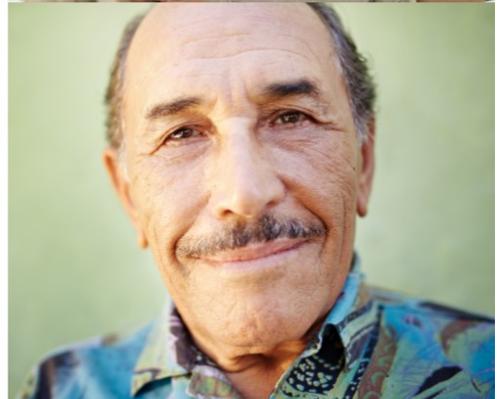


AGING HIV & LONG-TERM SURVIVORS

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Oregon
Health
Authority



Introduction

More than 30 years into the HIV epidemic, scientific and clinical advances have helped HIV-infected individuals live longer — most people living with HIV (PLWH) in the United States now die of diseases not specifically related to HIV. However, diseases of aging typically occur in HIV-infected individuals at higher rates and at younger ages than in the general population. This may have negative impacts on the quality of life of older PLWH. HIV-infected individuals who were diagnosed before the advent of highly active antiretroviral therapy in 1996 — a group often referred to as long-term survivors — may be more likely to experience accelerated aging because of longer exposure to the virus and its treatment, in addition to issues they experience by simply being older. This white paper summarizes research on the health and social challenges and opportunities for older people living with HIV (many of whom are also long-term survivors) and provides a description of older PLWH in Oregon.

Aging with HIV/AIDS

With the success of antiretroviral medications (ART), PLWH are living longer than ever before. In addition, improved screening methods have helped to identify more new cases of HIV in older adults.¹ Both of these factors have contributed to a growing population of PLWH over the age of 50. Additional facts:

- Survival rates continue to improve for PLWH, with life expectancies among PLWH who are successfully treated with ART approaching those of HIV negative people.²

- Deaths among PLWH are increasingly related to tobacco use, hypertension, diabetes, and liver-related causes—risk factors which often can be controlled through behavior change or medication.³
- In Oregon, as in the U.S., over 50% of PLWH are 50 and older; the average age of people living with HIV in Oregon is now 49 years.^{4,5}
- More than 10% of PLWH worldwide are 50 and older.⁶

Many older PLWH are part of a group known as long-term survivors (LTS). LTS are typically defined as those who have been living with HIV for more than 10 years and/or who were diagnosed prior before the advent of highly active antiretroviral therapy (i.e., 1996). In Oregon, nearly a quarter of PLWH were diagnosed before 1996. Although not all LTS are older adults – for example, people now in their 20s and 30s who acquired HIV at birth – when this white paper focuses on LTS, we refer to those age 50 and older.

Acceleration of the Aging Process with HIV

Older PLWH face many of the same health challenges as older individuals not infected with HIV. But many people with HIV experience at earlier ages the geriatric syndromes, immune changes, and inflammatory markers typically found in much older adults.⁷

Specific studies have found that HIV is associated with higher rates of:^{8, 9}

- Frailty
- Osteoporotic bone fractures
- Diabetes
- Hyperlipidemia
- Lipodystrophy
- Cardiovascular disease
- Cancer
- Liver disease
- Renal failure
- Anemia
- Neurocognitive disorder

A growing body of research has identified the many biological mechanisms through which HIV infection may accelerate the aging process. These include:^{10, 11, 12, 13, 14, 15, 16}

- Genetic instability
- Telomere shortening
- Epigenetic alterations
- Impaired homeostasis
- Deregulated nutrient sensing
- Mitochondrial dysfunction

- Cellular senescence
- Stem cell exhaustion
- Altered intercellular communication
- Abnormal endocrine and neuroendocrine signaling
- Immune dysregulation
- Chronic inflammation
- Oxidative stress
- Abnormal brain atrophy

Still, the extent to which the virus and its treatment is responsible for accelerated aging is yet to be fully understood. PLWH also tend to have higher rates of other risk factors for disease and accelerated aging, such as tobacco use, alcohol use, recreational and illicit drug use, and Hepatitis B and C infection.^{17, 18} In addition, many PLWH lack access to factors that can promote health, like stable housing, sufficient income, and enough food to eat (factors often referred to collectively as the social determinants of health). In general, PLWH experience a higher prevalence of homelessness, social isolation, stigma, discrimination, and psychological factors such as toxic stress/AIDS Survivor Syndrome (a disorder similar to post-traumatic stress disorder [PTSD]) – all of which may further contribute to poor physical and mental health.¹⁹ Although some studies do account for these factors, it's difficult to determine cause and effect.^{20, 21}

Age, Time Living with HIV, Health and Well-Being

Because the HIV virus and its treatment can impair biological function, it is reasonable to think that living with HIV longer may be associated with worse health outcomes, and that LTS would be more likely to suffer these consequences than non-LTS.* In addition, LTS are often older than non-LTS. How do we disentangle the effects of aging from the effects of long-term HIV infection?

