Caring for Older Adults with HIV in the 21st Century

It's Time for a Geriatric Approach

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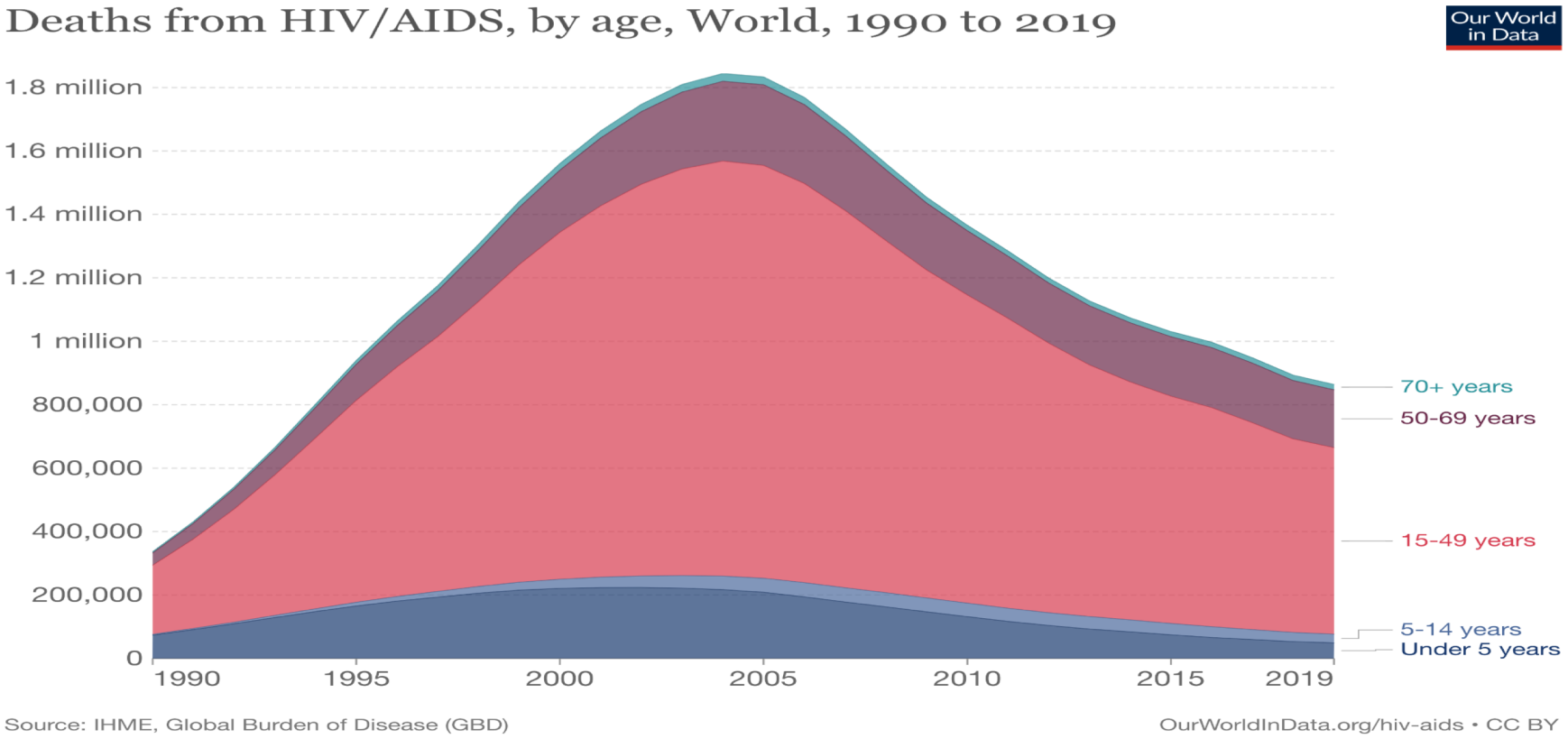
Department of Geriatrics and Palliative Medicine
Icahn School of Medicine at Mount Sinai

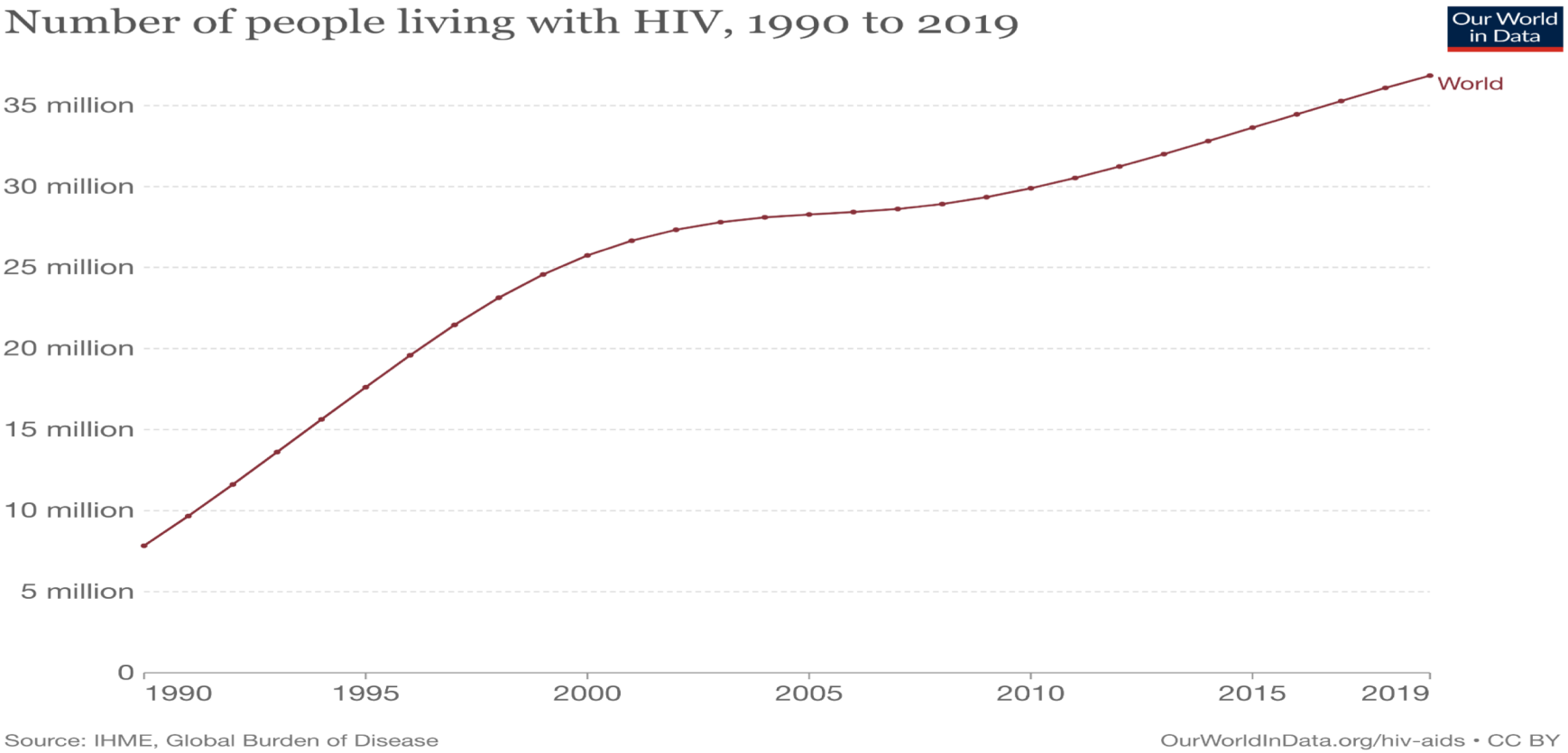
Objectives:

- 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**

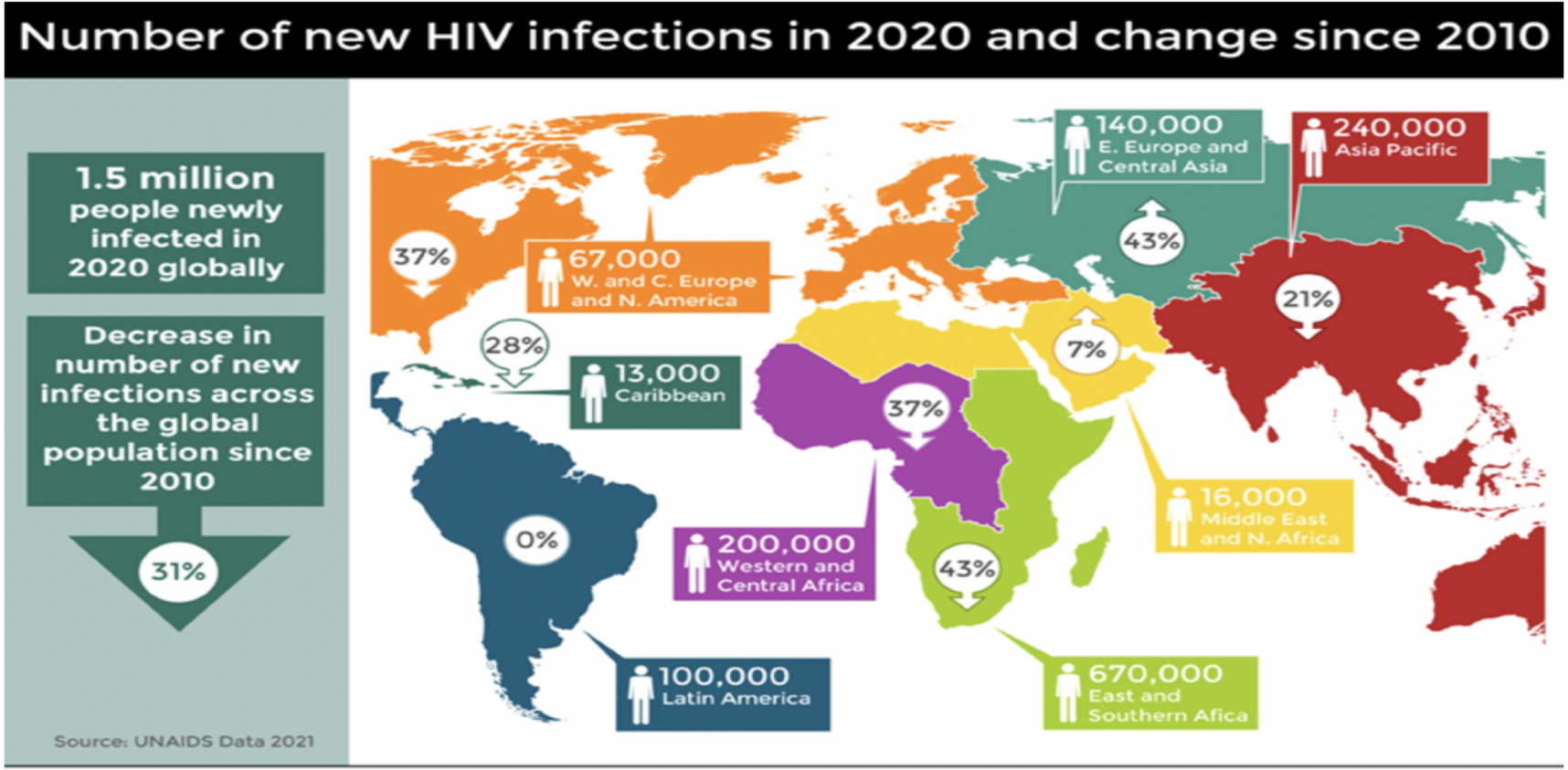
The care of HIV is improving all over the world.



The number of people living with HIV is increasing.

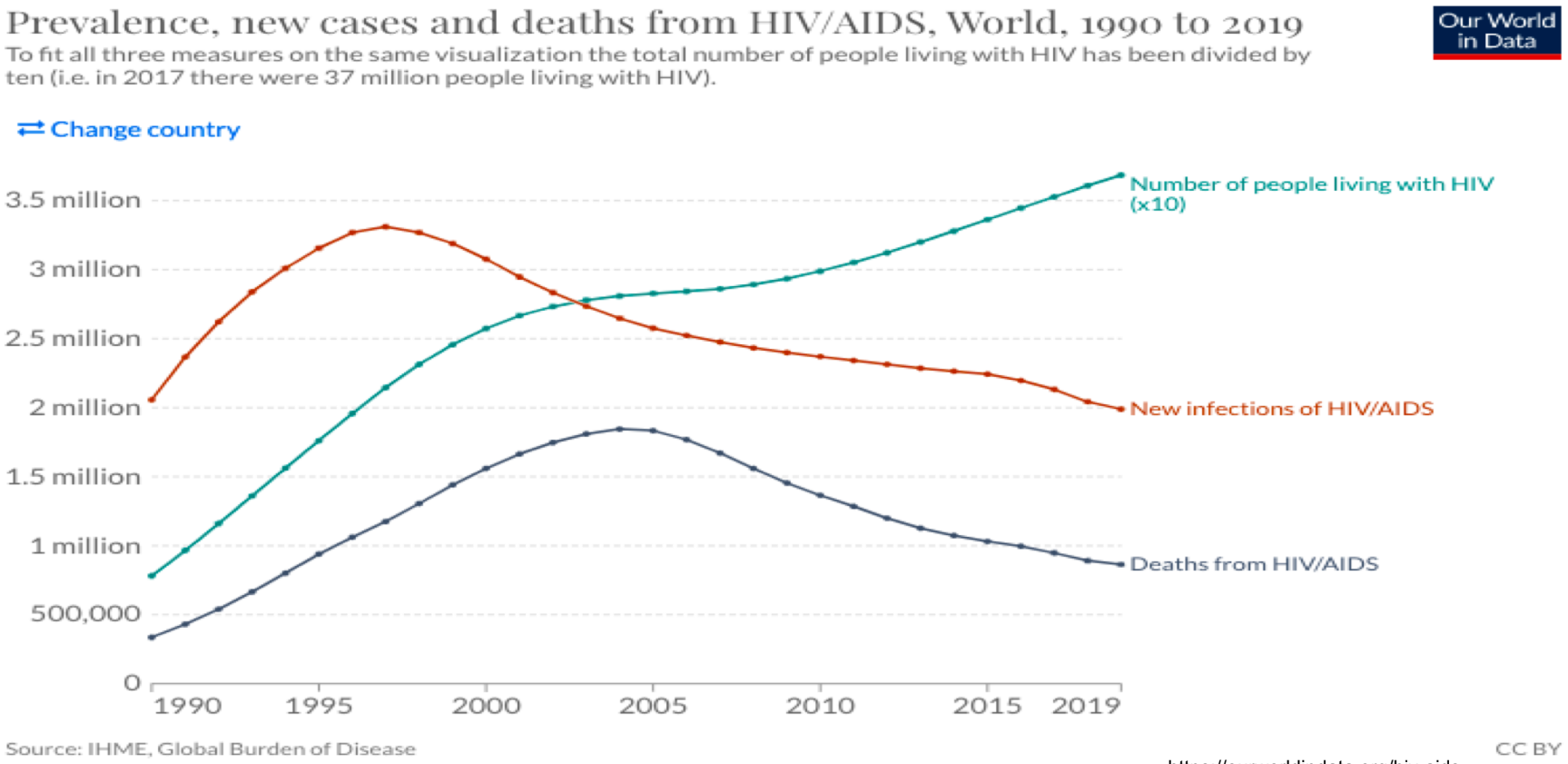


The number of new HIV infections is decreasing.



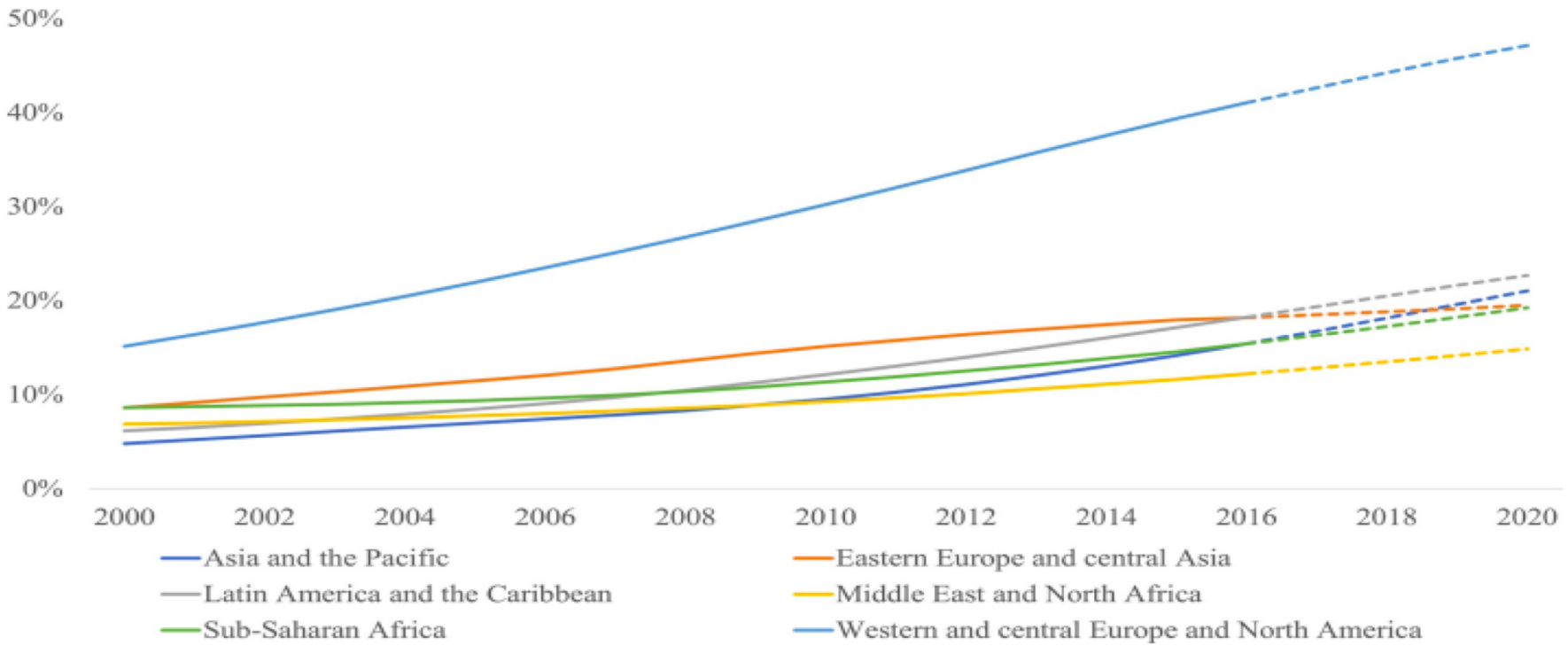
https://www.avert.org/global-hiv-and-aids-statistics

People all over the world are aging with HIV.



https://ourworldindata.org/hiv-aids

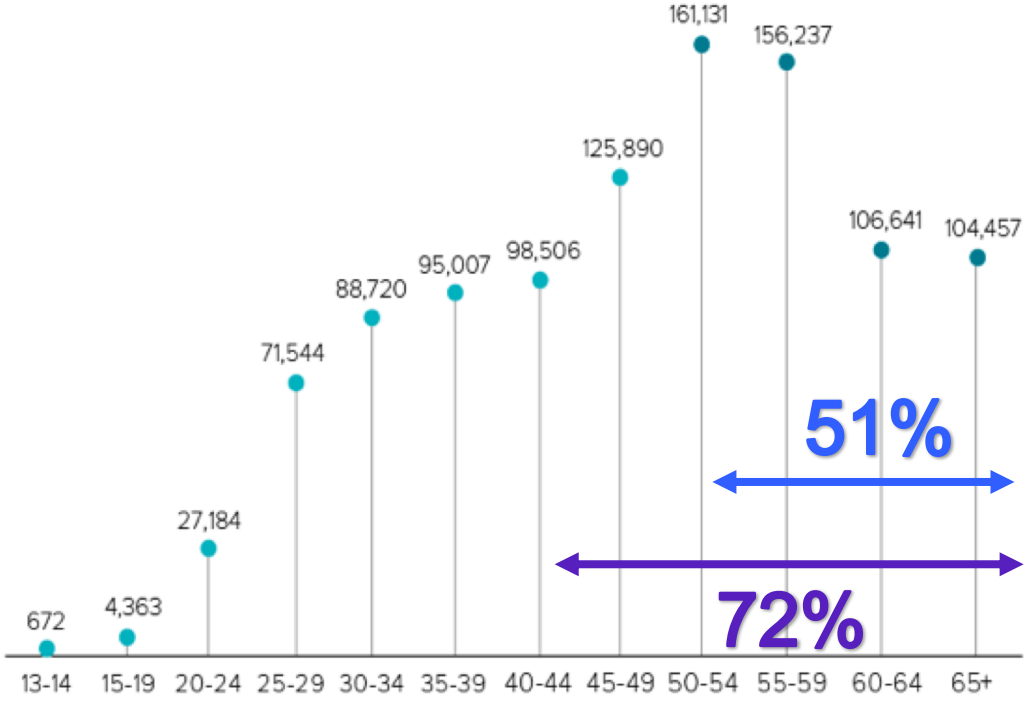
The number of PLWH who are 50+ is increasing.



