Multimorbidity, Polypharmacy, and an Approach to Deprescribing

Andrea Berg, MD
Assistant Professor
Department of Geriatrics
Disclosures

- None
OBJECTIVES

Be able to describe:

- Multimorbidity and its clinical implications
- Approach to evaluating and managing older adults with multimorbidity
- Anticholinergic symptoms and ways to measure anticholinergic burden
- How to assess and initiate deprescription when appropriate
An Aging Population

Jan 1, 2011

• 78 million Baby Boomers turned 65 years old

Dec 31, 2029

• 1 in 5 Americans (20%) older than 65

2050

• 7% of US population older than 80

U.S. Census Bureau, 2008
Boult et al., 2009; Cohn & Taylor, 2010
WHO NEEDS A GERIATRICS APPROACH TO CARE?

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>The presence of an additional condition in relation to an index condition in one individual.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complexity</td>
<td>The overall impact of different conditions in an individual, taking into account their severity as well as other health-related attributes, such as serving in a caregiver role, cultural background, etc.</td>
</tr>
<tr>
<td>Frailty</td>
<td>A condition of reduced strength, endurance, and physiologic reserve, characterized by an enhanced vulnerability to minor stressors. Specific definitions of frailty vary.</td>
</tr>
<tr>
<td>Disability</td>
<td>An impairment that results in activity limitations (eg, affecting mobility, manual dexterity, continence, and other ADL functions) or restricted participation in life. It reflects the interaction between a person and his or her social and physical environment.</td>
</tr>
</tbody>
</table>
MULTIMORBIDITY

- Defined as $\geq 3$ chronic diseases: Affects more than 50% of older adults

- Has distinctive cumulative effects for each individual

- Associated with increased rates of:
  - Death
  - Disability
  - Adverse treatment effects
  - Institutionalization
  - Use of health care resources
  - Decreased QOL
Older adults with multimorbidity are heterogeneous in terms of:

- Illness severity
- Functional status
- Prognosis
- Personal priorities
- Risk of adverse events

Multimorbidity requires a flexible approach to care

- Individuals are heterogeneous, even with the same conditions
- Treatment Options vary
Case Study
### Home Medications

- Azelastine nasal spray as needed
- Calcium carbonate – Vitamin D 600-800 mg-unit daily
- Coenzyme Q10 200 mg daily
- Colchicine 0.6 mg BID
- Donepezil 10 mg nightly
- Levocetirizine 5 mg nightly
- Lininopril/HCTZ 10mg/25mg daily
- Levothyroxine 50 mcg daily
- Lorazepam 0.5 mg twice daily PRN
- Uribel 118 mg Q6H PRN bladder discomfort
- Omega-3 Fatty Acids mg daily
- Acetaminophen 1000mg TID
- Tolterodine 4 mg daily
- Simvastatin 20mg daily
Key domains:

- Patient preferences
- Interpreting the evidence
- Prognosis
- Optimizing therapies and care plans
Guiding principle: Elicit and incorporate patient preferences into medical decision-making

Care provided in accordance with clinical guidelines may not adequately address patients’ individual preferences

Older adults with multimorbidity should have the opportunity to evaluate choices and prioritize their preferences for care, within personal and cultural contexts
Most CPG focus on management of only **one** disease

Older adults with multimorbidity are regularly excluded or under-represented in clinical trials and observational studies, which translates to less representation in meta-analyses, systematic reviews, and guidelines

**CPG-based care may be cumulatively impractical, irrelevant, or even harmful for individuals with multimorbidity**
Limitations of Clinical Guidelines

ASH Int Soc HTN 2013
- Less than 80 years: <140/90
- Older than 80: SBP 150
- < 140/90 with DM or CKD

JNC 8 2014
- Age 60 or older goal <150/90

JNC 8 2014
- Goal <140/90 in otherwise healthy
- Lifestyle changes
- > 80 years- SBP 140-145
  - Avoid SBP <130, DBP <65

ACCFA/AHA Consensus Panel 2011
- < 140/90 with DM or CKD
GUIDING PRINCIPLE #3: PROGNOSIS

- Guiding principle: Frame management decisions within the context of risks, burdens, benefits, and prognosis

- Prognosis = remaining life expectancy, functional status, QOL

- Discussion of prognosis can serve as an introduction to difficult conversations
  - Facilitate decision-making, advance care planning
  - Address patient preferences, treatment rationales, and therapy prioritization
GUIDING PRINCIPLE #3: PROGNOSIS

- Prognosis informs, but does not dictate, management decisions within the context of patient preferences

  ➢ The time horizon to benefit for a treatment may be longer than the individual’s projected life span, raising the risk of polypharmacy and drug-drug and drug-disease interactions

  ➢ Screening tests, too, may be non-beneficial or could be harmful if the time horizon to benefit exceeds remaining life expectancy, especially because associated harms and burdens increase with age and comorbidity
Tables that give average life expectancy based on current age provide a broad estimate of median survival in the general population.