First, not all aspects of aging result in poor health. A large body of research has found that older adults tend to have higher resilience than younger adults, which acts as a protective factor against disability, chronic illness, depression, and health-related quality of life.^{22, 23, 24, 25} In addition, studies show that PLWH experience protective factors, such as continuity and quality of medical care²⁶ and psychosocial factors, such as coping, acceptance, resilience, hardiness, spirituality, and social support^{27, 28, 29, 30, 31} that may reduce the impact of the adverse health consequences. None of these studies, however, specifically compared older LTS to older non-LTS.

To examine how resilience relates to older age and time living with HIV, and how these factors contribute to various outcomes, McGowen and colleagues examined self-reported resilience and physical and mental well-being in adults with and without HIV.³² Specifically, they separated the effects of advanced age from length of time diagnosed with HIV to see how much resilience people had and how resilience related to

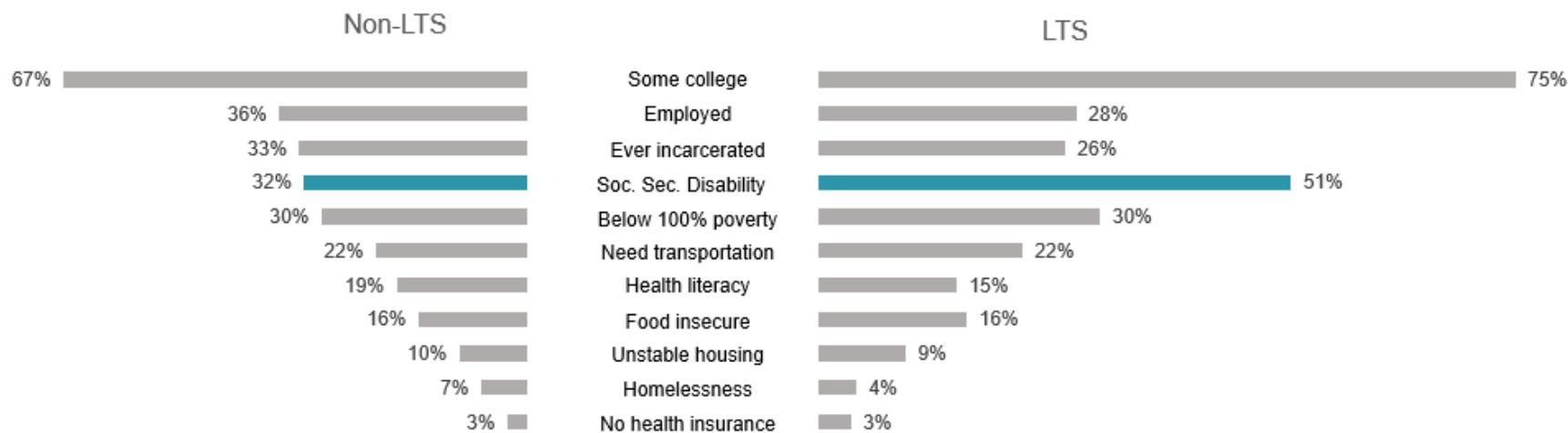
* There is an exception: older adults recently diagnosed with HIV are more likely to have less viral suppression that may result in poorer health outcomes because of compromised immune function associated with aging. (See: Guaraldi G, Zona S, Brothers TD, et al. Aging with HIV vs. HIV seroconversion at older age: a diverse population with distinct comorbidity profiles. *PLoS One*. 2015 Apr 13;10(4): e0118531. Althoff KN, Gebo KA, Gange SJ, et al. CD4 count at presentation for HIV care in the United States and Canada: are those over 50 years more likely to have a delayed presentation? *AIDS Res Ther*. 2010;7:45. The Lancet HIV editorial. 2017; 4:e277.

depression, anxiety, and functional status. They found that among PLWH, older age and shorter time with diagnosed HIV were associated with higher levels of resilience and lower levels of anxiety, depression, and functional limitations. Being diagnosed with HIV longer was associated with lower resilience scores and increased functional problems. In an earlier study, McGowen and colleagues also found that length of HIV diagnosis, rather than age, was related to higher symptom distress, depression, anxiety, and functional limitations.³³

The Oregon Experience

In Oregon, we looked at data from the HIV Medical Monitoring Project (MMP) to compare the health and social experiences of LTS and non-LTS. (Refer to Appendix 1 for a description of MMP methods). We controlled for the effects of aging by limiting our comparison to PLWH aged 50 and older. There were no significant differences between the groups by age, race (white vs. all other), gender, or sexual orientation. Figures 1-6 below compare additional health and social factors between the two groups. Factors for which there were significant differences are highlighted. A complete list of factors with p-values is provided in Appendix 2.

