a harm to self or others
- Removals
  - Chronic constipation
  - Lower urinary tract/BPH – inhaled anticholinergics

Nonbenzodiazepine hypnotics – changed from avoid > 90 days to avoid for any duration

- Sliding scale insulin – further clarified what a sliding scale regimen is

Additions

- Proton Pump Inhibitors – Avoid > 8 weeks without justification
- Desmopressin – Avoid in the treatment of nocturia or nocturnal polyuria

American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

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**Medications to be used with caution in older adults**

- No Changes
- 3 medications in all geriatrics
  - Aspirin for primary prevention of cardiac events in patients ≥ 80 (low, strong)
  - Prasugrel in patients ≥ 75 or with CrCl <30 mL/min (moderate, strong)
  - Dabigatran in patients ≥ 75 or with CrCl <30 mL/min (moderate, strong)
- Benefit in highest-risk may outweigh risk – i.e. diabetics, history of heart attack
- 2 conditions
  - SIADH or hyponatremia (moderate, strong)
  - Antipsychotics, diuretics, carbamazepine, oxcarbazepine, SNRIs, SSRIs, TCAs, cisplatin, cyclophosphamide, carboplatin
- Syncope – vasodilators (moderate, weak)

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**Potentially clinically important drug-drug interactions**

- Highly associated with bad outcomes in older adults
- Not intended to be comprehensive – 12 interactions
  - ≥ 3 other CNS active drugs defined – antipsychotics, benzodiazepines, Nonbenzodiazepine hypnotics, TCAs, SSRIs, opioids
  - Account for 4 interactions
  - ≥ 2 anticholinergics
  - Loop diuretics - Peripheral α1 blockers or lithium
  - NSAIDS – warfarin or corticosteroids (IV and oral)
  - Warfarin - amiodarone
  - ACEIs – amlodipine or trandolpene or lithium
  - Theophylline - cimetidine
- Most have moderate evidence
- All have strong recommendations

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**Medications to avoid/adjust dose in older adults based on kidney function**

- Adapted from previously published consensus guidelines
- Majority require action when CrCl <30 mL/min
  - Avoid – amiloride, Dabigatran, Fondaparinux, rivaroxaban, spironolactone, tramadol, duloxetine, pregabalin, gabapentin, tramadol (extended release)
  - Reduce dose – colchicine, tramadol (immediate release)
- Others
  - CrCl 25 mL/min – avoid apixaban
  - CrCl 30-50 mL/min – reduce edoxaban dose
  - CrCl < 30 mL/min or > 95 mL/min – avoid edoxaban
  - CrCl < 50 mL/min – reduce H2 receptor antagonist dose
  - CrCl < 60 mL/min – reduce pregabalin or gabapentin dose
  - CrCl ≤ 60 mL/min – reduce levetiracetam dose
- Recommendations are strong except tramadol and duloxetine (weak).
Question 2
Which of the following was a new addition to the 2015 Beers Criteria for Potentially Inappropriate Medication Use in Older Adults?

A. A table with clinically important hepatic dose adjustments
B. A table with clinically important drug-drug interactions
C. A table of medications to be used with caution
D. A recommendation to use the Beers Criteria as part of a performance appraisal for payment by insurance and payers

Misinterpretations of the Beers Criteria
• Clinicians – assume all medications listed are uniformly inappropriate
• Health Systems – quality improvement programs and clinical decision support software that considers any use of medications listed as inappropriate
• Insurance/Payers – require prior authorization for listed medications

Key Principles to Guide Use of Beers Criteria
• “A key theme underlying these recommendations is to use common sense and clinical judgement in applying the 2015 AGS Beers Criteria and to remain mindful of nuances in the criteria”
• Should be a “warning light” to identify medications with an unbalanced risk vs. benefit ratio
• Support – not replace – good clinical judgement
Key Principles to Guide Use of Beers Criteria

- Mediations listed are potentially inappropriate – not definitely inappropriate
  - Drug may almost always be a poor choice
  - There may be times where it is appropriate
  - Examples of potential appropriate use of Beers Criteria medications
    - Phenobarbital – refractory seizures
    - Lorazepam – after a myocardial infarction or end-stage COPD
    - Metoclopramide – short term use for refractory nausea/vomiting
    - Hydroxyzine – uremic itching


