HIV in 2018: It’s Not Over Yet – What Every Physical Therapist Needs to Know

American Physical Therapy Association
Combined Sections Meeting 2018

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Learning Objectives

After course, participants will be able to:
1. Describe the basic disease process and impact of pharmacologic agents on HIV disease
2. Explain basic epidemiological profile of HIV disease
3. Identify HIV disease impact on multi-system involvement and associated PT-related impairments: integumentary, cardiovascular, musculoskeletal, neurological, chronic pain, and age-related impairments.
4. Incorporate PT interventions for common HIV-related impairments and evaluate typical PT diagnoses within the larger context of HIV disease.

HIV/AIDS: Background and Musculoskeletal Considerations

HIV/AIDS definitions

• HIV: Human Immunodeficiency Virus. Progressive failure of the immune system that allows life-threatening opportunistic illnesses (cancers, PCP, toxoplasmosis) to thrive. Untreated, HIV progresses to AIDS.

• AIDS: Acquired Immunodeficiency Syndrome. Immune system is severely compromised and vulnerable to opportunistic illnesses.

• PLHIV – People Living with HIV

HIV/AIDS definitions

• CD4+ ("T-helper cell"): type of white blood cell that fights infection. Measured in cells/mm³.
  – Move throughout the body identifying/destroying germs such as viruses and bacteria
  – HIV binds to and enters CD4 cells → makes copies of itself → gradual decline of CD4 cells and immune system
  – Healthy CD4+ is 500-1600 cells/mm³.

• Viral load: measurement of HIV copies in a blood sample. Measured in copies/mL
  – Declared “undetectable” if it is under 40-75 copies/mL, BUT person is still HIV+ and needs to stay on ART

• Opportunistic Infections: Infections associated with severe immunodeficiency, as they take advantage of a weakened immune system. Ie pneumocystis carinii pneumonia (PCP)

HIV/AIDS Timeline

1981: 270 cases of “severe immune deficiency” among MSM. 121 of those individuals have died.

HIV/AIDS: historical overview

1980s-1990s: birth of grassroots organizations to fight HIV/AIDS and put pressure on government to recognize the crisis AND on the FDA to approve HIV drugs: “SILENCE= DEATH”

1997 – highly active antiretroviral therapy (HAART/ART/ARVs) becomes primary treatment for HIV/AIDS
  – AIDS-related deaths decreased by 47% from the year before (1996)

History of HIV/AIDS

• March 2012: Report at Conference on Retroviruses and Opportunistic Infections (Seattle, WA)
  – Life expectancy with treatment once CD4+ reaches 500 cells/mm³ = to HIV negative counterpart
• July 2012 – FDA approves Pre-exposure Prophylaxis (PrEP)
  – One pill each day (same medication used to treat HIV)
  – Risk of HIV up to 92% lower for those who take the pill consistently

Virological Profile

• **Infection**: the HIV virus attacks the immune system, while simultaneously destroying the CD4 (T-cells) that protect the body from illness. HIV then uses the CD4 cell to replicate.

Virological Profile

• **Replication**: Once a person is infected with HIV, the virus begins to attack and destroy the CD4 cells.
  – If HIV is not treated with antiretroviral treatment - prevents the virus from replicating - then the body is exposed to opportunistic infections which can cause serious illnesses.

Stages of HIV Infection

**Stage I: Acute HIV Infection** (weeks 2-4 post infection):
  – Massive inflammatory response to initial viral exposure
  – Develop severe flu-like symptoms
  – Large amounts of HIV in the blood and immune system
  • Body produces HIV antibodies and cytotoxic lymphocytes
  • Greatest transmission risk

**Stage II: Chronic HIV Infection** (aka clinical latency/asymptomatic infection):
  – HIV reproduces at low levels
  – People may be asymptomatic but still able to transmit
  – Without treatment, usually progresses to AIDS in ~10 years

Immune involvement

• **AIDS – Final stage of HIV**
  – HIV has destroyed immune system
  – CD4+ < 200 cells/mm³ (normal CD4+ 500-1600 cells/mm³).
  – 1 or more opportunistic illnesses such as: encephalopathy, tuberculosis, pneumoystis pneumonia (PCP), mycobacterium avium complex (MAC), lymphoma, herpes → AIDS-related death
  – Life expectancy without treatment with AIDS diagnosis = 3 years

• CD4 count is no longer considered a criterion of when to start therapy. Current guidelines: Initiate ART in all HIV-infected adults who are willing/ready to start therapy.
Pharmacological Profile

- Antiretroviral therapy (ART) is recommended for all individuals with HIV, regardless of CD4 count, to reduce the morbidity and mortality associated with HIV infection (AI).
- ART can’t cure HIV, but HIV medicines help people with HIV live longer, healthier lives. HIV medicines also reduce the risk of HIV transmission.

ARVs: What PTs need to know

- Ask ALL HIV+ patients:
  - Which ARVs are you taking?
  - Taking as prescribed?
  - Any trouble paying for or getting ARVs?
- Most side effects from HIV medicines are manageable, but a few can be serious. The benefits of HIV medicines far outweigh the risk of side effects.
- Possible short-term side effects: fatigue, nausea, vomiting, diarrhea, headache, fever, myalgia, dizziness, insomnia

ARVs: What PTs need to know

- Potential long-term side-effects: Kidney problems, including kidney failure, hepatotoxicity, heart disease, diabetes, hyperlipidemia, lipodystrophy, osteoporosis, Nervous system and psychiatric effects, depression, and suicidal thoughts
- If patient c/o side effects → advise them DO NOT stop medications or reduce dose. Contact ID provider. Stopping ARV allows HIV to multiply and can lead to drug resistance.