Autenrieth CS, Beck EJ, Stelzle D, Mallouris C, Mahy M, Ghys P. Global and regional trends of people living with HIV aged 50 and over: Estimates and projections for 2000-2020. *PLoS One*. 2018;13(11):e0207005-e0207005.

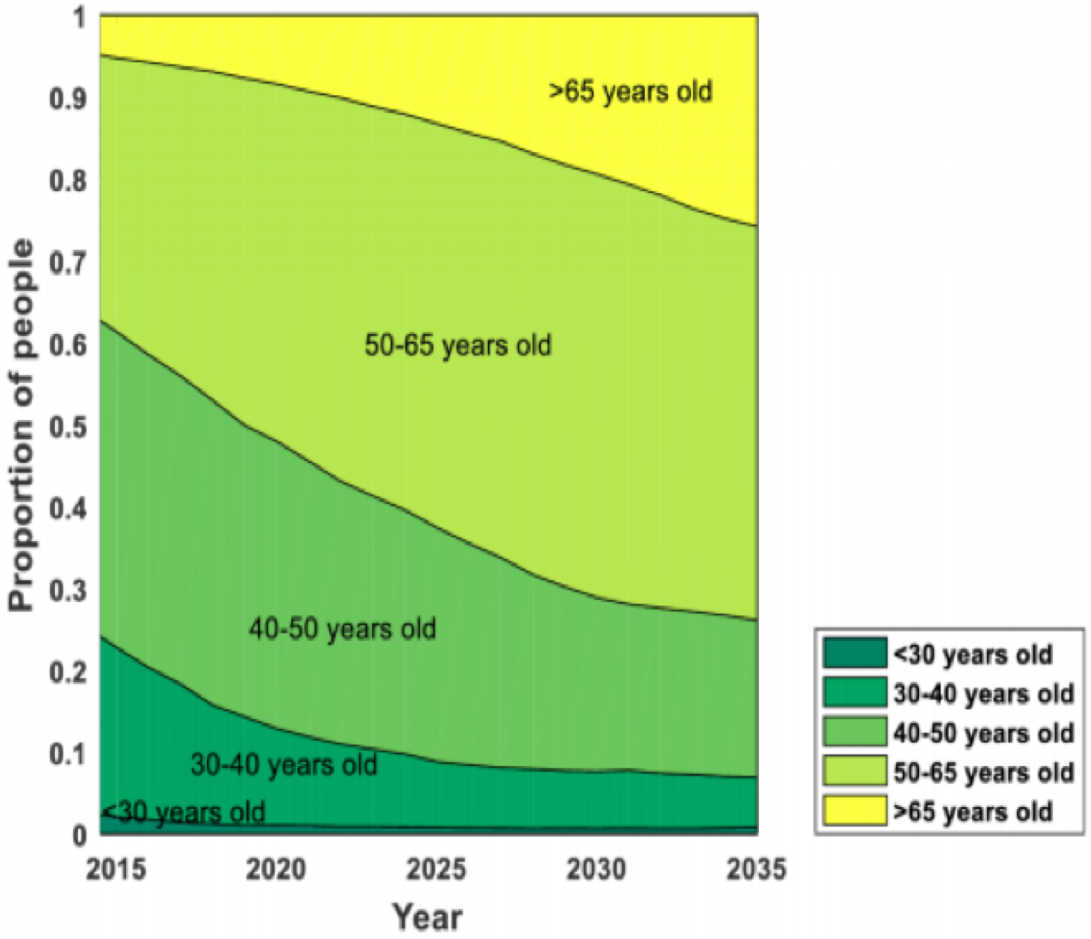
Adults and Adolescents with Diagnosed HIV in the US and Dependent Areas by Age, 2018

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



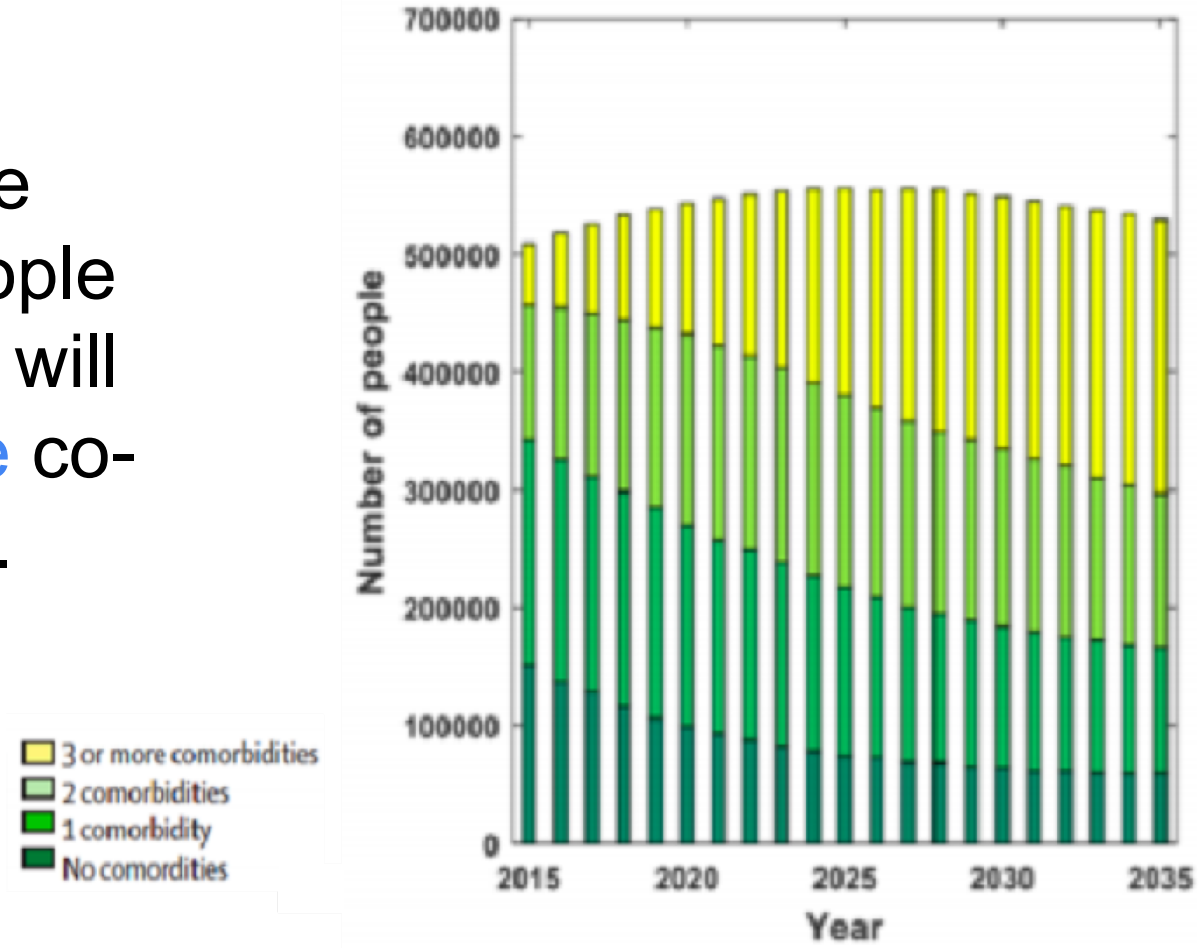
Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2018 (updated). *HIV Surveillance Report* 2020;31.

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



Smit M, Cassidy R, Cozzi-Lepri A, Quiros-Roldan E, Girardi E, Mammone A, et al. (2017) Projections of non-communicable disease and health care costs among HIV-positive persons in Italy and the U.S.A.: A modelling study. PLoS ONE 12(10): e0186638. https://doi.org/10.1371/journal.pone.0186638

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



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There’s no better time to talk about aging.

http://www.longlonglife.org/en/transhumanism-longevity/aging/biological-causes-aging-lifespan-limitation/attachment/biological-causes-of-human-aging-and-lifespan-limitation-a-review-about-longevity

Who is OLD?

Having lived for many years

Not young

https://www.britannica.com/dictionary/old

Who is OLD?

When I think about an older adult with HIV, I think about a person aged ____ or older.

A) 45

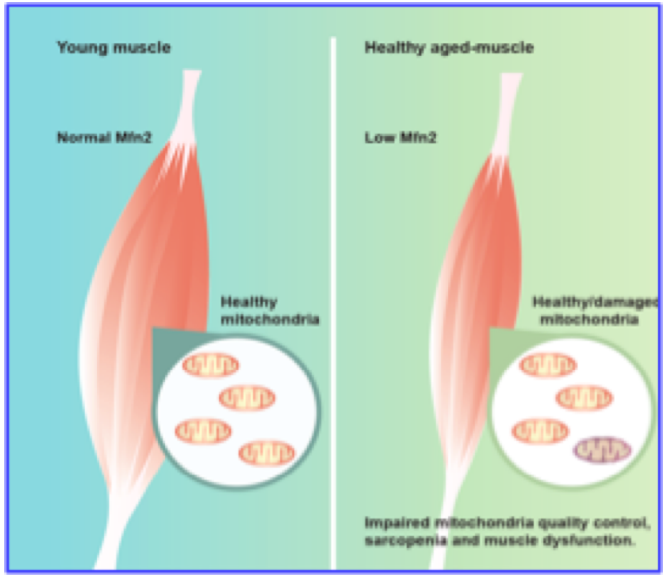
B) 50

C) 65

D) 70

Aging is a process: both chronologic and physiologic.

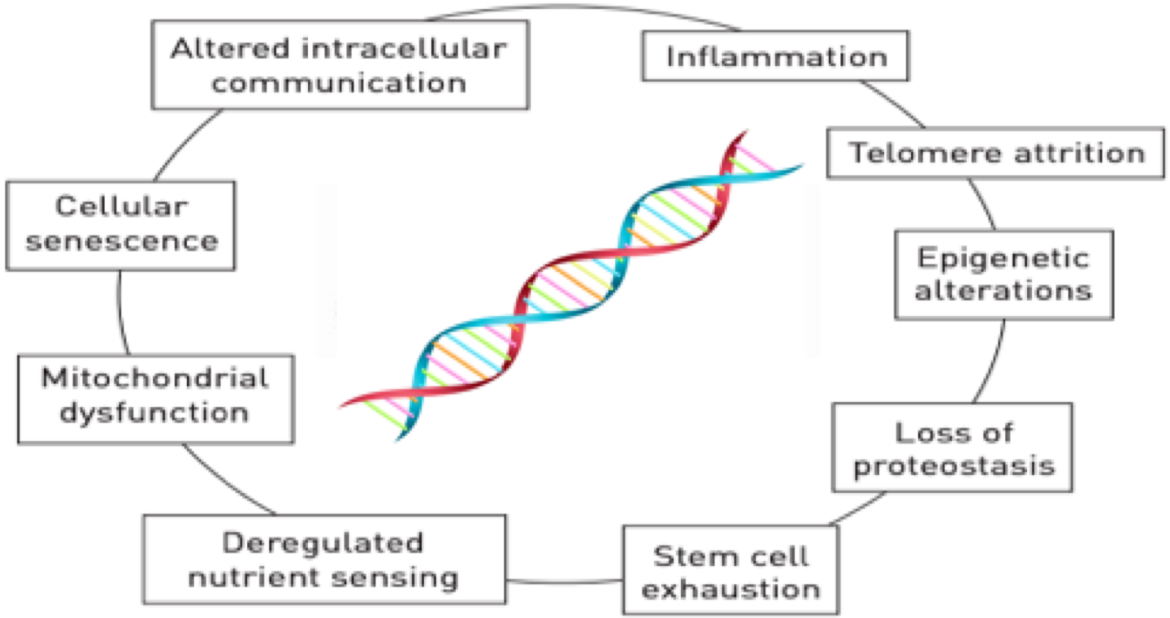
https://www.sbpdiscovery.org/news/beaker-blog/slowing-down-aging-clock



https://www.irbbarcelona.org/en/news/the-absence-of-a-single-protein-spurs-muscle-aging-in-mice

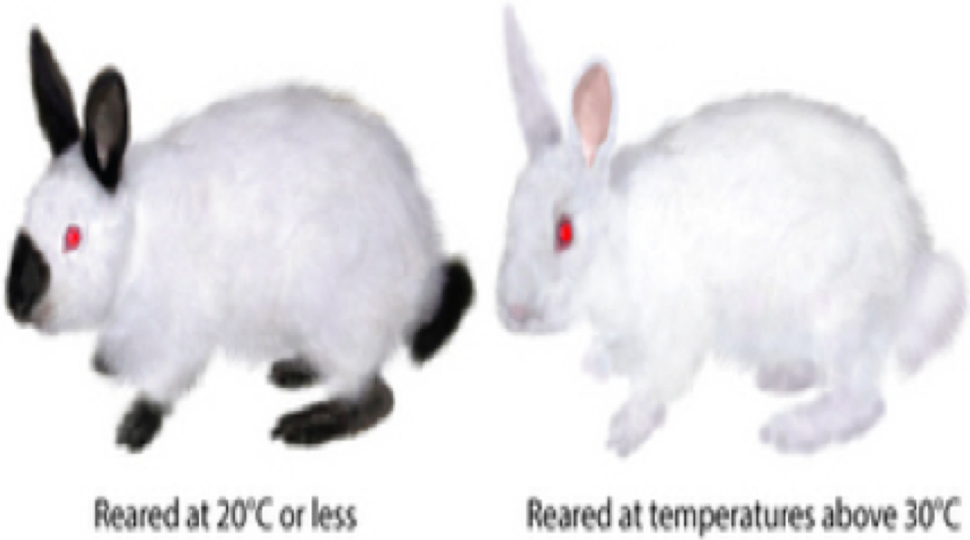
It’s more than just a number!

Genes play a large role in the rate of aging processes.



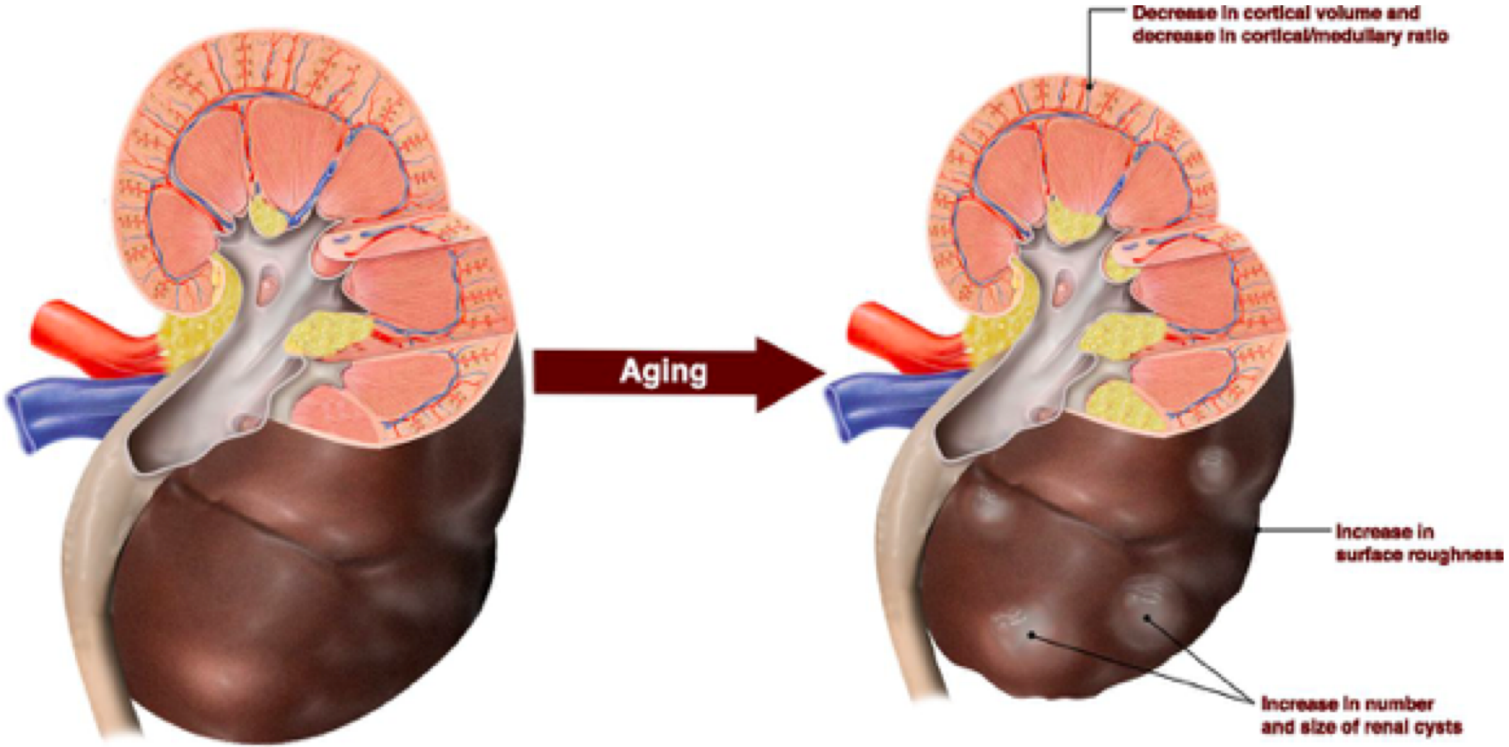
MacNee W, Rabinovich RA, Choudhury G. Ageing and the border between health and disease. *European Respiratory Journal.* 2014;44(5):1332-1352.

It’s more than just your genes!



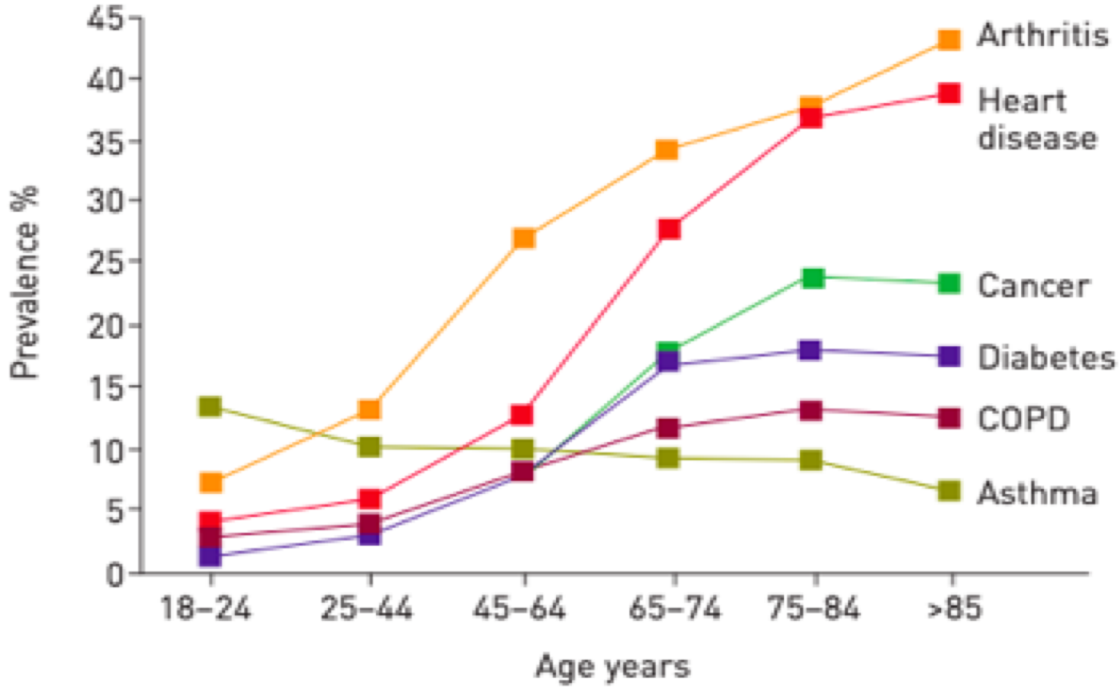
https://www.nature.com/scitable/topicpage/environmental-influences-on-gene-expression-536/

Aging is not a disease.



https://jasn.asnjournals.org/content/28/10/2838

Aging is a risk factor for chronic diseases.