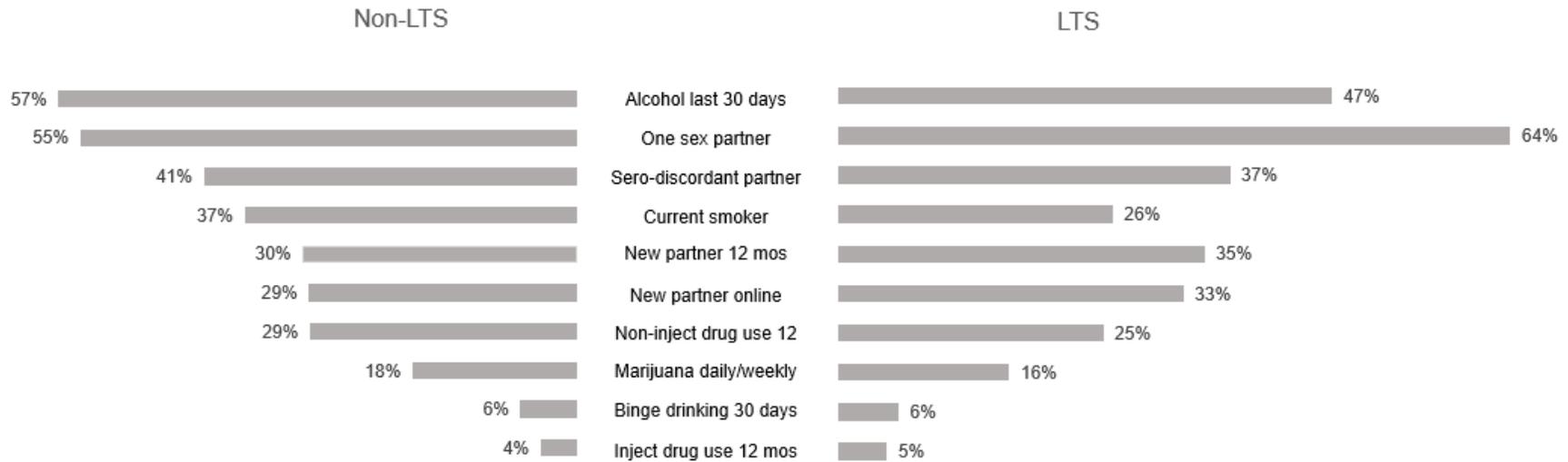
Figure 1. Comparison of demographic and social factors between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276



Key Finding: The proportion of LTS receiving Social Security Disability benefits was significantly higher than for non-LTS. There were no other significant differences.

Note: Some college=some college or higher; Need transportation=needed transportation services; Health literacy= somewhat/little bit/not a bit confident in filling out medical forms by yourself; Food insecure= often/sometimes true that "the food (I/we) bought didn't last and (I/we) didn't have money to get more" in the previous 12 months; Unstable housing= past-year experience of homelessness and/or 2 or more past year moves; Homelessness= past-year experience of homelessness; No health insurance= not having any health insurance/coverage at any time during the past 12 months.

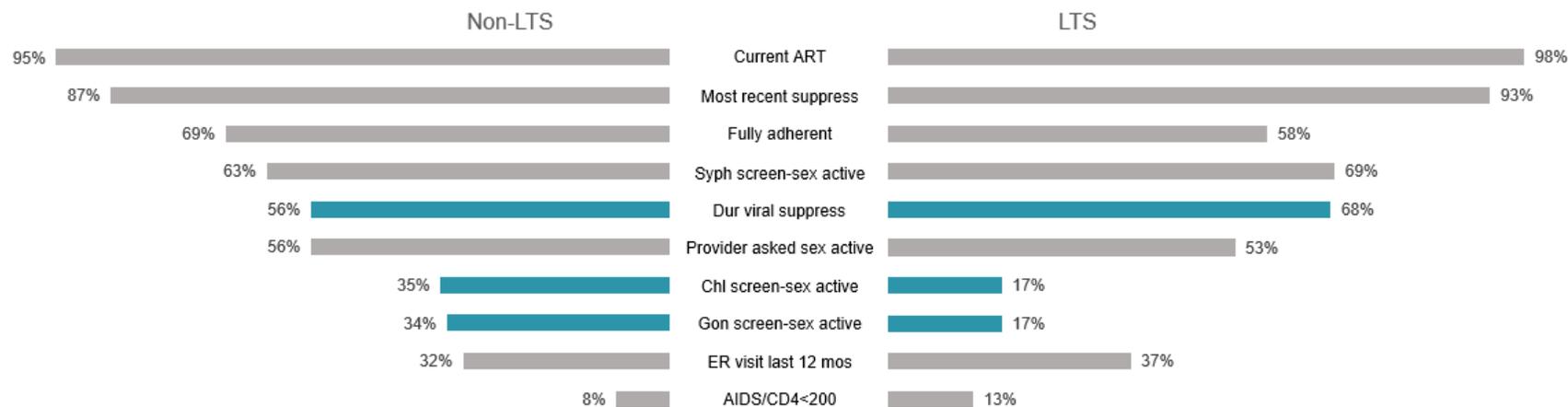
Figure 2. Comparison of health behaviors between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276