Epidemiological Profile

- An estimated 1,122,900 adults and adolescents were living with HIV at the end of 2015. Of those, 162,500 (15%) are unaware of their diagnosis.
- Young people are especially at risk of HIV transmission and HIV progression: Among people aged 13-24 who were living with HIV, an estimated 44% didn’t know.
- In 2016, 18,160 people received an AIDS diagnosis

Current HIV statistics: CDC

- Highest risk communities: economically disadvantaged urban areas in the U.S., MSM (men who have sex with other men) and African-Americans (12% of U.S. population; 41% of HIV infections), Southeastern U.S. bears the greatest geographical HIV burden.
- Cities with greatest HIV prevalence:
  1. Miami
  2. Baton Rouge, LA
  3. New Orleans, LA
  4. Jackson, Miss
  5. Atlanta, GA
- Geriatric population (55 or older) = 26% of all HIV infections in U.S.
Current Statistics: Age and Income

New HIV Diagnoses in the United States by Age, 2016

HIV Prevalence Rate, by Income

Physiological Profile

- HIV disease manifests itself in various physiological contexts
- Musculoskeletal
- Neurological/cognitive
- Psychiatric

Triage of HIV-related impairments

- Infectious disease provider: initiate HAART, manage/screen for opportunistic infections
- Family medicine/Internal medicine outpatient management
  - referral for symptoms/side effects
- Orthopedics/Physiatry/Physical therapy/neurology/psychiatry
- Goals: increase functional independence, decrease/eliminate pain, independent self-management of impairments, improve QOL

HIV as Chronic Disease

- Effects from the disease itself and its pharmacological treatment can cause long-term and acute health complications.
- However - less than 1/3 of deaths among PLH are attributed to HIV-related causes ie Kaposi’s sarcoma
- Increasing role of primary care in long-term management of HIV and non-HIV-related impairments
- Increasing role of physical therapy, occupational therapy, mental health providers
- Collaborative effort between disciplines and AIDS Service Organizations for comprehensive care

HIV as Chronic Disease

- In the era of highly active anti-retroviral therapy (HAART/ART), people can increasingly live longer with HIV, delay or avoid opportunistic infections, and live with HIV as a chronic health condition
- However...research shows that quality of life decreases with age, mostly related to physical decline, lower levels of independence and poorer emotional wellbeing
- Chronic inflammation due to long-term HIV infection
  - Autoimmune dysfunction, cardiovascular disease, neurocognitive disease, osteoporosis/frailty, liver disease, kidney disease and some cancers
Chronic HIV Infection

- Increased chronicity of HIV → increased life expectancy → increasingly experiencing common health problems seen in the general population that must be addressed.
- The treatment of HIV disease depends on:
  - Disease stage
  - Any concomitant opportunistic infections
  - Goal of treatment is to prevent the immune system from deteriorating to the point of opportunistic infections.
  - ART compliance

HIV as a Chronic Disease

- Effects from the disease itself and its pharmacological treatment can cause long-term and acute health complications
- Greater prevalence calls for an increasing role for physical therapy in the continuum of care for PLWHA
- Studies highlight potential benefits of physical therapy for PLWHA:
  - Improve cardiovascular health, strength, weight, and psychological status and neurocognitive function
  - Enhance quality of life by decreasing pain and fatigue

HIV as a Prevalent Disease

- Physical therapists may treat PLHIV of all ages and in various clinical settings
  - For example:
    - Pediatric patient in the NICU
    - Geriatric patient in an orthopedic outpatient clinic
- HIV/AIDS may be simply listed as a comorbidity, or the patient may have an HIV-related impairment as the primary diagnosis of referral

Commission on Accreditation in Physical Therapy Education

- CAPTE requires each program’s curriculum to include “content about the cardiovascular, pulmonary, endocrine, metabolic, gastrointestinal, genitourinary, integumentary, musculoskeletal, and neuromuscular systems....”
- The HIV/AIDS disease process affects all of the above listed systems
- Consistent incorporation of HIV/AIDS into a program’s curriculum equips graduating students with the knowledge and skills to treat PLWHA

Episodic disability

- “Episodic Disability” in HIV → described by O’Brien et al., as “episodic...health related consequences experienced as a result of HIV and its treatments” which can occur in multiple dimensions”.
- Not necessarily a linear decline as we saw in pre-ART times
- Increased chronicity of HIV → increased disability

What PTs Need to Know

- With proper therapy/treatment, HIV can be a chronic, survivable diagnosis
- HIV affects multiple systems and is best treated with a multidisciplinary approach
- ALL PLHIV should be followed by an infectious disease physician
Physical therapists’ management of the HIV-positive patient

**Key point:** Treating HIV-related comorbidities vs. treating "typical" PT diagnoses within the context of HIV disease.

- Some common HIV-related comorbidities are peripheral neuropathy (PN), avascular necrosis, and chronic pain.
  - Co-morbidities that are *direct result* of HIV
  - Important to know: viral load, ARV compliance, recent ARV changes, worsening symptoms

PT Exam: Is it different for an HIV+ vs HIV- patient?

**PMH:** May include HIV in the chart; however, patient may not wish to disclose this information.

Ask patient if they have recently been hospitalized for any HIV-related issues ie. Pneumonias, MAC,

“How do I ask about it?”

- Mention that you see it in their PMH, alongside other things. How would you ask about HTN? (“I see that hypertension is listed here in your chart…”)
  - *DO:* ask about medications: which ones, any side effects, any trouble with medication compliance, if they are followed by an infectious disease doctor
  - *DO NOT:* ask how they were infected

Secondary diagnoses

- PLWHA can have any and all of the same secondary diagnoses as non-PLWHA
  - Arthralgia
  - Myalgia
  - Osteoporosis
  - Low Back Pain
  - Neuropathy
  - Vestibular Dysfunction
  - Decreased Cardiovascular Endurance

Mental health

- Increased prevalence of mental health disorders in PLH, especially depression, Alzheimer’s, dementia, PTSD
- HIV proteins alter the response to stressors and cortisol production
- Exercise has emerged as a significant protective factor for HIV-related cognitive decline
- HIV-positive MSM who survived the 1980s have are likely to have lost 90% of their social group to AIDS
- For this cohort, the majority have clinical symptoms consistent with PTSD diagnosis

Social support

- This is especially important for PLWHA. It can affect both mental and physical health, including medication compliance.
- Stigma
- Past trauma re: receiving diagnosis.
- Long term survivors often have particular traumatic histories, including devastating losses of friends, partners, community.
Musculoskeletal involvement

- The increased life expectancy of PLWHA increases the possibility of age-related arthritis, as well as other chronic musculoskeletal impairments as complications of HIV virus and/or because of expected age-related symptoms.
- Recent research suggests that the probability of PLH developing osteoporosis is three times higher compared to their HIV-negative counterparts.

