Caring for Older Adults with HIV in the 21st Century

It’s Time for a Geriatric Approach

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Objectives:

- Discuss the changing *demographics* of HIV
- Highlight the challenges of *aging* with HIV
- Describe the domains of *geriatric medicine* and models of *HIV-geriatric care*
- Review *HIV pharmacotherapy*
- Discuss medications that can affect *cognition* and how to address *polypharmacy*
The care of HIV is improving all over the world.
The number of people living with HIV is increasing.

Number of people living with HIV, 1990 to 2019

Source: IHME, Global Burden of Disease
The number of new HIV infections is decreasing.

People all over the world are aging with HIV.
The number of PLWH who are 50+ is increasing.
Over half of people with diagnosed HIV were aged 50 and older.

As we reach 2035, adults age 50-65 yrs old will make up the greatest percentage of people living with HIV.

By 2035, the majority of people living with HIV will have **2 or more co-morbidities**.

There’s no better time to talk about aging.
Who is OLD?

Having lived for many years

Not young

https://www.britannica.com/dictionary/old
When I think about an older adult with HIV, I think about a person aged ____ or older.

A) 45
B) 50
C) 65
D) 70
Aging is a process: both chronologic and physiologic.


It’s more than just a number!
Genes play a large role in the rate of aging processes.
It’s more than just your genes!

https://www.nature.com/scitable/topicpage/environmental-influences-on-gene-expression-536/
Aging is not a disease.
Aging is a risk factor for chronic diseases.
Aging is a risk factor for geriatric syndromes.

Geriatric Syndromes:
clinical conditions in older adults that do not fit into discrete disease categories

- Delirium
- Falls
- Incontinence
- Dizziness
- Functional decline

Geriatric Syndrome

Falls

- Dizziness
- Impaired vision
- Arthritis
- Hypotension
- Weakness
- Neuropathy
Unique Challenges of Aging with HIV

Accelerated Aging

Accentuated Aging

Accelerated & Accentuated Aging

Older adults with HIV have increased risk of multimorbidity.

Older adults with HIV develop comorbidities at younger ages.


Older adults with HIV are experiencing geriatric syndromes.

Older adults with HIV develop dementia at younger ages.

Average age at dx:
- 67 yrs with HIV
- 78 w/o HIV

Geriatric Medicine
Geriatric Approach to Care

Disease

- Kidney disease
- Dementia
- Diabetes
- Hypertension
- Atrial fibrillation

Psychosocial

- Gait instability
- Recurrent falls
- Social support
- Depression
- Financial stress
- Housing

Function

- ADLs
- IADLs
- DME
- Gait instability
- Recurrent falls
- Anxiety
- Depression
- Social support
- Financial stress
- Housing

Atrial fibrillation

Hypertension

Diabetes

Dementia

Kidney disease

ADLs

IADLs

DME

Gait instability

Recurrent falls

Anxiety

Depression

Social support

Financial stress

Housing
Psychosocial Disease Function

Disease
- Atrial fibrillation
- Hypertension
- Diabetes
- Dementia
- Kidney disease

Psychosocial
- ADLs
- IADLs
- DME
- Gait instability
- Recurrent falls
- Anxiety
- Depression
- Social support
- Financial stress
- Housing

Function
- ADLs
- IADLs
- DME

Social support
- Anxious
- Depression
- Financial stress
- Housing
Geriatric 5 M’s

Mind  Mobility  Medications  Matters Most

Multi-complexity

https://britishgeriatricssociety.wordpress.com/2017/10/13/the-geriatric-5ms-the-5-simple-words-every-geriatrician-needs-to-know-the-new-mantra/
Geriatric-HIV Medicine 6 M’s

Mind   Mobility   Medications

Multi-complexity

Modifiable

Matters Most

Comprehensive Geriatric Assessment

1. Medical
2. Functional
3. Psychological
4. Sexual
5. Spiritual
6. Social
7. Environmental
8. Goals of Care

Assessment

Problem list
Review
Interventions
Care Plan

https://www.cgakit.com/cga
Models of HIV-Geriatric Care

01 Outpatient Referral
- Simplicity

02 Multidisciplinary Clinic
- Coordination
- Access

03 Dually Trained Providers
- No additional consultations needed
- Access

Comprehensive Program of Integrated Care for Older Adults with HIV

Keith Haring Foundation

Interdisciplinary Team
- Geriatrician
- Nurse
- Pharmacist
- Social Worker

https://www.haring.com/!/art-work/886
Comprehensive Program of Integrated Care for Older Adults with HIV

Keith Haring Foundation

Services
- Comprehensive Geriatric Assessment
- Cognitive Evaluation
- Mobility Assessment
- Medication Management
- Advance Care Planning
- …and more!

https://www.kingandmcgaw.com/prints/keith-haring/
Comprehensive Program of Integrated Care for Older Adults with HIV

Keith Haring Foundation

Referrals
- Average age 67
- 58% Male
- 51% Cognitive evaluation
- 29% Mobility
- 15% Polypharmacy
- 4% Multimorbidity
- 1% Advance care planning

https://www.artsy.net/artist/keith-haring
71 yr old man referred for a comprehensive geriatric assessment
Mr. B

