Deprescribing: the good, the bad, the ugly

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We are all getting older.

Population Aged 65 and Over for the United States: 2012 to 2050

We are taking more medications....

*Data from National Health and Nutrition Examination Survey (NHANES)  ** N=37,959
Set it and forget it!!

But Wait...
There’s more

http://bluesky.chicagotribune.com/originals/chi-ron-popeil-ronco-mccormick-place-bsi-20140317,0,0.story
Objectives

- Review the pharmacokinetic changes that occur with aging
- Define polypharmacy and prescription cascade
- Understand the concept of deprescribing
- Become aware of useful resources for triaging inappropriate medication usage in PACE participants
Review of Pharmaco-Terminology

PharmacoKINETICS
(Pharmacy math)
- Absorption
- Distribution
- Metabolism
- Elimination

PharmacoCOLOGY
(Study of drugs)
- Mechanism
- Effect
- Uses
- Kinetics
- Dynamics
- Toxicology

PharmacoDYNAMICS
(Therapeutic effects)
- Biochemical/physiological effects

How medications interact with receptors to produce a response

Shargel L, Yu Andrew. Applied Biopharmaceutics and Pharmacokinetics. 7 eds (2016)
Pharmacokinetic Changes in Geriatrics

Absorption

• Rate of absorptions determines peak levels

• Reduced
  • Gastric acid production
    • Reduced tablet dissolution
    • Decrease the absorption of drugs (e.g. ferrous to ferric iron)
  • Gastric-emptying rate/GI motility
    • Increased toxicity of ulcerogenic drugs (e.g. NSAIDS, bisphosphonate)
    • Increased degradation prior to absorption
  • Active transport mechanisms
  • GI blood flow (e.g. ADHF pt on oral furosemide)

Murphy JE et al. Clinical Pharmacokinetics. 5th eds (2012)
Image: https://upload.wikimedia.org/wikipedia/commons/1/1d/Stomach.png
Pharmacokinetic Changes in Geriatrics

*Distribution*

- Decreased binding proteins
  - Albumin decreases with age and is significantly lower in nursing facility residents.
  - Increased unbound (free) fraction of highly protein bound substances
    - Calcium (calculation to correct for low albumin)
    - Phenytoin (calculation to correct for low albumin)
    - Naproxen

- Changes lean body weight to fat ratio
  - Total body water is decreased
  - Total body fat is increased
  - Changes distribution phase = changes onset and duration of action
    - Fat soluble drugs would have delayed onset and prolonged duration
      - Tricyclic antidepressants, barbiturates, benzodiazepines and phenothiazines)

Murphy JE et al. Clinical Pharmacokinetics. 5th eds (2012)
Pharmacokinetic Changes in Geriatrics

**Hepatic metabolism**

- Hepatic metabolism dependent on blood flow
  - Decrease blood flow = decreased metabolism
    - Increased concentration for active compounds
    - Decreased concentration of pro-drugs
  - Variable blood flow (e.g. heart failure) = variable concentrations

- Reduced hepatic metabolic enzymes
  - Phase I metabolism is reduced (biotransformation)
    - CYP 450 enzymes
  - Phase II is stable (conjugation)
  - Drugs that only undergo phase II metabolism would thus be preferred
    - LOT benzodiazepine
      - Lorazepam, Oxazepam and Temazepam

*Murphy JE et al. Clinical Pharmacokinetics. 5th ed. (2012)*

Image: https://upload.wikimedia.org/wikipedia/commons/6/69/Liver_%28transparent%29.png
Pharmacokinetic Changes in Geriatrics

Renal metabolism

- Renal function decline in a linear fashion with age
- Numerous drugs require renal dose adjustments
- Cockcroft and Gault is preferred for drug dosing
- Rounding creatinine to 1 mg/dl underestimates renal function
- I recommend for obese patients calculating a “functional range” utilizing ideal body weight and an adjusted body weight

\[
\text{CrCL} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{\text{SCr (mg/dL)} \times 72} \quad (x0.85 \text{ if female})
\]

http://www2.kidney.org/professionals/kdoqiguidelines_ckd/Gif_File/kck_f9.gif
Dowling TC et al. Glomerular Filtration Rate Equations Overestimate Creatinine Clearance in Older Individuals Enrolled in the Baltimo.... Pharmacotherapy. 2013 Sep;33(9):912-21
Pharmacokinetic Changes in Geriatrics

**Therapeutic Drug Monitoring (TDM)**

- Drugs for which levels can be drawn for dose adjustments
  - Antibiotics (vancomycin, gentamicin)
  - Antidepressants (TCA)
  - Antiepileptics (phenytoin, phenobarbital, carbamazepine, VPA)
  - Digoxin
  - Anticoagulants (heparin, LMWH, warfarin)
  - Lithium
  - Theophylline
  - Others