MacNee W, Rabinovich RA, Choudhury G. Ageing and the border between health and disease. *European Respiratory Journal*. 2014;44(5):1332-1352.

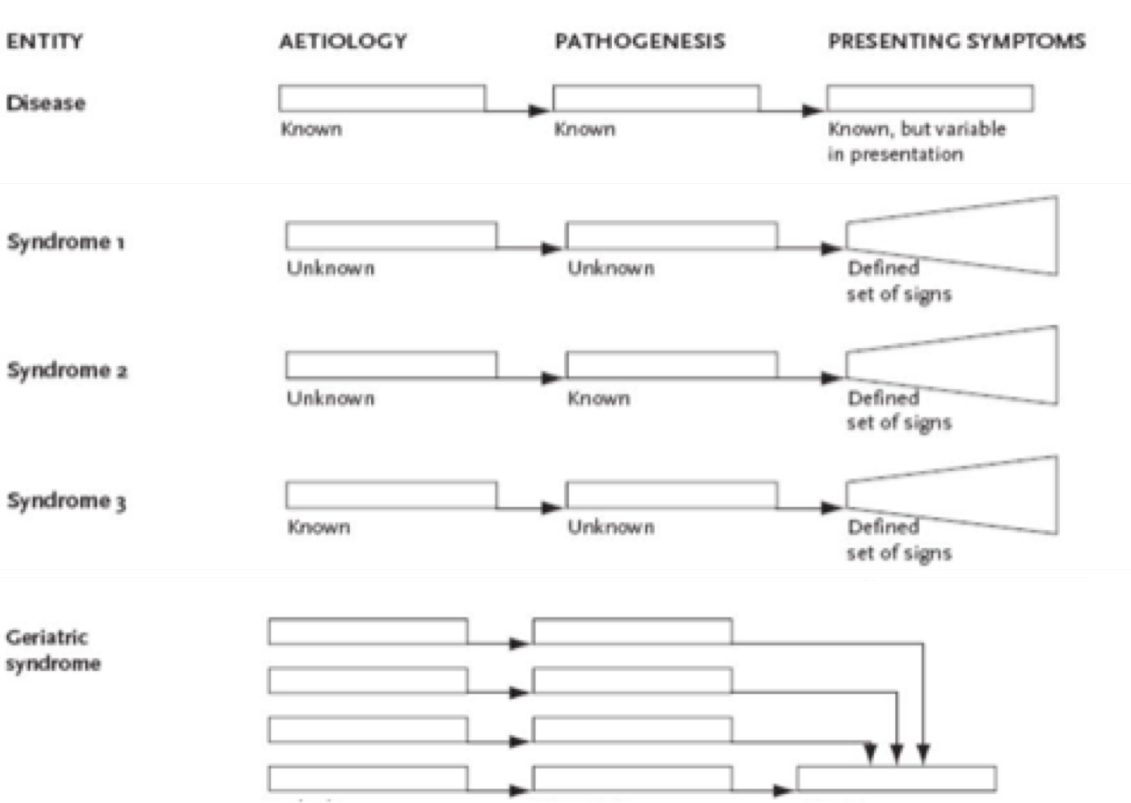
Aging is a risk factor for geriatric syndromes.

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

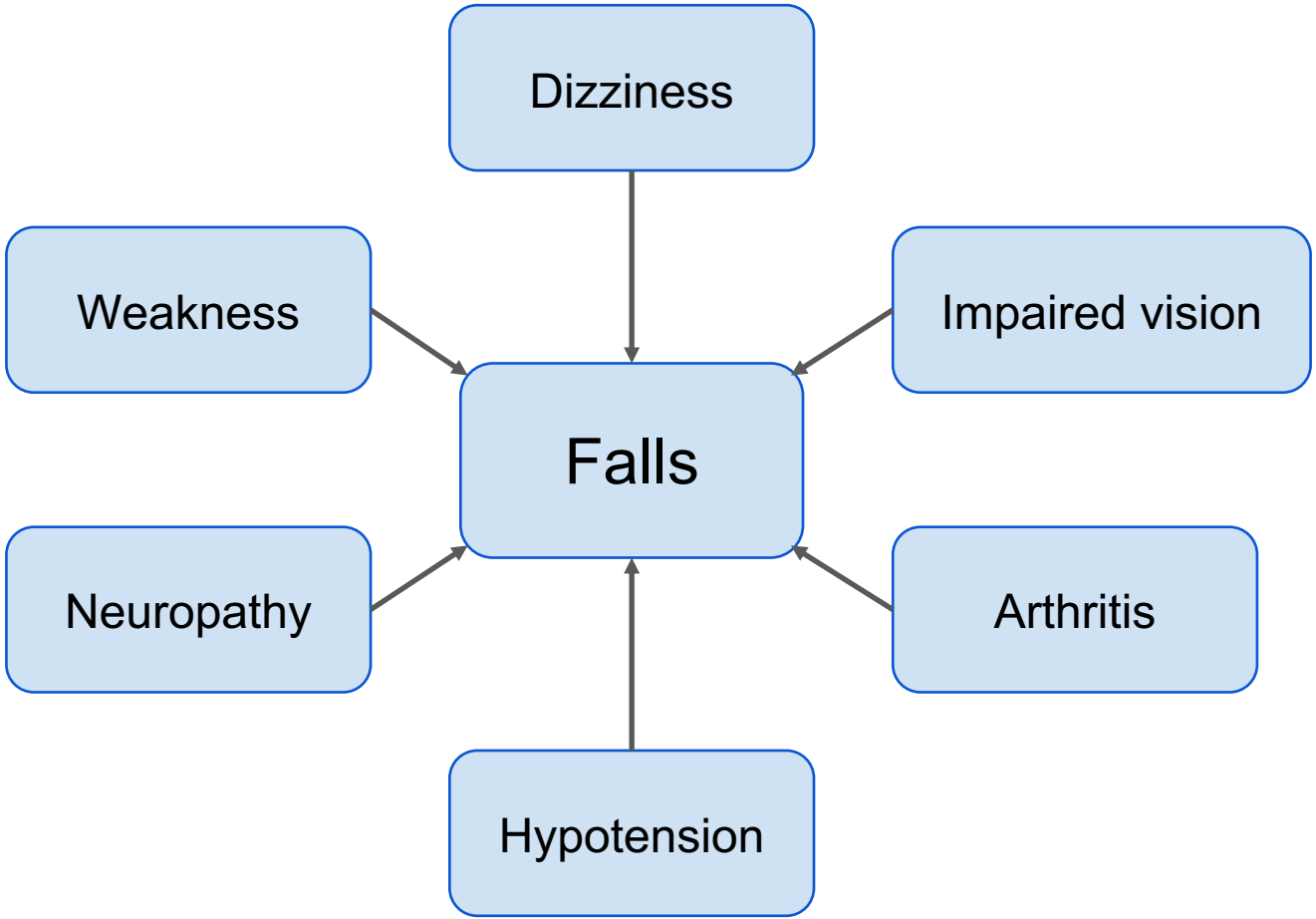
- Delirium
- Falls
- Incontinence
- Dizziness
- Functional decline

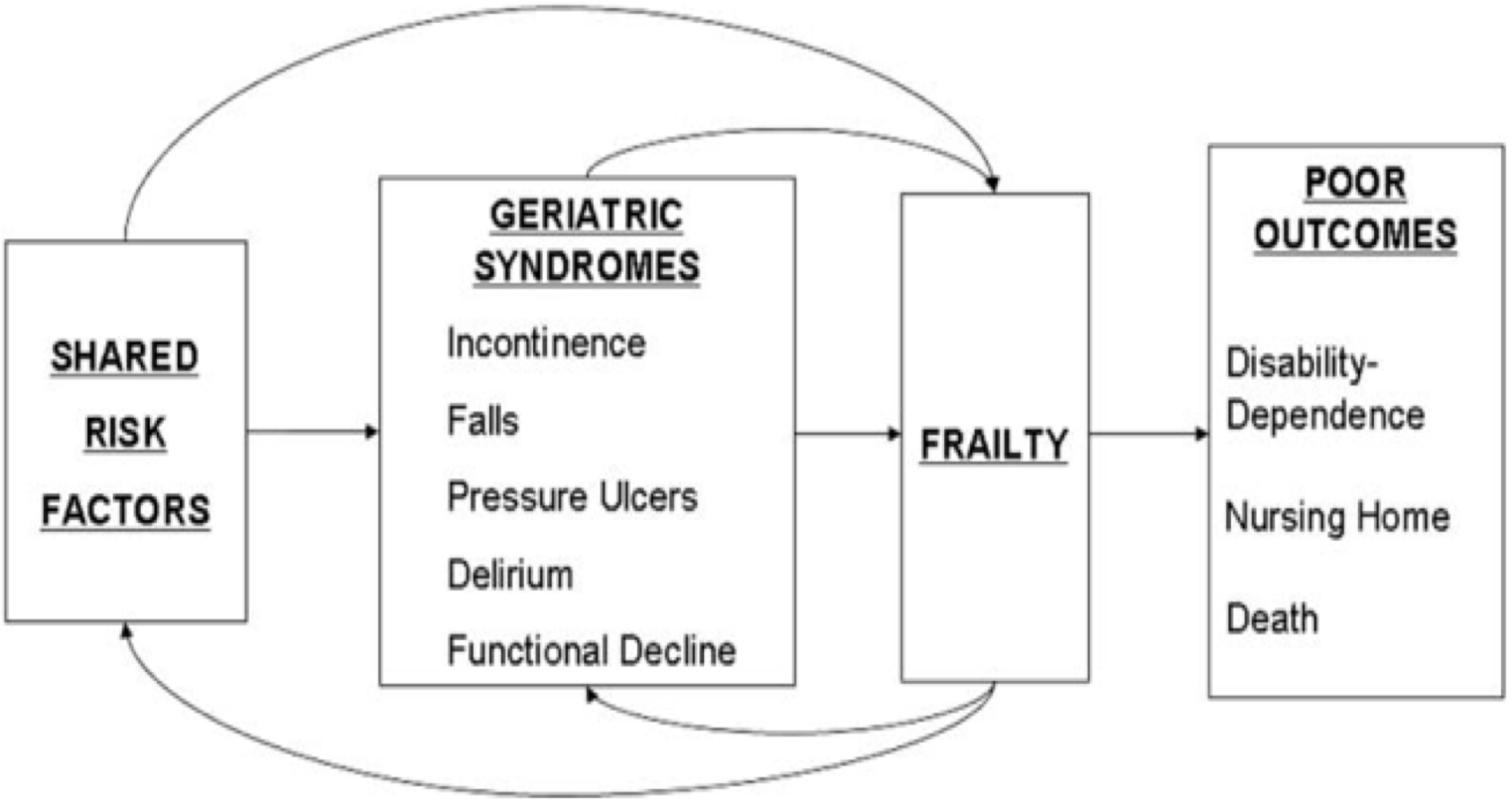
Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *Journal of the American Geriatrics Society.* 2007;55(5):780-791.

Geriatric Syndrome



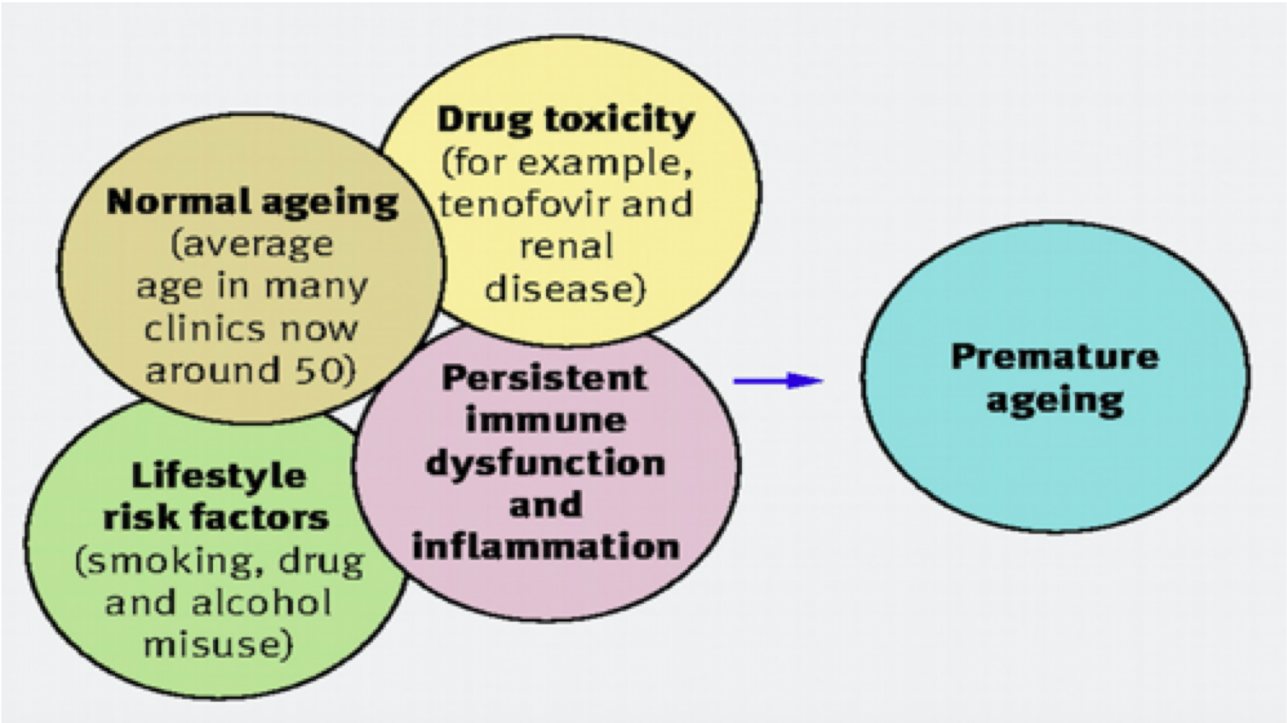
Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *Journal of the American Geriatrics Society.* 2007;55(5):780-791.


Dizziness
Weakness
Impaired vision
Falls
Neuropathy
Arthritis
Hypotension



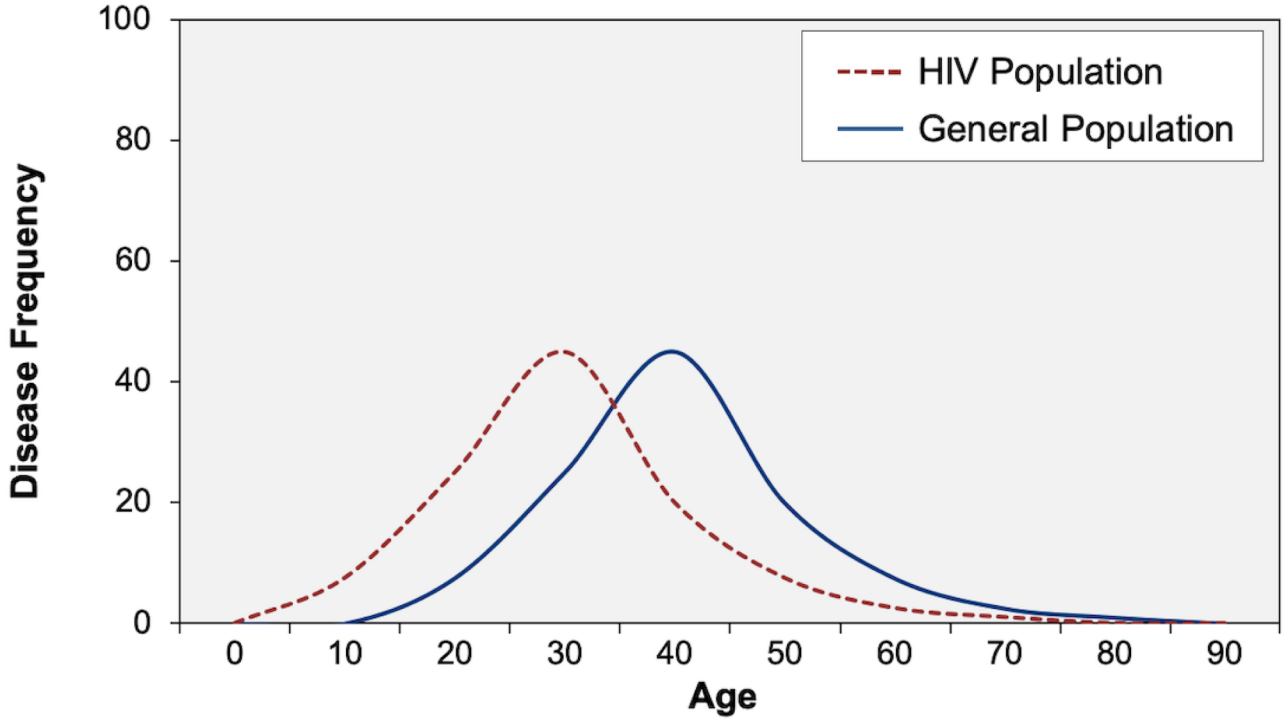
Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *Journal of the American Geriatrics Society.* 2007;55(5):780-791.

Unique Challenges of Aging with HIV



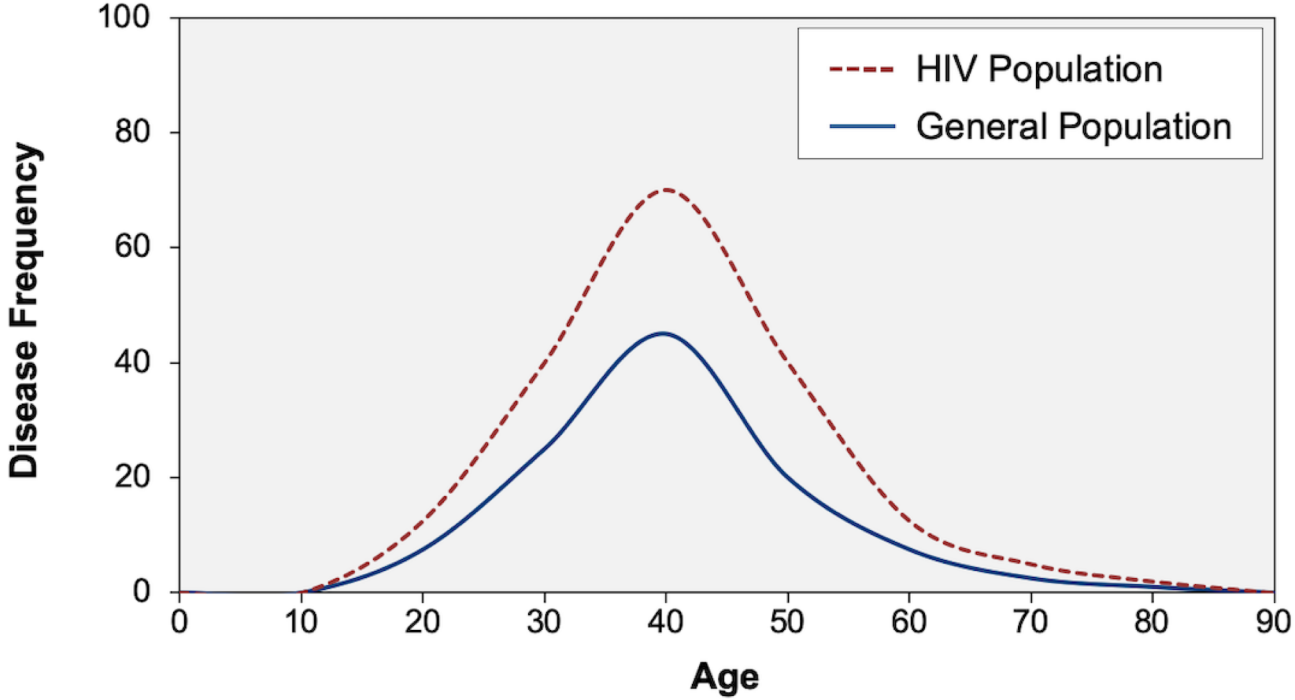
Deeks SG, Phillips AN. HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity. *Bmj.* 2009;338:a3172

Accelerated Aging



Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? *J Gerontol A Biol Sci Med Sci.* 2014;69(7):833-842.