Key Principles to Guide Use of Beers Criteria

- Read the rationale and recommendation statements
  - Nitrofurantoin – only PIM if CrCl <30 ml/min or for long-term prophylaxis
  - Peripheral α1 blockers – only PIM for treatment of hypertension
  - Clonidine – only PIM if using it for 1st line for hypertension
  - Proton pump inhibitors – only PIM > 8 weeks in low risk patients
  - NSAIDs – only PIM for arthritis if nothing else tried/failed and only if the patient is not on something to protect the stomach


Key Principles to Guide Use of Beers Criteria

- Understand why medications are included – adjust approach to those medications accordingly - Read the rationale
  - Consider the quality of evidence
  - Consider the strength of recommendation

Key Principles to Guide Use of Beers Criteria
• Beers Criteria should be a starting point for a comprehensive process of identifying and improving medication appropriateness and safety
  • It should not be the only thing used
  • Does not provide a comprehensive review of medications
  • Does not evaluate appropriate doses/frequencies for most medications
  • Does not address directions or adherence
  • Not individualized to the patient

Steinman et al.. J Am Geriatr Soc. 2015;63:e1-e7

Key Principles to Guide Use of Beers Criteria
• Access to medications listed should not be excessively restricted by prior authorization or health plan coverage policies
  • Some Medicare Part D plans are restricting Beers Criteria medications to beneficiaries < 65 years (i.e. disability, renal failure).
  • Clinicians who prescribe Beers Criteria medications often get low quality ratings
• ASCP recommends a pharmacist with geriatric expertise be included on any group that determines which drugs require prior authorizations
• Minimal benefit
  • Prior authorizations often increase total health care costs

Steinman et al.. J Am Geriatr Soc. 2015;63:e1-e7

Examples of Prior Authorization Policies
• BCBS of Alabama
  • Antipsychotics
  • Benzodiazepines—clonazepam, diazepam
  • Digoxin 0.25 mcg
  • Hydroxyzine
  • Promethazine
  • Phenobarbital

https://www.myprime.com/content/dam/prime/memberportal/forms/2016/FullyQualified/Other/ALL/BCBSAL/MEDICARE_D/ALBACPPO/EALH0104_BAC_prior_authorization_criteria.pdf
Key Principles to Guide Use of Beers Criteria

• Beers Criteria are not equally applicable to all countries
  • Developed based on medications available in United States
  • Medications available in other countries may be potentially appropriate


Key Principles to Guide Use of Beers Criteria

• For optimal application – identify where appropriate safer nonpharmacologic and pharmacologic strategies
  • Include counseling and lifestyle changes
  • 2015 – first ever offering of alternatives to Beers Criteria medications


Alternative Medications for Medications in the Use of High-Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly Quality Measures

• Developed as a list of alternatives to medications included in the use of two national quality measures
  • Use of High-Risk Medications in the Elderly
  • Potentially Harmful Drug-Disease Interactions in the Elderly

• Comprehensive literature review: 2000-2015
  • Authors also searched personal files.
  • Recommendations from American Geriatric Society, Beers Criteria Panel, National Committee on Quality Assurance, and Pharmacy Quality Alliance

• Includes references
Table 1 – alternatives to 15 medication classes
Table 2 – alternatives to 10 medication classes involved in drug-disease interactions
Table 3 – resources for non-pharmacologic alternatives


Examples:
• Instead of Benztropine – use carbidopa/levodopa
• Instead of glyburide – use glipizide
• Instead of 1st generation antihistamines – used 2nd generation antihistamines, intranasal saline, or intranasal steroids
• Instead of meperidine – use morphine or tramadol
• Instead of chronic NSAIDs – consider topical NSAIDs or lidocaine
• Instead of older anticonvulsants in a patient with falls – use lamotrigine or levetiracetam with calcium/vitamin D
• Instead of H2RAs in dementia, use a PPI
• Instead of oral estrogen – use vaginal estrogen