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Murphy JE et al. Clinical Pharmacokinetics. 5th eds (2012)
Pharmacokinetic Changes in Geriatrics

Pharmacodynamic changes

- Decreased acetylcholine, dopamine and serotonin
- Decreased enzymatic degradation of monoamine oxidase
- Impaired baroreceptor response to blood pressure changes
- Decreased responsiveness of beta-adrenergic receptors
- Decreased antibody response to vaccination
- Decreased insulin sensitivity
- Decreased cortisol suppression
- Enhanced responsiveness to warfarin and heparin
- Enhanced responsiveness to thrombolytics

Murphy JE et al. Clinical Pharmacokinetics. 5th eds (2012)
Pharmacokinetic Changes in Geriatrics

End result

- When starting new medications:
  - Be aware of those that are to be avoided due to increased risks in the elderly (Beer’s Criteria / STOPP Criteria)
  - Start low and go slow
  - Review medication dosing recommendations in the elderly
  - Estimate GFR regularly and make dose adjustment
  - Utilize therapeutic drug monitoring (TDM) when possible
  - Expect uncertainty and variations in response especially as the patients condition changes
Objectives

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• **Define polypharmacy and prescription cascade**

• Understand the concept of deprescribing

• Become aware of useful resources for triaging inappropriate medication usage in PACE participants
My Pathway to addressing Polypharmacy

• And learning the art of deprescribing
Reaching New Goals!

Rehabilitation Specialist and Resident

Excellence In Health Care For The 1990's
Complex Simulated Medication Regimen (Circa 1991)
My Ah-ha moment

• Bedside rounds

• Routine transfer of care
• Uneventful skilled nursing facility admission status post hip fracture
• Case presentation
• Review of medication list.
I AM YOUR Hospitalist

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Robert McKinney, D.O.
Are you experienced?

No idea but started to find resources and like minded people...

My indispensable resource, my Clinical Pharmacist.

• Not knowing what can be safely discontinued or should be discontinued
• Who is responsible?
• Fast and furious or slow and deliberate
• Drugectomy
• Evidence free Zone
• Wild West
The Dangers of “Polypharmacy” the Ever-Mounting Pile of Pills

• “We spend an awful lot of money and effort trying to figure out when to start medications,” Dr. Alexander said, “and shockingly little on when to stop.”

• “tracking prescription drug use from 1999-2012, Harvard researchers reported that 39% of those older than 65 now use 5 or more medications—a 70% increase in polypharmacy over 12 years”
What is polypharmacy?

- No consensus definition

- Generally defined as administration of more medicines than clinically indicated, representing unnecessary drug use

- Research definition-taking more than 5 medications

- Can be the consequence of the “Prescription Cascade”
What is the Prescription Cascade?

The process whereby the side effects of drugs are misdiagnosed as symptoms of another problem resulting in further prescriptions and further side effects and unanticipated drug interactions. This may lead to further misdiagnoses and further symptoms.
Cascade example

- Arthritis/NSAID → Hypertension/CCB. → Ankle edema/diuretic → Gout/Allopurinol
Adverse Geriatric Outcomes Secondary to Polypharmacy in a Mouse Model: The Influence of Aging.

• Do the meds themselves cause harm?

• Both young and old mice were administered a ‘polypharmacy diet’ which consisted of therapeutic doses of five commonly prescribed medications: simvastatin, metoprolol, omeprazole, acetaminophen and citalopram.

• They found significant declines in mobility, balance and strength in the older polypharmacy diet group (compared to an older group fed a control diet), but no differences in the younger groups.
Clinical consequences of polypharmacy in Elderly

• Nearly 50% of older adults take 1 or more medications that are not medically necessary

• Consequences of polypharmacy
  • Increase health care costs- approximate 30% increase in total medical costs
  • Adverse drug events- 5 or more medications added 88% increased risk of an adverse drug reaction
  • Classes associated with adverse drug effects included
    • Anticoagulants NSAIDs. Cardiovascular medications, diuretics, antibiotics, anticonvulsants, benzodiazepines and hypoglycemic medications
Clinical consequences of polypharmacy in Elderly

- Drug interactions - increase in the number of medications
  - Hospitalized older adults 5-9 medications a 50% increased probability of a drug interaction approaching 100% when >20 meds
  - Community dwelling elderly - patients had a potential drug interaction of nearly a 50%
  - Preventable cause of hospitalizations

- Medication non-adherence
  - Rates and community dwelling elderly adults have been reported between 43 and 100%
  - Greater than 4 medications one study documents 35%, rate of non-adherence
  - Medication non-adherence is associated with potential disease progression, treatment failure hospitalization, and adverse drug events
Clinical consequences of polypharmacy in Elderly

• Functional status
  • Polypharmacy in older patients- diminished ability to perform instrumental activities of daily living and decrease physical functioning

• Cognitive impairment.
  • 5 or more medications showed 22% reduction in cognition
  • taking 6-9 medications 33% reduction in cognition
  • more than 10 medications 54% reduction in cognition

• Falls
  • Number of medications, associated with increased risk of falls
  • Demented patients who fall have increase incidence of polypharmacy
  • “Caution should be using prescribing new medications to those who are risk of falling.”
Objectives

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• **Understand the concept of deprescribing**

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What is Deprescribing?