HIV Sequela (Musculoskeletal)

- Four common HIV-specific syndromes:
  - HIV arthritis,
  - Painful articular syndrome,
  - Diffuse-infiltrative lymphocytosis syndrome (DILS)
  - Immune reconstitution inflammatory syndrome (IRIS).
- It is currently unknown whether HIV causes its own primary arthritis.
- Avascular necrosis and osteoporosis are common comorbidities of HIV.
- *Walker-Bone Rheumatology, Volume 56, Issue 10, 1 October 2017, Pages 1648–1661*

Musculoskeletal Involvement

- Literature suggests that musculoskeletal conditions will affect 72% of HIV-infected individuals during their lifespan.
- Musculoskeletal and orthopedic complications have emerged as potential results of the disease itself and/or the ART treatment regimen.  
  - ie, low bone mineral density (BMD) has been associated independently with HIV disease itself and as a direct effect of ART

Musculoskeletal Involvement

- Most commonly seen MSK impairments are myalgia, arthralgia, low back pain, osteoporosis, avascular necrosis of femoral head.
- HIV virus affects bone remodeling → bone fragility
- PLH have a higher prevalence of fractures compared to HIV(-) peers
- Muscle wasting is now mostly seen in untreated, advanced disease → the changing face of the disease
- Lipoatrophy may be observed

Musculoskeletal considerations: surgery

- Orthopedic surgeries in HIV+ individuals are more likely due to increased chronicity of HIV
- Bone and joint infections account for ~67% of musculoskeletal infections in PLWHA
- HOWEVER: Recent findings → statistically insignificant differences in orthopedic postoperative complications of HIV-positive versus negative individuals*
  - HIV status may not be a reason to delay/forego orthopedic surgery based on HIV status alone

lipoatrophy

*Source: US Department of Veterans Affairs, HIV/AIDS Image Library*
Musculoskeletal: bone mineral density screening

- People with HIV should be screened carefully for low BMD – especially those with a history of bone disease and “traditional” risk factors
- At present, dietary and exercise advice, and vitamin D and calcium supplementation are the main preventive strategies, while treatment of established bone disease is similar to that in the general population.

Musculoskeletal considerations: surgery

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“the Changing face of AIDS”

- “from wasting to obesity” → changing face of AIDS: up to 70% of PLH on ARVs have central obesity
- Figure: Subjects in an urban AIDS clinic in the Southeastern U.S. (n=179) with chronic pain. (Pullen, 2016)

Cardiovascular Consideration in People Living with HIV/AIDS

R. Sandoval PT PhD

Objectives

- Systems review check as part of the evaluation.
- CVD prevalence and risk factors in people living with HIV/AIDS
- Impact of lipid abnormalities
- Clinical screening recommendations
- Treatment recommendations

Case

- 42 yo male
- HIV+ for 4 years
- VL: 4000 RNA copies/mm³
- CD4: 300 cells/mm³
- CD4 cell percentage: 12%
- Triglycerides: 200 mg/dl
- HDL: 38 mg/dl
- LDL: 135 mg/dl
- Cholesterol/HDL ratio: 5.0
- HT: 5'10", wt 175 lbs
- BP at rest: 149/90
- HR: 85 bpm
- HIV meds: Stribild (Elvitegravir/cobicistat/tenofovir/EFV)
- Social: Smokes ½ pack day and drinks socially
- Hx of cocaine use in the past, has been clean for the past 7 years.
Artery

HIV and atherosclerosis

Patient case
• Modifiable and non-modifiable risk factors

CVD risk factors

Risk factors of heart and cardiovascular disease
• Smoking
  • Physical inactivity
  • Obesity
  • Suboptimal diet
  • Hypertension
• Elevated serum total cholesterol
• Elevated low-density lipoprotein (LDL)
• Decreased high-density lipoprotein (HDL)
• Diabetes
• Family history
• Age
• Gender
• Male risk is higher until females reach menopause; then risk is equal
• Stress

**BOX 3-3  Risk factors associated with sudden death**

<table>
<thead>
<tr>
<th>Undiagnosed CHD population</th>
<th>Diagnosed CHD population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Decreased left ventricular ejection fraction (LVEF) (&lt;35%)</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td></td>
</tr>
<tr>
<td>(elevated)</td>
<td></td>
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<td>Vital capacity (low, especially a factor in females)</td>
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<tr>
<td>Cigarettes consumed daily</td>
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</tr>
<tr>
<td>Relative weight</td>
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</tr>
</tbody>
</table>

**Patient case**

- Medication and classes of medications
  - Elvitegravir/cobicistat/tenofovir/emtricitabine
  - Or integrase inhibitor+p450 inhibitor+1st NRTI+2nd NRTI

**ARV and risk for CVD**

**ARV risk factor for CVD**


**CVD risk associated with PI’s**

CVD risk associated with NRTI's

<table>
<thead>
<tr>
<th>Study</th>
<th>Relative Risk (95% CI)</th>
<th>Weight</th>
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<tr>
<td>Study 1</td>
<td>1.50 (1.10, 2.00)</td>
<td>5.5</td>
</tr>
<tr>
<td>Study 2</td>
<td>1.20 (0.90, 1.60)</td>
<td>3.5</td>
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CVD risk associated with NNRTI's

<table>
<thead>
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<th>Study</th>
<th>Relative Risk (95% CI)</th>
<th>Weight</th>
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<tbody>
<tr>
<td>Study 1</td>
<td>1.70 (1.30, 2.20)</td>
<td>8.0</td>
</tr>
<tr>
<td>Study 2</td>
<td>1.40 (1.00, 2.00)</td>
<td>6.0</td>
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CVD risk associated with Ziagen™ (Abacavir, NRTI)

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Patient case

- Lipid profile in labs
  - Triglycerides: 200 mg/dl
  - HDL: 38 mg/dl
  - LDL: 135 mg/dl
  - Cholesterol/HDL ratio: 5.0
  - Ht: 5'10", wt 175 lbs

ARV and their impact on lipids

<table>
<thead>
<tr>
<th>ARV</th>
<th>Effect on lipids</th>
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<tbody>
<tr>
<td>abacavir</td>
<td>increase</td>
</tr>
<tr>
<td>lamivudine</td>
<td>decrease</td>
</tr>
<tr>
<td>zidovudine</td>
<td>decrease</td>
</tr>
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</table>