STOPP/START criteria for potentially inappropriate prescribing in older people: version 2

• Screening Tool of Older People’s Prescriptions (STOPP)
  • Version 1 – 2008
  • Version 2 – 2014/15

• Screening Tool to Alert to Right Treatment (START)
**Rationale for update**
- Criteria no longer completely accurate or relevant
- 12 Criteria were lacking in clinical importance or prevalence
- Important criteria missing
- Increase applicability throughout Europe

**Goal**
- To create a complete and up-to-date set of PIMs that may have serious negative effects on the health and well being of geriatrics in most settings

**19 member panel from 13 European countries**

**Panel members**
- Commented on 2008 STOPP/START criteria – including current validity and relevance
- Proposed new criteria
- Commented on methods to improve structure and content of criteria

**Literature search**
- For all proposed new criteria (n=51) and all 2008 criteria recommended to retain (n=87)
- Pubmed, Embase, and Cochran library database
- Recently published textbooks, British National Formulary, NCIE guidelines, and SIGN guidelines (through March 1, 2014)
3 members of research team read selected articles
- Included principal author and 2 postgraduate students under supervision
- Ensured suitability as support evidence
- Removed criteria without clear evidence support (n=11)
- All references made available to panel via Dropbox® - read at discretion of panel member
- Reference evidence quality not rated
- Remaining criteria organized according to physiologic system

Review process
- Round 1 – first draft sent to each panel member for review. Feedback submitted through SurveyMonkey®
- Each criteria presented as a statement
  - Panel member chose his/her level of agreement (0= don’t know, 1 = strongly agree to 5 = strongly disagree)
  - Criteria with median value of 1 or 2 AND a 75% value of not >2 retained
  - 124 had median scores 1 or 2; 107 had 75% values not > 2
  - Round 2 – 17 criteria without 75% values not > 2
  - Achieved consensus on 7 criteria

15 STOPP/START version 1 criteria removed

114 total criteria
- All criteria considered potential, but not absolute
- No indication of clinical relevance/severity – all considered potentially serious
- Criteria found in supplementary data
  - Includes citations from which recommendation based on
  - Divided into sections based on type and/or major organ system
**STOPP/START criteria for potentially inappropriate prescribing in older people: version 2**

- Types of criteria
  - Drug-disease interactions - ***most common***
  - Drug-drug interactions
  - Maximum dose – aspirin, digoxin
  - Role (or avoidance) in therapy
  - Lack of benefit
  - Duration of therapy
Structured History taking of Medication use (SHiM)

- Uses STOPP criteria
- Tool for taking medication history in geriatrics
- 21 questions — current and recent medication use, medication knowledge, medication beliefs, allergies/intolerances
  - Most are yes/no
- Originally tested in inpatients
- Adapted for community pharmacists


General questions
- Adherence. If yes, reasons for non-adherence
- Side effects
- Other medications including non-prescriptions, herbals, those that belong to others
- Use of PRN medications
- Continued use of drugs that were stopped by prescriber

About medication use
- Independent use
- Use of dosage system
- Difficulty taking

Medication difficulties
- Type of dosage systems
- Difficulties using dosing systems
- Forgetfulness of dosing

Others
- Allergies and intolerances
  - Drugs/classes
  - Symptoms/effects

Drenth-van Maanen et al.
- 100 patients
- Discrepancies found in 92% of patients
- 72% of discrepancies were clinically relevant
- 21% of patients experienced harm from a discrepancy

Structured History taking of Medication use (SHiM)

- Cullinam et al
- 123 patients > 65 presenting to 5 emergency departments with ≥ 3 chronic diseases not under care of a geriatrician
- 200 discrepancies found
- 73% patients had ≥ 2 discrepancy
- 66% discrepancies (n=132) related to non-prescription medications
- Prescription medication discrepancies mostly inhalers, ophthalmic drops, antihypertensives, and antidepressants
- 65.5% of discrepancies were omissions
- 1% of discrepancies had potential to cause severe harm; 72.5% discrepancies has potential to cause moderate harm

EU(7)-PIM List

- Intention
  - To develop an expert-consensus list of PIMs covering the drug markets of 7 European countries
  - Countries – Finland, Estonia, Netherlands, France, Spain, Sweden