The process of tapering, stopping, discontinuing, or withdrawing drugs, with the goal of managing polypharmacy and improving outcomes.
Definition of deprescribing

The systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing for potential benefits within the context of an individual patient’s care goals, current level of functioning, life expectancy, values and preferences.
Elements of deprescribing

• Similar to medication initiation
  
  • Positive. Patient centered intervention

  • Involves inherent uncertainties

  • Requires shared decision making, informed patient consent and close monitoring of effects

JAMA Internal Med. 2015 May;175(5):827-34
Reducing inappropriate polypharmacy: the process of deprescribing

- Inappropriate polypharmacy reads a substantial burden of adverse drug events. Ill health, disability, hospitalization, and death

- The single most important predictor of inappropriate prescribing and risk of adverse drug events in older patients as the number of prescribed drugs

JAMA Internal Med. 2015 May;175(5):827-34
Reducing inappropriate polypharmacy: the process of deprescribing

• A deprescribing protocol is proposed in this article comprising of 5 steps:

1. **Ascertain all drugs the patient is currently taking in the reasons for each one** (OTC, Herbals, Supplements)
2. Consider overall risk of drug induced harm in individual patients, in determining the required intensity of the deprescribing intervention
3. Assessment each drug’s current or future benefit potential compared with the current or future harm or burden potential
4. Prioritize drugs for discontinuation that have the lowest benefit harm ratio and the lowest likelihood of adverse withdrawal reaction or disease, rebound syndromes
5. Implemented discontinuation regimen and monitor patient’s closely for improvement in outcomes, or onset of adverse effects
Low hanging fruit

- Medications that are:
  - not indicated
  - not effective
  - therapeutic duplications

- Potential Examples:
  - NSAIDS
  - PPI
  - H2-blockers
Challenges of deprescribing in the multimorbid patient

• Multi-morbidity often equals polypharmacy
  Co-occurrence of 2 or more chronic conditions

• One of the most common recommendations after medication review, discontinuation of medication or deprescribing- is one of the least likely to be followed.

• Barriers identified include multiple prescribers intra-professional relationships, Patient perspectives and lack of evidence

Challenges of deprescribing in the multimorbid patient

• An abundance of prescribing guidelines

1. They are based on trial data involving younger patients
2. Provide only a standardized set of recommended medications for each indication, regardless of patient’s additional comorbidities
3. Too disease specific
4. They do not include recommendations for deprescribing
Objectives

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Step 1 – Medication Reconciliation

“Unfortunately, medication reconciliation has often been misperceived as a superficial administrative accounting task with a pre-occupation with completing forms, resulting in the implementation of ineffective processes”

• Each provider has a medication list
  • Primary care
  • Specialist
  • Pharmacy
  • Hospital
• At each visit a new list is created
  • Updated before provider assessment
  • Does list get updated after assessment and plan?
• What is the patient actually taking vs. what you document?
• How many list does your patient have?

Image: http://allthefreestock.com/
Step 1 – Medication Reconciliation
How accurate are medication lists?

• Ask the patient?
  • Study of patients in the emergency department showed 64% of patient reported medication histories were inaccurate¹
  • Only 10% of patients in a diabetes clinic could provide an accurate list²

• Use your pharmacies?
  • Often do not contain over-the-counter medications, supplements or samples
  • Often dose adjustments and discontinuation are not communicated
    • Study of EHR electronic prescriptions showed that 1.5% (1000 orders) were dispensed after medication was discontinued³

• Check E-prescribing and 3rd party (PBM) records?
  • Have the same error rate as paper systems⁴-⁵
  • Do not capture samples, paper prescriptions (CII), self-pay (no electronic claim submitted)

How accurate are medication lists?

• Review clinic records?1-4
  • **Omissions** are very common due to failure to document medication changes (e.g. take two pills instead of one)
    • Lack of OTC, supplements
    • Lack of communication between specialists and primary care

• Use hospitals discharge medication list?5-6
  • Medication **errors on admission are passed on** to primary and specialty care
  • Most **patients** after discharge are **unaware of intended** medication changes

**Review all of the above and more**

Obtain “Best Possible Medication List”

• More than a list
  • ...you take x, y and z correct?
  • ...are you on the same medications?