There is substantial heterogeneity in life expectancy among older adults within the same age category.

To partially account for this, practitioners can use tables that separate life expectancy into quartiles, then use clinical judgment to decide whether an individual is in the healthiest quartile, least healthy quartile, or one of the middle quartiles.
## Average Life Expectancy

Based on Estimates of Health

<table>
<thead>
<tr>
<th>Age</th>
<th>Quartile of Life Expectancy (years)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Women</td>
<td></td>
<td>Men</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>75th</td>
<td>50th</td>
<td>25th</td>
<td>75th</td>
<td>50th</td>
<td>25th</td>
</tr>
<tr>
<td>65</td>
<td>26.9</td>
<td>21.2</td>
<td>14.2</td>
<td>24.3</td>
<td>18.3</td>
<td>11.4</td>
</tr>
<tr>
<td>70</td>
<td>22.2</td>
<td>16.9</td>
<td>10.7</td>
<td>19.8</td>
<td>14.4</td>
<td>8.5</td>
</tr>
<tr>
<td>75</td>
<td>17.8</td>
<td>12.9</td>
<td>7.6</td>
<td>15.6</td>
<td>10.8</td>
<td>6.0</td>
</tr>
<tr>
<td>80</td>
<td>13.6</td>
<td>9.3</td>
<td>5.1</td>
<td>11.8</td>
<td>7.7</td>
<td>4.0</td>
</tr>
<tr>
<td>85</td>
<td>9.9</td>
<td>6.3</td>
<td>3.2</td>
<td>8.5</td>
<td>5.2</td>
<td>2.5</td>
</tr>
<tr>
<td>90</td>
<td>6.9</td>
<td>4.1</td>
<td>1.9</td>
<td>5.9</td>
<td>3.4</td>
<td>1.6</td>
</tr>
<tr>
<td>95</td>
<td>4.7</td>
<td>2.6</td>
<td>1.2</td>
<td>4.1</td>
<td>2.2</td>
<td>1.0</td>
</tr>
</tbody>
</table>
Using clinical trial results to generate a prognosis may be worthwhile if the patient’s clinical characteristics, such as age and comorbidities, closely match those of the study’s patient population.

Studies can be especially helpful in quickly advancing fields, such as oncology, in which new therapeutics are dramatically improving life expectancy.

Generalizability is a concern because patients with functional or cognitive limitations, and/or significant comorbidities, are often excluded from clinical trials.
Prognostic indices are validated tools that use select characteristics from a particular population, such as functional status and comorbidities, to calculate a prognostic estimate.

When used for mortality predictions in older adults, tools that incorporate functional status tend to perform better than those that rely only on factors normally captured in an electronic medical record.

A collection of these types of indices can be found at ePrognosis, https://eprognosis.ucsf.edu
Use of an prognostic index requires understanding of its accuracy, validity, and generalizability.

Example: Indices developed to estimate risk of mortality for nursing-home residents do not apply to community-dwelling adults.

For patients with one dominant life-limiting condition, disease-specific indices are often valuable.

Otherwise, nondisease-specific indices tailored to populations residing in different settings (community, nursing home, hospital, hospice) may be most useful.
## COMMON PROGNOSTIC INDICES: DISEASE-SPECIFIC (1 of 2)

<table>
<thead>
<tr>
<th>Prognostic index</th>
<th>Patient population</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palliative Performance Scale</td>
<td>Cancer and noncancer patients in clinics, hospitals, and hospices</td>
<td><a href="http://www.ePrognosis.org">www.ePrognosis.org</a></td>
</tr>
<tr>
<td>Seattle Heart Failure Model</td>
<td>Outpatients without significant other comorbidities. May overestimate prognosis in the old-old.</td>
<td><a href="http://depts.washington.edu/shfm">http://depts.washington.edu/shfm</a></td>
</tr>
<tr>
<td>EFFECT Model</td>
<td>Inpatients hospitalized with acute decompensated heart failure</td>
<td><a href="http://www.ccourt.ca/Research/CHFRiskModel.html">http://www.ccourt.ca/Research/CHFRiskModel.html</a></td>
</tr>
</tbody>
</table>
### COMMON PROGNOSTIC INDICES: DISEASE-SPECIFIC (2 of 2)

