Rational polypharmacy for the cancer patient with comorbidities

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Key Points
- Polypharmacy is not a disease, and it cannot be "cured."
- We must learn to distinguish bad polypharmacy from good polypharmacy.
- Optimizing medication use means
  - Avoiding harmful drugs
  - Avoiding preventable adverse drug reactions
  - Using drugs most likely to be of benefit that concord with a patient’s goals and preferences

Sometimes you have to follow the signs.

Polypharmacy: the prescribing cascade

- Adverse drug reactions
- Use of inappropriate medications
- Poor adherence
- Functional decline / geriatric syndromes
- Increased cost
- Undertreatment

There is no consensus as to the definition of polypharmacy.

Comorbidities require
- "Polytherapy"
  - Heart failure
  - Diabetes
  - Coronary artery disease
- Underutilization
  - Clinical inertia
- Clinical Practice Guidelines

Hazzard, Principles of Geriatric Medicine and Gerontology
Why polypharmacy is a problem in cancer

- Comorbid conditions: HTN, OA, DM, CAD
- Pharmacokinetics
  - Absorption: mucositis
  - Distribution: weight loss and fat redistribution
  - Metabolism: cytochrome P450 interactions
  - Excretion: renal dysfunction

Why polypharmacy is a problem in cancer

- Drug interactions
  - 1 or more interactions in 27% of 405 patients
  - 87% involved non-cancer agents
  - Warfarin, steroids, antihypertensives, anticonvulsants
  - Only 13% involved chemotherapeutic drugs

Drugs metabolized by P450 enzymes

- Cyclophosphamide
- Taxanes
- Etoposide
- Irinotecan
- Aromatase inhibitors
- Vinca alkaloids
- Bicalutamide
- Imatinib, gefitinib, erlotinib

Drugs metabolized by P450 enzymes

- CYP3A
  - Metabolizes >60% of drugs: Calcium channel blockers, certain beta-blockers, most statins, warfarin, amiodarone

- CYP2D6
  - Metabolizes: metoprolol, propranolol, tramadol, codeine, oxycodone, TCAs, SSRIs
Why polypharmacy is a problem in cancer

- Impact of cancer [cancer treatment] on comorbidities
  - Androgen deprivation and the metabolic syndrome
  - Tyrosine kinase inhibitors and hypertension or heart failure
- What we need to know: the impact of aggressive control of comorbid illness on cancer outcomes
  - CRC outcomes for A1c <7.5% = patients without DM but A1c ≥7.5% had more aggressive cancer


Life expectancy after stage I colorectal cancer diagnosis according to age, number of comorbidities, and sex


Reconsidering meds in patients with cancer and comorbidity

- High stakes
  - Diminishing remaining life expectancy
  - Multiple competing/interacting comorbidities
  - Survival in a more functionally dependent state?
- Patient-centered care
  - Changing goals and preferences as new diagnoses are made and chronic diseases worsen
  - Focusing on outcomes important to improve quality of life

Most palliative patients will have medicines ADDED

- 4.9 meds at baseline, 2.5 added for symptoms
- Use of “inappropriate meds” increased from 29% to 48%


Essential Drugs in Palliative Care

- Acetaminophen
- Amitriptyline
- Bisacodyl
- Carbamazepine
- Citalopram
- Codeine
- Dexamethasone
- Diazepam
- Diclofenac
- Diphenhydramine
- Fentanyl
- Gabapentin
- Haloperidol
- Hyoscine
- Ibuprofen
- Levomepromazine
- Loperamide
- Lorazepam
- Megestrol
- Methadone
- Metoclopramide
- Midazolam
- Mineral oil enema
- Mirtazapine
- Morphine
- Octreotide
- Oral rehydration salts
- Oxycodone
- Prednisolone
- Senna
- Tramadol
- Trazodone
- Zolpidem


Drugs to Avoid in the Elderly

- Acetaminophen
- Amitriptyline
- Bisacodyl
- Carbamazepine
- Citalopram
- Codeine
- Dexamethasone
- Diazepam
- Diclofenac
- Diphenhydramine
- Fentanyl
- Gabapentin
- Haloperidol
- Hyoscine
- Ibuprofen
- Levomepromazine
- Loperamide
- Lorazepam (dose)
- Megestrol
- Methadone
- Metoclopramide
- Midazolam
- Mineral oil enema
- Mirtazapine
- Morphine
- Octreotide
- Oral rehydration salts
- Oxycodone
- Prednisolone
- Senna
- Tramadol
- Trazodone
- Zolpidem

Fick DM Arch Intern Med 2003;163:2716-2724
Beers MH Arch Intern Med 1997;157:1531-1536
Individualized Patient Assessment

- Will the patient benefit from the drug?
  - Does remaining life expectancy exceed time until benefit of drug is achieved?
- Is the drug a logical part of the patient’s treatment plan?
  - Compare goals of care to the medication treatment target

Survival according to risk factors for mortality in frail elderly

- Male
- Age
- Toileting
- Dressing
- Cancer
- COPD
- CHF
- Renal disease

Time until benefit

- Minutes/Hours:
  - Analgesics
- Months
  - Bisphosphonates in osteoporosis
- Years
  - Tight control in diabetes mellitus
- More difficult for others:
  - Statins?

Treatment Target Should Match Goals of Care

Goals of Care
- Prolong life
- Prevent morbidity
- Slow disease progression
- Prevent decline
- Comfort

Treatment Targets
- Primary prevention
- Secondary prevention
- Control chronic diseases
- Treat acute disease
- Medications for symptoms

Patient preferences for treatment are the ultimate determinates of medication use.
Deprescribing

Indication to Stop Drug
Identify and Prioritize Drug to Stop
Stop Drug and Monitor

Sometimes you have to stop a drug to know if it’s needed.

124 VA outpatients on ≥5 meds
26% of stopped meds caused ADWEs
36% of ADWEs led to admission, ER, or urgent care

Pruning vs. Peeling

The Patient: Life expectancy
Complexity of care

The Drug: Dependence
Inadequate physiologic compensation
Risk of exacerbation

Summary

• Use caution when a patient takes ≥9 meds.
• Avoid excessive combinations of sedatives, anticholinergic drugs, and psychotropic medications.
• Consider whether a patient is likely to benefit (or be harmed) from a drug and whether the treatment fits with their goals and preferences.

Thank you
• Mimi Rodin, Supriya Mohile, Elizabeth Lamont
• SIOG