



Canada's source for  
HIV and hepatitis C  
information

La source canadienne  
de renseignements sur  
le VIH et l'hépatite C

## CATIE-News

CATIE's bite-sized HIV and hepatitis C news bulletins.

### **Frailty, nerve injury and falls in middle-aged and older HIV-positive people**

12 September 2017

More HIV-positive people are living longer thanks to the use of potent combination anti-HIV therapy (ART). As HIV-positive people enter their middle age and senior years, they will have to grapple with one or more aging-related issues. One issue that can have a large impact on the health and quality of life of older people is falling. Older people who fall can injure themselves, and according to U.S. researchers, such injuries can make pre-existing problems, such as physical inactivity or weakness, worse.

Some studies with middle-aged and older HIV-positive people suggest that being frail and physically impaired are relatively common. One study found that HIV-positive adults whose average age was 52 years were at a similar risk of falling as HIV-negative adults 65 years or older.

#### **The present study**

In a U.S. study code-named ACTG A5322 researchers enrolled more than 900 middle-aged and older HIV-positive people to study their health. One report that emerged from this research concerns frailty and falling. The researchers found that frailty was uncommon, occurring in 6% of participants. However, nearly 40% of participants were becoming physically weaker and labelled as "pre-frail" by the researchers.

Statistical analysis found that people who were frail or pre-frail were at increased risk of falling. People who were frail and had injured nerves in their feet/legs (peripheral neuropathy) were also at elevated risk for falling.

The study underscores one aspect of aging and that some HIV-positive people, even in middle age, will need screening for factors linked to an increased risk for falls.

#### **Study details**

Researchers enrolled participants from across the U.S. between November 2013 and July 2014. Participants visited study clinics every six months where they were interviewed, completed questionnaires, underwent a physical exam and had blood drawn for analysis. Participants were also assessed for the presence of co-existing health conditions and, in particular, neurocognitive problems.

On average, participants were in their mid-50s; 80% of participants were men and 20% were women.

Researchers defined falls as "an unexpected event in which the individual loses their balance and lands on the floor, ground or at a lower level and/or hits an object." The researchers did not count falls that occurred because of a stroke or because a person was pushed or shoved.

The researchers used a validated method of assessing frailty that included the following:

- the strength of a person's grip (using a dynamometer)
- how fast or slow they walked for a distance of four metres (this is called gait speed)
- self-reported unintentional weight loss
- self-reported exhaustion
- self-reported limitations in various physical activities

## Results—Falls

Researchers analysed data collected from 967 people and found that 174 people (18%) had at least one fall in the past year. The distribution of falls was as follows:

- 106 people (11%) – one fall in the past year
- 68 people (7%) – more than one fall in the past year

Among the 174 people who fell, 21% sought medical help as a result of falling. About 5% were found to have at least one broken bone.

## Frailty

After assessing all study participants for frailty, here is what the researchers found:

- 55% were non-frail
- 39% were pre-frail
- 6% were frail

The distribution of frailty and falls was as follows:

- among non-frail people – 12% fell at least once in the past year
- among pre-frail people – 22% fell at least once in the past year
- among frail people – 49% fell at least once in the past year

Researchers found that participants with weak grip strength were more likely to have recurring falls than people without weak grip strength.

Also, participants who walked slowly were more likely to have had recurrent falls than people who walked at a normal pace.

## Peripheral neuropathy (PN)

People with HIV can develop injured nerves in their feet, legs and hands. There are many reasons PN can occur, including the following:

- HIV-related reasons: Experiments with monkeys infected with a virus closely related to HIV called SIV (simian immunodeficiency virus) have found that monkeys can develop nerve injury because of proteins produced by SIV-infected cells. So it is very likely that proteins produced by HIV-infected cells can cause inflammation and injury in susceptible nerve cells, leading to PN in people with HIV. Furthermore, some studies have found that high viral loads are associated with an increased risk for PN.
- past use of one or more of a group of older anti-HIV drugs called “D-drugs”—ddC (zalcitabine, Hivid), ddI (didanosine, Videx, Videx EC) and d4T (stavudine, Zerit). Although the use of D-drugs is no longer recommended by treatment guidelines in high-income countries, PN can be a lingering legacy of exposure to this group of medicines.
- co-infection with a common member of the herpes virus family – CMV (cytomegalovirus)
- type 2 diabetes
- deficiency of vitamin B<sub>12</sub>
- excessive exposure to alcohol
- shingles (herpes zoster)
- impaired thyroid gland functioning
- exposure to some antibiotics used for treating TB

After assessing participants, researchers found that 39% (373 people) had PN. Furthermore, the researchers stated that people who were frail and who had PN “were significantly more likely to experience falls than non-frail people.”