Key Finding: There were no significant differences in health behaviors between LTS and non-LTS.

Note: One sex partner=one past-year sex partner among sexually active; Sero-discordant partner=past-year condomless sex with a partner of negative or unknown HIV status among sexually active; New partner 12 mos=new sex partner in past year among sexually active; New partner online=met new past-year sex partner at a public venue or online; Non-inject drug use 12=past-year non-injection drug use, including marijuana.

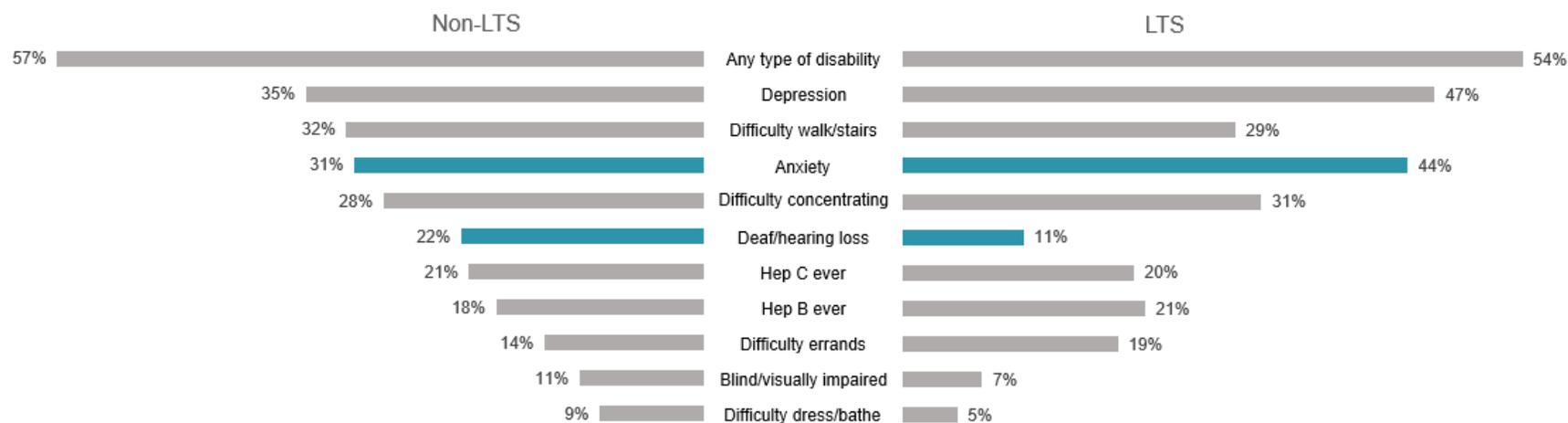
Figure 3. Comparison of clinical characteristics and health care utilization between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276



Key Findings: LTS were significantly less likely to receive screening for some sexually transmitted infections, but a higher proportion of LTS achieved durable viral suppression compared to non-LTS. The average number of annual outpatient visits (not shown) was 3.4 for non-LTS and 3.5 for LTS, and there were no significant differences in other important markers of care, such as use of antiretroviral therapy, hospital visits, or satisfaction with HIV medical care.

Note: Most recent suppress=last viral load <200 copies/ml; Fully adherent= did not miss a dose of ART past 30 days; Syph screen-sex active= past-year syphilis screening among sexually active; Dur viral suppress=at least 2 past-year tests and all viral loads <200 copies/mL; Provider asked sex active= HIV provider asked if sexually active; Chl screen-sex active= past-year chlamydia screening among sexually active; Gon screen-sex active=past-year gonorrhea screening among sexually active; ER visit last 12 mos=any past year visit to ER for own health reason; AIDS/CD4<200=lowest past-year CD count <200.