Accentuated Aging



Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? *J Gerontol A Biol Sci Med Sci.* 2014;69(7):833-842.

Accelerated & Accentuated Aging

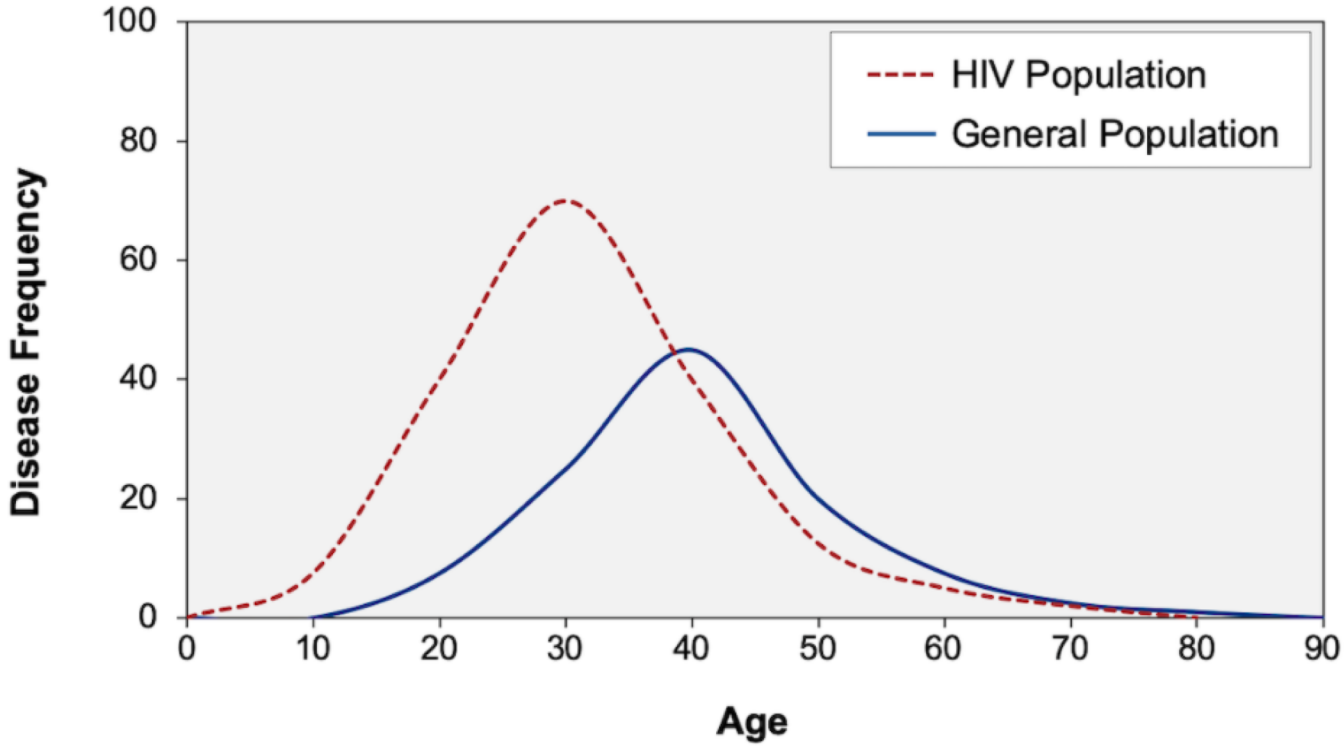
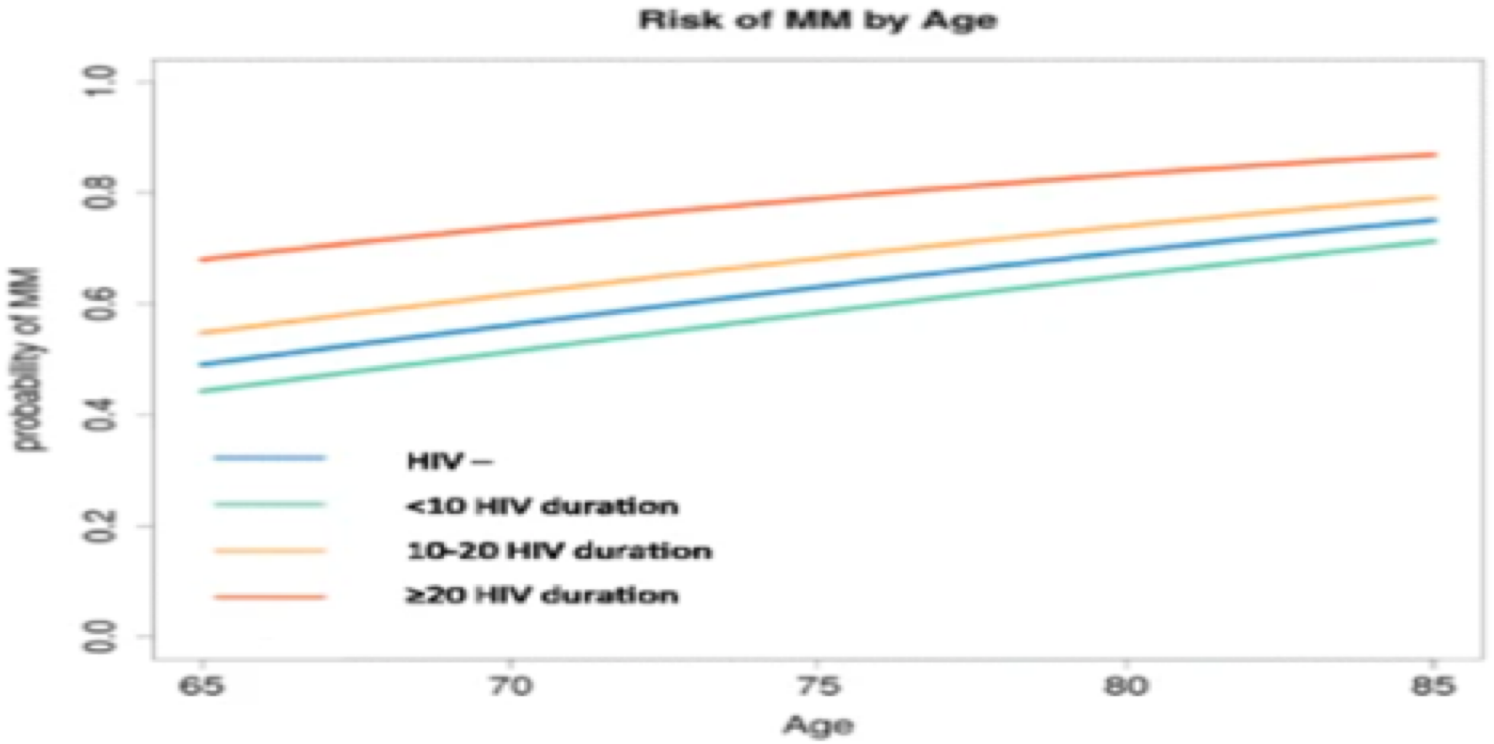


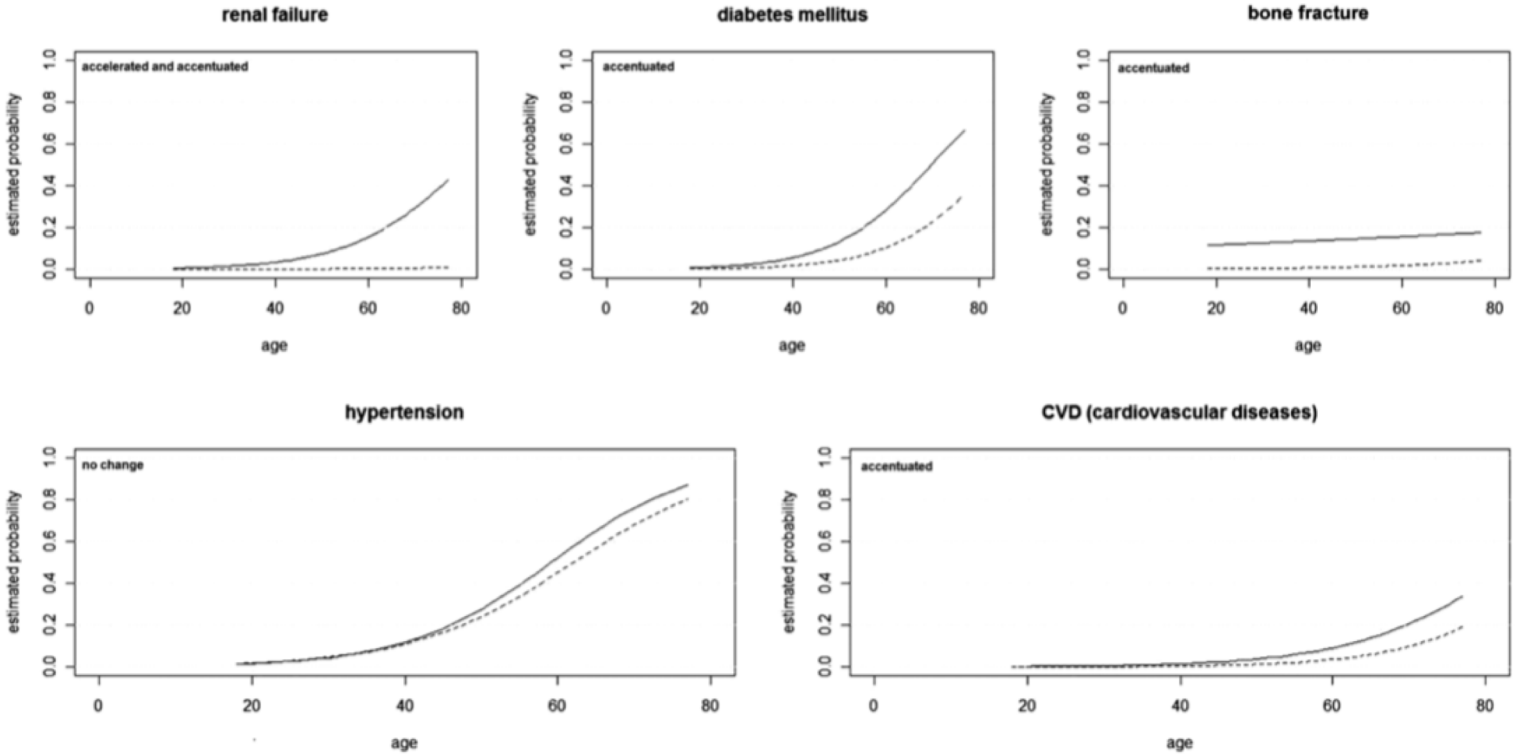
Image based on model from: Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? J Gerontol A Biol Sci Med Sci. 2014;69:833-42.

Older adults with HIV have increased risk of multimorbidity.



Guaraldi G, Malagoli A, Calcagno A, et al. The increasing burden and complexity of multi-morbidity and polypharmacy in geriatric HIV patients: a cross sectional study of people aged 65 - 74 years and more than 75 years. *BMC Geriatr.* 2018;18(1):99.

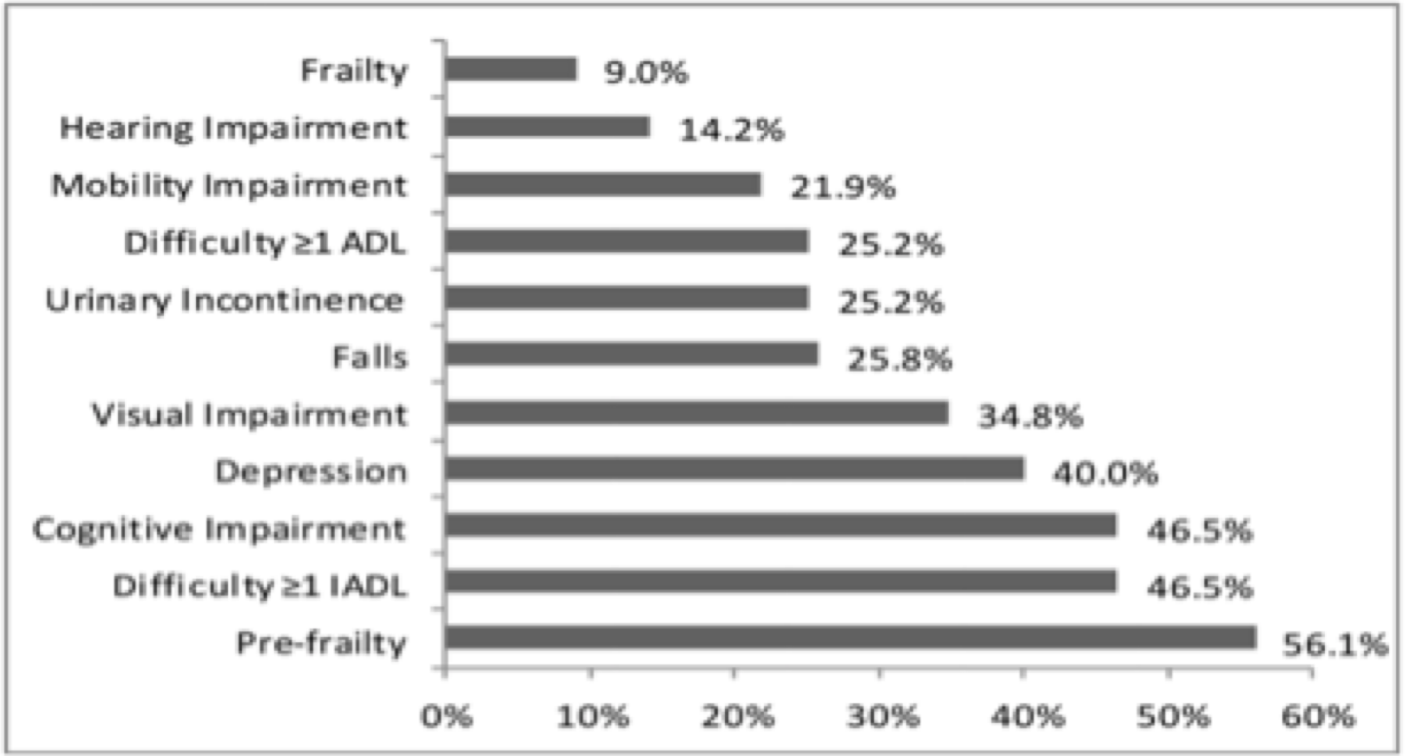
Older adults with HIV develop comorbidities at younger ages.



Pathai S, Bajillan H, Landay AL, High KP. Is HIV a model of accelerated or accentuated aging? *J Gerontol A Biol Sci Med Sci.* 2014;69(7):833-842.

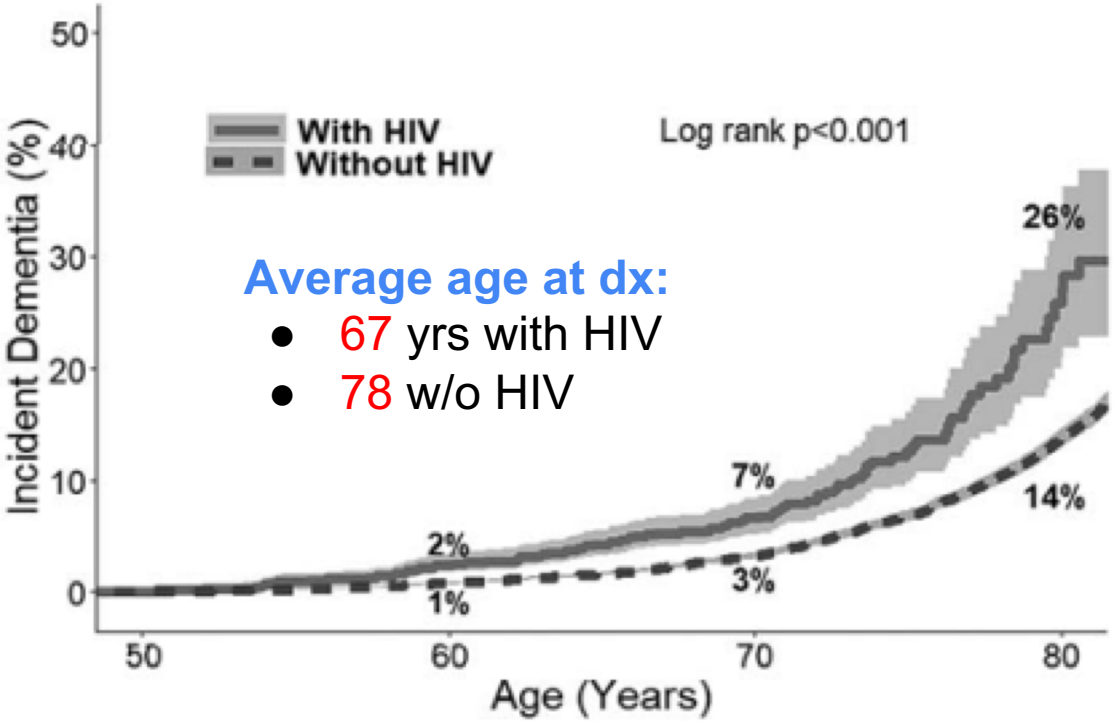
Guaraldi G, Orlando G, Zona S, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clin Infect Dis.* 2011;53(11):1120-1126.

Older adults with HIV are experiencing geriatric syndromes.



Greene M, Covinsky KE, Valcour V, et al. Geriatric Syndromes in Older HIV-Infected Adults. *J Acquir Immune Defic Syndr.* 2015;69(2):161-167.

Older adults with HIV develop dementia at younger ages.