- 4 member research team and 33 member expert panel
- Preliminary PIM list
  - Developed by research team
  - 85 PIMs from PRISCUS list
  - 99 PIMs from Laroche criteria, 1997 and 2003 Beers Criteria, and McLeod Criteria
EU(7)-PIM List

- Methods
  - Expert panel added drugs to PIM list that were not already represented (through May 2012)
  - Two-round Delphi survey
    - Round 1
      - Experts rated each medication (1 = strongly agree to 5 = strongly disagree)
      - Experts provided suggestions for dose adjustments and safer alternatives for medications viewed as PIM
    - Round 2
      - Experts assessed appropriateness of medications classified as questionable PIM in round 1 and 8 new criteria from 2012 Beers Criteria
      - Experts provided suggestions for dose adjustments and safer alternatives for medications viewed as PIM
      - Medications classified as PIM, non-PIM, or questionable-PIM
  - Final list – included medications whose 95% CI did not cross over 3


EU(7)-PIM List

- 282 potentially inappropriate medications
- Listed by drug class or use
  - Example – drugs for peptic ulcer and gastroesophageal reflux
- Brief main reason
- Dose adjustment or special considerations
- Alternatives

EU(7)-PIM List

- Difference from Beers Criteria
  - Ranitidine only H2RA listed
  - Senna – removed from Beers Criteria with 2012 version
  - Glimepiride and sitagliptine
  - Ferrous sulfate > 325 mg/day - removed from Beers Criteria with 2012 version
  - Propranolol and sotalol
  - Nifedipine SR – Beers Criteria only includes immediate release
  - Benzodiazepines with dose limits – changed to regardless of dose with 2012 Beers Criteria

**Fit fOR The Aged (FORTA)**

- Developed in Europe
- Intention
  - Screen for unnecessarily, inappropriate, or harmful medication and omissions in geriatrics in an everyday clinical setting
- Contains positive and negative labeling

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**Fit fOR The Aged (FORTA) Classification**

- Class A: A-bsolutely
  - Indispensable medication with clear-cut benefit in terms of safety/efficacy ratio proven in geriatrics for a given indication
- Class B: B-eneficial
  - Medication with proven or obvious efficacy in geriatrics, but limited extent of effect of safety concerns
- Class C: C-areful
  - Medication with questionable efficacy/safety profile in geriatrics.
  - To be avoided or omitted in the presence of too many drugs, lack of benefits, or emerging side effects
  - Review/find alternatives
- Class D: D-on't
  - Avoid in geriatrics
  - Omit first
  - Review/find alternatives

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**Fit fOR The Aged (FORTA) List**

- Two-round Delphi consensus process
- German speaking physician experts
- Original list developed by primary authors
- List sent out to panel in questionnaire form
- Panel reviewed FORTA labels and agreed/disagreed with proposals
- Panel proposed new medications and indications not already listed
- Consensus based on Likert scale
Fit FOR The Aged (FORTA) List

- 190 medications in 20 main indication groups
- Each is assigned a FORTA classification
- Divided by disease state
- Most common medications for that disease state management are listed
- Includes average panel rating
- Includes expert panel comments for some drugs
- Includes statements on cost, cautions, contraindications, role in therapy, metabolism, etc.
- Many psychiatric medications include doses

Wehling M et al. Age and Ageing. 2016;0:1-6

FORTA Disease States

- Hypertension
- Heart failure
- Coronary artery disease and stroke
- Post myocardial infarction
- Atrial fibrillation
- Parkinson's disease
- Incontinence
- Epilepsy
- GI illness
- Bipolar disorder
- COPD
- Osteoporosis
- Diabetes
- Dementia
- Sleep disorders
- Depression
- Pain
- Cancer
- Anemia