Figure 4. Comparison of physical and mental health between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276

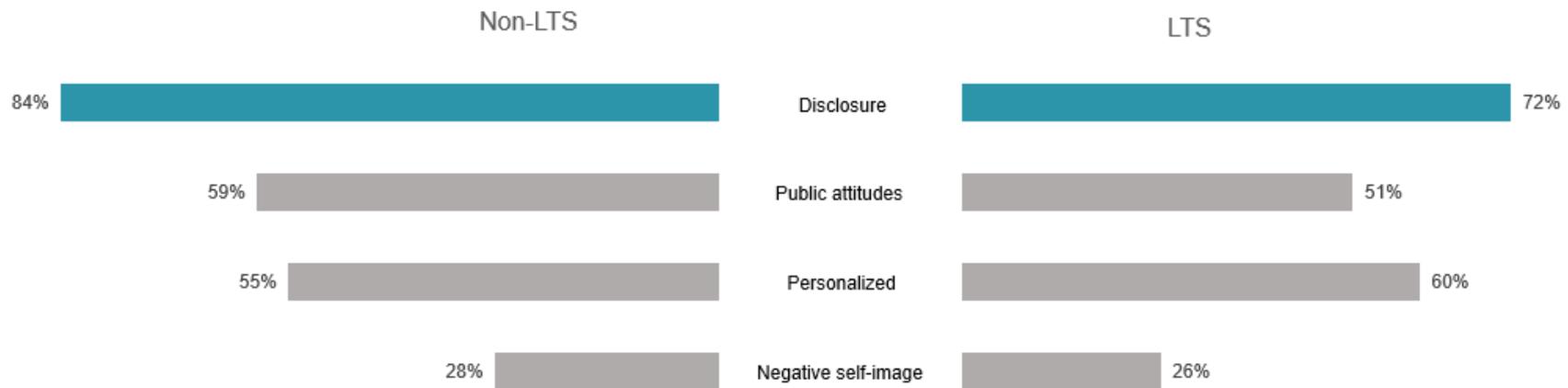


Key Findings: LTS were significantly more likely than non-LTS to experience anxiety. There were also significant differences in self-reported hearing loss. The average number of disabilities (not shown) was 1.2 for non-LTS and 1.0 for LTS.

Note: Any type of disability= a tally of any of the six types of disabilities (i.e., deaf/hearing loss, blind/visually impaired, and difficulty walking/stairs, concentrating, errands, and dress/bathe); Depression=diagnosis or treatment for depression; Anxiety=diagnosis or treatment for anxiety; Hep C ever=self-reported history of hepatitis C infection; Hep B ever=self-reported history of hepatitis B infection.

Figure 5a. Comparison of stigma between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276

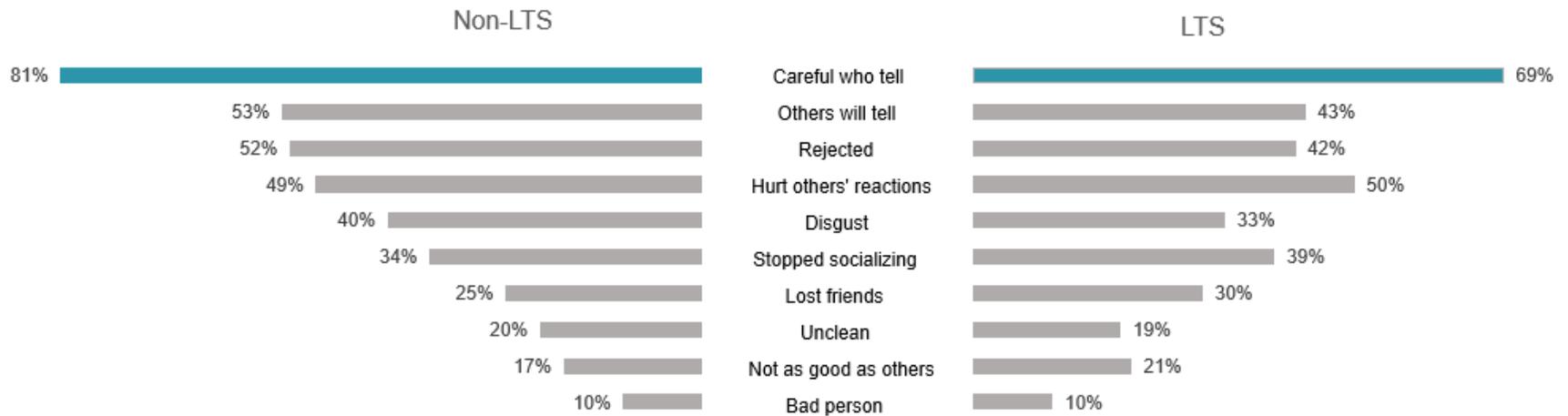
Responses to questions about stigma were grouped into four categories: personalized stigma (hurt by how people reacted, stopped socializing because of others’ reactions, and/or lost friends by telling about HIV status); disclosure stigma (careful who you tell about HIV status, worry people who know will tell others); negative self-image stigma (feel not as good as others, feel unclean, feel like you are a bad person); and public attitudes stigma (perceptions that others think that a person with HIV disgusting and/or that people with HIV are rejected).