Average age at dx:

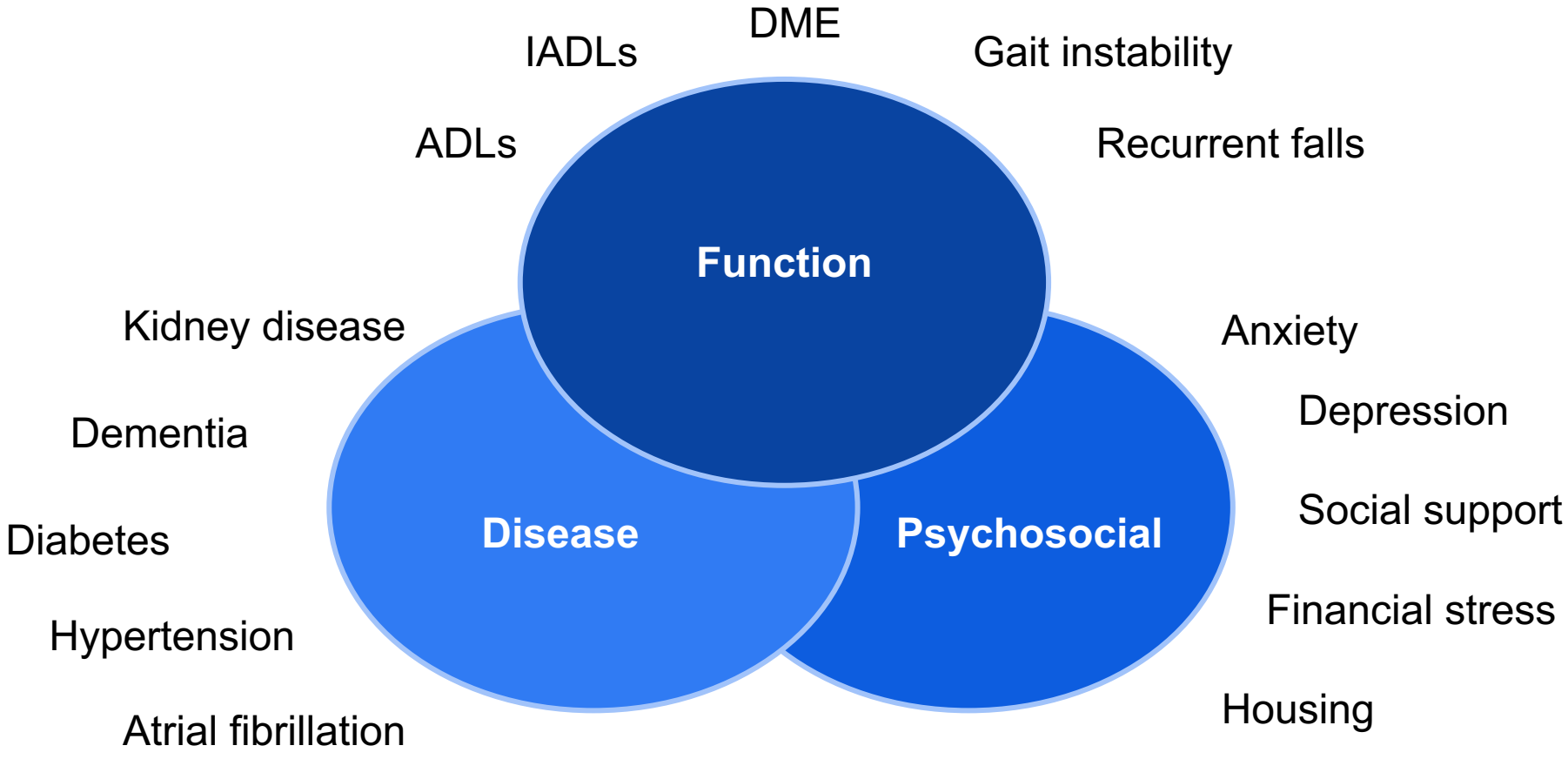
- 67 yrs with HIV
- 78 w/o HIV

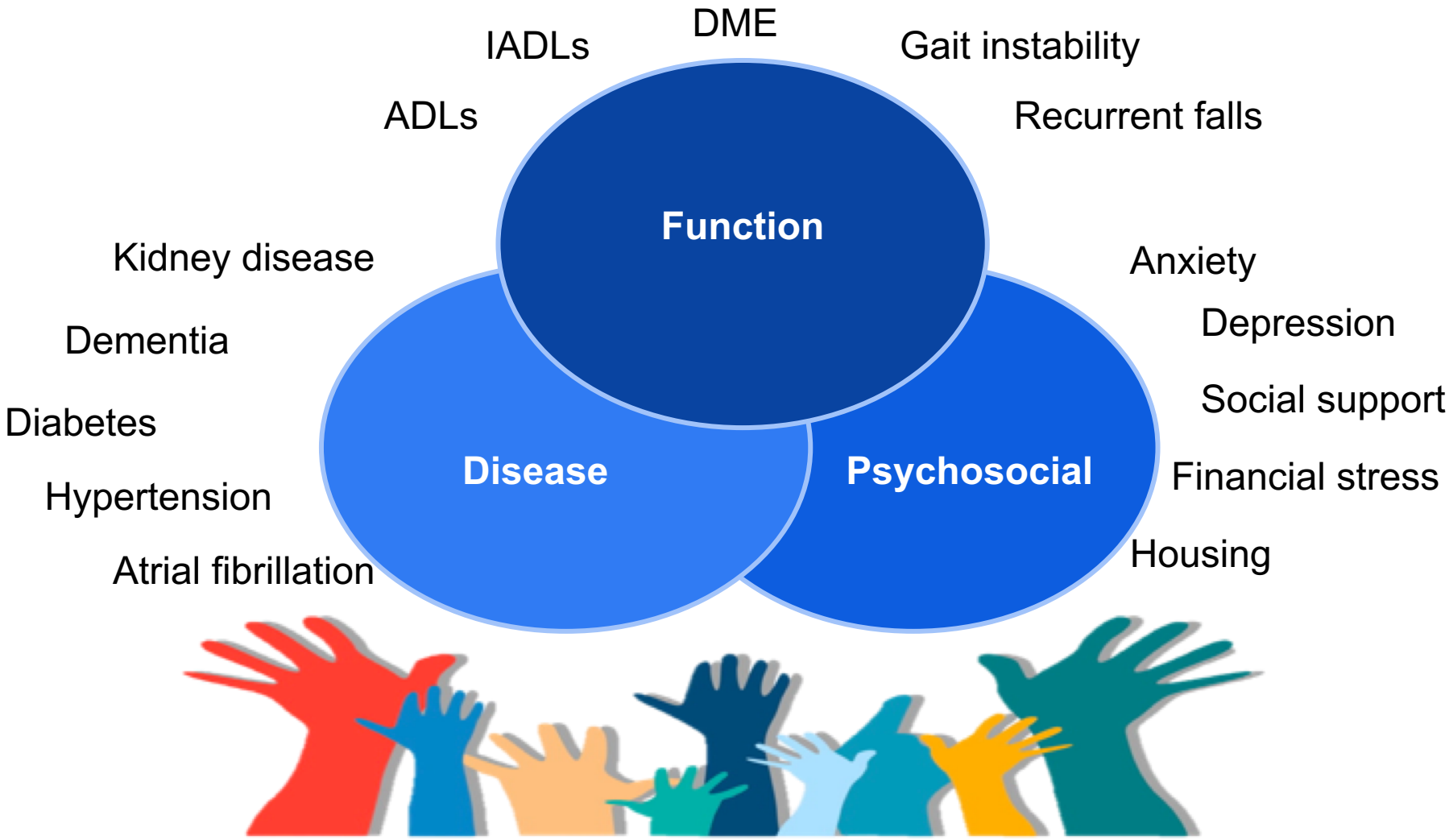
Lam JO, Hou CE, Hojilla JC, et al. Comparison of dementia risk after age 50 between individuals with and without HIV infection. *AIDS*. 2021;35(5):821-828

Geriatric Medicine

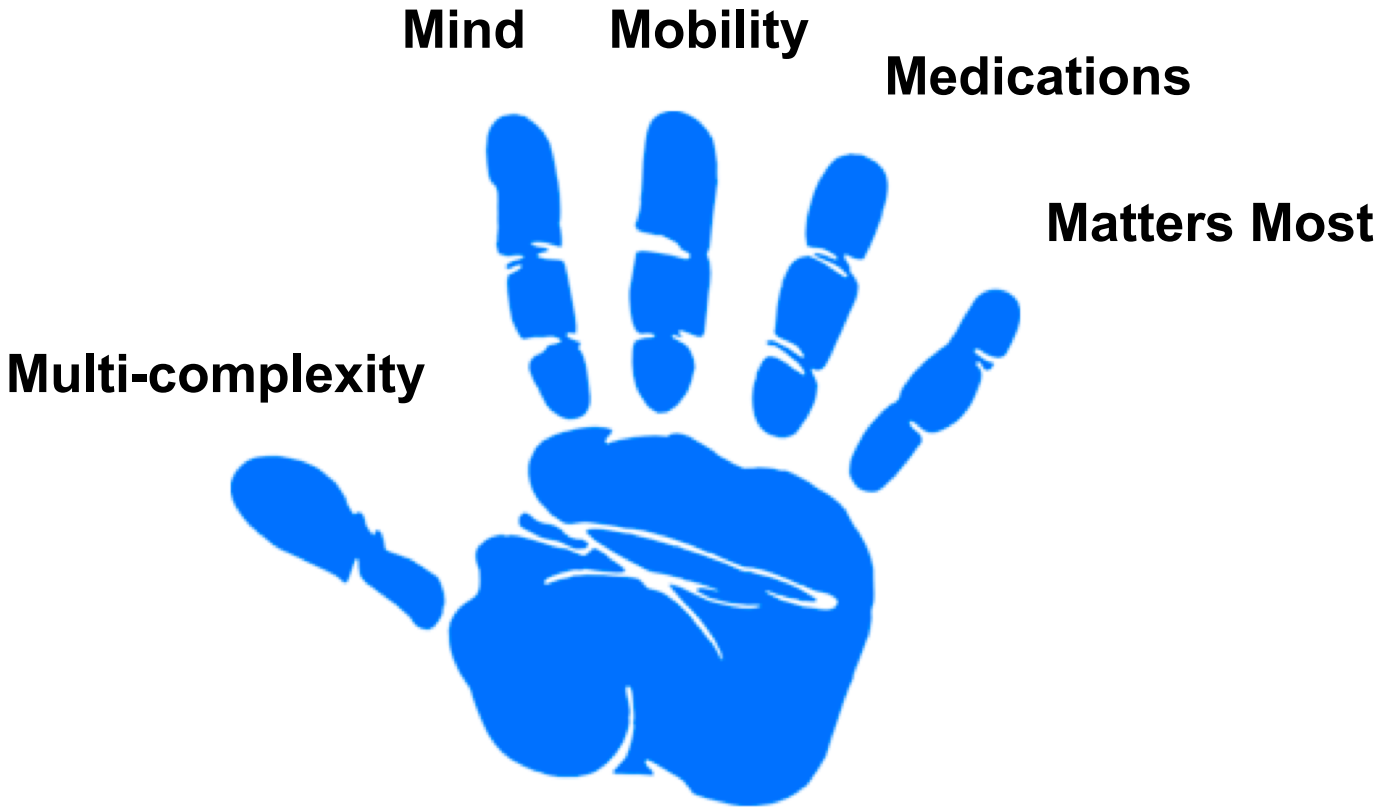
https://creativemarket.com/ssstocker/669281-Caring-for-elderly-patients?u=radcat

Geriatric Approach to Care



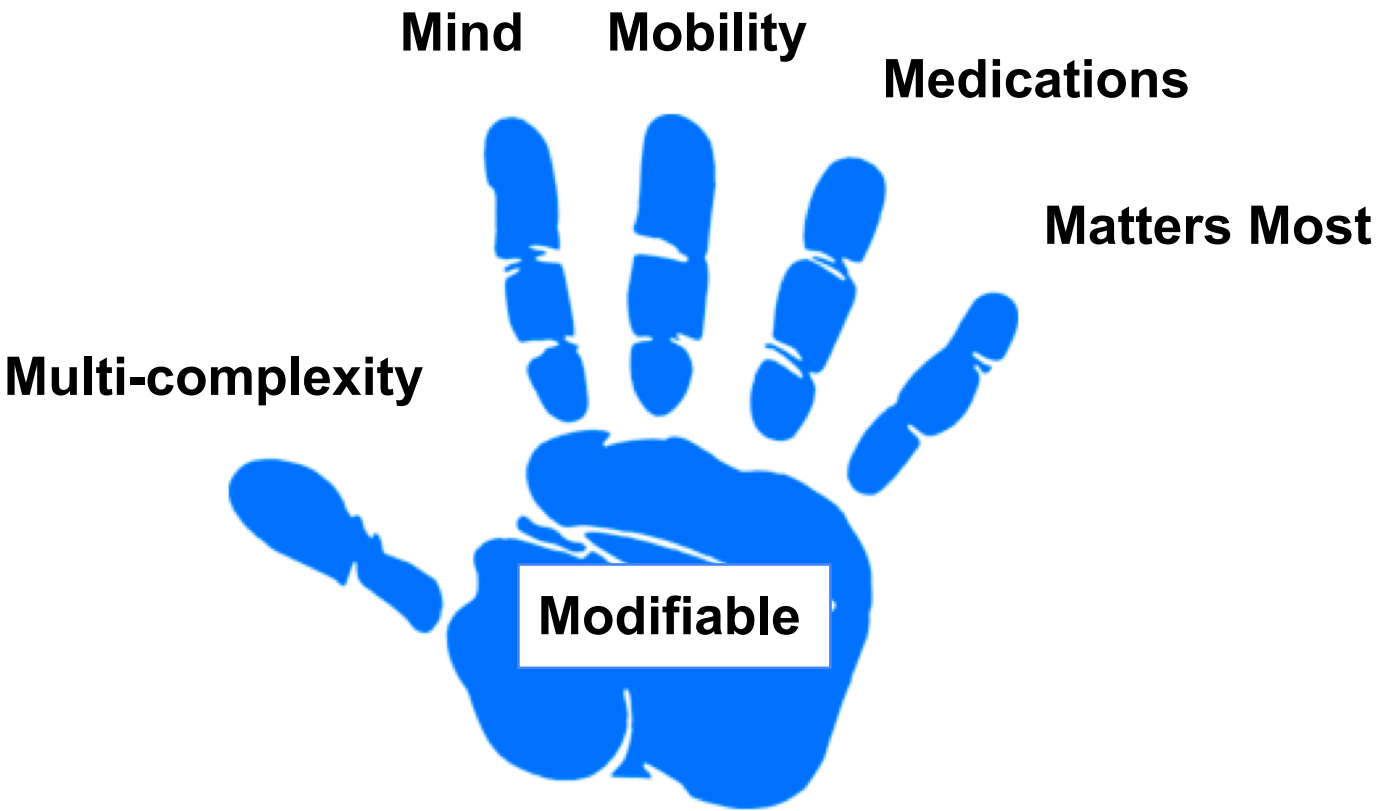

DME
IADLs
Gait instability
ADLs
Recurrent falls
Function
Kidney disease
Anxiety
Dementia
Depression
Diabetes
Social support
Disease
Psychosocial
Hypertension
Financial stress
Atrial fibrillation
Housing

Geriatric 5 M’s



https://britishgeriatricssociety.wordpress.com/2017/10/13/the-geriatric-5ms-the-5-simple-words-every-geriatrician-needs-to-know-the-new-mantra/

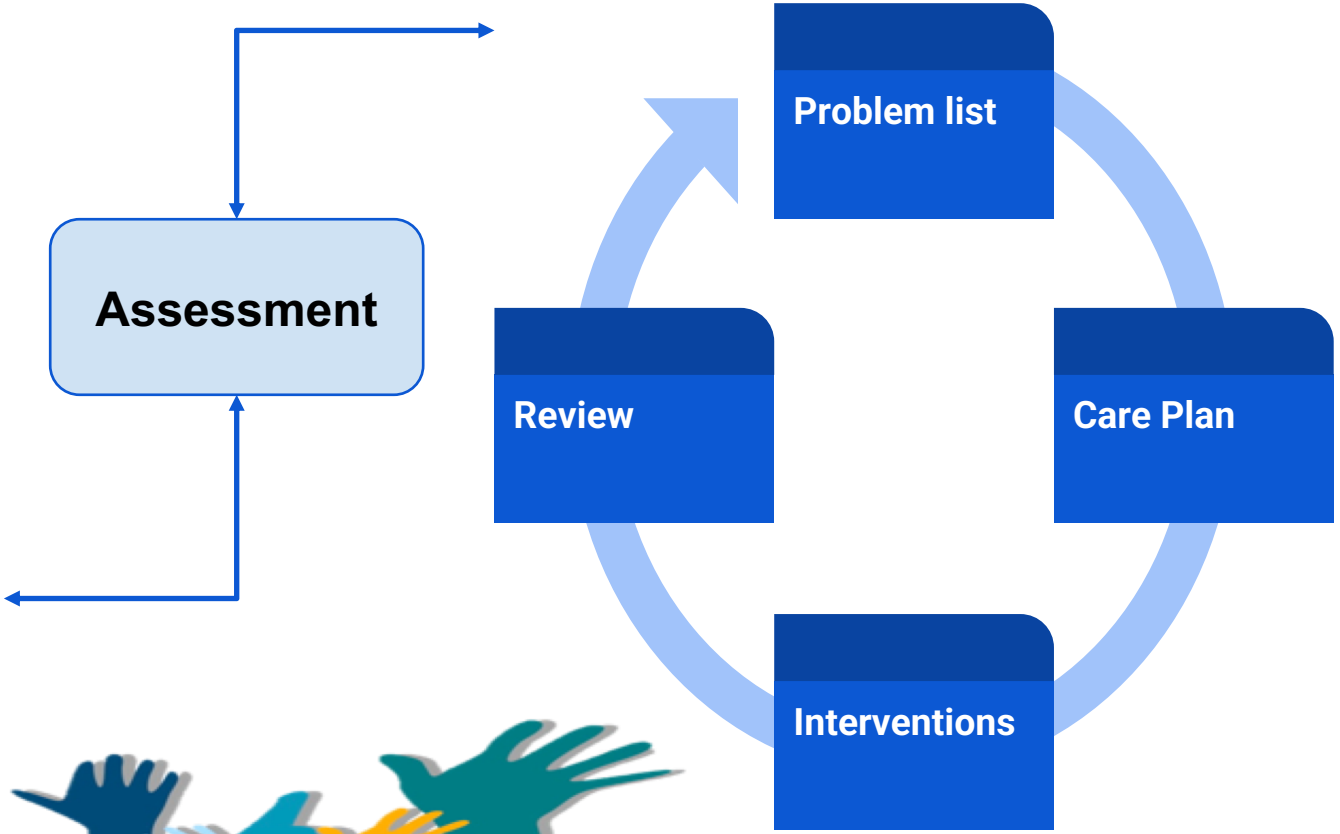
Geriatric-HIV Medicine 6 M's



Erlandson KM, Karris MY. HIV and Aging: Reconsidering the Approach to Management of Comorbidities. *Infect Dis Clin North Am.* 2019;33(3):769-786.

Comprehensive Geriatric Assessment

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



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

Davis AJ, Greene M, Siegler E, et al. Strengths and Challenges of Various Models of Geriatric Consultation for Older Adults Living With Human Immunodeficiency Virus. *Clinical Infectious Diseases.* 2021;74(6):1101-1106.