Cholesterol management

- Ghanem F1, Vodnala D2, K Kalavakunta J3,4, Durga S3 et al.
  Cholesterol crystal embolization following plaque rupture: a systemic disease with unusual features.
Lipid management options

### Clinical Presentation

- Similar to general population except
  - <50 years of age
- Higher risk if associated with dyslipidemia, HTN and DM
- Soft plaques are more prevalent in HIV+ individuals (more prone to rupture/thrombus formation)
- No chest pain or pain with exertion
- Additional behavioral risk factors
  - Cocaine use
  - Tobacco use

Bloomfield SG, Leung C. Cardiac Disease Associated with Human Immunodeficiency Virus Infection. *Cardiol Clin.* 2017, (35), 59–70

### Patient Client Management

**BOX 3-3 Risk factors associated with sudden death**


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### Screening recommendations BP

<table>
<thead>
<tr>
<th>Classification of Blood Pressure for Adults</th>
<th>Normal</th>
<th>Prehypertension</th>
<th>Stage 1 hypertension</th>
<th>Stage 2 hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure (mm Hg)</td>
<td>&lt;120</td>
<td>120-139</td>
<td>140-159</td>
<td>≥160</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mm Hg)</td>
<td>&lt;80</td>
<td>80-89</td>
<td>90-99</td>
<td>≥100</td>
</tr>
</tbody>
</table>

(Goodman 575)


### CVD Heart Disease Prevention Target Measurements

<table>
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<tr>
<th>Risk Factors</th>
<th>Targets</th>
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<tr>
<td>Body Measurements</td>
<td></td>
</tr>
<tr>
<td>• Body mass index (BMI): multiply your weight in pounds by 703, then divide that number by the square of your height in inches</td>
<td>18.5-24.0</td>
</tr>
<tr>
<td>• Waist-to-hip ratio (WHR): divide your waist measurement in inches by your hip measurement in inches</td>
<td>≤0.8</td>
</tr>
<tr>
<td>Lipids, Lipoproteins</td>
<td></td>
</tr>
<tr>
<td>• Total cholesterol</td>
<td>&lt;200 mg/dL</td>
</tr>
<tr>
<td>• HDL cholesterol</td>
<td>≥40 mg/dL (men)</td>
</tr>
<tr>
<td>• LDL cholesterol</td>
<td>≥50 mg/dL (women)</td>
</tr>
<tr>
<td>• Triglycerides</td>
<td>≤150 mg/dL (men), ≤135 mg/dL (women)</td>
</tr>
<tr>
<td>• Total cholesterol/HDL ratio</td>
<td>&lt;5.0 mg/dL (men), &lt;4.5 mg/dL (women)</td>
</tr>
</tbody>
</table>

(Goodman 575)

Auscultation

Carotid artery

Carotid bruises as a prognostic indicator of cardiovascular death and myocardial infarction: a
Pickett, Christopher A et al. The Lancet, Volume 371, Issue 9624, 1587 - 1594

Exercise recommendations (Geriatrics)

[Diagram showing exercise recommendations]

Moderate Cardio training impact

- Circuit training
  - Focusing initially on local muscular endurance (if severely deconditioned) or hypertrophy adaptations
  - Shifting focus to strength adaptations (low volume/higher loads)
  - Introduce power activities (ballistic/plyometrics) later in the program

- Cardio
  - Moderate training intensity ~80% of predictive max HR for age or when using Karvonen formula

Table 2: MIXED trial and groups mean±SD for percent and postural values (N=36)

<table>
<thead>
<tr>
<th>Session</th>
<th>35±5</th>
<th>Follow</th>
</tr>
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<tbody>
<tr>
<td>BP (sitting)</td>
<td>150.2±12.5</td>
<td>118.0±13.9</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>72.6±9.6</td>
<td>65.3±9.3</td>
</tr>
<tr>
<td>VO2 max (ml/kg/min)</td>
<td>29.3±6.9</td>
<td>28.7±6.5</td>
</tr>
</tbody>
</table>

*Significant at p<0.05: BP - Systolic blood pressure, SBP - Systolic blood pressure, DBP - Diastolic blood pressure, HR - Heart rate

Romero-Arenas S*, Martinez-Pascual M, Alcaraz PE. Impact of resistance circuit training on neuromuscular, cardiopulmonary and body composition adaptations in the

Summary

• CVD prevalence and risk factors
• Impact of lipid abnormalities
• Clinical screening recommendations
• Treatment recommendations

Questions or comments:
RSandovalPTPhD@outlook.com

Chronic Pain and Peripheral Neuropathy in People Living with HIV (PLHIV)

Dave Kietrys, PT, PhD, OCS, FCPP
Associate Professor; Assistant Vice-Chair, Rutgers School of Health Professions
kietrydm@shp.rutgers.edu

Chronic Pain in PLHIV

• Prevalence estimates of chronic pain in PLHIV range from 39% to 55%.
• Higher prevalence and severity of pain in indigent population
• Concurrent psychiatric illness → 40% more likely to have pain
• Concurrent substance abuse → higher pain severity and disruption of daily function

Chronic Pain in PLHIV

• Associated with decreased quality of life
• Often underestimated and undertreated
• PLHIV and pain 87% less likely to be adherent to ART

Issues in Dealing with Chronic Pain

• Stigma
• Provider Bias
• Substance Use Disorders

Disparities in Chronic Pain Management

Less attention (by providers) given to inquiry about chronic pain and treatment of chronic pain to:

• Non-Caucasian
• Women
• Poor
• Incarcerated
• Immigrants
• Disability
• Multiple Chronic Conditions

References:


Multifactorial Etiology of Chronic Pain in PLHIV

- Direct effects of HIV infection
- Chronic inflammation and immune activation
- Side-effects of ART drugs or other drugs
- Neurologic mechanisms
- Comorbidities / Multi-morbidity
- Opportunistic infections
- Aging
- Psychosocial influences
- Prescription opioid misuse and heroin use
- Gender and ethnic differences in perception & expression of pain


Merlin et al. (2013) Prospective cohort, N=1,903

Pain independently associated with increased odds of impairment in 3 domains of physical function

- Mobility (aOR 10.5)
- Self-care (aOR 4.1)
- Usual activities (aOR 5.4)


Self-Reported Disability in HIV+ Persons in the United States and South Africa

Kemto, Myezwa, Fawzi, Davis, O'Brien, Lante, Masera, and Gal安排

Secondary analysis of data sets from:
- US cohort (southern NJ) N=127
- South African cohort (Johannesburg) N=1016

Analysis of potential predictors of disability based on theoretical considerations and data common to the 2 cohorts

- Depression
- Muscle pain
- Adherence to ART
What factors were related to presence of disability?