1. HIV on ARVs
2. CAD
3. HFrEF (EF 30%)
4. COPD
5. Neuropathy
6. Chronic back pain
7. Lumbar spinal stenosis
8. Osteoporosis
9. Compression fractures
10. Active tobacco use disorder

Goals of care
- Functional
- Social
- Environmental
- Psychological
- Spiritual
- Sexual
Guidance for Addressing the Needs of Older Patients in HIV Care

Lead author: Eugenia L. Siegler, MD, with the Medical Care Criteria Committee, July 2020
Multicomplexity

Guiding Principles for the Care of Older Adults with Multimorbidity: An Approach for Clinicians

American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity*

- Patient preference
- Limitations
- Harms, burdens, benefits
- Prognosis
- Treatment complexity and feasibility
- Optimize benefit, minimize harm, enhance quality of life

Multicomplexity

- Identify
- Align
- Decide

Matters Most

Mr. K's healthcare team wants him to:

- Stop beta-blocker
- Increase beta-blocker
- Psychiatric Nurse Practitioner
- Start insulin

Cardiologist
Endocrinologist
Primary Care Doctor

Each clinician is focused on treating his individual conditions.

Is this what Mr. K wants?

https://patientprioritiescare.org/how-it-works/infographic/
Matters Most

**IDENTIFY HEALTH PRIORITIES**
- Values (What Matters most to the patient)
- Actionable, specific, realistic health outcome goals
- Health care preferences (which care the patient finds helpful and which burdensome) and any tradeoffs
- “One Thing” – the health goal the patient most wants to address to help achieve what Matters most

**ALIGN CARE WITH HEALTH PRIORITIES**
- Consider if current and potential care is:
  - Consistent with health outcome goals including patient’s “One Thing”?
  - Consistent with care preferences?
- Use the patient’s priorities:
  - As the focus for communication with the patient
  - As the goal for serial trials to start, stop or continue interventions
  - To prioritize care decisions, especially where differing perspectives exist

Update components as needed

https://patientprioritiescare.org/how-it-works/the-process/
Matters Most

My quality of life is more important than the quantity.

I want to maintain my independence & functional ability.
Matters Most

Advance Care Planning

VACS Index

Health Care Proxy

Appointing Your Health Care Agent in New York State

ePrognosis

Estimating Prognosis for Elders

MOLST

MEDICAL ORDERS FOR LIFE-SUSTAINING TREATMENT
A POLST Paradigm Program
### Mind

<table>
<thead>
<tr>
<th>Cooking</th>
<th>House Cleaning</th>
<th>Taking Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooking, planning, and preparing meals</td>
<td>Keeping living space free of clutter and dirt</td>
<td>Taking medications as prescribed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laundry</th>
<th>Shopping</th>
<th>Personal Finances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Washing linens, towels, and articles of clothing</td>
<td>Purchasing groceries, clothing, and other items</td>
<td>Paying bills and budgeting accurately</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Communication</th>
<th>Transportation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Making and returning telephone calls</td>
<td>Driving a car, calling a cab, using public transportation</td>
</tr>
</tbody>
</table>

[https://info.eugeria.ca/en/what-are-iadls-and-how-are-they-different-from-adls](https://info.eugeria.ca/en/what-are-iadls-and-how-are-they-different-from-adls)
Mind

Instructions for Administration & Scoring

Step 1: Three Word Registration

Look directly at person and say “Please listen carefully I am going to say three words that I want you to repeat back to me now and try to remember. The words are [select a list of words from the versions below]. Please say them for me now.” If the person is unable to repeat the words after three attempts, move on to Step 2 (clock drawing).

The following and other word lists have been used in one or more clinical studies. For repeated administrations, use of an alternative word list is recommended.

Step 2: Clock Drawing

Say “Next, I want you to draw a clock for me. First, put in all of the numbers where they go.” When that is completed, say “Now, set the hands to 10 past 11.”

Use preprinted circle (see next page) for this exercise. Repeat instructions as needed as this is not a memory test. Move to Step 3 if the clock is not complete within three minutes.

Step 3: Three Word Recall

Ask the person to recall the three words you stated in Step 1. Say “What were the three words I asked you to remember?” Record the word list version number and the person’s answers below.