Comprehensive Program of Integrated Care for Older Adults with HIV

Keith Haring Foundation

https://www.haring.com/!/art-work/886

Interdisciplinary Team

- Geriatrician
- Nurse
- Pharmacist
- Social Worker

Comprehensive Program of Integrated Care for Older Adults with HIV

Keith Haring Foundation

https://www.kingandmcgaw.com/prints/keith-haring/

Services

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

Comprehensive Program of Integrated Care for Older Adults with HIV

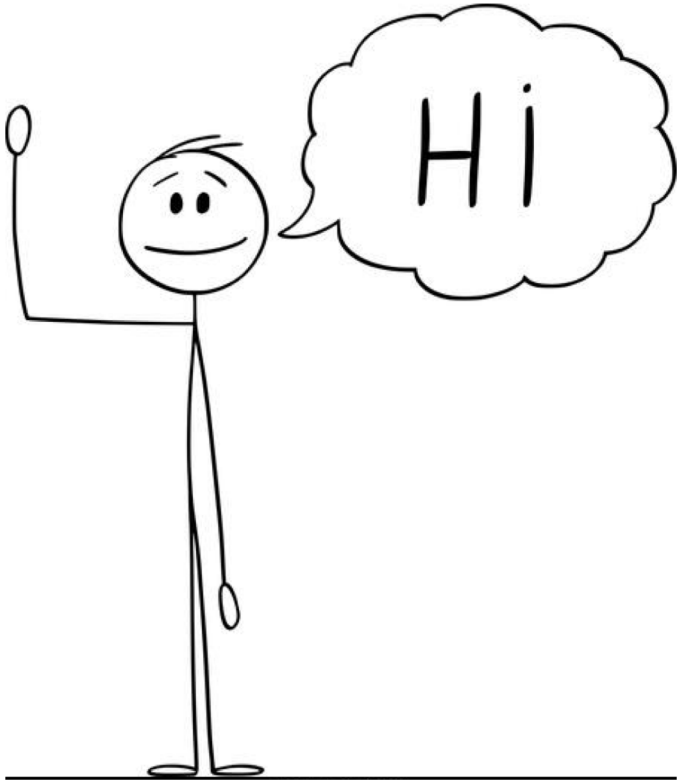
Keith Haring Foundation

https://www.artsy.net/artist/keith-haring

Referrals

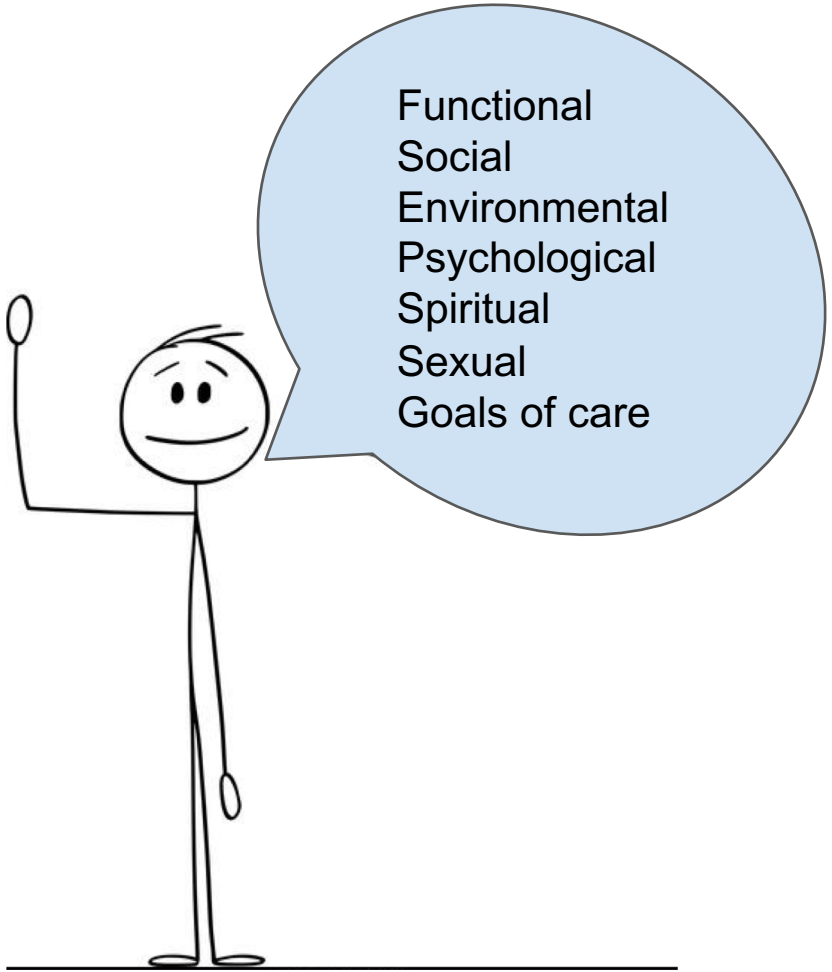
- Average age 67
- 58% Male
- 51% Cognitive evaluation
- 29% Mobility
- 15% Polypharmacy
- 4% Multimorbidity
- 1% Advance care planning

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



CLINICAL GUIDELINES PROGRAM

NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE | HIV · HCV · SUBSTANCE USE · LGBT HEALTH

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

https://www.hivguidelines.org/hiv-care/aging-guidance/

Multicomplexity

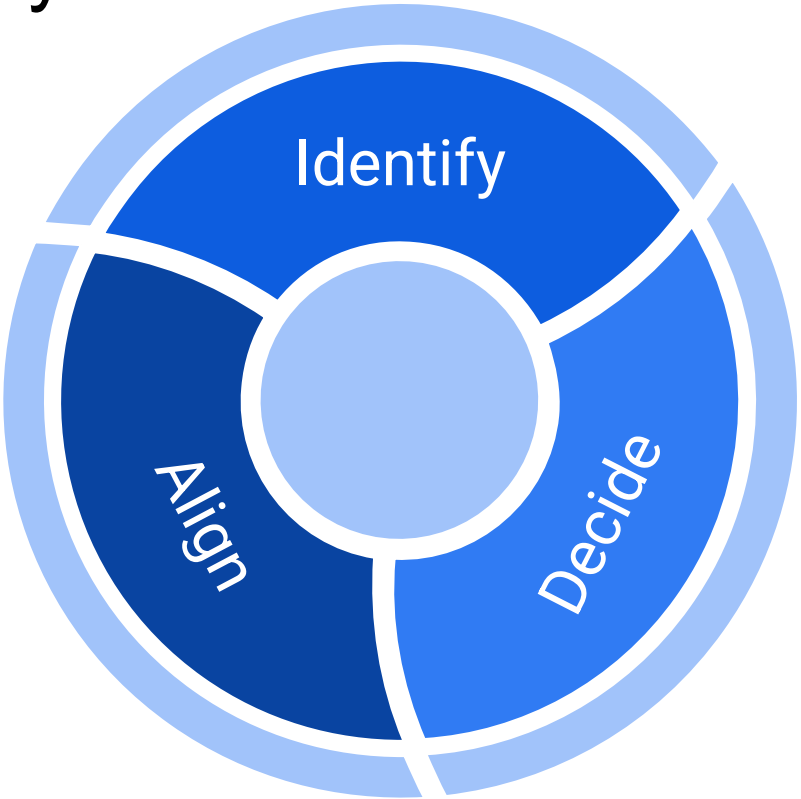
Guiding Principles for the Care of Older Adults with Multimorbidity: An Approach for Clinicians

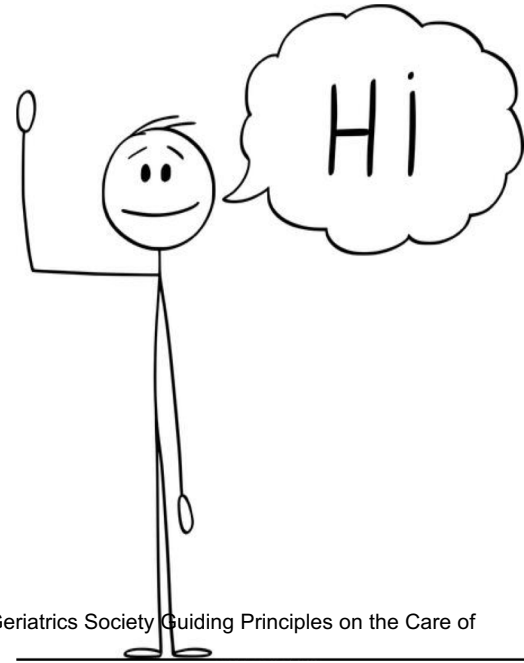
American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity*

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

Boyd C, Smith CD, Masoudi FA, et al. Decision Making for Older Adults With Multiple Chronic Conditions: Executive Summary for the American Geriatrics Society Guiding Principles on the Care of Older Adults With Multimorbidity. *Journal of the American Geriatrics Society.* 2019;67(4):665-673.

Multicomplexity

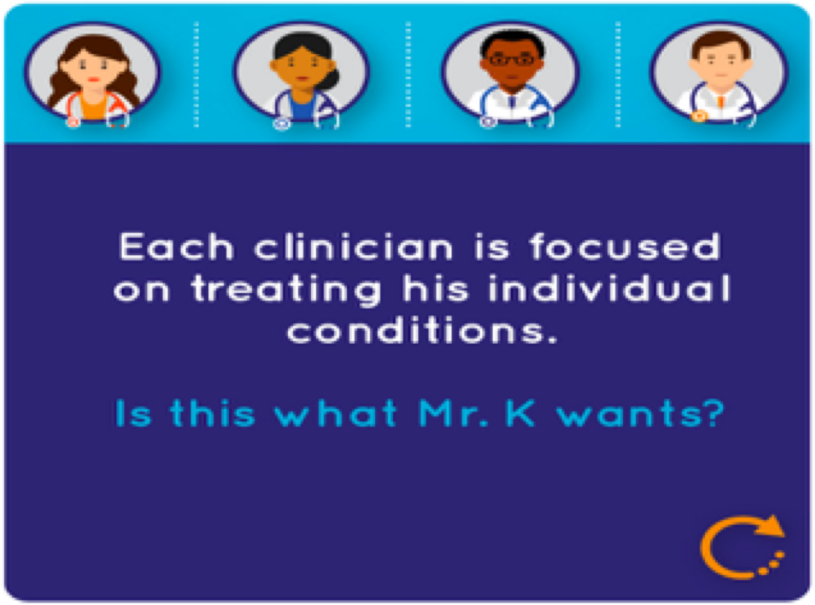




Boyd C, Smith CD, Masoudi FA, et al. Decision Making for Older Adults With Multiple Chronic Conditions: Executive Summary for the American Geriatrics Society Guiding Principles on the Care of Older Adults With Multimorbidity. *Journal of the American Geriatrics Society.* 2019;67(4):665-673.

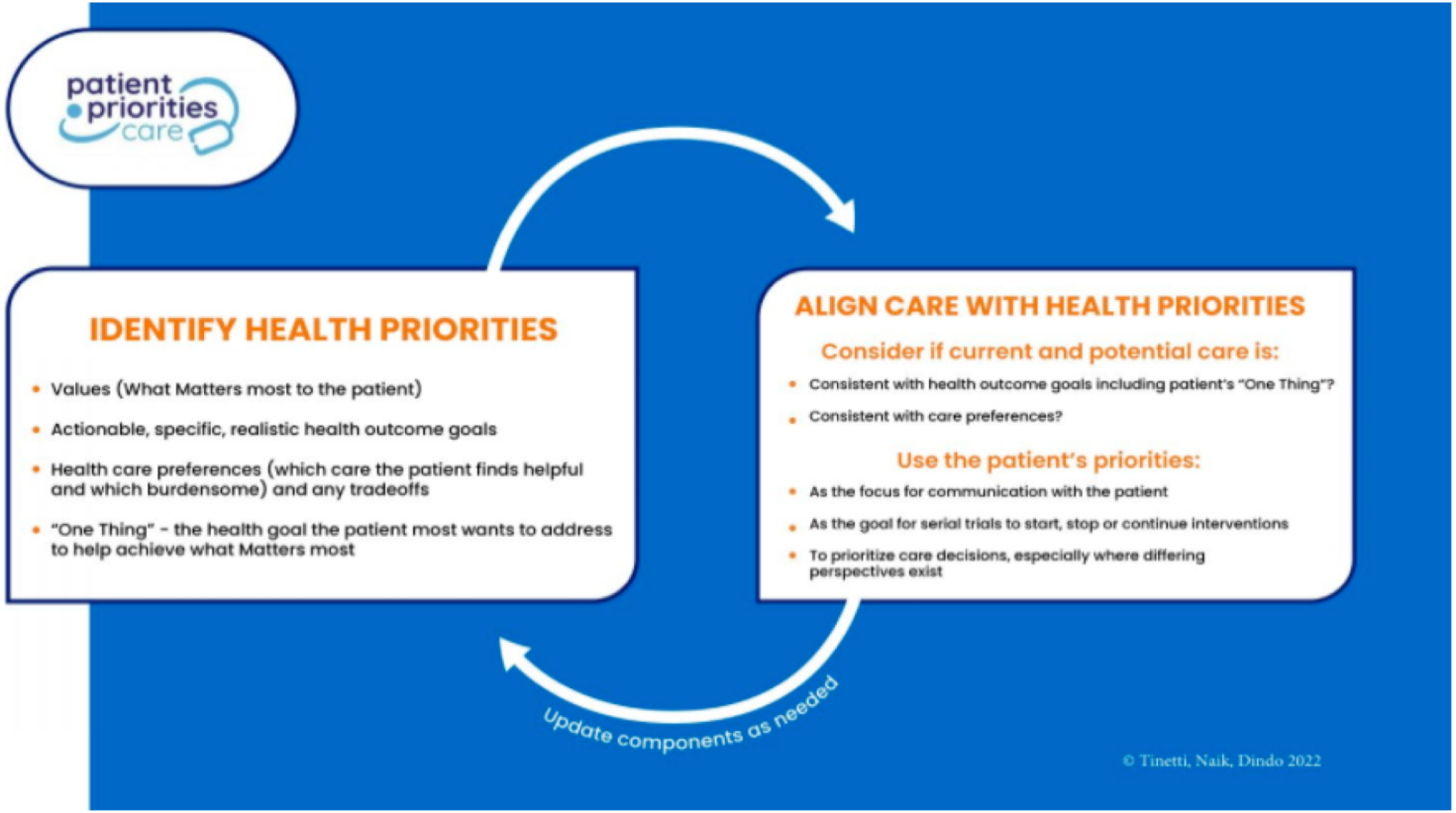
Matters Most

patient priorities care | Choosing what matters. Doing what works.



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

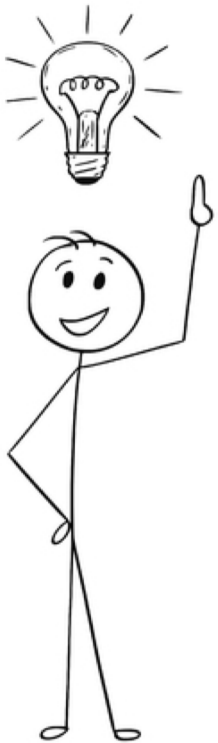
Matters Most



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

MOLST

MEDICAL ORDERS FOR
LIFE-SUSTAINING TREATMENT

A POLST Paradigm Program

Health Care Proxy

Appointing Your Health Care Agent in New York State

ePrognosis | Estimating Prognosis for Elders

Mind

https://info.eugeria.ca/en/what-are-iadls-and-how-are-they-different-from-adls

Mind

Mini-Cog©

Instructions for Administration & Scoring

ID: _____ Date: _____

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.[1-3] For repeated administrations, use of an alternative word list is recommended.

Version 1	Version 2	Version 3	Version 4	Version 5	Version 6
Banana	Leader	Village	River	Captain	Daughter
Sunrise	Season	Kitchen	Nation	Garden	Heaven
Chair	Table	Baby	Finger	Picture	Mountain

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."

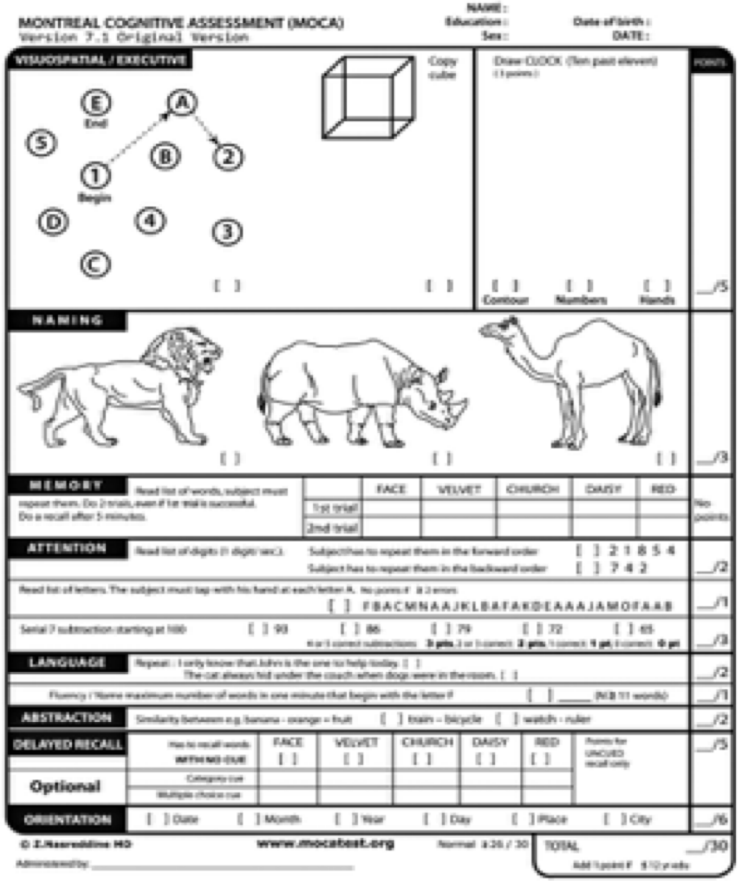
Use preprinted circle (see next page) for this exercise. Repeat instructions as needed as this is not a memory test. Move to Step 3 if the clock is not complete within three minutes.

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: _____ _____ _____

https://mini-cog.com/mini-cog-instrument/standardized-mini-cog-instrument/



MONTREAL COGNITIVE ASSESSMENT (MOCA)

Version 7.1 Original Version

NAME :
Education :
Sex :
Date of birth :
DATE :

VISUOSPATIAL / EXECUTIVE

Copy cube

Draw CLOCK (Ten past eleven)

Contour | Numbers | Hands

NAMING

MEMORY

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

FACE | VELVET | CHURCH | DAISY | RED

1st trial

2nd trial

ATTENTION

Read list of digits (1 digit/sec.)

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train - bicycle [ ] watch - ruler

DELAYED RECALL

Has to recall words (NOT FIVE NO-CUE)

FACE | VELVET | CHURCH | DAISY | RED

Optional

Category cue

Multiple choice cue

Points for UNCUED recall only

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL /30

Add 1 point if ≤ 12 yr edu

Administered by: _____

https://www.sciencedirect.com/topics/nursing-and-health-professions/montreal-cognitive-assessment

Mind

MOCA 21/30

https://stock.adobe.com/search?k=stick+figure+thinking

Mind

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

(For office coding: Total Score T____ = ____ + ____ + ____)

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use "✔" to indicate your answer)*	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING 0 + _____ + _____ + _____