- **Gender**
  - Female gender: 61% more likely to report disability

- **Number of years living with HIV**
  - 3.5% increase in odds of reporting disability with EACH additional year living with HIV

- **Muscle Pain**
  - 82% more likely to report disability if experiencing muscle pain

- **Depression**
  - 67% more likely to report disability if depressed

What **DOESN’T** work for management of chronic pain

- **Opioid “Pain Killers”**
  - Not efficacious for chronic pain
  - Risk of:
    - Side-effects
    - Dependency
    - Addiction
    - Overdose
    - Paradoxical hyperalgesia
    - Synergistic effect with ETOH
    - Drug-drug interactions

Many HIV+ patients with a history of chronic pain have been taking prescription opioids for a long time, and may have developed tolerance and/or physical and/or emotional dependency, and yet still have chronic pain.

What do we do?

**Biopsychosocial Model of Chronic Pain**

- **Biological**
  - Tissue pathology (e.g. neuropathy, AVN of bone, chronic myalgia)
  - Co-morbidities
  - Central and peripheral sensitization

- **Psychological**
  - Fear
  - Fear Avoidance of Activity
  - Anxiety
  - Depression
  - Trauma

- **Social**
  - Stigma
  - Environmental Stressors

A Conceptual Framework for Understanding Chronic Pain in Patients with HIV

Jessica S. Merlin, MD, MBA\(^\text{a,b}\); Anne Zinski, PhD\(^b\); Wynne E. Norton, PhD\(^b\); Christine S. Ritchie, MD, MSPH\(^b\); Michael S. Srugo, MD\(^b\); Michael J. Mugavero, MD, MHS\(^b\); Glenn Greenspan, MD, PhD\(^b\); W. Michael Hsia, MD\(^{a,b}\)

Pain Practice, Volume 14, Issue 3, 2014 207–216

When working with patients who have chronic pain, communication is key

- **Trust**
- **Therapeutic Relationship**
- **Shared Medical Decision Making**
  - Goal Setting
  - Motivational Interviewing
Assessment of Chronic Pain

- Interview
  - Onset
  - Alleviating or provoking factors
  - Quantitative and qualitative descriptions
    - Severity
    - Location(s) Radiating?
  - Timing
  - Current management strategies including pharmaceuticals
  - Work and activity status

- Self-report instrument
  - Brief Pain Inventory

Brief Pain Inventory


Widely used in study of cancer, HIV disease and neuropathic pain.

| Mean severity score (items 3-6) | Mean interference score (items 9A-9G) |

Mean severity score (items 3-6)          Mean interference score (items 9A-9G)


What have our patients been doing to deal with their chronic pain?

- Physical activity
- Cognitive and spiritual strategies
- Spending time with family and friends (social support)
- Avoidance of physical and social activity
- Medication-centric pain management
- Substance use

Non-pharmaceutical Management of Chronic Pain

A multidisciplinary / multi-modal approach may include:

- Physical Therapy
  - Exercise
  - TENS
  - Manual Therapy
- Self-Management Programs
- Diet / Nutrition
- Counseling (Cognitive Behavioral Therapy)
- Pharmaceuticals
- Surgery (for specific conditions for which surgery is indicated)
- Complementary and alternative therapies

Complementary and alternative therapies that may be considered in the management of chronic pain

- Mindfulness or other forms of meditation
- Yoga
- Acupuncture
- Yoga
- Hypnosis
- Biofeedback
- Massage
- Marijuana
- Topical Capsaicin (for neuropathic pain)


- 11 studies included; most low or very low quality
- 7 studies of pharmaceuticals
  - gabapentin
  - pregabalin
  - capsaicin
  - analgesics including opioids
- 4 studies of non-pharmaceutical
  - cognitive behavioral therapy
  - self-hypnosis
  - smoked cannabis

The only controlled studies with positive results were of capsaicin and cannabis.

Systematic Review of RCTs on Non-Pharmacological Interventions for PLHIV and Chronic Pain

Ketriya, Foster, McFarland, Milburn, Nguyen, Chiswick - Regent School of Health Professions

9 RCTs or pilot studies to date

- **Exercise** (aerobic and strengthening) (Parker et al., 2018)
  - No between group differences in pain, but exercise group showed a decrease in pain over time.

- **Self-management Program** (pilot study - Gifford et al., 1998)
  - No between group difference in pain, but self Mx group did experience decrease in pain over time.

- **Patient Education** (Nkohma et al. 2015)
  - Improvements in pain compared to control

- **Reiki with music** (Bremner et al. 2016)
  - Improvements in pain within treatment group (clinical meaningfulness)

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**HIV-related Peripheral Neuropathy**

Individuals with HIV-related DSP typically experience pain, numbness, paresthesia, reduced quality of life compromised function, and episodic disability.

Antiretroviral therapy may increase intensity and frequency of neuropathic symptoms.

- **Cognitive Behavioral Therapy** (Lechner, 2003; Doerfler & Goodfellow, 2016; Uebelacker et al., 2016)
  - Mixed results across 1 RCT and 2 pilot studies

- **Vibration** (foot platform) (Paice et al., 2000)
  - No between group differences in pain, but vibration group did experience decrease in pain over time.

- **Night splints** (feet / for neuropathic foot pain) (Sandoval et al., 2016)
  - No between group differences in pain, but splint group did experience decrease in pain over time.