Word List Version: Person’s Answers:


Mind

MOCA 21/30

https://stock.adobe.com/search?q=stick+figure+thinking
Patient Health Questionnaire (PHQ-2)

Over the past 2 weeks, have you often been bothered by:
1. Little interest or pleasure in doing things? □ Yes □ No
2. Feeling down, depressed, or hopeless? □ Yes □ No

GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems?
(Use "✓" to indicate your answer)

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeling nervous, anxious or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Being so restless that it is hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feeling afraid as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

For office coding: Total Score T = ___ + ___ + ___ + ___

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all □
Somewhat difficult □
Very difficult □
Extremely difficult □
Mind

MOCA 21/30

PHQ9 9

GAD7 7
Mobility
Mobility

- Eating
- Bathing
- Dressing
- Transferring
- Toileting
- Walking or moving around

https://www.elderneedslaw.com/blog/activities-of-daily-living-and-medicaid-eligibility
Mobility

STEADI Algorithm for Fall Risk Screening, Assessment, and Intervention among Community-Dwelling Adults 65 years and older

Available Fall Risk Screening Tools:
- Stay Independent: a 12-question tool
  [at risk if score ≥ 4]
  Important: If score ≤ 4, ask if patient fell in the past year
  (If YES: patient is at risk)
- Three key questions for patients (at risk if YES to any question)
  Feels unsteady when standing or walking?
  Worries about falling?
  Has fallen in past year?
  ▶ If YES ask, "How many times?" "Were you injured?"

Common ways to assess fall risk factors are listed below:

- Evaluate gait, strength, & balance
- Identify medications that increase fall risk
  (e.g., Beers Criteria)
- Ask about potential home hazards
  (e.g., throw rugs, slippery tub floor)
- Measure orthostatic blood pressure
  (Lying and standing positions)
- Check visual acuity
  Common assessment tool: Snellen eye test
- Assess feet/footwear
- Assess vitamin D intake
- Identify comorbidities
  (e.g., depression, osteoporosis)

Common assessments:
- 30-Second Chair Stand
- 4-Stage Balance Test

Reduce identified fall risk:
- Discuss patient and provider health goals
- Develop an individualized patient care plan (see below)

Below are common interventions used to reduce fall risk:

- Poor gait, strength, & balance observed
- Medication(s) likely to increase fall risk
- Home hazards likely
- Orthostatic hypotension observed
- Visual impairment observed
- Feet/footwear issues identified
- Comorbidities documented

PREVENT future risk by recommending effective prevention strategies.

- Educate patient on fall prevention
- Assess vitamin D intake
  [If deficient, recommend daily vitamin D supplement]
- Refer to community exercise or fall prevention program
- Reassess yearly, or any time patient presents with an acute fall

INTERVENE to reduce identified risk factors using effective strategies.

Follow up with patient in 30-90 days.
Discuss ways to improve patient receptiveness to the care plan and address barriers.

Frailty

<table>
<thead>
<tr>
<th>F__atigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>R__esistance</td>
</tr>
<tr>
<td>A__mbulation</td>
</tr>
<tr>
<td>I___llnesses</td>
</tr>
<tr>
<td>L__oss of Weight</td>
</tr>
</tbody>
</table>

≥ 3 = frail / 1 - 2 = pre-frail / 0 = robust

Modifiable

Medications

1. Metoprolol
2. Sacubitril/Valsartan (Entresto®)
3. Spironolactone
4. Aspirin
5. Ezetimibe
6. Rosuvastatin
7. Bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy®)
8. Esomeprazole
9. Tiotropium (Spiriva®)
10. Alendronate
11. Lorazepam
12. Zolpidem

https://www.dreamstime.com/illustration/cartoon-pharmacist.html
71 yr old man referred for a comprehensive geriatric assessment

Multicomplexity
- Yes!
- Priorities

Matters Most
- Independence
- Prognosis
- ACP

Medications
- 12 daily meds

Mind
- IADLs
- PHQ9/GAD7
- MOCA

Mobility
- ADLs
- Falls screening

Modifiable
- Tobacco use
71 yr old man referred for a comprehensive geriatric assessment

**Problem list:**
- Chronic pain
- Hearing loss
- Depression/Anxiety
- Insomnia
- Polypharmacy
- Tobacco use

**Care Plan:**
- Referral to SW
- Referral to psychotherapy
- Referral to ENT

**Interventions:**
- Motivational interviewing
- Care coordination
Side Effects - Medications

- Possibility, not a certainty.
  - Possibility of side effects may increase based on factors such as pre-existing conditions, reduced kidney or hepatic function, higher dose, and drug or food interactions.

- Two classifications of side effects
  - Class-specific
  - Drug-specific
## Side Effects - NRTI (Nucleoside reverse transcriptase inhibitors)

**Class-specific:** Lactic acidosis, hepatic steatosis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>Hypersensitivity (rash/fever/fatigue/dyspnea/GI/cough/pharyngitis)</td>
</tr>
<tr>
<td>Didanosine</td>
<td>Peripheral neuropathy, pancreatitis (with heavy alcohol use)</td>
</tr>
<tr>
<td>Emtricitabine</td>
<td>Hyperpigmentation of palms/soles</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Stavudine</td>
<td>Peripheral neuropathy, pancreatitis</td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate</td>
<td>Acute renal failure, decreased bone mineral density, Fanconi syndrome</td>
</tr>
<tr>
<td>Tenofovir alafenamide</td>
<td>Increased serum creatinine and urinary protein, mineral density loss</td>
</tr>
<tr>
<td>Zalcitabine</td>
<td>Peripheral neuropathy, ulcerations, rash</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Bone marrow suppression</td>
</tr>
</tbody>
</table>
### Side Effects - NNRTI (Non-nucleoside reverse transcriptase inhibitors)