=Total Score: _____

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

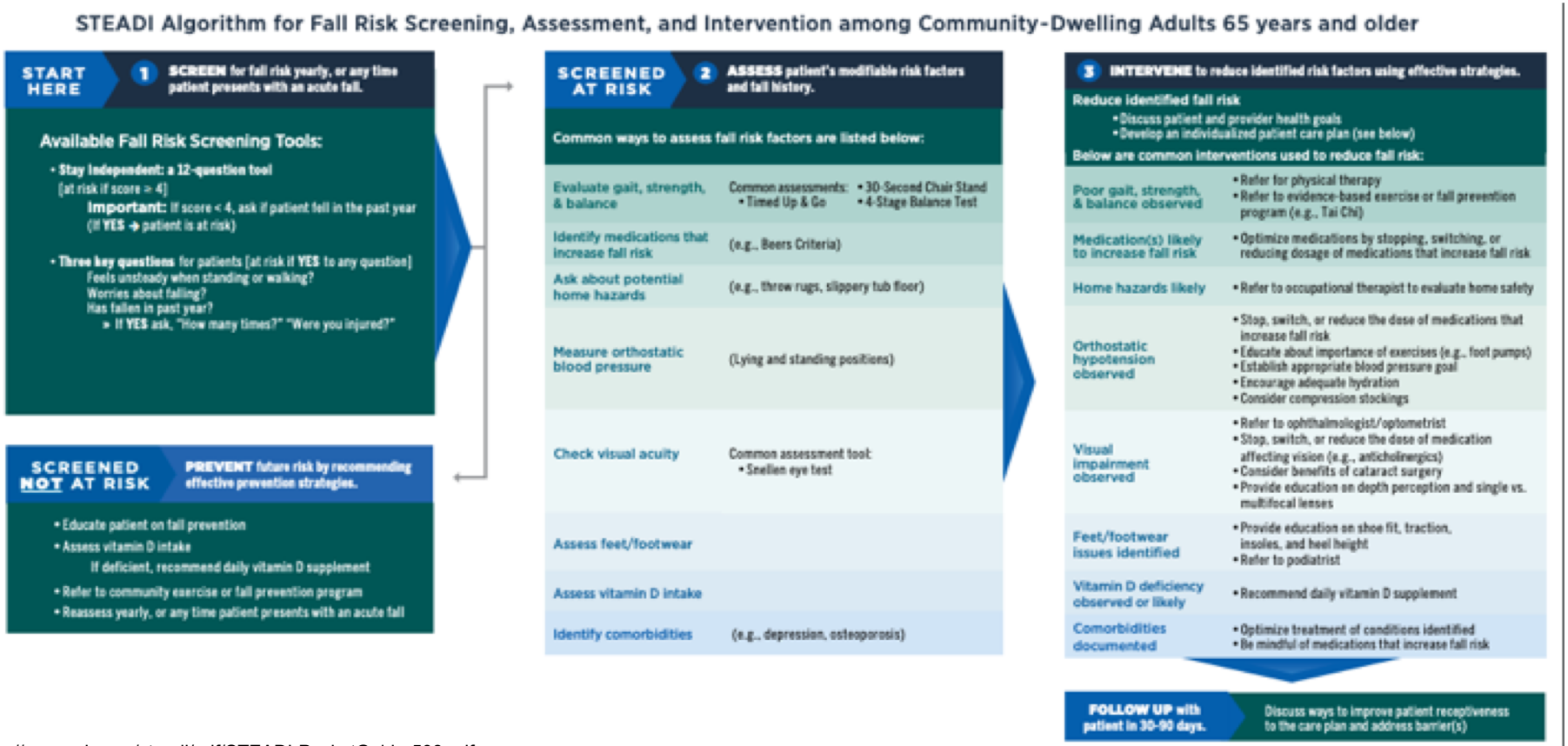
GAD7 7

Mobility

Mobility

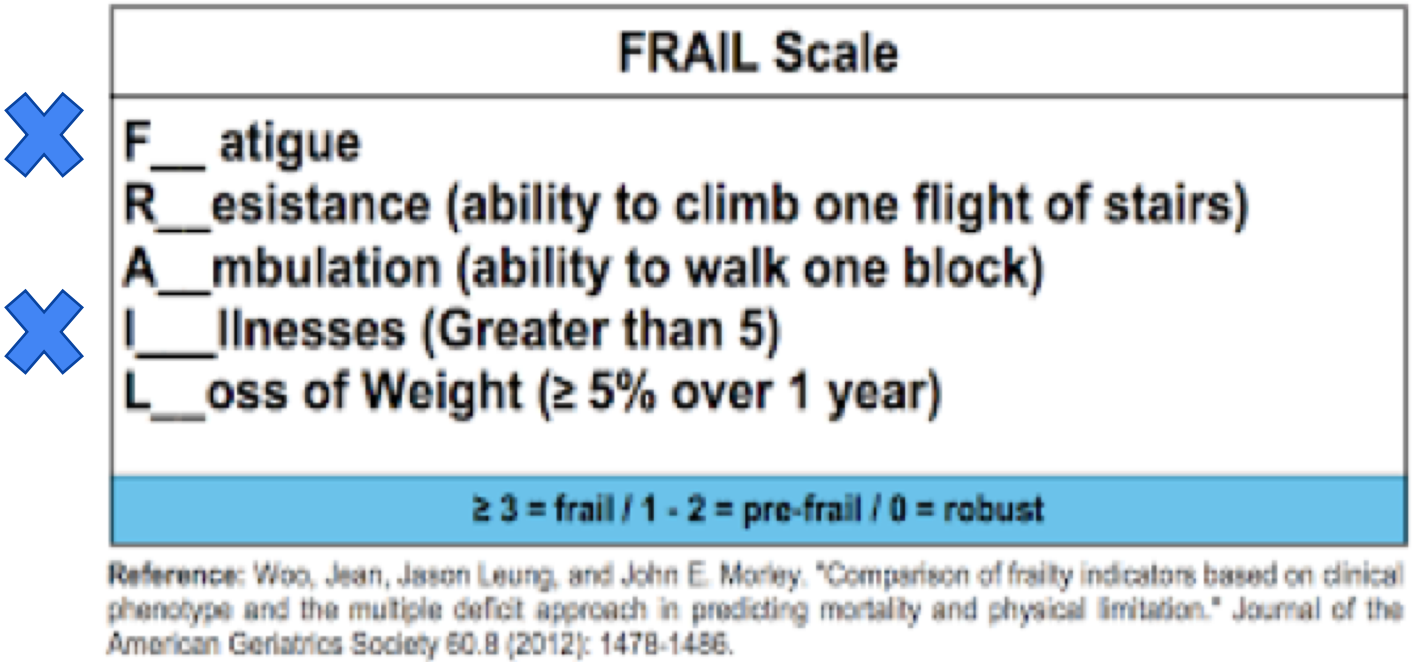
https://www.elderneedslaw.com/blog/activities-of-daily-living-and-medicaid-eligibility

Mobility



https://www.cdc.gov/steadi/pdf/STEADI-PocketGuide-508.pdf

Frailty



Reference: Woo, Jean, Jason Leung, and John E. Morley. "Comparison of frailty indicators based on clinical phenotype and the multiple deficit approach in predicting mortality and physical limitation." Journal of the American Geriatrics Society 60.8 (2012): 1478-1486.

https://sobramfa.com.br/wp-content/uploads/2019/08/WBFM16-32-Frailty.pdf

Modifiable

https://www.vectorstock.com/royalty-free-vector/healthy-lifestyle-cartoon-composition-vector-31271615

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

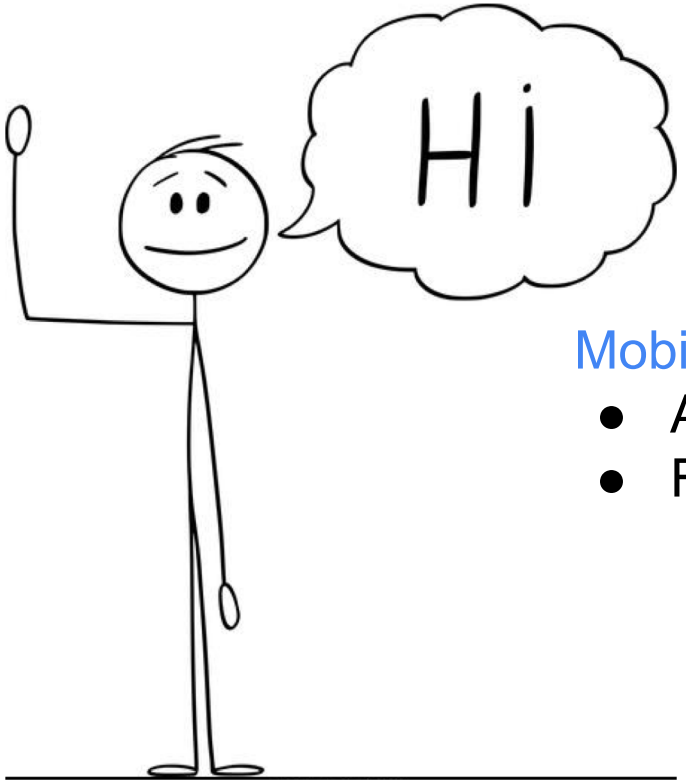
https://www.dreamstime.com/illustration/cartoon-pharmacist.html

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:

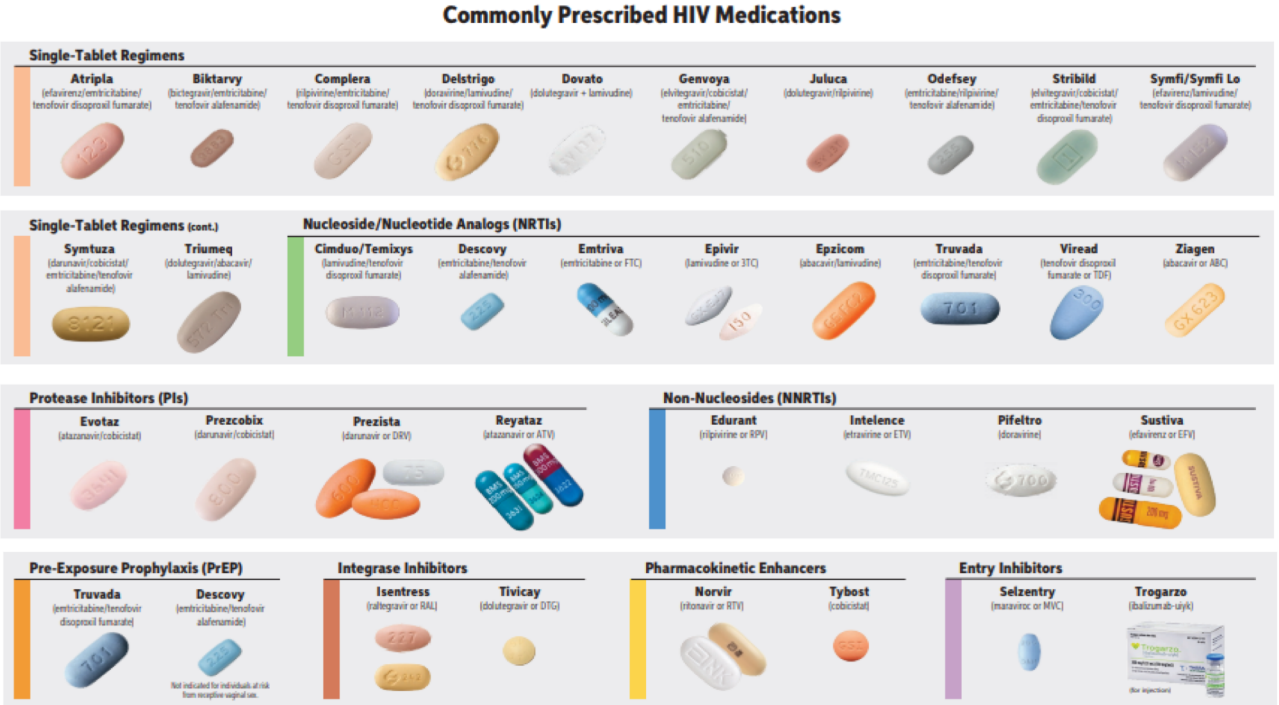
- Referral to SW
- Referral to psychotherapy
- Referral to ENT

Interventions:

- Motivational interviewing
- Care coordination

Alexander Lee - PharmD, JD, AAHIVP

HIV Pharmacotherapy



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

Abacavir	Hypersensitivity (rash/fever/fatigue/dyspnea/GI/cough/pharyngitis)
Didanosine	Peripheral neuropathy, pancreatitis (with heavy alcohol use)
Emtricitabine	Hyperpigmentation of palms/soles
Lamivudine	Pancreatitis
Stavudine	Peripheral neuropathy, pancreatitis
Tenofovir disoproxil fumarate	Acute renal failure, decreased bone mineral density, Fanconi syndrome
Tenofovir alafenamide	Increased serum creatinine and urinary protein, mineral density loss
Zalcitabine	Peripheral neuropathy, ulcerations, rash
Zidovudine	Bone marrow suppression

Side Effects - NNRTI (Non-nucleoside reverse transcriptase inhibitors)

Class-specific: Rash, hepatotoxicity, CNS symptoms

Delavirdine	Elevated transaminases and total bilirubin
Doravirine	Headache, nausea, diarrhea
Efavirenz	Neuropsychiatric (vivid dreams, altered mental state), depression, suicidal ideation
Etravirine	Elevated cholesterol/triglycerides/glucose, hepatotoxicity
Nevirapine	Hypersensitivity, hepatotoxicity
Rilpivirine	Depression, suicidal ideation, QTc prolongation, virologic failure

Side Effects - PI (Protease inhibitors)

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

Amprenavir	Rash, elevated triglycerides, diarrhea
Atazanavir	Jaundice, PR prolongation, decreased bone mineral density, cholelithiasis/nephrolithiasis
Darunavir	Elevated amylase/transaminases, hepatotoxicity
Fosamprenavir	Elevated transaminases
Indinavir	Nephrolithiasis, hyperbilirubinemia
Lopinavir	Diarrhea, nausea
Nelfinavir	diarrhea
Saquinavir	PR/QT prolongation
Tipranavir	Intracranial hemorrhage, hepatic toxicity

Side Effects - INSTI (Integrase strand transferase inhibitor)

Class-specific: Rash

Bictegravir	Elevated total bilirubin, serum creatine, renal insufficiency
Dolutegravir	Insomnia, mood disturbance, renal insufficiency
Elvitegravir	Elevated hepatic transaminase
Raltegravir	Fatigue, muscle aches, elevated pancreatic amylase and hepatic transaminase

Side Effects - Booster, CCR5I, FI, PAI

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

Side Effects - HIV Medications

	NRTI	NNRTI	PI	INSTI
Cognitive/Psychiatric		X		X
Kidney	X		X	
Liver		X	X	X
Pancreas	X			X
Bone	X		X	
Cardiovascular	X	X	X	X
Metabolic	X		X	

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

Statin	Protease Inhibitors (PI)	Cobicistat
Atorvastatin	OK except with tipranavir-ritonavir (Aptivus®) “Start low, go slow”	OK
Fluvastatin	No data	No data
Lovastatin	Contraindicated	Contraindicated
Pitavastatin	OK	No data
Pravastatin	OK. Use lowest dose with atazanavir or darunavir containing regimen.	No data
Rosuvastatin	OK “start low, go slow”	OK
Simvastatin	Contraindicated	Contraindicated

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:

	1A2	2C9	2C19	2D6	2E1	3A4	OATP1A	OATP2B1	P-gp
Inhibitor	Echinacea	Kava Kava Milk Thistle	Kava Kava	Golden Seal	Kava Kava	Echinacea Golden Seal	Green Tea Extract		Green Tea Extract
Inducer	Curcumin					Ginseng (Asian) St. John’s Wort		Black Cohosh	Garlic St. John’s Wort

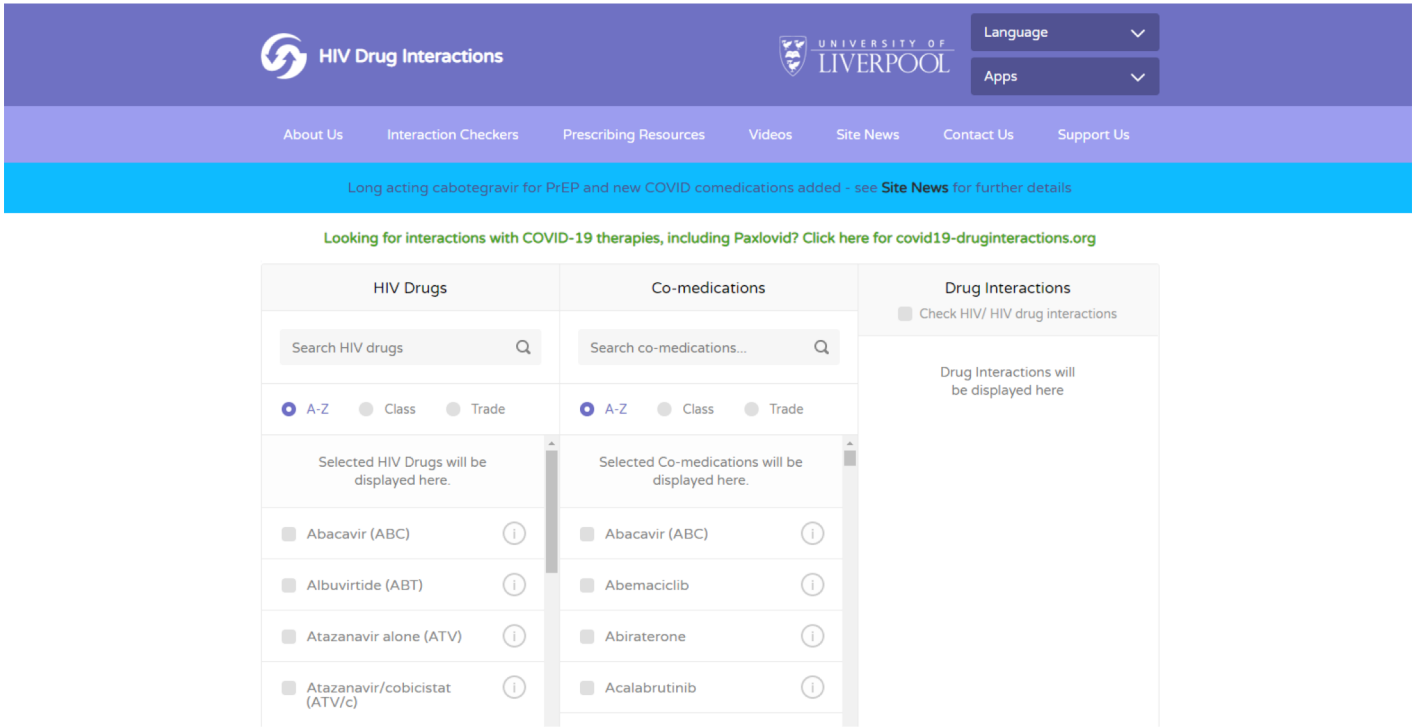
Archives of Gerontology and Geriatrics, Vol 59, Issue 2, September-October 2014, Pages 227-233
Am Fam Physician. 2017 Jul 15;96(2):101-107.

Minimizing Adverse Events From Drug Interactions

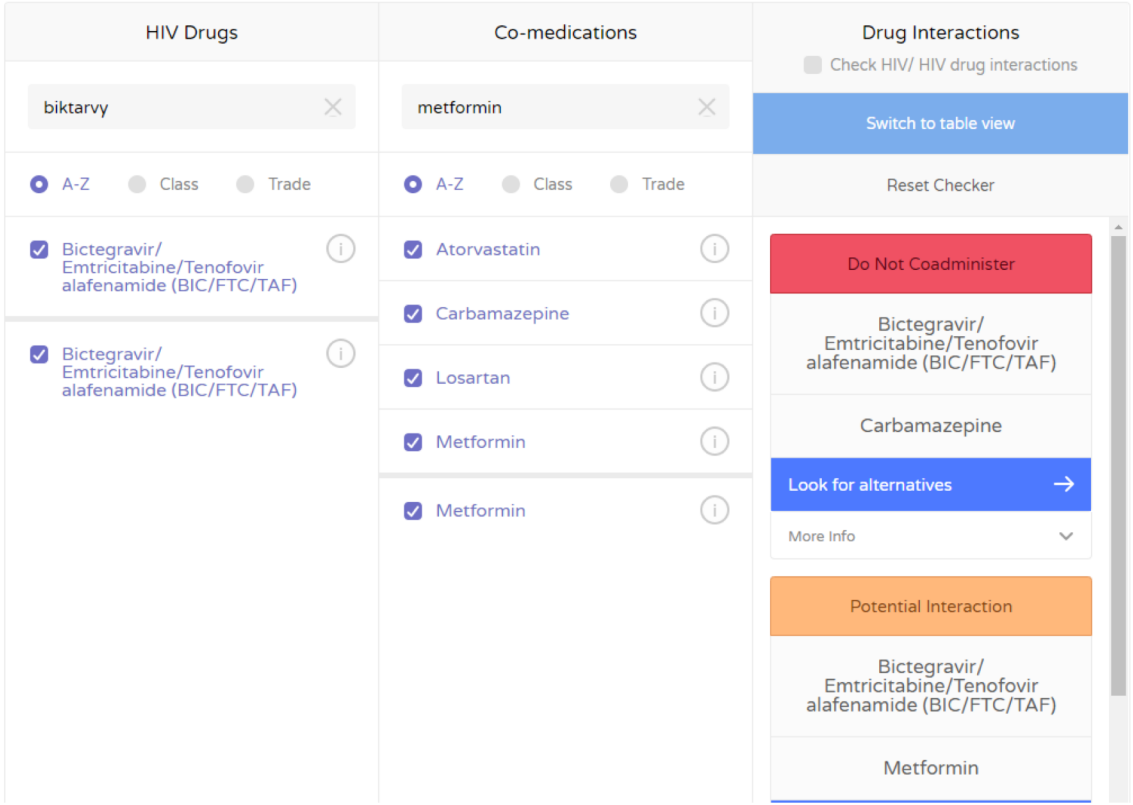
- When drug interactions exist, prescribers and pharmacists assess the clinical significance of the interactions, and may proceed with dispensing of the drug if benefits outweigh the risks.
- Provide full and accurate list of medications, including herbal supplements and vitamins.
- Use one pharmacy 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

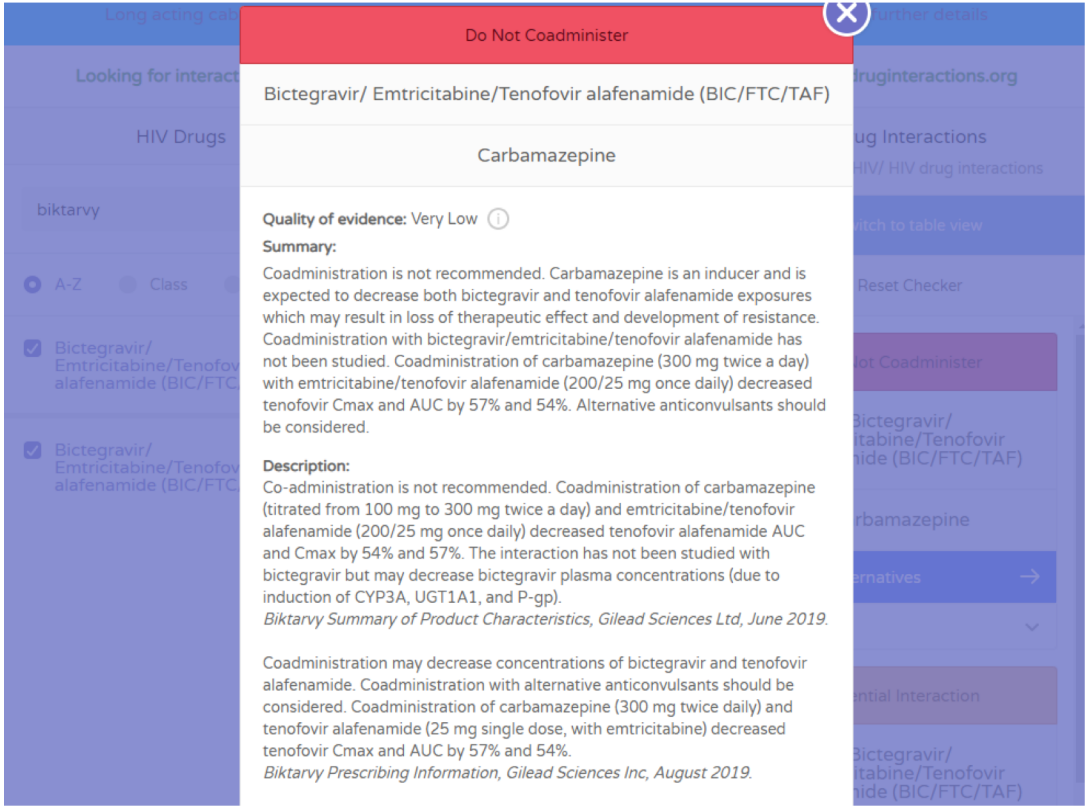
https://www.hiv-druginteractions.org/checker



Liverpool Interaction Checker



Liverpool Interaction Checker



Other comedications in the same class

Clicking on a symbol will show details of the interaction

The table below shows interactions with other drugs in the same class. The clinical suitability of a drug as an alternative may depend not only on its interaction profile, but also on patient specific information.