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**Distal Sensory Polyneuropathy (DSP)**

- The most common neurological comorbidity in PLHIV
- Prevalence: 30-60% in PLHIV
- Bilateral involvement at the extremities
- Clinical presentation:
  - Decreased DTR at the ankle
  - Decreased sensation
  - Usually without significant strength loss
  - No significant range of motion deficits
  - Paresthesias and/or numbness
  - Painful night cramps

---

**Pathophysiology of DSP is not fully understood, but has been related to:**

- Peripheral nerve damage related to HIV infection
- Toxic effects of certain anti-retroviral drugs
- Risk factors for DSP in people with HIV disease include
  - Advancing age
  - Past exposure to certain anti-retroviral drugs
  - Longer duration (history) of HIV infection
  - Advanced HIV disease
  - Substance abuse
  - Low CD4 nadir
  - The impact of DSP on QoL and function in individuals with HIV disease needs to be elucidated

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**References**

Physical impairments and functional limitations due to neuropathy are seen clinically and have been reported in the literature.

In patients with peripheral neuropathy:
- Manor et al. (2009)
  - Reduced gait performance
  - Impaired standing balance
- Manor et al. (2008)
  - Increased walking variability and local instability

In patients with HIV-related neuropathy:
- Galantino, Kietrys, et al. (2014)
  - Lower self-reported LE function
  - Lower physical health-related QoL
- Sandoval et al. (2014)
  - Moderate to severe pain, sleep disturbances, and limited ambulation distances

Self-Reported Disability in HIV+ Persons with and without HIV-related Distal Sensory Polyneuropathy
Kietrys, Galantino, Parrott, Davis, Levin, O'Brien & Tran

Prevalence of Neuropathy in our current study
As evidenced by reporting current p&n at need OR numbness in the feet and/or legs on the Subjective Peripheral Neuropathy Scale: YES 43.4%

Many tests available to screen for presence of neuropathy

**Brief Peripheral Neuropathy Screen**

**Total Neuropathy Score**

**Michigan Neuropathy Screening Instrument (MNSI)**

**Single Question Neuropathy Screen**

- "Do you experience tingling, burning, or numbness in your feet or hands?"
- Sensitivity 86%, specificity 80% in HIV+ patients

**DN4 Questionnaire**


Example: "Mitch" is a 72 year old male with HIV and peripheral neuropathy

**Impairments in body structure or function**
- Poor endurance, leg weakness, poor balance, foot pain

**Activity limitations (functional activity limitations)**
- Unable to walk without cane
- Unable to climb more than 3 stairs (using cane and handrail)

**Participation restrictions**
- Unable to attend church services
difficulty getting out of house to socialize

**Environmental factors**
- Church entrance has 12 stairs with no handrail

**Personal factors**
- Lives alone; sedentary and solitary lifestyle

**Subjective Peripheral Neuropathy Screen (SPNS)**

- 6 sections; all self-report
- Quick and inexpensive
- Validated in HIV+ patients

**Mean WHO-DAS scores**

<table>
<thead>
<tr>
<th></th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>those with neuropathy</td>
<td>30.8</td>
</tr>
<tr>
<td>those without neuropathy</td>
<td>15.5</td>
</tr>
</tbody>
</table>

**Example:**

Mitch is a 72 year old male with HIV and peripheral neuropathy. He experiences tingling, burning, and numbness in his feet and hands. He has difficulty walking, maintaining balance, and climbing stairs. He is unable to attend church services and has difficulty getting out of his house to socialize. He lives alone in a sedentary and solitary lifestyle.

**LANSS score for identifying pain of predominantly neuropathic origin**: validated for use in clinical and postal research. Journal of Pain, 2005; 6(9), 511-515.
Neuropathy Pain Scale

- Predictive and discriminative validity (score of >43 suggestive of neuropathy)
- Sensitive to change due to effect of treatments
- Can be scored 4 ways:
  - NPS-10: 0-100 point composite / global score; all items
  - NPS-8: only those items re: neuropathy pain
  - NPS-NA (non-alldynia): excludes "surface pain" and "skin sensitivity"
  - NPS-4 includes "sharp pain", "hot pain", "dull pain" and "deep pain"

Evidence for PT Interventions for Persons with HIV-related Neuropathy

Exercise

What do we know about exercise for neuropathy in general?

- Kluding et al. (2012)
  - 10 wks of aerobic/strengthening exercises in patients with diabetic neuropathy.
  - Improved neuropathic symptoms and cutaneous nerve fiber branching
- Streckmann et al. (2014)
  - Systematic review of exercise for patients with peripheral neuropathy
  - "exercise is feasible, safe, and promising supportive measure"
  - Balance exercise appears to have highest effect on motor and sensory symptoms
  - Endurance training has potential to prevent onset and delay progression of diabetic neuropathy

Exercise

Kietrys et al. (2015; 2016)

**TENS**

For patients with HIV-related neuropathy

  - Case series using microcurrent
  - Reduced or absent pain in 97% of patients; improved gait in 76% of patients
- Gale (2003)
  - 2 cases, bundled PT Tx including microcurrent TENS therapy was associated with significantly subjective improvement in overall neuropathic symptoms.
  - Reduced or absent pain in 97% of patients; improved gait in 76% of patients

**What do we know about TENS for diabetic neuropathy?**

Jin et al. (2014) Systematic review and meta-analysis of 3 RCTs

- Reductions in mean pain score were significantly greater in TENS group than in placebo TENS group in 4 weeks and 6 weeks follow-up (WMD -0.68, 95% CI (-0.92, -0.44))
- No TENS related adverse events were registered in TENS group
- TENS therapy may be an effective and safe strategy in treatment of symptomatic DPN.

**Night Splints**

HIV-related neuropathy

- Sandoval et al., 2016
  - RCT: Night splints vs. control (liner only)

![Figure 1: Pain scores](image)

**Manual Therapy**

For patients with HIV-related neuropathy

- Gale (2003)
  - 2 cases; soft tissue massage and joint mobilization as part of combination therapy
  - (to be summarized on a later slide)

**What do we know about manual therapy for diabetic neuropathy?**

- Chatchawan et al. (2015)
  - Thai foot massage (3x/wk for 2 wks) compared to control
  - Improved balance; improved sensation; improved knee and ankle toe range of motion

**Multi-modal Physical Therapy for HIV related neuropathy (Gale, 2003)**

- 2 patients with HIV related neuropathy
- STM + joint mobilization + stretching exercise + microcurrent + home program
- Case 1: decreased pain and numbness; improved stride length and ambulation tolerance
- Case 2: decreased pain; able to return to work despite progressive atrophy of foot intrinsic muscles at around 12 months

**YOGA FOR PERSONS WITH HIV-RELATED NEUROPATHY: A CASE SERIES**

Koelry, Galantino, Logan, Gauld-Rogerite, O’ Brien, Cohan, Jermy, & Parrott

**Inclusion Criteria**

- Age 18-65 years, HIV+ with controlled HIV disease status
- Clinical Diagnosis of DSP in the feet
- Average foot pain at least 6/10
- Stable pharmacologic management of pain
- Able to ambulate independently for 6-15 minutes

**Yoga Intervention:**

- 4 weeks of twice-weekly 90 minute yoga classes
- Home yoga practice on non-class days
Participants had improvements in several gait parameters (step length, stride length, stride velocity, walking velocity, and double limb support time) after the intervention, but persistence at 4-week follow-up was inconsistent.