**Class-specific:** Rash, hepatotoxicity, CNS symptoms

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delavirdine</td>
<td>Elevated transaminases and total bilirubin</td>
</tr>
<tr>
<td>Doravirine</td>
<td>Headache, nausea, diarrhea</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Neuropsychiatric (vivid dreams, altered mental state), depression, suicidal ideation</td>
</tr>
<tr>
<td>Etravirine</td>
<td>Elevated cholesterol/triglycerides/glucose, hepatotoxicity</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Hypersensitivity, hepatotoxicity</td>
</tr>
<tr>
<td>Rilpivirine</td>
<td>Depression, suicidal ideation, QTc prolongation, virologic failure</td>
</tr>
</tbody>
</table>
# Side Effects - PI (Protease inhibitors)

Class-specific: Metabolic (e.g., insulin resistance, dyslipidemia), lipodystrophy

<table>
<thead>
<tr>
<th>Medication</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amprenavir</td>
<td>Rash, elevated triglycerides, diarrhea</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>Jaundice, PR prolongation, decreased bone mineral density, cholelithiasis/nephrolithiasis</td>
</tr>
<tr>
<td>Darunavir</td>
<td>Elevated amylase/transaminases, hepatotoxicity</td>
</tr>
<tr>
<td>Fosamprenavir</td>
<td>Elevated transaminases</td>
</tr>
<tr>
<td>Indinavir</td>
<td>Nephrolithiasis, hyperbilirubinemia</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>Diarrhea, nausea</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>diarrhea</td>
</tr>
<tr>
<td>Saquinavir</td>
<td>PR/QT prolongation</td>
</tr>
<tr>
<td>Tipranavir</td>
<td>Intracranial hemorrhage, hepatic toxicity</td>
</tr>
</tbody>
</table>
Side Effects - INSTI (Integrase strand transferase inhibitor)

Class-specific: Rash

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bictegravir</td>
<td>Elevated total bilirubin, serum creatine, renal insufficiency</td>
</tr>
<tr>
<td>Dolutegravir</td>
<td>Insomnia, mood disturbance, renal insufficiency</td>
</tr>
<tr>
<td>Elvitegravir</td>
<td>Elevated hepatic transaminase</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>Fatigue, muscle aches, elevated pancreatic amylase and hepatic transaminase</td>
</tr>
</tbody>
</table>
# Side Effects - Booster, CCR5I, FI, PAI

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritonavir (booster)</td>
<td>Abnormal taste sensation, numbness around mouth/extremities, PR prolongation</td>
</tr>
<tr>
<td>Cobicistat (booster)</td>
<td>Jaundice, hyperbilirubinemia, elevated serum creatinine, renal insufficiency</td>
</tr>
<tr>
<td>Maraviroc (chemokine receptor type 5 inhibitor)</td>
<td>Cough, upper respiratory tract infections, rash, musculoskeletal pain, MI, hepatitis</td>
</tr>
<tr>
<td>Enfuvirtide (fusion inhibitor)</td>
<td>Injection site reaction, fatigue diarrhea, nausea, insomnia, pneumonia, eosinophilia</td>
</tr>
<tr>
<td>Ibalizumab-uiyk (post-attachment inhibitor)</td>
<td>Diarrhea, dizziness, nausea, rash, elevated serum creatinine</td>
</tr>
</tbody>
</table>
## Side Effects - HIV Medications

<table>
<thead>
<tr>
<th></th>
<th>NRTI</th>
<th>NNRTI</th>
<th>PI</th>
<th>INSTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive/Psychiatric</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Pancreas</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Metabolic</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
Drug-Drug Interactions

- Drugs can interact with other medication in various ways
  - May increase the absorption → Higher chance of adverse effects
  - May decrease the absorption → Higher chance of treatment failures

- HIV medications may interact with non-HIV medications
  - Statins: lowers cholesterol
  - Acid-Suppressive agents: helps with heartburn
  - Antiepileptics: prevent/treat seizures
  - Methadone: pain and addiction
  - Antidepressants: mood, depression, anxiety
  - PDE-5 inhibitors: erectile dysfunction
  - Fluticasone & salmeterol: allergies, asthma
  - Others
## Drug-Drug Interactions

### Statins

<table>
<thead>
<tr>
<th>Statin</th>
<th>Protease Inhibitors (PI)</th>
<th>Cobicistat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>OK except with tipranavir-ritonavir (Aptivus®) “Start low, go slow”</td>
<td>OK</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>OK</td>
<td>No data</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>OK. Use lowest dose with atazanavir or darunavir containing regimen.</td>
<td>No data</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>OK “start low, go slow”</td>
<td>OK</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Contraindicated</td>
<td>Contraindicated</td>
</tr>
</tbody>
</table>
Drug-Drug Interactions

- **Acid-suppressive agents**
  - Increases the pH (makes less acidic) of the gastrointestinal tract, which can lead to decreased absorption of some HIV medications, which leads to virologic failure.
  - Acid-suppressive agents include histamine-2 blockers (famotidine, ranitidine, etc.), proton pump inhibitors (omeprazole, lansoprazole, pantoprazole, esomeprazole, etc.), and antacids (calcium carbonate, aluminum hydroxide, magnesium carbonate, etc.).