• Comprehensive history of all prescribed and nonprescribed medications (including vitamins, supplements, etc)

• Systematic patient interview
  • What prescription medication do you take regularly?
  • What prescription medication do you take as needed?
  • What do you take when you have pain, cough, cold, allergies…?
  • What supplements, vitamins or over the counter medications do you use?
  • Tell me about the pharmacies that you use?
  • Who are all of the providers you have seen in the last year that have prescribed, recommended or modified any of your medications?

Obtain “Best Possible Medication List”

• Verification of information from more than one source
• Inspection of
  • Medication vials
  • Electronic health records, prescription record (e.g. pharmacy history)
• Documentation includes
  • Drug name
  • Dose
  • Frequency
  • Route of administration
  • Patients actual use compared with prescribed use (e.g. patient uses PRN instead of daily)
• Adherence assessment
  • “It’s hard for everyone to remember to take our medications each day, how often would you say you miss a dose…?”

Complete a Comprehensive Review

• Review the patients' problem list

• Is there
  • A medication for every indication?
    • What do you take for your XXXX?
  • An indication for every medication?
    • Why do you take XXXX?
  • Any medication that may be the cause of or contributing to the patients problem list?
  • Opportunities to taper or discontinue medications for problems that are in remission or have resolved?

• Review the goals of therapy and progress towards those goals
  • How well do you think XXX is working for your XXXX?
  • How have your symptoms changed since we started XXXX?
  • What do you think of XXXX?
  • Do you have any concerns about your medications?

• Deprescribe
How to accomplish effective deprescribing

• American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults
  • 13 Member interdisciplinary team of experts in geriatric care, and pharmacotherapy
  • Consensus on each existing and new criterion
  • A goal of closer monitoring of drug use in older adults
  • Available online and smartphone applications

• STOPP-START criteria, version 2 (UK, 2015) Screening tool of older persons prescriptions
  • Up to date literature review and consensus validation among a European panel of experts
Discuss the following with the patient/guardian

- An evidence-based consensus exists for using the drug for the indication given in its current dosing rate in this patient’s age group and disability level, and the benefit outweighs all possible known adverse effects

  - No/Not sure

    - Indication seems valid and relevant in this patient’s age group and disability level

      - No

        - STOP DRUG

      - Yes

        - Do the known possible adverse reactions of the drug outweigh possible benefit in old, disabled patients?

          - No

            - ANY adverse symptoms or signs that may be related to the drug?

              - Yes

                - SHIFT TO ANOTHER DRUG

              - No

                - Is there another drug that may be superior to the one in question?

                  - Yes

                    - Can the dosing rate be reduced with no significant risk?

                      - No

                        - Continue with the same dosing rate

                      - Yes

                        - Reduce dose

                  - No

                    - Continue with the same dosing rate
Free phone app from AGS/GAYF

- Recognize opportunities to stop a medication:
  - Care transitions
  - Annual/semiannual medication review (eg, annual wellness visit)
  - Review existing medications before starting a new medication
  - Presentation or identification of a new problem or complaint

- D/C medication if:
  - Harms outweigh benefits
  - Minimal or no effectiveness
  - No indication
  - Not being taken, and adherence is not critical

- Plan, communicate, and coordinate:

  - Include patient, caregiver, and other healthcare providers
  - What to expect/intent
  - Instructions, eg, how to taper (if indicated)

- Monitor and follow-up:
  - Withdrawal reactions
  - Exacerbation of underlying conditions

Examples of medications eligible for de-prescribing: bisphosphonates, antiallergy (seasonal), PPIs and H₂ antagonists, cholinesterase inhibitors, memantine, iron, antipsychotics, and antidepressants.

Source: Adapted from Bain KT et al. JAGS 2008;56:1946–1952.
• Early exposure and education regarding polypharmacy and our collective philosophy regarding deprescribing
  • Community outreach
  • Enrollment coordinators
  • Pre-enrollment Assessment

• Acquisition of medication lists- multiple sources, well known issue with medication list reconciliation
  • In home RN populates medication list EHR
  • Finalized participant list submitted-Initial polypharmacy review with our clinical pharmacist (CareKinesis/EireneRx)

• Post-Enrollment/medications are initiated with attempted cycle synchronization-
  • WERM -(weekly event review meeting) clinical pharmacist phone conference
  • Semi-annual, annual
www.medstopper.com

- A web based tool designed to help prescribers and patient’s make decisions around polypharmacy by providing an approach to thinking about whether or not to reduce or stop medications
- University of British Columbia
The art of medicine is essentially composed of the clinical skills of listening and advocacy...
It is an art of no little importance, to administer medicines properly: but, it is an art of much greater and more difficult acquisition to know when to suspend or altogether to omit them.

Philippe Pinel (1745-1826)
BOHEMIAN POLYPHARMACY

A PARODY OF THE CLASSIC QUEEN SONG
BOHEMIAN RHAPSODY