<table>
<thead>
<tr>
<th>Prognostic index</th>
<th>Patient population</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>BODE</td>
<td>Outpatients with COPD. May be more accurate in patients with severe COPD.</td>
<td>Reference.medscape.com/calculator/bode-index-copd</td>
</tr>
<tr>
<td>Advanced Dementia Prognostic Tool (ADEPT)</td>
<td>Nursing-home residents with advanced dementia</td>
<td><a href="http://www.ePrognosis.org">www.ePrognosis.org</a></td>
</tr>
</tbody>
</table>
LAG TIME TO BENEFIT

- **Definition**: Interval between the time of a diagnostic or therapeutic intervention and the time when improved health outcomes may be expected.

- **Examples with regard to a preventive intervention**:
  - **Life expectancy is significantly less than the lag time**: The likelihood of harm rather than benefit is high.
  - **Life expectancy is significantly exceeds the lag time**: The likelihood of benefit is now much higher.
  - **Life expectancy approximately equals the lag time**: Further discussion of prognosis and patient goals of care may help guide decision making.
# LAG TIME TO BENEFIT FOR COMMON INTERVENTIONS

<table>
<thead>
<tr>
<th>Lag time to benefit</th>
<th>Intervention(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2 months</td>
<td>• SSRIs for depression</td>
</tr>
<tr>
<td>6 months</td>
<td>• Statins for secondary prevention of CVD</td>
</tr>
<tr>
<td></td>
<td>• Finasteride for benign prostatic hyperplasia</td>
</tr>
<tr>
<td>1–2 years</td>
<td>• BP control for primary prevention of CVD</td>
</tr>
<tr>
<td>1–3 years</td>
<td>• Strict BP and lipid control in type 2 DM</td>
</tr>
<tr>
<td></td>
<td>• Statins for primary prevention of CVD</td>
</tr>
<tr>
<td>2–5 years</td>
<td>• Statins for CV events</td>
</tr>
<tr>
<td>8–10 years</td>
<td>• Tight glycemic control for prevention of microvascular complications in type 2 DM</td>
</tr>
<tr>
<td>10 years</td>
<td>• Colon and breast cancer screening</td>
</tr>
</tbody>
</table>
GUIDING PRINCIPLE #4: OPTIMIZING THERAPIES, CARE PLANS

- Guiding principle: Choose therapies that maximize benefit, minimize harm, enhance QOL

- Older adults with multimorbidity are at risk of:
  - Polypharmacy
  - Suboptimal medication use
  - Potential harms from various interventions

- Reducing the number of meds can lower the risk of adverse drug reactions

- Nonpharmacologic interventions may be more burdensome than beneficial, if inconsistent with patient preferences
Polypharmacy

Anticholinergics

*J Gen Intern Med.* 2014;29(10);1379-1386.
Anticholinergic Symptoms

Can’t pee
Can’t see
Can’t spit
Can’t sh**

Hot as a hare
Dry as a bone
Blind as a bat
Red as a beet

Mad as a hatter

Shared with permission by Elizabeth Feldman PharmD
Peripheral Effects
- Dry mouth
- Dry eyes
- Blurred vision
- Constipation
- Fecal Impaction
- Urinary Retention
- Tachycardia

Central Effects
- Cognitive impairment
- Dizziness
- Confusion
- Delirium

Shared with permission by Elizabeth Feldman PharmD
What is the “anticholinergic burden”? 