- **HIV medications interacting with acid-suppressive agents**
  - **Histamine-2 blockers**: *Atazanavir* (boosted can be given at the same time or at least 10 hours after H2 blocker; unboosted should be taken at least 2 hours before or at least 10 hours after taking H2 blocker), *Rilpivirine* (H2 blockers should be given at least 4 hours before or 2 hours after).
  - **Proton pump inhibitors**: *Atazanavir* (12 hours apart), *Darunavir* (ritonavir boosted formulation), *Rilpivirine* (contraindicated), *Tipranavir* (not recommended).
  - **Antacids**: *Atazanavir* (2 hours before or 1 hour after antacid), *Bictegravir, Dolutegravir* (2 hours before or 6 hours after; can be taken with a calcium-containing antacid if taken with food), *Elvitegravir* (2 hours apart), *Raltegravir* (avoid aluminum or magnesium containing antacid), *Rilpivirine* (4 hours before or 2 hours after antacid).
Drug-Drug Interactions

- Antiepileptics
  - 1st generation antiepileptic drugs (carbamazepine, phenytoin, phenobarbital, valproic acid)
    - Carbamazepine: increased level when coadministered with PIs, particularly ritonavir.
      Decreased level when coadministered with efavirenz and nevirapine.
    - Phenytoin: decreased level when coadministered with lopinavir/ritonavir and nelfinavir.
    - Valproic acid: decreased level when coadministered with ritonavir.
    - PI, maraviroc, efavirenz, etravirine: decreased level when coadministered with carbamazepine, phenytoin, and phenobarbital.

- Limited data on newer antiepileptic drugs
Drug-Drug Interactions

- **Methadone**
  - Interacts with most PIs and NNRTIs
  - ~50% reduction in level of methadone when coadministered with lopinavir/ritonavir, nelfinavir, efavirenz, and nevirapine.
  - May lead to opioid withdrawal
    - Dose increase of methadone by 10 to 20mg at a time with careful monitoring needed

- **Antidepressants**
  - Ritonavir based regimen increases levels of various SSRIs (fluoxetine, citalopram, paroxetine, sertraline), trazodone and tricyclic antidepressants (amitriptyline, despiramine, doxepin, imipramine, nortriptyline, etc).
  - Efavirenz decreases levels of bupropion and sertraline
  - Fluvoxamine, fluoxetine, and paroxetine may increase level of PIs.
Drug-Drug Interactions

● PDE-5 inhibitor
  ○ PI increases the level of PDE-5 inhibitors
    ■ Saquinavir and ritonavir increased the AUC of sildenafil by 3.1-fold and 11-fold, and increased the Cmax by 2.4-fold and 3.9-fold respectively.
  ○ Limited data with vardenafil and tadalafil.

● Fluticasone & salmeterol
  ○ Nasal spray for allergies and oral inhaler for asthma
  ○ Ritonavir increases the fluticasone AUC by 350-fold, which causes systemic effects.
    ■ Can cause Cushing Syndrome (too much cortisol in the body - symptoms include upper body obesity, round face, and thin skin with bruising)
  ○ Ritonavir increases level of salmeterol
    ■ Palpitations, tachycardia, and QTc prolongation
Drug-Drug Interactions

- Herbal supplements - Just because it is “natural” does not mean it is safe to use with other medications!
- Common herbal supplements used by elderly population:
  - gingko biloba, garlic, ginseng, aloe vera, chamomile, spearmint, and ginger
- Herbal supplements with significant CYP450 interactions:

<table>
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<tr>
<th></th>
<th>1A2</th>
<th>2C9</th>
<th>2C19</th>
<th>2D6</th>
<th>2E1</th>
<th>3A4</th>
<th>OATP1A</th>
<th>OATP2B1</th>
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<td>Kava Kava</td>
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<td>Black Cohosh</td>
<td>Garlic</td>
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<td>St. John’s Wort</td>
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</table>

Archives of Gerontology and Geriatrics, Vol 59, Issue 2, September-October 2014, Pages 227-233
Minimizing Adverse Events From Drug Interactions

- When drug interactions exist, prescribers and pharmacists assess the clinical significance of the interactions, and may proceed with dispensing of the drug if benefits outweigh the risks.
- Provide full and accurate list of medications, including herbal supplements and vitamins.
- Use one pharmacy if possible.
  - If using multiple pharmacies, make sure to update every pharmacy with up to date medication list.
  - Let the pharmacist know if you have kidney or liver problems.
- Report side effects to the prescriber and the pharmacist.
Liverpool HIV Interaction Checker

https://www.hiv-druginteractions.org/checker
Liverpool Interaction Checker

<table>
<thead>
<tr>
<th>HIV Drugs</th>
<th>Co-medications</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>biktarvy</td>
<td>metformin</td>
<td></td>
</tr>
</tbody>
</table>