In general, researchers did not find evidence that other co-existing conditions, including neurocognitive impairment, had any significant impact on frailty and falls.

[A previous U.S. study](#) with about 650 HIV-positive women also found a link between the presence of PN and an increased risk of falls.

CATIE's [Practical Guide to HIV Drug Side Effects](#) has a section on PN that has useful options to consider.

## Points to consider

This study confirms that HIV-positive people who have some degree of frailty (that is, they were frail or pre-frail) are at increased risk for falling.

Two standardized and measurable aspects of frailty—strength and slow pace of walking (slow gait speed)—were significantly linked to an increased risk for falling.

It is possible that the participants in this study may not be reflective of patients that doctors see in clinics. This possibility arises because the researchers stated that many of the people who entered the present study had a history of volunteering for HIV-related clinical trials. Nevertheless, it is possible that some HIV-positive people outside of this study are at increased risk for frailty and falls.

## Advice from researchers

Based on the results of their study, the researchers encourage doctors and nurses to incorporate simple evaluations of frailty, such as grip strength and gait speed, as possible ways of identifying their HIV-positive patients at heightened risk for falling. Patients with this risk can then be given education to help prevent falls. Also, the researchers noted that HIV-positive people with PN might also need screening for their risk for falls.

## Bear in mind

The present study has uncovered two aging-related issues affecting HIV-positive people: frailty and falls. These problems are traditionally seen in elderly HIV-negative people but in the present study they occurred in some middle-aged HIV-positive people.

## An aging epidemic

Research suggests that by the early 1970s HIV had arrived in North America and its spread eventually led to the appearance of the first recognized cases of AIDS in 1981. HIV-positive people who survived that era are now well over the age of 50.

In several studies, despite the use of ART for many years with excellent adherence, researchers have found that HIV still persists in lymphatic tissues of participants and causes ongoing inflammation and activation of the immune system. This ongoing immune activation and inflammation may make some HIV-positive people more susceptible to aging-related complications. Therefore, researchers need to continue to engage in research with aging HIV-positive people to find ways to help them enter middle and old age with good quality of life.

—Sean R. Hosein

## Resources

[Factors linked to falling in HIV-positive women](#) - CATIE News

[Nerve pain and numbness](#) from *A Practical Guide to HIV Drug Side Effects*

[Unravelling the complexity of HIV and fatigue](#) - CATIE News

["America's other drug problem: Giving the elderly too many prescriptions"](#) - *Washington Post*

[Emerging issues in older HIV-positive people](#) - *TreatmentUpdate* 214

[Older people with HIV face different long-term health challenges](#) - CATIE News

[Denmark—unexpected trends in use of psychotropic medicines](#) - *TreatmentUpdate* 204

[Impressive gains in survival for older people with HIV but still less than general population](#) - *CATIE News*

[Danish study raises questions about accelerated aging in HIV](#) - *CATIE News*

[Quantification of biological aging in young adults](#) - *Proceedings of the National Academy of Science USA*

[Management of Human Immunodeficiency Virus Infection in Advanced Age](#) - *Journal of the American Medical Association*

[Long-term HIV infection and health-related quality of life](#) - *CATIE News*

[Dutch doctors explore intersection of aging and HIV](#) - *CATIE News*

[Geriatric syndromes found to be common among some people with HIV](#) - *CATIE News*

[HIV and Aging: State of Knowledge and Areas of Critical Need for Research. A Report to the NIH Office of AIDS Research by the HIV and Aging Working Group](#)

[The CIHR Comorbidity Agenda](#) - Canadian Institutes of Health Research (CIHR)

[CIHR's HIV Comorbidity Research Agenda: Relevant Research Areas](#)

[HIV and aging](#) - Healthy living tips for people 50 and over living with HIV

[Mental Health](#) from *HIV in Canada: A primer for service providers*

[HIV and brain-related issues](#) - *TreatmentUpdate* 204

[Longer life expectancy for HIV-positive people in North America](#) - *TreatmentUpdate* 200

[Factsheets on HIV and aging in Canada](#) - Canadian AIDS Society

[HIV & Aging: A 2013 Environmental Scan of Programs and Services in Canada - Community Report](#) - realize (formerly the Canadian Working Group on HIV and Rehabilitation - CWGHR)

[Directory of Promising Programs and Services for Older People Living with HIV in Canada](#) - realize

[Evidence-informed recommendations for rehabilitation with older adults living with HIV: a knowledge synthesis](#) - *BMJ Open*