Key Finding: A significantly higher proportion of non-LTS reported disclosure stigma—that is, they were more likely to express concerns about sharing their HIV status with others.

A detailed breakdown of the stigma items within in each of the four categories is shown below:

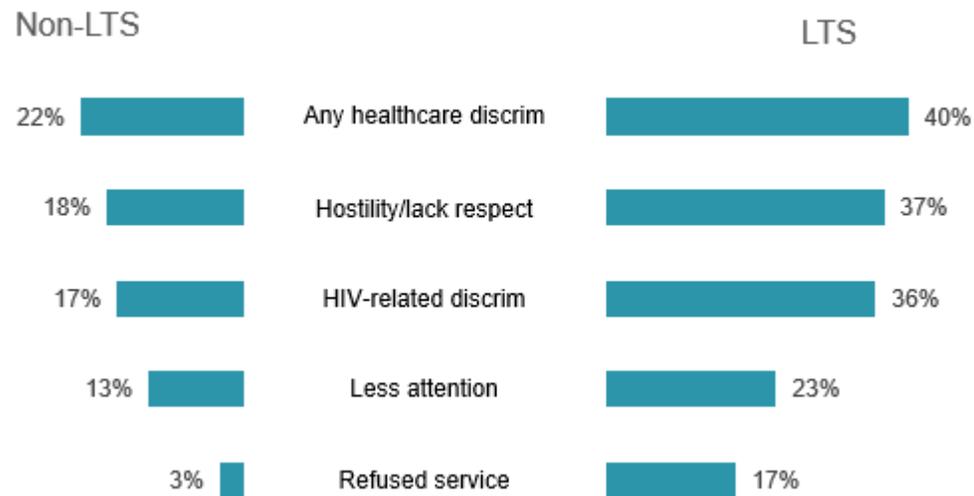
Figure 5b. Comparison of stigma between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276



Key Findings: Significantly higher proportions of non-LTS reported feeling the need to be very careful who they tell about their HIV status. The average stigma score for LTS was 36.6, which was not significantly different than the score of 40.9 for non-LTS.

Figure 6. Comparison of discrimination between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276

MMP collects data on participants' experiences of perceived discrimination within the health care setting. The question asks: "People with HIV sometimes sense discrimination from healthcare providers in different ways. Has anyone in the healthcare system done any of the following to you since testing positive for HIV: exhibited hostility or a lack of respect toward you; given you less attention than other patients; or refused you service?" For those who answered yes to any of those questions, a follow-up question asks, "Did the discrimination occur because of your HIV infection?"



Key Findings: Significantly higher proportions of LTS reported healthcare discrimination since testing HIV positive. There were no differences between LTS and non-LTS for reports of discrimination for demographic reasons; however, significantly higher proportions of LTS reported HIV-related discrimination in the health care setting.

Summary

The demographics of PLWH are shifting, with ever higher proportions of the population age 50 and above. Many PLWH over 50 are long-term survivors, who experienced decades of accumulated trauma as the HIV epidemic unfolded. Many have wondered if LTS possess specific characteristics that helped them survive while so many others died. Because chronological age is a confounding factor for health and well-being for older PLWH, we “removed” the effect of age, comparing people age 50 and older, by LTS status.

Mostly, we found no differences between the groups, although there were a few exceptions. The main difference was that LTS were more likely to report depression and anxiety than those more recently diagnosed. This finding supports the common wisdom of many long-term survivors, who describe a host of psychological symptoms that include depression and anxiety—but also lack of future orientation, survivor’s guilt, numbness and other symptoms. This group of symptoms has been dubbed AIDS Survivor Syndrome by Tez Anderson, founder of grassroots activist organization, Let’s Kick A*S*S.³⁵

Other differences also seemed related to historical experience; that is, whether one lived through the early years of the epidemic, when HIV was more stigmatized and survival more uncertain. Specifically, LTS were more likely to receive Social Security Disability Insurance benefits and to report ever having experienced discrimination in the health care setting. They were also less likely to report worrying about HIV status disclosure now.

Finally, LTS were less likely to receive STI screenings than more recently diagnosed people over 50. STI screenings, though recommended annually for PLWH, are low

overall in Oregon.³⁶ More recently diagnosed people may be more likely to receive all preventive care and recommended screenings, as they are newer to HIV medical care.

Although we are unable to determine causality with cross-sectional data, none of these characteristics would seem to specifically promote survival. Beginning in 2018, the Oregon Medical Monitoring Project added items to the survey related to resilience, social support, and social connectivity to identify whether any of these factors may be related to long-term survivorship.