Wehling M et al. Age and Ageing. 2016;0:1-6

Fit fOR The Aged (FORTA) Don’ts

- Hypertension – clonidine, minoxidil, verapamil
- MI – antiarrhythmics (except Amiodarone – C), Dihydropyridine calcium channel blockers
- Atrial fibrillation – Dihydropyridine calcium channel blockers
- COPD – chronic glucocorticoids, antitussives
- Osteoporosis – hormone replacement therapy
- Diabetes – rosiglitazone
- Dementia – selegiline, nimodipine, ginko, ergots, antioxidants, ginseng, testosterone, indomethacin, clozapine
- Depression – long-acting benzodiazepines St. John’s Wort
- Insomnia – oxazepam, triazolam, doxepine, diphenhydramine
- Pain – carbasamazine, amitryptiline, naproxen, celecoxib
- Epilepsy – phenytoin, oxcarbazepine, diazepam

Wehling M et al. Age and Ageing. 2016;0:1-6
VALFORTA Study

- Purpose – to further validate the FORTA concept regarding impact on medication quality and relevant clinical end points and on its teachability and implementation practicality vs. standard care
- Design – open, randomized controlled trial
- Setting – 2 geriatric clinics
- March 2013-August 2014
- 409 patients

VALFORTA Study: Methods

- Inclusion criteria
  - Age ≥ 65 years and ≥ 3 medications OR age ≥ 60 years and ≥ 6 medications
  - Hospitalized ≥ 5 days
  - ≥ 3 clinically relevant diagnosis
- Assessment of medication quality and adjudication of adverse drug reactions and clinical endpoints performed by FORTA-trained physicians
- Chart

VALFORTA Study: Endpoints

- Primary endpoint – FORTA-score
  - Composite measure of the major categories of therapeutic quality
  - For each patient and each medication – one point given if
    - An indication is not treated though beneficial options exist (undertreatment)
    - Prescription in the absence of appropriate indication (overtreatment)
    - If indication exists, a related rug is used but is not the best available FORTA category (mistreatment) (wrong drug or dose)
VALFORTA Study: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>FORTA (n=202)</th>
<th>Control (n=207)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>84</td>
<td>82</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Number diagnoses</td>
<td>10</td>
<td>8</td>
<td>P=0.0025</td>
</tr>
<tr>
<td>Barthel Index score (range 0-100)</td>
<td>55</td>
<td>60</td>
<td>P=0.05</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>66</td>
<td>90</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>85</td>
<td>64</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>49</td>
<td>76</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Depression</td>
<td>65</td>
<td>43</td>
<td>P&lt;0.01</td>
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</table>

VALFORTA Study: Primary Results

<table>
<thead>
<tr>
<th>Admission</th>
<th>Discharge</th>
<th>Change</th>
<th>In-group P value</th>
<th>P-value for group comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>FORTA</td>
<td>3.5 ± 2.7</td>
<td>0.8 ± 1.4</td>
<td>2.7 ± 2.25</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Control</td>
<td>3.4 ± 2.3</td>
<td>2.4 ± 2.2</td>
<td>1 ± 1.8</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

Withdrawal Algorithm

- No formal name
- Developed in Australia
- Algorithm – to identify and discontinue (through tapering and withdraw) potentially inappropriate high-risk medications
- Differences from explicit lists
  - Suggests alternatives
  - Highlights risk of withdrawal or disease recurrence syndrome
- Recommends appropriate tapering
Withdrawal Algorithm

- Methods
  - Provisional list of PIMs – 2012 Beers Criteria, McLeod Criteria, Laroche list, PRISCUS list, and Norwegian General Practice criteria.
  - Excluded medications not available or rarely used in Australia

- Literature Search -
  - Not intended to be systematic review – was structured
  - Pubmed – for each drug
    - In association with other key terms – falls, delirium, depression, cognitive impairment, activities of daily living, adverse health outcomes, adverse effects, geriatric syndromes
  - Citation search of relevant articles – Web of Science
  - For safe discontinuation
    - For each drug
    - In association with key terms – withdrawal, cessation, discontinuation, stopping, deprescribing.