Anticonvulsants	Bictegravir/ Emtricitabine/Tenofovir alafenamide (BIC/FTC/TAF)
Carbamazepine	●
Clonazepam	◆
Eslicarbazepine	●
Ethosuximide	◆
Gabapentin	◆
Lacosamide	◆
Lamotrigine	◆
Levetiracetam	◆
Oxcarbazepine	●
Phenobarbital (Phenobarbitone)	●
Phenytoin	●
Pregabalin	◆
Primidone	●
Tiagabine	◆
Topiramate	◆
Valproate	◆
Vigabatrin	◆
Zonisamide	◆

● Do Not Coadminister ■ Potential Interaction ▲ Potential Weak Interaction ◆ No Interaction Expected

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.

Koziolek, Mirko et al. "The mechanisms of pharmacokinetic food-drug interactions – A perspective from the UNGAP group" *European Journal of Pharmaceutical Sciences* vol 134 (2019): 31-59. doi.org/10.1016/j.ejps.2019.04.003.

Bushra, Rabia et al. "Food-drug interactions." *Oman medical journal* vol. 26,2 (2011): 77-83. doi:10.5001/omj.2011.21

Drug-Food Considerations

With food	Single tablet regimen: Complera®[1], Odefsey®[1], Genvoya®[2], Stribild®[2], Juluca®[3], Symtuza®[4] 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®[1], Symfi®[1], Symfi Lo®[1] NRTI: Didanosine NNRTI: Efavirenz PI: Amprenavir (suspension formulation for adult only), Indinavir

1. NNRTI/NRTI, 2. INSTI/NRTI, 3. INSTI/NNRTI, 4 PI/NRTI

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

Drugs Aging Jul 1999, 15(1):15-28

Anticholinergics

Allergies Cough/Cold Sleeping	Nausea	Overactive Bladder	Parkinson	Anti-psychotics	Anti-spasmodics	Muscle Relaxants	Depression
Diphenhydramine (Benadryl®, “PM”)	Meclizine (Bonine®)	Oxybutynin	Benztropine	Olanzapine	Atropine	Carisoprodol	Amitriptyline
Hydroxyzine	Dimen-hydrinate (Dramamine®)	Tolterodine	Trihexy-phenidyl	Quetiapine	Belladonna Scopolamine	Chlor-zoxazone	Despiramine
Promethazine	Prochlor-perazine	Trospium	Amantadine	Clozapine	Dicyclomine	Cyclo-benzaprine	Doxepin
Chlorpheniramine (Chlor-Trimeton®)	Trimetho-benzamide	Darifenacin		Chlor-promazine	Hyoscyamine	Metho-carbamol	Nortriptyline

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 agents on 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
JAMA Neurol. 2016;73(6):721-732.
JAMA Intern Med. 2015;175(3):401-407.

Benzodiazepines

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

Front. Psychiatry, 17 September 2020 | https://doi.org/10.3389/fpsyt.2020.00755
J Clin Psychiatry. 2005;66 Suppl 2:9-13. PMID: 15762814.
Am J Health Syst Pharm. 2018 Jan 1;75(1):e6-e12. doi: 10.2146/ajhp160381. PMID: 29273607.

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.

Pain Medicine, Volume 16, Issue suppl_1, October 2015, Pages S37–S43

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

Ment Health Clin. 2016 Jul; 6(4): 201–206.

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

Eur Arch Psychiatry Clin Neurosci. 2015 Aug;265(5):419-28. Epub 2014 Oct 24.
Associations between proton pump inhibitors and Alzheimer's disease: A nested case-control study using a Korean nationwide health screening cohort. Research Square. 2022 Mar 11. DOI: 10.21203/rs.3.rs-1435267/v1

H_2 Antagonists (Antacids)

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

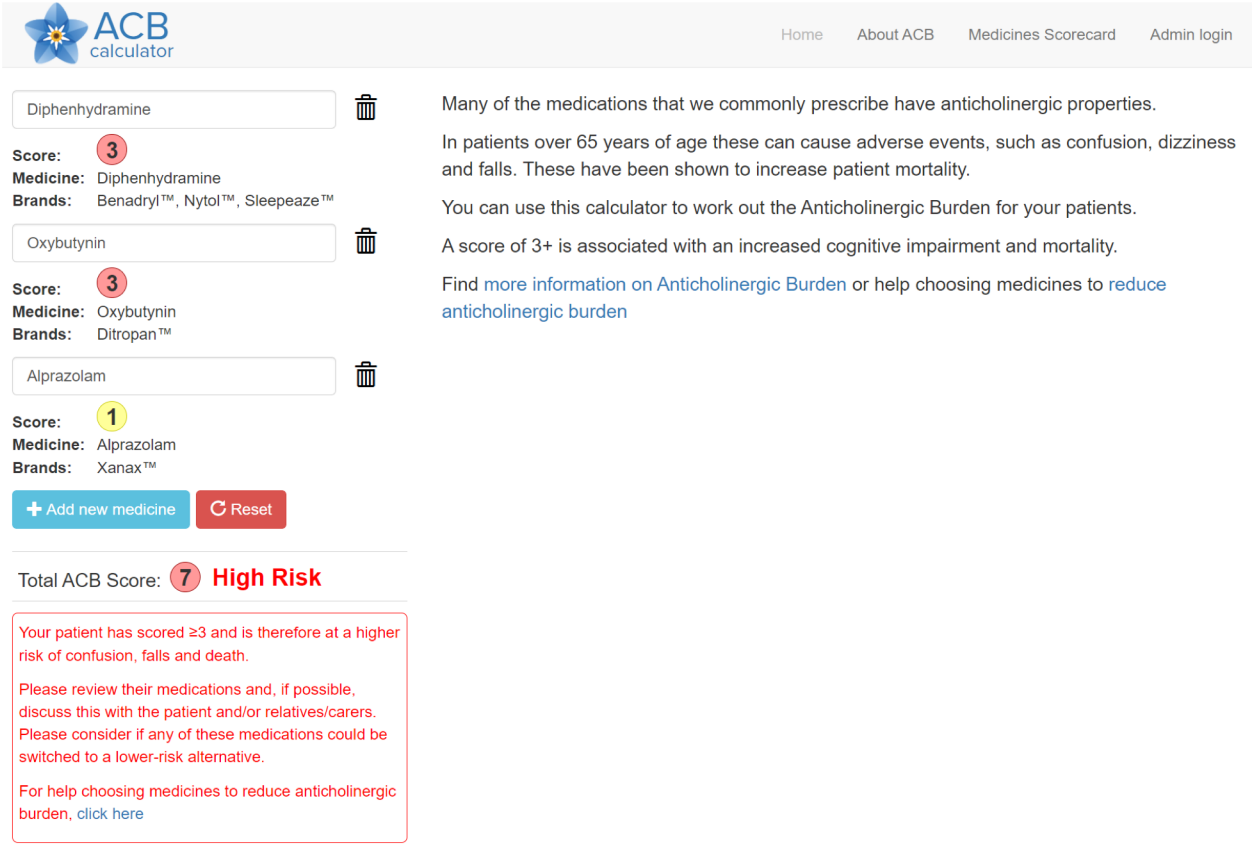
Ann Intern Med. 1991;114:1027–1034.
Gastroenterology. 1990;11:127–149

Tools to Calculate Anticholinergic Burden

ACB Calculator

ACBcalc.com

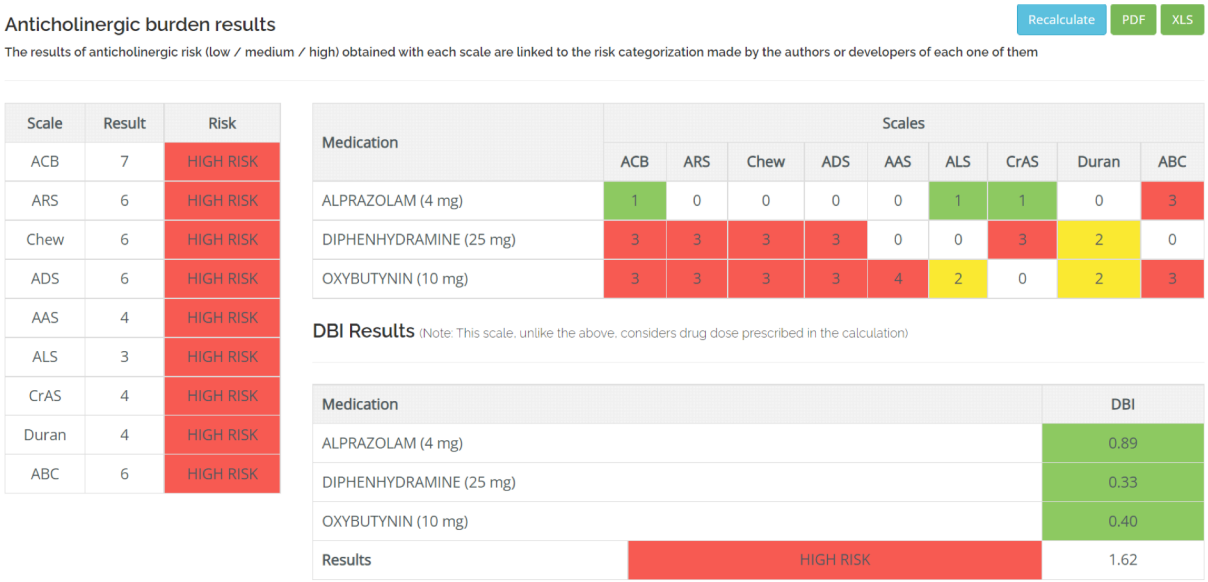
- Provides a score for medication with anticholinergic effects
- Score of 3+ is associated with increased cognitive impairment and mortality



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



Anticholinergic burden results

Recalculate PDF XLS

The results of anticholinergic risk (low / medium / high) obtained with each scale are linked to the risk categorization made by the authors or developers of each one of them

Scale	Result	Risk
ACB	7	HIGH RISK
ARS	6	HIGH RISK
Chew	6	HIGH RISK
ADS	6	HIGH RISK
AAS	4	HIGH RISK
ALS	3	HIGH RISK
CrAS	4	HIGH RISK
Duran	4	HIGH RISK
ABC	6	HIGH RISK

Medication	Scales								
	ACB	ARS	Chew	ADS	AAS	ALS	CrAS	Duran	ABC
ALPRAZOLAM (4 mg)	1	0	0	0	0	1	1	0	3
DIPHENHYDRAMINE (25 mg)	3	3	3	3	0	0	3	2	0
OXYBUTYNIN (10 mg)	3	3	3	3	4	2	0	2	3

DBI Results (Note: This scale, unlike the above, considers drug dose prescribed in the calculation)

Medication	DBI
ALPRAZOLAM (4 mg)	0.89
DIPHENHYDRAMINE (25 mg)	0.33
OXYBUTYNIN (10 mg)	0.40
Results	HIGH RISK 1.62

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
Brain Sci. 2019 Aug; 9(8): 195. Published online 2019 Aug 9. doi: 10.3390/brainsci9080195

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

AIDS: January 28, 2015 - Volume 29 - Issue 3 - p 253-261
Open Forum Infectious Diseases, Volume 6, Issue 7, July 2019, ofz277, https://doi.org/10.1093/ofid/ofz277
American Psychiatric Association. (2012). HIV and Cognitive Disorders [Fact Sheet].

HIV - High CNS Penetration Agents

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

0	1	2	3	4
Amprenavir	Tenofovir disoproxil fumarate	Didanosine	Abacavir	Zidovudine
Amprenavir/r	Tenofovir alafenamide[a]	Lamivudine	Emtricitabin	Nevirapine
Cobicistat	Zalcitabine	Stavudine	Efavirenz	Dolutegravir[a]
	Enfuvirtide	Etravirine	Delavirdine	Indinavir/r
	Ritonavir[b]	Rilpivirine[a]	Raltegravir	
	Saquinavir	Elvitegravir[a]	Maraviroc	
	Saquinavir/r	Fos-amprenavir	Fos-amprenavir/r	
	Tipranavir/r	Atazanavir	Indinavir	
	Nelfinavir	Atazanavir/r	Lopinavir/r	
			Darunavir/r	

NOTE: Adapted from Letendre et al [18] with permission.

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

[b]When used as a nonbooster.

Source: Open Forum Infect Dis. 2019;6(7):ofz277. Published 2019 Jul 8.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6612860/

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

https://geriatricscareonline.org/ProductAbstract/american-geriatrics-society-updated-beers-criteria-for-potentially-inappropriate-medication-use-in-older-adults/CL001

Polypharmacy

- No universal definition: ≥ 5 medications
- PLWH
  - Occurs ~10 years before the general population
  - High prevalence (≥ 5 non-HIV medications)

Reference	Age	N	Polypharmacy prevalence
McNicholl I et al. *Pharmacotherapy*. 2017.	≥50	248	94%
Cabanilla G et al. Presented at IAS 2019.	≥65	112	84%
Greene M et al. *J AM Geriatr Soc*. 2014.	≥60	89	74%

  - 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)

Lancet Healthy Longev 2021; 2: e639-50
J Am Geriatr Soc. 2014;62(3):447-453
Eur J Clin Pharmacol. 2020;76(3):305-318

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

Drugs Aging 36(3): 289–97.

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

Drugs Aging 36(3): 289–97.

Deprescribing Tool

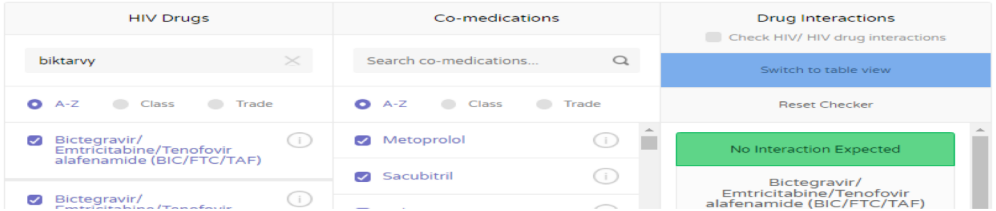
MedStopper
medstopper.com

- Provides stopping priorities and suggested taper approach

Stopping Priority RED=Highest GREEN=Lowest	Medication/ Category/ Condition	May Improve Symptoms?	May Reduce Risk for Future Illness?	May Cause Harm?	Suggested Taper Approach	Possible Symptoms when Stopping or Tapering	Beers/STOPP Criteria
	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
	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	Details

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**

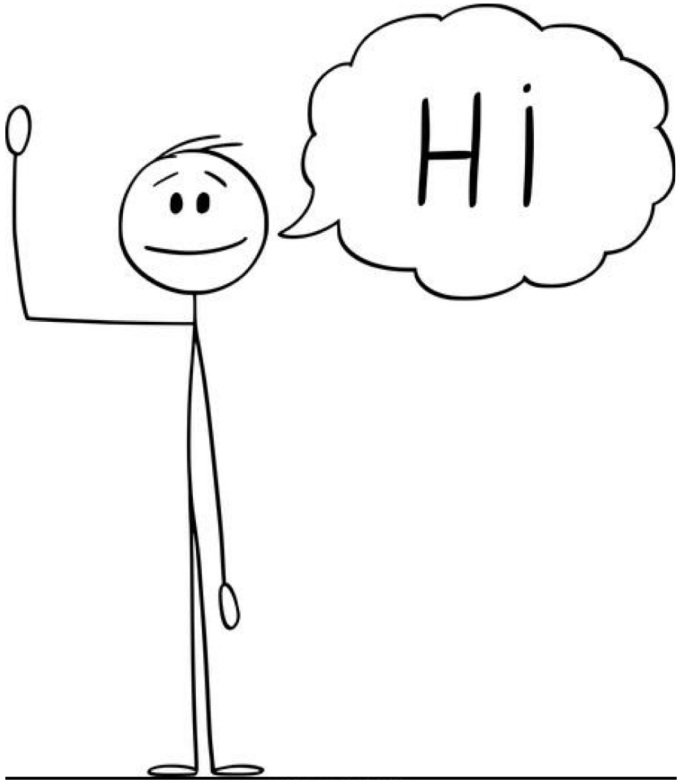


- Review the indications of each medication and the necessity of pharmacotherapy
- Conduct risk-benefit analysis

Benzodiazepines *Short and intermediate acting:* Alprazolam Estazolam Lorazepam Oxazepam Temazepam Triazolam *Long acting:* Chlordiazepoxide (alone or in combination with amitriptyline or clidinium) Clonazepam Clorazepate Diazepam Flurazepam Quazepam	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults May be appropriate for seizure disorders, rapid eye movement sleep behavior disorder, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, and periprocedural anesthesia	Avoid
Meprobamate	High rate of physical dependence; sedating	Avoid
Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (ie, "Z-drugs") Eszopiclone Zaleplon Zolpidem	Nonbenzodiazepine benzodiazepine receptor agonist hypnotics (ie, Z drugs) have adverse events similar to those of benzodiazepines in older adults (eg, delirium, falls, fractures); increased emergency room visits/ hospitalizations; motor vehicle crashes; minimal improvement in sleep latency and duration	Avoid

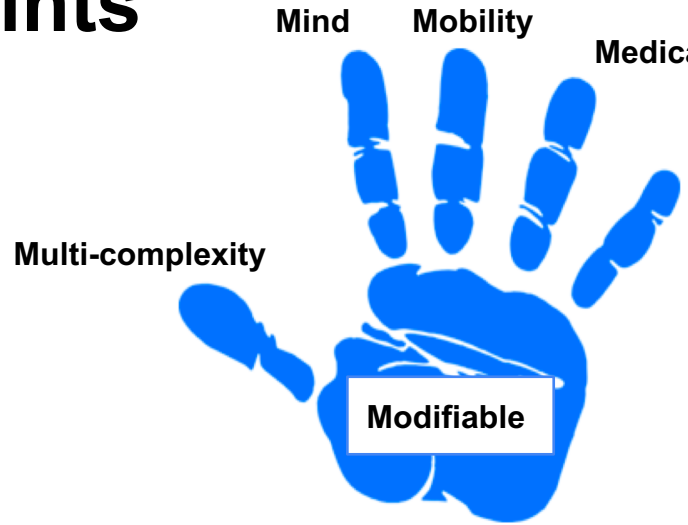
- Deprescribe as necessary

71 yr old man referred for a comprehensive geriatric assessment



Take Home Points

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



AGS BEERS CRITERIA® 2019