Aging is inevitable – but aging in the presence of HIV is more complicated, generally involving more comorbidities and a more rapid decline than observed in the general population. Assessment of aging-related health and functional impairment at younger ages combined with addressing modifiable risk factors, like alcohol, tobacco, and other drug use, may help slow the aging process.

Limitations

- We did not have a measure of resilience in the 2015-17 data but added one in 2018. We did examine measures of discrimination and stigma that may be related to resilience and coping.
- We limited our analysis to the population of PLWH over age 50 to control for the effects of aging among LTS and non-LTS. Age 50 as a cut point is consistent with other studies in the HIV and aging literature and seemed conceptually sound, since PLWH experience the effects of aging at younger ages than in the general population. We did not limit our analysis to an older age group (e.g., 65+) because of small numbers which would have limited our ability to conduct statistical comparisons between LTS and non-LTS groups.

- Although we did not compare health and aging-related factors to the non-HIV population of older adults in Oregon, the literature provides substantial evidence for these differences.
- Our study used cross-sectional data, which means we were unable to determine a causal relationship between advancing age and health and social factors.

Future Study

Starting in 2018, the data will include a measure of resilience that will augment responses to survey questions about social connection and isolation, discrimination, and stigma. We will continue to explore differences between LTS and non-LTS using these new questions. In addition, we may be able to combine additional years of data to generate a larger sample of older PLWH to allow for analysis of adults in different stages of older adulthood, such as age 50-60, 60-70, and >70 years.

APPENDIX 1

Methods

We used data from the HIV Medical Monitoring Project (MMP), which produces nationally and locally representative data to assess the clinical and behavioral characteristics of adults with diagnosed HIV infection in medical care in the United States and Puerto Rico. MMP uses a complex survey sample selected in two consecutive stages: (1) United States and dependent areas and (2) adults with diagnosed HIV infection aged ≥ 18 years reported to the National HIV Surveillance System (NHSS) as of December 31st of the year preceding data collection. Oregon is one of 23 participating project areas and has participated since 2008.

Persons were eligible for participation if, as of the sampling date, they had received a diagnosis of HIV, were aged ≥ 18 years, alive, and a resident of an MMP project area. Sampled persons were presumed to be eligible based on their information in NHSS unless data from another source contradicted this status. Persons were classified into 4 categories: (1) eligible respondents, (2) contacted nonrespondents, (3) nonrespondents who were not contacted, and (4) ineligible persons. These categories were used in calculating final response rates and contact rates in accordance with standard formulas.

Data used to generate national estimates were weighted for the probability of selection based upon known probabilities of selection of states and individuals within states. In addition, data were weighted to adjust for nonresponse by using predictors of response, including sex, race/ethnicity, age of most recent contact information, transmission category, and the person's receipt of care as documented by laboratory test results in NHSS records.

For a complete description of sampling and weighting methods see the Centers for Disease Control and Prevention's 2018 *HIV Surveillance Special Report*.³⁴

For the comparisons between LTS and non-LTS in this report, we combined data from 2015, 2016 and 2017 and conducted statistical comparisons of proportions using chi-square tests or comparisons of means using t-tests in Stata v. 15.

A stigma score was calculated by summing the 10 individual stigma items. Each item was scored 0 to 4 based on the level of agreement/disagreement with the statement and then each score was multiplied by 2.5. The stigma score is the sum of scores on the 10-items, ranging from 0 (no stigma) to 100 (high stigma). The mean stigma score for LTS and non-LTS was compared using a t-test.

APPENDIX 2

Data Table

Comparison of demographic, physical health, mental health, and social factors between long-term survivor and non-long-term survivor PLWH aged 50 and older, Oregon MMP 2015-17, n=276

Factor	% Non-LTS (n=138) [†]	% LTS (n=138) [†]	p-value
Socio-demographics			
Mean age [§]	58.4 [‡]	59.6 [‡]	0.131
Race/Ethnicity			0.190
White, non-Hispanic	79.0	71.5	
Black, non-Hispanic	4.9	6.0	
Hispanic/Latino	10.4	10.2	
Native Hawaiian, non-Hispanic	0.9	0.0	
American Indian/Alaska Native, non-Hispanic	0.5	0.0	
Multiracial, non-Hispanic	4.2	12.2	
White/Minority group			
White, non-Hispanic	79.0	71.5	0.189
Minority group	21.0	28.5	
Gender			
Male	85.8	87.3	0.394
Female	12.5	12.7	
Transgender	1.7	0.0	
Sexual orientation			
Lesbian/gay	54.8	52.7	0.736
Bisexual	12.1	12.9	
Heterosexual	33.1	29.1	
Something else	0.0	5.4	
Employed	35.8	27.6	0.160
Social Security Disability recipient	32.2	50.8	0.003 ^A
Educational attainment			
High school or less	38.2	28.1	0.029 ^A
Some college or higher	61.8	71.9	
Social Determinants of Health			
Health literacy	18.8	14.7	0.377
Below 100% poverty guideline	29.7	30.2	0.932
Food insecure	15.6	15.8	0.969