### A-Z  Class  Trade

- **Bictegravir/Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF)**
- **Atorvastatin**
- **Carbamazepine**
- **Losartan**
- **Metformin**

### Drug Interactions

- **Do Not Coadminister**
  - Bictegravir/Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF)
  - Carbamazepine
  - Metformin
  - Metformin

### Potential Interaction

- Bictegravir/Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF)
- Metformin

Switch to table view
Reset Checker
Liverpool Interaction Checker

Do Not Coadminister

Bictegravir/Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF)

Quality of evidence: Very Low

Summary:
Coadministration is not recommended. Carbamazepine is an inducer and is expected to decrease both bictegravir and tenofovir alafenamide exposures which may result in loss of therapeutic effect and development of resistance. Coadministration with bictegravir/emtricitabine/tenofovir alafenamide has not been studied. Coadministration of carbamazepine (300 mg twice a day) with emtricitabine/tenofovir alafenamide (200/25 mg once daily) decreased tenofovir Cmax by 57% and 54%. Alternative anticonvulsants should be considered.

Description:
Co-administration is not recommended. Coadministration of carbamazepine (titrated from 100 mg to 300 mg twice a day) and emtricitabine/tenofovir alafenamide (200/25 mg once daily) decreased tenofovir alafenamide AUC and Cmax by 54% and 57%. The interaction has not been studied with bictegravir but may decrease bictegravir plasma concentrations (due to induction of CYP3A, UGT1A1, and P-gp).

Biktarvy Summary of Product Characteristics, Gilead Sciences Ltd, June 2019

Coadministration may decrease concentrations of bictegravir and tenofovir alafenamide. Coadministration with alternative anticonvulsants should be considered. Coadministration of bictegravir/carbamazepine (300 mg twice daily) and tenofovir alafenamide (25 mg single dose, with emtricitabine) decreased tenofovir Cmax and AUC by 57% and 54%.

Drug-Food Considerations

- Taking certain medications with food or on an empty stomach can have clinically significant effect on the outcome of pharmacotherapy.
- Variations of instructions
  - Take with food
  - Take on an empty stomach
  - Take with food with calorie requirements (e.g., >390 calories) or restrictions (e.g., avoid high fat meal)
  - Avoid specific fruit or juice (e.g., grapefruit, seville oranges, starfruit, etc.)
- Recommendations may differ even for the same medication depending on the dosage formulation, ART regimen, and patient’s age.


## Drug-Food Considerations

| With food | Single tablet regimen: Complera®, Odefsey®, Genvoya®, Stibild®, Juluca®, Symtuza®  
NRTI: Tenofovir alafenamide, Etravirine, Rilpivirine (>390 calories)  
PI: Amprenavir (if taken with ritonavir or suspension for pediatric), Atazanavir, Darunavir, Indinavir (if taken with a booster), Lopinavir (solution formulation), Nelfinavir, Saquinavir, Tipranavir (if taken with ritonavir tablet formulation)  
INSTI: Elvitegravir |
|---|---|
| Empty stomach | Single tablet regimen: Atripla®, Symfi®, Symfi Lo®  
NRTI: Didanosine  
NNRTI: Efavirenz  
PI: Amprenavir (suspension formulation for adult only), Indinavir |
Medications and Cognition
Anticholinergics

- Class of medication with wide therapeutic use.
- Blocks neurotransmitter called acetylcholine in central and peripheral nervous system.

**Common Therapeutic Use**
- Allergy/Cough/Cold
- Asthma/COPD
- Antispasmodic - Bladder/Stomach/GI Tract
- Stomach & GI Tract Ulcer
- Insomnia
- Motion Sickness/Dizziness/Nausea

- Movement disorders
- Anxiety
- Muscle spasms/Relaxants/Pain
- Antipsychotics
- Antidepressants (Tricyclic)
- Antiarrhythmics
- Seizures

## Anticholinergics

<table>
<thead>
<tr>
<th>Allergies/Cough/Cold/Sleeping</th>
<th>Nausea</th>
<th>Overactive Bladder</th>
<th>Parkinson</th>
<th>Anti-psychotics</th>
<th>Anti-spasmodics</th>
<th>Muscle Relaxants</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenhydramine (Benadryl®, “PM”)</td>
<td>Meclizine (Bonine®)</td>
<td>Oxybutynin</td>
<td>Benztropine</td>
<td>Olanzapine</td>
<td>Atropine</td>
<td>Carisoprodol</td>
<td>Amitriptyline</td>
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<tr>
<td>Hydroxyzine</td>
<td>Dimenhydrinate (Dramamine®)</td>
<td>Tolterodine</td>
<td>Trihexyphenidyl</td>
<td>Quetiapine</td>
<td>Belladonna Scopolamine</td>
<td>Chloroxazone</td>
<td>Despiramine</td>
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<tr>
<td>Promethazine</td>
<td>Prochlorperazine</td>
<td>Tropium</td>
<td>Amantadine</td>
<td>Clozapine</td>
<td>Dicyclomine</td>
<td>Cyclobenzaprine</td>
<td>DOXEPIN</td>
</tr>
<tr>
<td>Chlorpheniramine (Chlor-Trimeton®)</td>
<td>Trimethobenzamide</td>
<td>Darifenacin</td>
<td>Chlorpromazine</td>
<td>Hyoscyamine</td>
<td>Methocarbamol</td>
<td>Nortriptyline</td>
<td>DOXEPIN</td>
</tr>
</tbody>
</table>
Anticholinergics