- The cumulative effect of taking multiple medications with anticholinergic properties.
Anticholinergic Burden

Genetics

Comorbidities

Medications

Shared with permission by Elizabeth Feldman PharmD
How do we quantify this burden?
An impractical but accurate way

- **Gold Standard:** Measurement of serum anticholinergic activity by radiographic assay

- **SAA:** Serum Anticholinergic Activity
  - Radioreceptor assay
  - Measured in term of atropine equivalents
    - Range 0.25 pmol/mL – 25.0 pmol/mL

- **Limitations**
  - Intra-laboratory variability
  - Endogenous substances can affect measurement
  - SAA impact on cognition → unclear
A More Practical Approach: Anticholinergic Risk Scales

- Anticholinergic Cognitive Burden Scale (ACB)*
- Anticholinergic Drug Scale (ADS)*
- Anticholinergic Risk Scale (ARS)*
- Chew 2009
- Clinician-Rated Anticholinergic Scale (CRAs)*
- Anticholinergic Burden Classification (ABC)*
- Anticholinergic Load Scale (ALS)
- Anticholinergic Activity Scale (AAS)*
- Drug Burden Index (DBI)

Scoring Considerations

- High variability between scales

- Drugs included: #27 – 128

- Scoring Range: 0-3
  - 0 = no anticholinergic potency
  - 3 = high potency

Anticholinergic Drug Scale (ADS)

- Level 1 = potentially anticholinergic as evidenced by receptor binding sites
- Level 2 = anticholinergic adverse events sometimes noted, usually at excessive doses
- Level 3 = markedly anticholinergic

Anticholinergic Drug Scale (ADS)

<table>
<thead>
<tr>
<th>Level 3 Drugs</th>
<th>Level 3 Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>amitriptyline</td>
<td>oxybutynin</td>
</tr>
<tr>
<td>atropine</td>
<td>proscycline</td>
</tr>
<tr>
<td>benztropine</td>
<td>promethazine</td>
</tr>
<tr>
<td>brompheniramine</td>
<td>propantheline</td>
</tr>
<tr>
<td>carbinoxamine</td>
<td>protriptyline</td>
</tr>
<tr>
<td>chlorpheniramine</td>
<td>pyrilamine</td>
</tr>
<tr>
<td>chlorpromazine</td>
<td>scopolamine</td>
</tr>
<tr>
<td>clemastine</td>
<td>thioridazine</td>
</tr>
<tr>
<td>clomipramine</td>
<td>tolterodine</td>
</tr>
<tr>
<td>clozapine</td>
<td>trihexyphenidyl</td>
</tr>
<tr>
<td>darifenacin</td>
<td>trimipramine</td>
</tr>
<tr>
<td>desipramine</td>
<td></td>
</tr>
</tbody>
</table>

Anticholinergic Burden Classification (ABC)

- Assess potential of anticholinergic drugs as a cause of non-degenerative mild cognitive impairment in elderly
- 10% of people on AC drugs
  - Multiple cognitive deficits
  - High likelihood of being diagnosed with mild cognitive impairment
  - Probability of evolution to dementia?
- Pro-cholinergic drugs to treat effects of cholinergic agents?

## High Anticholinergic Load: *Clinical Implications*

<table>
<thead>
<tr>
<th>Scale</th>
<th>Cognitive Function</th>
<th>Functional Outcome</th>
<th>Side Effects</th>
<th>Hospitalization</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carnahan USA, 2006 (ADS)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Han USA, 2008 (CrAS)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rudolph USA, 2008 (ARS)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Boustani, USA 2008 (ACB)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Ehrt, Norway 2010 (AAS)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

# High Anticholinergic Load: Clinical Implications

<table>
<thead>
<tr>
<th>Scale</th>
<th>Cognitive Function</th>
<th>Functional Outcome</th>
<th>Side Effects</th>
<th>Hospitalization</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carnahan USA, 2006 (ADS)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Han USA, 2008 (CrAS)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rudolph USA, 2008 (ARS)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Boustani, USA 2008 (ACB)</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Ehrt, Norway 2010 (AAS)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

"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 1745-1823
A Necessary Continuum

Deprescribing  Prescribing
Deprescribing Strategies
Home Medications

- Azelastine nasal spray as needed
- Calcium carbonate – Vitamin D 600-800 mg-unit daily
- Coenzyme Q10 200 mg daily
- Colchicine 0.6 mg BID
- Donepezil 10 mg nightly
- Levocetirizine 5 mg nightly
- Lixinopril/HCTZ 10mg/25mg daily
- Levothyroxine 50 mcg daily
- Lorazepam 0.5 mg twice daily PRN
- Uribel 118 mg Q6H PRN bladder discomfort
- Omega-3 Fatty Acids mg daily
- Acetaminophen 1000mg TID
- Tolterodine 4 mg daily
Medication decision making