Evidence-Based Recommendations for Patients with HIV-related neuropathy

- **Recommended with reservations**
  - **Night splints** (based on a single RCT)
  - **Exercise** (based on expert opinion and extrapolation from research on pts with diabetic neuropathy)
  - **Combined Physical Therapy treatments** (soft tissue massage, joint mobs, stretching, microcurrent, and desensitization) (based on a single case series)
  - **Electro-acupuncture** (based on a single case series)
  - **Yoga** (based on a single case series with mixed findings)

Mortality and Lifespan

- People with HIV are living longer with the success of ART.
- In 2012, 40% of people living with HIV were greater than 50 years of age in the US. In 2015, 50% were greater than 50.
- Mortality rate has fallen and life expectancy has increased for people living with HIV.
- Despite these improvements, there is still a difference between the life expectancy of a HIV+ and HIV- individual.

Impact of Antiretroviral Therapy (ART)

- Antiretroviral Drugs or ART is a type of combination therapy that utilizes three or more drugs to treat HIV. This combination therapy is paramount because of HIV’s ability to multiply forming many copies that may possess mutations.
- This medical treatment does NOT cure HIV but will inhibit the growth of the virus.
- Hindering the growth of HIV will subsequently slow down the disease itself.

HIV+ individuals are at an Increased Risk of Comorbidities:

- Cardiovascular disease and stroke
- Osteoporosis and fracture
- Metabolic syndromes and diabetes mellitus
- Renal disease
- Neuropathy
- Malignancies
- Geriatric syndromes and frailty
Comorbidities in HIV Disease

Compared to the general population, PLWH have a 2-fold higher risk of CV disease, a 3-fold increased risk of fracture, and a risk of kidney disease that is comparable to that in diabetes.

(Van Epps et. al, 2017)

Frailty in HIV

Frailty is recognized by a decrease in the ability to perform basic day to day activities and a reduced functional capacity.

- Encompasses physical weakness and increased vulnerability because of increased age.
- Negative consequences include: increased hospitalization risk, increased risk of falling, depression, and a decreased ability for self-care.
- Frailty entails multiple negative health outcomes, affects more women than men, and is linked with people of lower income and those who are in current poor health conditions.
- Present in 4-10% of all PLWH patients and about 50% of PLWH over the age of 50.

(Van Epps, Overton, and Saag, 2016)

Frailty and Fall Risk

- Used a 4-m walk, grip strength, and self-reported weight loss, exhaustion, and low physical activity and classified into 3 categories based on their results: frail, pre-frail, and non frail.
- Aging HIV-infected pre-frail and frail individuals are at significantly increased risk of falls.
- Incorporation of frailty assessments or simple evaluations of walk speed or grip strength in clinical care may help identify individuals at greatest risk for falls.
- Peripheral neuropathy further increases fall risk among frail persons, defining a potential target population for closer fall surveillance, prevention, and treatment.

(Niempapoulos et. al, 2007)

FRP

HIV infection is strongly correlated with the frailty-related phenotype (FRP)

HIV infection is associated with an earlier occurrence of a phenotype that resembles the phenotype of frailty in older adults without HIV infection.

(Dosquilbet et. al, 2007)

Impact on Cognitive Function

Frail individuals have higher risk of cognitive impairment; however, it is not known if early-onset frailty in those infected by HIV could also increase the risk of cognitive impairment.

(Zamudio et. al, 2017)

Further Research

- Phenotypes (dimensions of behavior, closely related to fundamental mechanisms, may be more informative than chronological age)
- Comorbid aging and cognitive aging, though other phenotypes (i.e., disability, frailty, accelerated aging, successful aging)
- Conclusions:
  - Phenotypes, comorbid aging and cognitive aging, are distinct from each other, yet overlapping
  - Associative relationships are the rule in HIV for comorbid and cognitive aging phenotypes
  - HIV behavioral interventions for both comorbid aging and cognitive aging have been limited.

(Stoff et. al, 2017)
Assessment and Early Intervention

- Emphasis on:
  - Early diagnosis and treatment
  - Prevention of comorbidities
  - Improvement of quality of life
- Management should increasingly focus on geriatric concerns.

Physical Therapy Interventions and Nutritional Considerations

Physiology of Frailty

- Cycle of Frailty – sarcopenia, decreasing metabolic rate and decreased total energy expenditure
- 1) molecular and genetic (mitochondria, genetics senescence, autophagy) 2) physiology (high IL-6, CRP, WBC clotting, angiotensin, glucose intolerance) 3) syndrome 4) outcomes
- Key stress response systems underlie vulnerability (inflammation, SNS, HPA axis and angiotensin system which relates to the inflammatory process
- IL-10 inflammation managed – without, age quicker with skeletal muscle and mitochondrial decline

Goals for Frailty Intervention

1. Target Specific biological processes that drive frailty (inflammation/RAS)
2. Prevent worsening chronic disease and functional decline

Clinical Scales to Assess Frailty

- Frailty Phenotype
- Edmonton Frail Scale
- Frailty Index
Dosage of Exercise, Medication & Nutrition

Total time spent for exercises should be prescribed to prevent adverse effects; however, it remains unclear what type of exercise, and at what dose, is most appropriate and feasible to treat and/or prevent frailty in older adults with HIV.

Polypharmacy (5+ medications) has been shown to increase frailty in HIV-negative populations. This finding suggests that ART medication could contribute to the development of fragility but further research is needed to confirm this relationship.

Alterations to dietary factors have only been studies in a limited amount of clinical trials. Nutrition effectiveness to address frailty in the context of HIV infection remains unknown.