- Associated with poorer cognition, reduced cerebral glucose metabolism, increased brain atrophy, and clinical decline in cognitive normal older adults.
- Taking at least one anticholinergic agent on a regular basis was 47% more likely to develop mild cognitive impairment, which is a precursor to dementia.
- Taking an anticholinergic for the equivalent of 3 years or more increased the risk of dementia by 54% than taking the same dose for 3 months or less.

Neurology Oct 2020, 95(16) e2295-e2304
Benzodiazepines

● Conflicting findings
● Cognitive impairment shown with
  ○ Long-acting benzodiazepines
    ■ chlordiazepoxide, clorazepate, diazepam, flurazepam.
  ○ Long-term use (> 3 years)
  ○ Abuse

Opioids

- Cognitive decline on the Mini Mental State Examination in patients using long-term opioid therapy or combined opioid and benzodiazepines.
- Other studies suggest that there are minimal effects on cognitive function.
Cardiac Agents

- **Antiarrhythmics - via anticholinergic effects**
  - Disopyramide, procainamide, quinidine

- **Hypertensives**
  - Low cerebral perfusion
    - All antihypertensives
  - Fluid, electrolytes, and acid-base imbalance
    - Diuretics
  - Neurotransmitter imbalance in the CNS
    - Reserpine, methyldopa, clonidine

- **Digoxin - via Na+/K+ ATPase disruption**
Proton Pump Inhibitors

- Omeprazole (Prilosec®), Esomeprazole (Nexium®)
- A study in 2014 showed a significant increased risk of any dementia with PPI use.
  - Multiple subsequent studies have failed to find association between PPI use and increased risk of dementia
  - One study published in 2022 (pending peer review) found that the incidence of Alzheimer’s disease was higher for patients exposed to PPIs regardless of duration of exposure
H₂ Antagonists (Antacids)

- Ranitidine (Zantac®), Cimetidine (Tagamet®)
- Long-term use (>2 years)
- Two possible mechanisms:
  - Anticholinergic effects
  - Interfere with absorption of Vitamin B₁₂

Tools to Calculate Anticholinergic Burden

ACB Calculator
ACBcalc.com

- Provides a score for medication with anticholinergic effects
- Score of 3+ is associated with increased cognitive impairment and mortality

Many of the medications that we commonly prescribe have anticholinergic properties. In patients over 65 years of age these can cause adverse events, such as confusion, dizziness and falls. These have been shown to increase patient mortality.

You can use this calculator to work out the Anticholinergic Burden for your patients. A score of 3+ is associated with an increased cognitive impairment and mortality.

Find more information on Anticholinergic Burden or help choosing medicines to reduce anticholinergic burden.
Tools to Calculate Anticholinergic Burden

Anticholinergic Burden Calculator
anticholinergicscales.es

- Assesses risk based on multiple scales and indices developed by various scholars
- Considers total daily dose of each medication
HIV - Efavirenz (Sustiva®, Atripla®, Symfi®)

- Associated with cognitive and psychiatric side effects
- Poorer cognitive function with long-term use and high efavirenz plasma level
- Switching to non-efavirenz combination improved general CNS symptomatology

Neurology Apr 2011, 76 (16) 1403-1409; DOI: 10.1212/WNL.0b013e31821670fb
HIV - High CNS Penetration Agents

- Most studies show that higher CNS penetration agents lead to improved cognition
- American Psychiatric Association suggests that some HIV agents (zidovudine and efavirenz) cause CNS complications due to its ability to penetrate the CNS
- Zidovudine, lamivudine, indinavir, and abacavir associated with amyloid plaques in neuronal cell culture experiment
- One study shows no association
# HIV - High CNS Penetration Agents

**Table 1. Central Nervous System Penetration Effectiveness Scores for Antiretroviral Agents Used to Date**

<table>
<thead>
<tr>
<th></th>
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<td>Tenofovir disoproxil fumarate</td>
<td>Didanosine</td>
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<tr>
<td>Amprenavir/r</td>
<td>Tenofovir alafenamide&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Lamivudine</td>
<td>Emtricitabine</td>
<td>Nevirapine</td>
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<tr>
<td>Cobicistat</td>
<td>Zalcitabine</td>
<td>Stavudine</td>
<td>Efavirenz</td>
<td>Dolutegravir&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Enfuvirtide</td>
<td>Etravirine</td>
<td>Delavirdine</td>
<td>Indinavir&lt;sup&gt;r&lt;/sup&gt;</td>
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<tr>
<td>Ritonavir&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Rilpivirine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Raltegravir</td>
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<td>Saquinavir</td>
<td>Elvitegravir&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Saquinavir/r</td>
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<tr>
<td>Tipranavir/r</td>
<td>Atazanavir</td>
<td>Indinavir</td>
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<tr>
<td>Nelfinavir</td>
<td>Atazanavir&lt;sup&gt;r&lt;/sup&gt;</td>
<td>Lopinavir&lt;sup&gt;r&lt;/sup&gt;</td>
<td>Darunavir&lt;sup&gt;r&lt;/sup&gt;</td>
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**NOTE:** Adapted from Letendre et al [18] with permission.