Withdrawal Algorithm

- Table 1 – Potentially inappropriate medications in older adults
  - Alphabetically by class – 85 drugs total
  - Main concern – brief statement
  - References
Withdrawal Algorithm

- Table 2 – Withdrawal regimens for commonly used medications in older people

- 14 groups or categories
- 14 medication classes (as a whole) plus 26 individual medications
- Only 3 groups/drugs have specific tapering instructions
  - Available – opioids, anxiolytics/hypnotics/benzodiazepine, Amiodarone
  - All others – “Taper slowly with caution”


Withdrawal Algorithm

For Symptoms
- Immediate symptomatic benefit (i.e. analgesics)
- Prevent rapid symptomatic deterioration (i.e. diuretics in heart failure)
- Assess for discontinuation on a case-by-case basis
- Balance immediate symptom benefit vs. magnitude of short-term harm vs. availability of equally effective non-pharmacologic options

Prevent Long-term Complications
- Medium-long-term future
- Assess for discontinuation in almost all cases
- Exception – risk of catastrophic disease event is very high and likely to occur within 6-12 months

Withdrawal Algorithm

- Table 3 – alternatives
  - Includes references
  - Includes mediation and non-pharmacologic alternatives
  - Not all alternatives available in the United States

(PRIMA)-eDS Tool

- "Polypharmacy in chronic diseases – Reduction of Inappropriate Medication and Adverse drug events in older populations" electronic Decision Support tool
- Targeted at primary care settings
- Provides recommendations regarding drug discontinuation or modification
- Currently being studied in clinical trial

(PRIMA)-eDS Tool

- Analyzes patient’s:
  - Diagnoses
  - Current medications
  - Symptoms
  - Biometric measurements (BMI, blood pressure)
  - Laboratory values
- Performs a comprehensive review
(PRIMA)-eDS Tool
- May recommend drug discontinuation/modification based on:
  - Indication and contraindication check – per diagnoses
  - Uses European Medicines Agency approved indications
  - 40 evidence-based rules and recommendations on the most commonly prescribed medications in older adults
  - 95 rules and recommendations from the Evidence-Based Medicine electronic Decision Support (EBMeDS) database
  - Based on NICE guidelines
  - RENBASE renal dosing decision support software
  - Swedish, Finnish, Interaction-X-referencing (SFINX) interaction check decision support software
  - PHARAO decision support software on adverse drug reactions
  - EU(7)-PIM list

(PRIMA)-eDS Tool Study
- Multicenter cluster-randomized controlled trial
- 5 study sites in Germany, United Kingdom, Austria, and Italy
- Inclusion criteria - Patients ≥ 75 years taking ≥ 8 medications in the primary care or nursing home setting
- Exclusion criteria – life expectancy < 1 year, chemotherapy/radiation, dementia with inability to provide consent

(PRIMA)-eDS Tool Study
- Groups
  - Physicians of enrolled patients with access to PRIMA-eDS tool
  - Physicians of enrolled patients with access to PRIMA-eDS tool
- Primary endpoint –
  - 1st non-elective hospital admission or death with an observation time of 2 years
(PRIMA)-eDA Tool Study

- Objectives
  - Primary – to test the hypothesis that reduction of polypharmacy and inappropriate prescribing using the PRIMA-eDS tool will improve clinical outcomes for older patients.
  - Secondary
    - All-cause mortality and non-elective hospital admissions individually
    - Number/Severity of falls
    - Fractures
    - Quality of life (SF-12v2)
    - Number and types of medications – total #, # discontinued, # continued despite recommendation, # re-administered for symptom control
    - Adverse event rate
    - Medication costs over observation period

(SPRIN)-eDS Tool Study

- Measurements
  - PRIMA-eDS group – record of recommendations adopted.
  - Control – Physicians record medication and other data. Usual care.
  - Follow-up – 8, 16, and 24 months

Question 3

Which of the following tools was not created for use in Europe?

A. STOPP
B. EU(7)-PIM
C. Withdrawal Algorithm
D. FORTA
E. (PRIMA)-eDS tool
Summary & Other Key Points

• No big comparisons (yet) of the new Beers Criteria and STOPP
• Tools are meant to be helpful – not punitive
• Use common sense
• Bonus features
  • Alternatives – Beers Criteria, EU(7)-PIM list, Withdrawal algorithm
  • Incorporated into software – Beers Criteria, STOPP/START, EU(7)-PIM list, PRIMA-eDS

Questions