Medication Decision Making

[Diagram showing case scenarios]

Medication Decision Making

Home Medications

No Benefit

- Azelastine nasal spray as needed
- Calcium carbonate – Vitamin D 600-800 mg-unit daily
- Coenzyme Q10 200 mg daily
- Colchicine 0.6 mg BID
- Donepezil 10 mg nightly
- Levocetirizine 5 mg nightly
- Lininopril/HCTZ 10mg/25mg daily

- Levothyroxine 50 mcg daily
- Lorazepam 0.5 mg twice daily PRN
- Uribel 118 mg Q6H PRN bladder discomfort
- Omega-3 Fatty Acids mg daily
- Acetaminophen 1000mg TID
- Tolterodine 4 mg daily
- Simvastatin 20mg daily
Home Medications

Harm Outweighs Benefit

- Azelastine nasal spray as needed
- Calcium carbonate – Vitamin D 600-800 mg-unit daily
- Coenzyme Q10 200 mg daily
- Colchicine 0.6 mg BID
- Donepezil 10 mg nightly
- Levocetirizine 5 mg nightly
- Lininopril/HCTZ 10mg/25mg daily
- Levothyroxine 50 mcg daily
- Lorazepam 0.5 mg twice daily PRN
- Uribel 118 mg Q6H PRN bladder discomfort
- Omega-3 Fatty Acids mg daily
- Acetaminophen 1000mg TID
- Tolterodine 4 mg daily
- Simvastatin 20mg daily
Algorithm for Deprescribing

1. **No benefit**
   - Significant toxicity OR no indication OR obvious contraindication OR cascade prescribing?
   - **Yes**
   - **No**

2. **Harm outweighs benefit**
   - Adverse effects outweigh symptomatic effect or potential future benefits?
   - **Yes**
   - Withdrawal symptoms or disease recurrence likely if drug therapy discontinued?
     - **Yes**
     - Taper dose and monitor for adverse drug withdrawal effects
     - **No**
   - **No**

3. **Symptom or disease drugs**
   - Symptoms stable or nonexistent?
   - **Yes**
   - **No**

4. **Preventive drugs**
   - Potential benefit unlikely to be realized because of limited life expectancy?
   - **Yes**
   - Discontinue drug therapy
   - **No**

Continue drug therapy

Symptoms stable or nonexistent?

Restart drug therapy

Home Medications
Still Indicated?

- Azelastine nasal spray as needed
- Calcium carbonate – Vitamin D 600-800 mg-unit daily
- Coenzyme Q10 200 mg daily
- Colchicine 0.6 mg BID
- Donepezil 10 mg nightly
- Levocetirizine 5 mg nightly
- Lininopril/HCTZ 10mg/25mg daily
- Levothyroxine 50 mcg daily
- Lorazepam 0.5 mg twice daily PRN
- Uribel 118 mg Q6H PRN bladder discomfort
- Omega-3 Fatty Acids mg daily
- Acetaminophen 1000mg TID
- Tolterodine 4 mg daily
- Simvastatin 20mg daily
**Home Medications Preventative**

- Azelastine nasal spray as needed
- Calcium carbonate – Vitamin D 600-800 mg-unit daily
- Coenzyme Q10 200 mg daily
- Colchicine 0.6 mg BID
- Donepezil 10 mg nightly
- Levocetirizine 5 mg nightly
- Lininopril/HCTZ 10mg/25mg daily
- Levothyroxine 50 mcg daily
- Lorazepam 0.5 mg twice daily PRN
- Uribel 118 mg Q6H PRN bladder discomfort
- Omega-3 Fatty Acids mg daily
- Acetaminophen 1000mg TID
- Tolterodine 4 mg daily
- Simvastatin 20mg daily
More than 50% of older adults have 3 or more chronic diseases, referred to as “multimorbidity”

Multimorbidity is associated with increased rates of death, disability, adverse effects, institutionalization, use of healthcare resources, and impaired QOL

Older adults with multimorbidity are heterogeneous in terms of illness severity, functional status, prognosis, personal priorities, and risk of adverse events
Treatment of older adults with multimorbidity requires a flexible approach because of heterogeneity among patients and inadequacy of most clinical practice guidelines.

The domains of evaluating and managing older adults with multimorbidity are to:

- Consider patient preferences
- Interpret relevant evidence
- Consider prognosis
- Optimize therapies and care plans
Thank you