<sup>a</sup>Letendre et al [35] with permission and personal communication from Dr. Scott Letendre (unpublished data), written communication (22 June 2018).

<sup>b</sup>When used as a nonbooster.

Beers Criteria

- Lists potentially inappropriate medication use in older adults
- Guide to reduce polypharmacy, drug interactions, and adverse drug reactions
  - Provides recommendations and evidence-based rationale
- Improves risk-benefit ratio of pharmacotherapy
Polypharmacy

- No universal definition: ≥ 5 medications
- PLWH
  - Occurs ~10 years before the general population
  - High prevalence (≥ 5 non-HIV medications)
  - Higher risk of polypharmacy-associated hospitalization in PLWH
  - Higher prevalence of taking potentially inappropriate drugs (52-63% compared to 29% in uninfected patients)
  - Higher prevalence of anticholinergic risk score ≥ 3 (17% compared to 4% in uninfected patients)
  - Higher number of non-HIV medications (8 compared to 6 medications in uninfected patients)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>N</th>
<th>Polypharmacy prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>McNicholl I et al. <em>Pharmacotherapy</em>. 2017.</td>
<td>≥50</td>
<td>248</td>
<td>94%</td>
</tr>
<tr>
<td>Cabanilla G et al. Presented at IAS 2019.</td>
<td>≥65</td>
<td>112</td>
<td>84%</td>
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<tr>
<td>Greene M et al. <em>J AM Geriatr Soc</em>. 2014.</td>
<td>≥60</td>
<td>89</td>
<td>74%</td>
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Age

<table>
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<tr>
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<tr>
<td>≥60</td>
<td>74%</td>
</tr>
</tbody>
</table>

Reference

Lancet Healthy Longev 2021; 2: e639-50
Polypharmacy

● Higher chance of drug-drug interactions
  ○ May increase the risk of side effects or therapy failure
  ○ Limits pharmacotherapy options

● Additive effects
  ○ “Anticholinergic Burden”
  ○ Common weak anticholinergic medications:
    ■ warfarin, metoprolol, furosemide, venlafaxine, loratadine

● Potential burden on kidney and liver
Polypharmacy

- Prescribing Inertia
  - Amotivation to discontinue a medication that patient has been taking for a long time or prescribed by another provider

- Prescribing Cascade
  - Starting a medication to treat a side effect from another medication

- Patient’s desire to maintain the status-quo
  - Want to continue the current regimen because it has been working for them
Deprescribing Tool

MedStopper
medstopper.com

- Provides stopping priorities and suggested taper approach

---

|-------------------|---------------------------------|-----------------------|-------------------------------------|-----------------|---------------------------|---------------------------------------------|----------------------|
| RED=Highest  
GREEN=Lowest    | oxybutynin ( Ditropan) / Incontinence / incontinence | 😞 | 😞 | 😞 | If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose. | return of symptoms | None |
|                   | acetaminophen ( Tylenol) / Acetaminophen / general pain/osteoarthritis | 😞 | 😞 | 😞 | Tapering not required | None | None |
|                   | omeprazole ( Prilosec, Losec) / Proton pump inhibitor / heartburn/GERD | 😁 | 😞 | 😞 | If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose. | return of symptoms, heartburn, reflux | None |

MedStopper is a deprescribing resource for healthcare professionals and their patients.
Let’s Apply the Knowledge!

1. Metoprolol - anticholinergic score: 1
2. Sacubitril/Valsartan (Entresto®)
3. Spironolactone - Beer’s list
4. Aspirin
5. Ezetimibe
6. Rosuvastatin
7. Bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy®)
8. Esomeprazole - Beer’s list
9. Tiotropium (Spiriva®)
10. Alendronate
11. Lorazepam - Beer’s list
12. Zolpidem - Beer’s list

- Review the indications of each medication and the necessity of pharmacotherapy
- Conduct risk-benefit analysis
- Deprescribe as necessary
71 yr old man referred for a comprehensive geriatric assessment
Take Home Points

Multi-complexity

Mind
Mobility
Medications

Matters Most

Over half of people with diagnosed HIV were aged 50 and older.

Normal ageing (average age in many clinics now around 50)
Drug toxicity (for example, tenofovir and renal disease)
Lifestyle risk factors (smoking, drug and alcohol misuse)
Persistent immune dysfunction and inflammation

Premature ageing

Modifiable

AGS BEERS CRITERIA’2019