#### REFERENCES:

1. Tassiopoulos K, Abdo M, Wu K, et al. Frailty is strongly associated with increased risk of recurrent falls among older HIV-infected adults: a prospective cohort study. *AIDS*. 2017; *in press*.
2. Amato AA, Barohn RJ. Chapter 459. Peripheral neuropathy. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson J, Loscalzo J. eds. *Harrison's Principles of Internal Medicine*, 19e. New York, NY: McGraw-Hill; 2015.
3. Lichtenstein KA, Armon C, Baron A, et al. Modification of the incidence of drug-associated symmetrical peripheral neuropathy by host and disease factors in the HIV outpatient study cohort. *Clinical Infectious Diseases*. 2005 Jan 1;40(1):148-57.
4. Malvar J, Vaida F, Sanders CF, et al. Predictors of new-onset distal neuropathic pain in HIV-infected individuals in the era of combination antiretroviral therapy. *Pain*. 2015 Apr;156(4):731-9.
5. Ellis RJ, Rosario D, Clifford DB, et al. Continued high prevalence and adverse clinical impact of human immunodeficiency virus-associated sensory neuropathy in the era of combination antiretroviral therapy: the CHARTER Study. *Archives of Neurology*. 2010 May;67(5):552-8.
6. Hitchcock SA, Meyer HP, Gwyther E. Neuropathic pain in AIDS patients prior to antiretroviral therapy. *South African Medical Journal*. 2008 Nov;98(11):889-92.
7. Yuan SB, Shi Y, Chen J, et al. Gp120 in the pathogenesis of human immunodeficiency virus-associated pain. *Annals of Neurology*. 2014 Jun;75(6):837-50.
8. Dorsey JL, Mangus LM, Hauer P, et al. Persistent peripheral nervous system disease in simian immunodeficiency virus-infected macaques receiving antiretroviral therapy. *Journal of Neuro pathology and Experimental Neurology*. 2015 Nov;74(11):1053-60.

9. Worobey M, Watts TD, McKay RA, et al. 1970s and 'Patient 0' HIV-1 genomes illuminate early HIV/AIDS history in North America. *Nature*. 2016 Nov 3;539(7627):98-101.
10. Faria NR, Rambaut A, Suchard MA, et al. HIV epidemiology. The early spread and epidemic ignition of HIV-1 in human populations. *Science*. 2014 Oct 3;346(6205):56-61.
11. Lorenzo-Redondo R, Fryer HR, Bedford T, et al. Persistent HIV-1 replication maintains the tissue reservoir during therapy. *Nature*. 2016 Feb 4;530(7588):51-56.
12. Folkvord JM, Armon C, Connick E. Lymphoid follicles are sites of heightened human immunodeficiency virus type 1 (HIV-1) replication and reduced antiretroviral effector mechanisms. *AIDS Research and Human Retroviruses*. 2005 May;21(5):363-70.
13. Kline C, Ndjomou J, Franks T, et al. Persistence of viral reservoirs in multiple tissues after antiretroviral therapy suppression in a macaque RT-SHIV model. *PLoS One*. 2013 Dec 18;8(12):e84275.
14. Fletcher CV, Staskus K, Wietgreffe SW, et al. Persistent HIV-1 replication is associated with lower antiretroviral drug concentrations in lymphatic tissues. *Proceedings of the National Academy of Sciences USA*. 2014 Feb 11;111(6):2307-12.
15. Khoury G, Fromentin R, Solomon A, et al. Human immunodeficiency virus persistence and T-cell activation in blood, rectal, and lymph node tissue in human immunodeficiency virus-infected individuals receiving suppressive antiretroviral therapy. *Journal of Infectious Diseases*. 2017 Mar 15;215(6):911-919.
16. Hong JJ, Silveira EL, Amancha PK, et al. Early initiation of antiretroviral treatment post SIV infection does not resolve lymphoid tissue activation. *AIDS*. 2017 Aug 24;31(13):1819-1824.

## Produced By:



Canada's source for  
HIV and hepatitis C  
information

555 Richmond Street West, Suite 505, Box 1104  
Toronto, Ontario M5V 3B1 Canada  
Phone: 416.203.7122  
Toll-free: 1.800.263.1638  
Fax: 416.203.8284  
www.catie.ca  
Charitable registration number: 13225 8740 RR

## Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to ensure they have the most current information. Users relying solely on this information do so entirely at their own risk. Neither CATIE nor any of its partners or funders, nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. Any opinions expressed herein or in any article or publication accessed or published or provided by CATIE may not reflect the policies or opinions of CATIE or any partners or funders.

Information on safer drug use is presented as a public health service to help people make healthier choices to reduce the spread of HIV, viral hepatitis and other infections. It is not intended to encourage or promote the use or possession of illegal drugs.

## Permission to Reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: *This information was provided by CATIE (the Canadian AIDS Treatment Information Exchange). For more information, contact CATIE at 1.800.263.1638.*

© CATIE

Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

Available online at:  
<http://www.catie.ca/en/catieneews/2017-09-12/frailty-nerve-injury-and-falls-middle-aged-and-older-hiv-positive-people>