Factor	% Non-LTS (n=138) [†]	% LTS (n=138) [‡]	p-value
No health insurance for any time past 12 months	2.7	3.3	0.731
Unstable housing	9.7	9.2	0.906
Homelessness	6.5	3.9	0.323
Need transportation services	21.8	21.8	0.995
Ever incarcerated	32.9	26.4	0.252
Clinical Characteristics/Health Care Utilization			
AIDS/Lowest CD4 <200 copies/mL past year	8.0	12.9	0.204
Durable viral suppression past 12 months	55.6	68.1	0.051 ^A
Most recent viral load <200 copies/mL	86.8	92.7	0.149
Average # outpatient visits to HIV provider	3.4 [¶]	3.5 [¶]	0.817
Currently taking ART	95.3	98.0	0.221
Fully adherent (0 days missed past 30 days)	68.9	58.3	0.276 ^{**}
Provider asked if sexually active	55.6	53.3	0.713
ER visits past 12 months	31.9	37.2	0.363
Syphilis screening - among sexually active	62.5	68.7	0.521
Gonorrhea screening – among sexually active	34.4	17.3	0.045 ^A
Chlamydia screening – among sexually active	35.4	17.3	0.036 ^A
Physical/Mental Health Status			
History of hepatitis B infection	18.4	21.2	0.580
History of hepatitis C infection	20.8	20.2	0.909
Hearing impaired, deaf	21.5	10.5	0.012 ^A
Visually impaired, blind	11.0	6.9	0.239
Difficulty concentrating, remembering	28.4	31.4	0.610
Difficulty walking or climbing stairs	31.7	29.1	0.674
Difficulty dressing or bathing	9.2	4.7	0.176
Difficulty doing errands along	14.1	18.8	0.351
Any type of disability	57.4	54.3	0.619
Depression, treatment or diagnosis	35.3	46.6	0.073
Anxiety, treatment or diagnosis	31.0	44.2	0.032 ^A
Health Behaviors			
Any anal or vaginal sex past 12 months	42.5	40.2	0.710
One sex partner among sex active past 12 mos	54.6	63.6	0.346
Sero-discordant sex	41.0	37.0	0.685
New partner past 12 months	30.1	34.6	0.618
Met new sex partner public venue or online	29.4	32.6	0.721
Current cigarette user	36.5	25.9	0.065
Alcohol past 30 days	57.0	46.7	0.106
Binge drinking past 30 days	6.1	5.6	0.863
Use non-injection drugs past 12 months	29.3	25.0	0.431
Use injection drugs past 12 months	3.9	4.5	0.766
Marijuana use (daily/weekly)	18.0	16.1	0.350
Stigma			
Average stigma score	40.9 [¶]	36.6 [¶]	0.134

Factor	% Non-LTS (n=138) [†]	% LTS (n=138) [‡]	p-value
Personalized	54.7	60.2	0.370
hurt by others' reactions	48.5	49.6	0.869
stopped socializing	34.2	39.2	0.424
lost friends by telling	24.6	29.8	0.392
Disclosure	83.7	72.3	0.029 ^Δ
careful who tell	80.7	69.1	0.034 ^Δ
others will tell	52.8	43.2	0.130
Negative self-image	28.4	26.0	0.678
not as good a person	17.3	20.5	0.544
feel unclean	20.3	19.1	0.823
feel bad person	9.8	10.2	0.920
Public attitudes	58.7	51.4	0.239
disgust	39.5	32.7	0.278
rejected	51.8	41.9	0.113
Discrimination			
Discrimination from health care providers			
hostility/lack of respect	18.4	37.1	0.001 ^Δ
gave less attention	12.8	22.7	0.039 ^Δ
refused service	3.3	17.3	0.000 ^Δ
any reason	21.9	40.3	0.002 ^Δ
Discrimination occurred because of HIV infection	16.7	36.4	0.001 ^Δ

*weighted survey data

† non-LTS includes 8 (3%) recently diagnosed within past 5 years and 130 (48%) intermediate diagnosed >5 to <=10 years.

‡There are 171 individuals in the sample classified as LTS. 33 of them are under the age of 50.

§Mean age of 3 groups: Recently diagnosed 64, Intermediate 58, LTS 60.

¥Not a %

Δ Statistically significant difference between groups where p-values are <=0.05.

** p-value for group of comparisons

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