(Willig, Overton, and Saag, 2016)

Exercise & Neurocognitive Function

- 80 HIV+ subjects ages 50-79
- Neurocognitive & physical activity assessments
- Findings:
  - Moderate physical activity is associated with less executive dysfunction among older HIV+ adults
  - Physical activity may directly impact frontal systems (e.g., neurogenesis), or may work indirectly via reduction of risk factors for neurocognitive impairment (e.g., vascular comorbidities)

(Fazeli et al., 2015)

Aerobic and Resistance Exercise in Men with HIV

- A 2006 study by Fillipas et al, examined the effects of supervised, aerobic and resistance exercise, twice weekly, in men living with HIV over a 6 month period
- At the end of six months, the experimental group had improvements in self-efficacy, in cardiovascular fitness, and in 2 dimensions of QOL

(Filipas et al., 2006)

Progressive Resistive Exercise

- A 2008 systematic review reported that PRE or a combination of PRE and aerobic exercise may lead to statistically significant increases in body weight and arm and thigh girth.
- Notes progressive resistive exercises appears to be safe and may be beneficial for medically-stable adults living with HIV.

(O'Brien, Tyanan, and Glazier, 2008)

Aerobic Exercise

- Concerns about aerobic exercise increasing the body's metabolic rate and thus increasing additional muscle loss can be overcome with a balanced high-calorie diet and incorporating a sound nutritional program.
- The key determinant of weight loss in HIV infection-related wasting they concluded was reduced energy intake, not increased energy expenditure.
Nutrition

• Proper caloric intake must set the standard for each type of exercise to meet the energy expenditure required for the activity.

Nutrition

• WHO recommendations on micronutrient requirements:
  – Balanced, healthy diet is strongly encouraged
  – Intake of micronutrients at RDI may be insufficient to correct nutritional deficiencies
  – Evidence shows some supplements, vitamin A, zinc, and iron, can have adverse effects in people infected with HIV/AIDS
  – Safe upper limit of daily intake micronutrients has not been defined

(Polo et. al., 2007)

Nutrition Guidelines for People with HIV

• Most importantly, eat more because extra muscle weight will help individuals fight HIV.
• Eat starches, proteins and moderate amount of fats.
  – Proteins help build and maintain muscle.
  – Carbohydrates gives a person energy.
  – Fats provide extra energy.
• A moderate exercise routine will help the body turn food into muscle.
• Drinking plenty of fluids is another important factor.
  – Extra water can help reduce the side effects of medications.

(InfoNet, 2014)

Wasting, Obesity, and Frailty

The pathogenesis of poor nutrition in HIV-infected patients depends on caloric intake, intestinal nutrient absorption/translocation & resting energy expenditure, which are features seen in all chronic diseases.

Optimal nutrition is an important part of HIV care to support the immune system, limit HIV-associated complications as well as maintain better QOL and survival.

Patients with HIV have presented in three ways over the past 30 years as changes to diet have been altered: wasting syndrome, lipodystrophy and frailty.

(Mankal & Kotler, 2014)

Optimal Protein Intake

• An evidence-based study done by Bauer et al. shows that older population require more dietary protein than do younger populations.
• Increase in protein intake is paramount in maintaining proper function in activities and to mitigate various illnesses.
• The European Union Geriatric Medicine Society performed a review on dietary protein needs (>65):
  Recommended a range of 1.0-1.2 grams of protein per kilogram of body weight.
  Resistance and endurance exercises; however with increased physical activity there will need to be slightly higher protein intake levels.

(Bauer et al., 2013)

Case Study

Lena is a 70-year-old woman with end-stage renal disease (ESRD) from hypertension on dialysis, chronic obstructive pulmonary disease (COPD) on 2L oxygen with recurrent pulmonary Mycobacterium Avium Intracellulare (MAI) infection failing past therapies, coronary artery disease s/p stent placement 1 year prior with congestive heart failure (ejection fraction of 40%), right hip osteoarthritis and HIV well-controlled on ART. Patient is in your clinic with her daughter who is her health care proxy for a pre-operative assessment of an elective ventral hernia repair. The daughter tells you the surgeon mentioned that Lena looks frail and wants her optimized before the surgery.

Questions to Consider:
1. How do you determine if this patient is frail?
2. How is frailty different in HIV-infected individuals compared to the general population?
3. What is the effect of frailty on health outcomes?
Case Study Continued...

Lena lost 20 lbs in the past 3 months due to recurrent MAI infections in her lungs. She spends most of her time at home due to weakness and fatigue, except on dialysis days when she gets transported to the dialysis center. She is unstable on her feet and usually holds on to other people when she walks outside her apartment. Lena feels depressed due to her decline in health and her dependence on dialysis, although she denies suicidal or homicidal ideation. She does not have pain related to the hernia or her other medical conditions. On exam, her pulse was 78, BP 120/65, oxygen saturation 90% on 2L. Her 6MWT distance was 300m. Her albumin was 3.0 g/dL.

Questions to consider?
1. Is Lena frail? What frailty measure would you use to answer this question?
2. What would you do to optimize Lena for her upcoming surgery?
3. How would you counsel Lena’s daughter regarding the prognosis?

HIV Care Model: The Grady Ponce de Leon Center, Atlanta, GA

Grady Ponce de Leon Center
A Publicly Funded, Tertiary HIV Care clinic

Atlanta HIV cluster

- 60% of all PLH in Atlanta live in a 4-county radius
- Rate of HIV in the cluster is 1.34 % → World Health Organization’s description of a “generalized epidemic” (>1 %).
- More than 70% of HIV-infected patients who live in Atlanta live within two miles of the Ponce clinic

Future directions

- Multi-disciplinary collaboration to ensure that needs of this diverse population are met.
  - Palliative care model
- HIV management in primary care
- HIV Prevention and screening at all life stages
  - PrEP
  - Screening older patients for sexual health-related risks
- National study: adults > age 50 at risk for HIV are 80% less likely to be tested for HIV than younger people
Future directions

• Continued vaccine research
• More federal research/funding
  — Effects of stigma on physical/emotional health
  — Effects of ARV on aging adults
  — Effects of HIV on aging adults
• Public health campaigns targeting older adults and minority MSM for prevention, screening and interventions
• Treatment of long-term effects of HIV by multidisciplinary teams including rehab medicine/PT

References